UNIVERSITY COLLEGE LONDON

PLANTS USED TO TREAT DIABETES IN SRI LANKAN SIDDHA MEDICINE

Thesis submitted by

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Declaration

"I, Saravanan Vivekanandarajah, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis."

Saravanan Vivekanandarajah

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Abstract

In recent decades diabetes, most notably type 2, has become a considerable health problem in countries like Sri Lanka. Siddha Medicine is one of the four traditional medicines practised in Sri Lanka. α-Glucosidase inhibitors are one of the drugs types currently used to treat type 2 diabetes. However, they cause adverse side effects. The aims of this project are to identify, document, and make publicly available the plants historically and currently utilised to treat diabetes in Sri Lankan Siddha Medicine and identify one or more compounds capable of inhibiting α-glucosidase from the various plants studied. Historical documents used as Siddha Medicine degree textbooks in Sri Lankan universities were employed to obtain details on the plant species historically utilised. Apart from this, an ethnobotanical survey was carried out in the Eastern Province of Sri Lanka to identify the plant species currently used by Siddha empirical healers. Based on both the information from the historical documents and survey as well as the elimination of globally distributed and very well studied plant species, *Achyranthes aspera, Coccinia grandis, Ipomoea aquatica, Mukia maderaspatana,* and *Artocarpus heterophyllus* were selected for further study. The α-glucosidase inhibition assay was used to test inhibitory activity and Nuclear Magnetic Resonance spectroscopy was employed for metabolite profiling. In addition, Orthogonal Partial Least Square - Discriminant Analysis was employed to identify the compounds that showed α-glucosidase inhibition. Overall 171 species in 73 families were identified from the historical documents. Among them, *Senna auriculata* had been the most frequently cited species and the largest number of taxa was from the Fabaceae. Consultations with 27 Siddha empirical healers revealed 88 species from 46 families are currently used, while *Syzygium cumini* was the most frequently reported species. Remarkably, one-third of the currently used species was not listed in the historical documents. Again, Fabaceae yielded the largest number of species applied. The literature review of the documented plant species revealed that the majority of the species had *in vivo* antidiabetic evidence and the most number of studies were conducted in Type 1 diabetes models. The methanol extract of mature *A. heterophyllus* leaf exhibited the highest α-glucosidase inhibitory activity among the various extracts tested. Additionally, 38 samples of mature *A. heterophyllus* leaves had a range of IC_{50} values from 7.56 to 185.03 µg/ml. There was a correlation observed between the α-glucosidase inhibitory

activity and the climatic conditions of the region from which the plant specimens used to prepare the extract was collected and the phytochemical composition. Metabolite profiling identified that Artoheterophyllin B might be the α-glucosidase inhibitory compound found in the mature *A. heterophyllus* leaves. Hence, further phytochemical and pharmacological studies should be carried out to confirm this. This work created the foundation for more efficient studies of antidiabetic Sri Lankan SM preparations and the plants utilised in the future.

Research impact statement

The population has diabetes is rising globally and diabetes causes life-threatening complications with increased treatment costs. Traditional medicines have been used over centuries to treat numerous illenesses. Siddha Medicine (SM) is the traditional medicine which is mostly practised in the regions of Sri Lanka (SL) where the Tamils reside. Siddha empirical healers keep SM knowledge as secret and pass it to their next generation. Consequently, there is a need to identify, document, and make publicly available this knowledge to prevent from the future disappearance. Currently, Acarbose is one of the α-glucosidase inhibitors utilised to treat type 2 diabetes (T2D) and it causes adverse side effects including diarrhoea, abdominal bloating, flatulence, and distention. Thus, an urgent need search for natural α-glucosidase inhibitors with no or less side effects.

A huge number of plant species used to treat diabetes were identified from the Sri Lankan SM historical documents and the ethnobotanical survey carried out in the Eastern Province in SL in this study. A comparison study between these two sources revealed that there were changes and continuity in the SM diabetes treatment. Documentation of plants currently utilised to treat diabetes in the Eastern Province prevented the disappearance of this knowledge in the future. On top of that, the literature review conducted for several documented plant species showed that there was only a limited scientific evidence currently available. Therefore, this study suggests several potential plant species as the source for diabetes for future drug discovery studies.

There was a massive variation of α-glucosidase inhibitory activity observed in 38 samples of mature *A. heterophyllus* leaves. This suggests that a preliminary bioactivity screening should be performed to several plant samples to identify the most effective sample. This outcome can also be used to recognise mature *Artocarpus heterophyllus* leaves with more antidiabetic effects to make SM preparations.

Finally, this work identified an α-glucosidase inhibiting plant extract (the methanol extract of mature *Artocarpus heterophyllus* leaves showed the maximum α-glucosidase inhibitory activity) with 20 times more effect than the currently utilised one of the α-glucosidase inhibitors (Acarbose).

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List of Abbreviations

db/db: diabetic dyslipidaemia

fa/fa: Zucker fatty

IC_{50}: Half maximal inhibitory concentration

KKAy: Kyoji Kondo A^y/a

MVDA: Multivariate Data Analysis

NMR: Nuclear Magnetic Resonance

OLETF: Otsuka Long-Evans Tokushima Fatty

OPLS-DA: Orthogonal Partial Least Square - Discriminant Analysis

PCA: Principle Component Analysis

ppm: parts per million

rpm: revolutions per minute

SEH: Siddha empirical healer

SL: Sri Lanka

SM: Siddha Medicine

T1D: Type 1 diabetes

T2D: Type 2 diabetes

TM: Traditional medicine

Chapter 1

Aims and objectives

1.1. Aims

The aims of this study are:

1. To identify, document, and make publicly available (the knowledge is kept as a secret) the plants used to treat diabetes in Sri Lankan Siddha Medicine (SM) to prevent this knowledge in future disappearance
2. To identify natural α-glucosidase inhibitors (with from a documented plant species

1.2. Objectives

The objectives of this study are as follows:

1. Identifying, documenting, and making publicly available the plants historically (Chapter 4) and contemporarily (which is kept as a secret) (Chapter 5) used to treat diabetes in Sri Lankan SM.
   - Knowledge of medicinal plant use in the Traditional Medicines (TMs) in Sri Lanka (SL) is at risk of disappearing due to the fast-socioeconomic changes and keeping the medicinal plant knowledge as a secret. Thus, there is a need to document this knowledge and make it available to the wider scientific community. More specifically, with the fast increase in diabetes globally and importantly in SL, it is essential to document and analyse both modern and historical uses of medicinal plants in the treatment of diabetes. Specifically, it is essential to describe the complex preparations used for the treatment of the condition and plant species included in these preparations.

2. Assessing the level of antidiabetic scientific evidence for the documented plant species (Chapter 6)
   - Besides, with the majority of the rural population in SL still relies on TMs as their primary source of health care (Perera, P.K., 2012), such research can potentially provide alternative methods for primary care management of early stages of diabetes. This requires an assessment of

the current scientific knowledge of the pharmacological effects and possible clinical efficacy of the plants utilised.

3. Identifying the natural α-glucosidase inhibitory compound/s from a selected plant species using metabolite profiling technique (Chapter 7)

- Natural α-glucosidase inhibitors could be an economical, effective, and a safe way to control Type 2 Diabetes (T2D). Therefore, this project also aims to identify the natural α-glucosidase inhibitory compounds from a documented plant species used to treat diabetes in Sri Lankan SM using a rapid method (metabolite profiling).

Chapter 2

Introduction

2.1. Impact of diabetes globally

Diabetes is causing increased strain on social and economic development in several developing countries. Undiagnosed diabetes cases increase the health cost of treatments and may also result in dangerous complications. In 2017, there were 425 million people living with diabetes globally. In other words, one in eleven people has diabetes. Unfortunately, half of the people (i.e. 212 million) have diabetes are undiagnosed (IDF, 2017). Furthermore, the most common type of diabetes is Type 2 diabetes (T2D), accounting for up to 90% of diagnosed diabetes cases (Bruno et al., 2005; Evans et al., 2000; Holman et al., 2015). The majority of people diagnosed with diabetes live in the Western Pacific region (159 million) followed by South East Asia (82 million), Europe (58 million), North America and the Caribbean (46 million), Middle East and North Africa (39 million), South and Central America (26 million), and finally Africa (except North Africa) (16 million) (IDF, 2017). The large proportion of diabetics (77%) live in low and middle-income countries due to limited access to biomedical health care (IDF, 2014). Additionally, the majority (two thirds) of the people with diabetes live in urban areas (279 million) with the rest living in rural areas (146 million). It has been found that those of working age (aged between 20 and 64 years) account for 327 million of the people living with diabetes. In 2045, the diabetic population is projected to increase to 629 million with a global increase of 48%. Moreover, in 2017 diabetes caused 4 million deaths worldwide in the age range between 20 to 79 years and global treatment costs for the disease amounted to US$ 727 billion (IDF, 2017).

2.2. Impact of diabetes on Sri Lanka

In 2017, there were 1.2 million people living with diabetes in Sri Lanka (SL) (20 to 79 years) (IDF, 2017) and there were 625,000 undiagnosed cases in 2015 (IDF, 2015). In 2016, it was found that diabetes was responsible for up to 7% of the deaths in SL (WHO, 2016), with the annual cost of treatment per person with diabetes is US$ 429.20 (IDF, 2015).

2.3. Diabetes in biomedicine

Diabetes similarly referred to as hyperglycaemia, is defined by chronically elevated blood glucose concentrations (DeFronzo et al., 2015) in biomedicine (the definiation of biomedicine is stated in glossary). The insulin is secreted by the β-cells in the pancreas and released into the bloodstream. The blood glucose concentration will usually increase in cases where cells are unable to respond appropriately to the secretion of insulin. If untreated, diabetes can lead to various complications and may affect the nervous system, blood vessels, eyes, gums and teeth, heart, kidneys, or feet and skin (Zaccardi et al., 2015). The likelihood of suffering from diabetes can be lowered by both diet control and increased physical activity (WHO, 2017).

Diabetes can be categorised into three types:

1. Type 1 Diabetes or insulin-dependent diabetes:

Type 1 Diabetes (T1D) is caused by the destruction of insulin-secreting β-cells in the pancreas by an autoimmune response. Hence, only very little or no insulin is secreted by the β-cells.

2. Type 2 Diabetes or noninsulin dependent diabetes:

T2D occurs when tissues develop insulin resistance and there is decreased secretion of insulin from the β-cells.

3. Gestational diabetes:

Gestational diabetes can occur during pregnancy. Pregnancy-related hormones such as human placental lactogen can interfere with insulin sensitivity (CDCP, 2017).

Diabetes is diagnosed using various blood tests in biomedicine, these include:

1. Glycohaemoglobin (A1C) Test:

This blood test measures the average blood glucose concentration over a two to three-month period. The result is expressed as a percentage and the normal level is below 5.7%, prediabetes is between 5.7 - 6.4%, and patients are diagnosed as being diabetic if their blood glucose concentration is over 6.5%.

2. Fasting Plasma Glucose (FPG) Test:

This diagnosis involves measuring the fasting blood glucose concentration. The standard fasting blood glucose level is between 70 and 100 mg/dl for nondiabetics and 126 mg/dl for diabetics.

3. Oral Glucose Tolerance Test (OGTT):
This test measures the blood glucose concentration before and after two hours of drinking a sweet drink containing 75 g of sugar. The normal serum glucose level is lower than 140 mg/dl, between 140 – 100 mg/dl for pre-diabetes, and 200 mg/dl and above for those with diabetes.
4. Random Plasma Glucose Test:
This blood test measures the blood glucose concentration of a non-fasting person. The normal blood glucose concentration is between 79 – 160 mg/dl, between 160 – 200 mg/dl is considered as pre-diabetes, and above 200 mg/dl is considered as diabetes (ADA, 2016).

Currently, treatments are available for all types of diabetes. T1D is treated by injecting insulin and islet transplantation (Shahani and Shahani, 2015). T2D is commonly treated with oral drugs. Some of the different classes of drugs include:
1. Insulin secretagogues:
These drugs encourage the β-cells to secrete more insulin.
E.g. Sulphonylureas, Meglitinides (glinides), and Incretins.
2. Insulin sensitisers:
These drugs decrease the production of glucose in the liver and assist the insulin to labour better in the fat and muscle.
E.g. Thiazolidinediones (glitazones) and Metformin®.
3. Direct plasma glucose reducers:
These drugs reduce the amount of glucose produced by the liver and decrease the blood glucose levels.
E.g. Sodium-Glucose Cotransporter-2 (SGLT2) inhibitors and Metformin® (Bailey et al., 2016).

2.4. α-Glucosidase inhibitory activity

The enzyme α-glucosidase in the brush border of the small intestine is directly associated with glucose metabolism and soluble carbohydrate digestion. Oligosaccharides like disaccharides and polysaccharides and other carbohydrates (starch) are broken down into glucose (a monosaccharide) by the α-glucosidase enzyme (a carbohydrate-hydrolase). α-Glucose is released by hydrolysis of terminal non-reducing (1→4)-linked α-glucose residues by the α-glucosidase enzyme. The released glucose is then absorbed into the intestine and then released into the bloodstream (Bischoff et al., 1985). Therefore, the α-glucosidase inhibitory activity can decrease postprandial glucose concentrations in the bloodstream. By this, inhibiting α-glucosidase enzyme activity reduces the glucose absorption in the small intestine (Hanhineva et al., 2010). Currently, α-glucosidase inhibitors as an illustration, Acarbose (Figure 2.1) are prescribed in biomedicine. Mechanism of action of α-glucosidase inhibitors (Acarbose) is shown in Figure 2.2. However, the currently available α-glucosidase inhibitors cause unwanted adverse side effects such as abdominal pain, diarrhoea, abdominal bloating, flatulence and distention (Bischoff et al., 1985). Notably, using natural α-glucosidase inhibitors could be an economical way to control postprandial hyperglycaemia and may cause fewer side effects compared to synthetic drugs (Matsui et al., 2006). Moreover, plants have a high α-glucosidase inhibitory activity which could be used to manage T2D (Kwon et al., 2006).

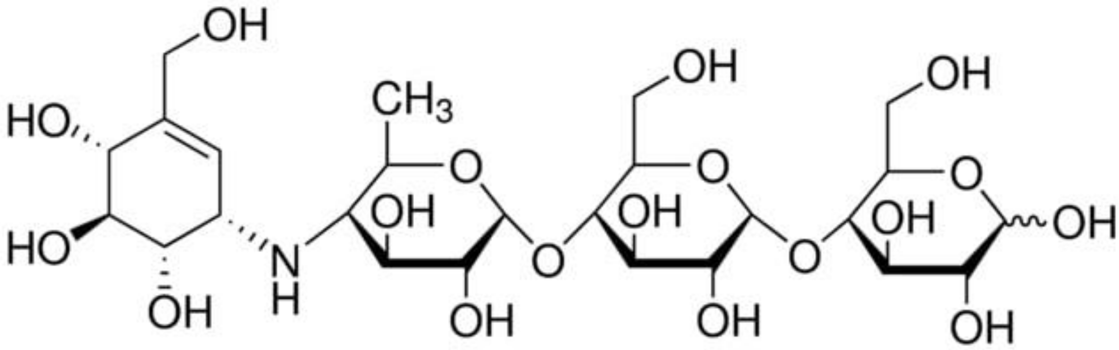

Figure 2. 1 Chemical structure of Acarbose. Adapted from: https://www.sigmaaldrich.com/catalog/product/sigma/a8980?lang=en&region=GB

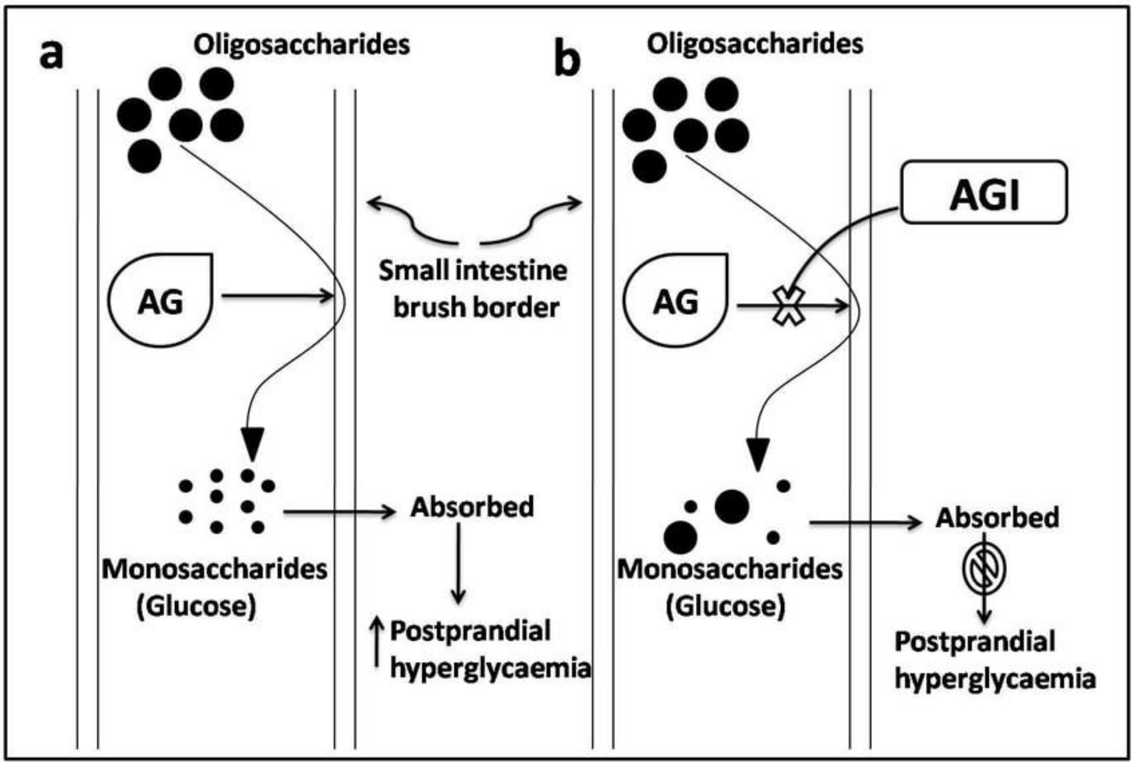

Figure 2. 2 Mechanism of action of α-glucosidase inhibitors. (a) Oligosaccharides are broken down by α-glucoside to monosaccharides, which are simply absorbed in the small intestine brush border (the absence of an α glucosidase inhibitor (Acarbose)). (b) Oligosaccharides are not broken down by α-glucosidase to monosaccharides while the presence of an α-glucosidase inhibitor (Acarbose). Hence, production and absorption of monosaccharides are decreased in the small intestine brush border. AG: α-Glucosidase, AGI: α-Glucosidase inhibitor (Acarbose). Adapted from: Arungarinathan et al. (2011).

2.5. Plants and diabetes – the big picture

Plants have been utilised for centuries in traditional medicines (TMs) to treat several illnesses, including diabetes (Nearing, 1985), whereby its treatments have to a great extent vanished in developed countries. In spite of the changes over the years, some patients still take food supplements based on traditional medicinal knowledge and some preparations are prescribed by the alternative medicinal practitioners (Bailey and Day, 1989). In the USA, 22% of people living with diabetes use herbal therapy while 31% use dietary supplements (Shane-McWhorter, 2009). Conversely, it has been found that plants are still widely used in developing countries to treat diabetes due to the limited access to biomedicine (Ajiboye A.T. et al., 2016a). Other factors that contribute to the use of plants in developing countries is that fact that plants are easily available and affordable (Nearing, 1985).

Several plants utilised in TMs have shown positive antidiabetic effects linked to managing T2D (Jia et al., 2003; Yeh et al., 2003). Thus, plants are a more suitable natural source for antidiabetic drug discovery (Harvey, 2010). Metformin is a biguanide currently used as the primary drug for control of T2D in biomedicine and was developed from galegine (a guanidine) isolated from *Galega officinalis* L. (Fabaceae) (Witters, 2001).

The most of the terpenoids and flavonoids isolated from natural sources showed antidiabetic activity (Yin et al., 2014). Approximately, 1200 plant species have been identified as being able to treat diabetes in TM. On top of that, 80% of TM preparations have shown antidiabetic activity in pharmacological studies (Marles and Farnsworth, 1995). TM preparations may, therefore, provide the foundation for developing new antidiabetic medications and dietary supplements (Bailey and Day, 1989).

Examples of antidiabetic compounds isolated from plants and their mechanisms are discussed further. Cinnamaldehyde belongs to the lignan class of compounds and is isolated from *Cinnamomum verum* J.Presl (Lauraceae). Oral administration of 3 mg/kg body weight to Streptozotocin-induced diabetic rats for 45 days significantly decreased (63.29%) blood glucose concentration in a dose-dependent way compared to Glibenclamide (0.6 mg/kg). Besides, cinnamaldehyde (20 mg/kg body weight) notably reduced concentrations of glycosylated haemoglobin (A1C), triglyceride, and total cholesterol in the blood. It also elevated levels of hepatic glycogen, high-density lipoprotein cholesterol, and insulin in the blood, which returned the levels of enzymes such as alanine aminotransferase, alkaline phosphatase, acid phosphatase, aspartate aminotransferase, and lactate dehydrogenase to the usual level (Subash Babu et al., 2007).

In another study carried out by Noor Shahida et al. (2009), Bruceine D (a terpenoid) was isolated using the bio-assay guided isolation technique from the seeds of *Brucea javanica* (L.) Merr.. Oral administration of 1 mg/kg of Bruceine D to Streptozotocin-induced diabetic rats for 8 hours exhibited a notable plasma glucose reduction of (88%). Glibenclamide (3 mg/kg) was utilised as a positive control and was found to reduce blood glucose levels by up to 47%.

2.6. Biodiversity of Sri Lanka

SL is a South Asian island situated in the Indian Ocean. It has an area of 65 610 km^2 and a population of 21.2 million. The largest ethnic group is Sinhalese (75%), followed by Sri Lankan Tamil (11%), Sri Lankan Moor (9%), and Indian Tamil (4%). The official and national languages of SL are Sinhala and Tamil. The major and official religion is Buddhism (70%) followed by Saivism (13%), Islam (10%), and Christianity (7%) (DCSSL, 2017).

SL has three climate zones, namely dry, intermediate, and wet zones. These zones have been classified based on the amount of annual rainfall experienced in the regions. Furthermore, the principle topographies determined by the elevations from the sea level and there are three types of topographies: coastal (0 to 30 m), plain (31 to 200 m), and highland (above 200 m) (DMSL, 2016). Added to that, the major soil groups include red-yellow podzol, reddish brown latosol, red and yellow latosol, and red-brown earths (Panabokke, 1996).

SL is one of the 34 ‘biodiversity hotspots’ in the world and it possesses a great number of endemic plant species (IUCN, 2016). So far, 4,143 plant species from 214 families have been identified. In these plant species, 75% are indigenous to SL while 25% of them are either introduced or exotics. Besides, 32% have become naturalised and 68% have been cultivated (Senaratna, 2001). In 2010, nearly 29.7% of the Sri Lankan land area was covered by natural forests. The vegetation can be categorised as follows, according to the impact of soil and elevation: Montane, submontane, lowland rain, moist monsoon, dry monsoon, riverine dry, sparse and open, and mangrove forests (FDSL, 2017). The main export crops are *Camellia sinensis* (L.) Kuntze (Theaceae) (tea), *Hevea brasiliensis* (Willd. ex A.Juss.) Müll.Arg.

(Euphorbiaceae) (rubber), and *Cocos nucifera* L. (Arecaceae) (coconut) (MFSL, 2017).

2.7. Siddha Medicine

Siddha Medicine (SM) is also called Tamil Medicine and it is originated in the main Tamil land in India from BCE 10,000 to 4,000. It is believed to be the premier medicinal system around the world (NIS, 2018). Yet, it is currently practised mostly in Tamil speaking regions in India and SL (AYUSH, 2018). SM has been recognised as a main Alternative East Indian Medicine within Tamils (Stephen, 2005). At present, SM is suitable for the treatment of all disorders apart from emergency cases (AYUSH, 2018).

Siddha means “heavenly bliss” or “attaining perfection in life”. Siddhars are considered as superhumans who have supernatural powers, great scientists, and preservers of the globe. They had a huge intelligence. Siddhars are believed to have the ability to predict the future and they developed SM by including Yoga, rejuvenation therapy, astrology, philosophy, alchemy, and astronomy (NIS, 2018). There are 18 Siddhars who have contributed to SM: Agathiyar (அகத்தியர்), Thirumoolar (திருமூலர்), Bogar (போகர்), Konganar (கொங்கணர்), Therayar (தேரையர்)¸ Korakkar (கோரக்கர்), Karuvooraar (கருவூரார்) , Idaikkaadar (இடைக்காடர்), Sattamuni (சட்டைமுனி), Suntharaananthar (சுந்தரானந்தர்), Iraamathevar (இராமதேவர்), Paampaatti (பாம்பாட்டி), Machchamuni (மச்சமுனி), Kuthampai (குதம்பை), Aluhannar (அழுகண்ணர்) , Ahappe (அகப்பே), Nanthithevar (நந்திதேவர்), and Kahapusundar (காகபுசுந்தர்) (Uthamaroyan, 1992). There are a few notable Sri Lankan Siddhars who lived in the Eastern and Northern Provinces of SL. Especially, Yogarswami (யோகர்சுவாமி) who lived half a century ago and his guru Sellappaswami (செல்லப்பாசுவாமி); both lived in Jaffna and are reknown around the world (Anonymous, 2015).

SM is based on Saiva philosophy. Saivism is one of the six branches of Hinduism and it reveres Sivaperuman as the main God. In SM, a human body is considered as a miniature of the universe (‘universe-body’ principle). In other words, the association between the universe and the human body

(Narayansami, 1975). The human body is composed of five principal elements: earth, water, fire, wind, and sky, whereas the human body functions are retained by three forces or faults, which are wind, bile, and phlegm. Nonequilibrium of these three forces are the cause of illnesses and Siddhar Yugimuni identified 4,448 disorders in SM (Ramanathan, 2008).

SM places equal importance on body, mind, and spirit. It aims to make the body perfect and promote longevity by reinstating the essential balance between the mind and the human body. Lifestyle and diet are very important in treating illnesses as well as preserving health. There are some common philosophical concepts of Siddhars as “food is medicine, medicine is food” and “sound mind makes a sound body” (Sivasanmugarajah, 2001).

SM treatments are considered as individual treatments. They are provided to patients based on their environment, age, gender, lifestyles, habitat, mental state, meteorological condition, appetite, physiological structure, and physical state (AYUSH, 2018). Moreover, SM has three types of treatments: divine, rational, and surgical treatments. In divine treatments, inorganic substances such as mercury and sulphur are used in the preparations. On the other hand, botanical ingredients are utilised in the preparations in rational treatments, whereas, surgical treatments, heat implementation, leech application, incision, bloodletting, and excision are employed. Ameliorative treatments in SM are further classified into fasting, purgative, steam, emetic, solar, oleation, Yoga, physical, and bloodletting therapies. In addition to these three tyes of treatments, the other type is called Varma, which is available for accidental injuries and traumatology. Such treatment is based on the concept of 100 essential points (Varma points) which are the joints of ligaments, tendons, nerves, blood vessels, and bones. The principle behind this treatment is concentrating life energy (energy retains the body powerful and alive) on these joints during the manipulation to provide healing (Sivasanmugarajah, 2002).

SM has eight different ways through which diagnosis is performed, these include the examination of the tongue, skin, pulse, speech, complexion, eye, urine, and stool. The pulse examination is the most significant diagnosis technique when determining the illness. A urine examination technique called

Neerkkuri (நீர்க்குறி) used in SM is unique and involves releasing a drop of sesame oil onto the collected urine (usually the patient's first urine of the day) after which the shape and pattern of spreading are observed. The fundamental principle behind this diagnosis is linked to the surface tension of the urine (Narayansami, 1975).

SM preparations are grouped into three classes: miracle, sophisticated, and common preparations. Miracle preparations are rare and they must be learned directly from a guru. A guru is a person who has achieved perfections in everything by experiencing all types of risks of the traineeship. Sophisticated preparations are produced precisely and prescribed by a trained Siddha practitioner without any hazard. Common preparations are the most economic and simple preparations widely utilised by the public, especially in the rural regions (Ramanathan, 2008).

Ingredients used in the SM preparations are categorised into three herbal, inorganic (metals and minerals), and animal (incorporating marine organisms) materials. There are 32 types of internal and external treatment techniques employed in SM and they include cold and heat application, bloodletting, bath, ointments, suction, counter-irritation, decoctions, creams, dexterous procedures like Yoga and Varma (see above), diet and sanitation focus, emetics and purgatives use, precautionary techniques for grey hair, ageing and wrinkle formation, and illnesses, as well as deferring death for a desired length of time. In addition, pilgrimage, mountaineering, and peregrination are likewise utilised as practical treatment techniques (Sivasanmugarajah, 2001).

2.8. Siddha Medicine in Sri Lanka

The Sri Lankan Ministry of Health equally recognises both biomedicine and TMs (Sivashanmugarajah, 2000). In biomedicine, blood tests, x-rays, scanning, and surgeries are provided free of charge for all the citizens receiving treatment in state hospitals. Importantly, TM services are also provided free of charge in specialised hospitals. The Ministry of Indigenous Medicine is part of the Ministry of Health, Nutrition, and Indigenous Medicine and is responsible for TM services (Ministry of Health, Nutrition, and Indigenous Medicine, 2018). There are four

TMs (Ayurveda, Siddha, Unani, and Deshiya Chikitsa) currently practised with Desheeya Chikitsa known as the native TM of SL (Weragoda, 1980).

SM is mostly practised in the Eastern and Northern Provinces of SL where the majority of Tamils reside. SM is recognised as the second-ranked TM by the Sri Lankan government (Sivashanmugarajah, 2001). Even so, SM preparations are manufactured and supplied to the state Siddha hospitals by the SL Ayurveda Drugs Corporation (SLADC, 2018).

Both Siddha graduates and Siddha empirical healers (SEHs) currently provide SM treatments in SL (see below). Both services are accepted by the government, still, there is no association between them. The illnesses are diagnosed based on the SM clinical knowledge of both Siddha graduates and SEHs. Additionally, some of the preparations and ingredients used are not the same. Siddha graduates and SEHs must register with the Ayurvedic Medical Council functioning as a part of the Ministry of Health, Nutrition, and Indigenous Medicine before starting the medical practice. Siddha graduates can directly register. Anyhow, all the SEHs currently practising must pass a standard nationwide examination in SM conducted by the Ministry of Indigenous Medicine to register with the Ayurvedic Medical Council. As of 2008, there still were some, mostly older SEHs, who were not registered with the Ayurvedic Medical Council (Ramanathan, 2008). Although, specific latest data are not available.

SEHs practise both in urban and rural regions. Despite that, the majority of them reside in the rural regions. They are self-employed and practise from their homes. Information about the ingredients in the preparations, preparation methods, and their properties, processing, purification, antidote, toxicity, dosage, and clinical administration are conserved in verse form and this information is only passed on within the family and to the future generations of the SEHs. As such, the details include the ingredients and preparations utilised by SEHs is not publicly known. The Ministry of Indigenous Medicine has been carrying out workshops and seminars about good practice for registered SEHs. The ministry also has been gathering information about the difficulties experienced by the SEHs in obtaining and collecting ingredients to improve the service provided by the SEHs to the public (Ramanathan, 2008).

There are two universities that offer a Bachelor of SM and Surgery (BSMS) degree - the Eastern University of SL in Eastern Province and the University of Jaffna in the Northern Province. This is a five-year degree course that comprises a year of internship at state Siddha hospitals. In both universities, separate Siddha faculties have been established similar to the faculties of biomedicine. In spite of that, the first two years for both SM and biomedicine students are taught together. For example, anatomy and biochemistry. Only SM graduates (i.e. not SEHs) can work as doctors at state Siddha hospitals (Ramanathan, 2008).

2.9. Diabetes in Siddha Medicine

The causes, signs, and symptoms of diabetes in terms of SM principles differ from biomedicine. For this reason, in this context terms in biomedicine like T1D and T2D are not meaningful. In SM diabetes is called Neerilivu (நீரிழிவு) or Salakkalichchal (சலக்கழிச்சல்) (losing water), Salaroham (சலரோகம்) (water-related disease), and Mathumeham (மதுமேகம்) (sweet urine). Based on these concepts it is characterised by frequently passing hot urine and passing foamy urine, like a pearl (drop) of fresh honey in the water. Diabetes is likewise seen as an incurable disease and it is classified as one of the 20 types of polyuria (மேகரோகம் - Meharoham) related conditions. These 20 types are categorised into three groups: fire (six types), wind (four types), and water-related (ten types). Diabetes is considered one of the four types of wind-related polyuria related conditions (Anonymous, 2003).

2.9.1. Causes of diabetes

Diabetes (Neerilivu) is considered to be caused by excess consumption of foods which increase the coolness of the body, such as ghee, curd, and milk, sour foods, meat, and Irasam (இரசம்), irregular eating, eating disorder, not applying oil on the body, excessive walking in the sun, and excessive sexual intercourse (Anonymous, 2000).

Irasam is a decoction (commonly utilised as a gravy on diverse dishes) prepared using *Cuminum cyminum* L. dried fruit (Apiaceae), *Coriandrum sativum* L. dried fruit, *Allium cepa* L. (Amaryllidaceae) fresh bulb, *A. sativum* L. dried bulb, *Tamarindus indica* L. (Fabaceae) dried fruit juice, *Piper nigrum* L. (Piperaceae) dried fruit, *Murraya koenigii* (L.) Spreng. (Rutaceae) fresh leaf, *Capsicum annuum* L. (Solanaceae) dried fruit, and *Curcuma longa* L. (Zingiberaceae) dried rhizome powder (Anonymous, 2000).

2.9.2. Signs of diabetes

The signs of diabetes are believed to invlove feeling lazy, excessive sweating, body odour, tiredness, grease formation on tongue, sweet taste in mouth, desiring to consume cold drinks and foods, dry tongue, chest, and throat, rapid growth of hair and nails, ants and flies gather around the urine, burning sensation in the stomach, paleness of body skin, weight loss, loss of consciousness, feeling thirsty, nocturia, difficulty in walking, blurred vision on humid, foggy, and rainy days, excessive urination, feeling depressed, desire to quench thirst by drinking buttermilk and coconut water, loss of appetite, body ache, passing clear and foamless urine during day and night, extreme pain, ear congestion, insomnia, passing urine with properties of coconut water during the night, and body weakness and it may cause death (Anonymous, 2000; Anonymous, 2003).

2.9.3. Types of diabetes

In SM, 24 types of diabetes are distinguished and grouped into seven categories. The categories are based on the elements of the human body and the types are based on the taste and odour of the urine. The seven categories are:

1. Wind associated diabetes, which includes three types and the urine is characterised by:

- An odour of *Mangifera indica* L. (Anacardiaceae) flower and sour taste
- An odour of *Crocus sativus* L. (Iridaceae) flower and sour-bitter taste

2. Wind-fire associated diabetes which contains four types and the urine is characterised by:

- An odour of *Curcuma longa* L. rhizome (Zingiberaceae) and sour-bitter taste
- An odour of *Nerium oleander* L. (Apocynaceae) flower and sweet-pungent-bitter-sour-astringent taste
- An odour of milk and buttery taste
- An odour of the brain and bitter taste

3. Fire associated diabetes which contains three types and the urine can be characterised by:

- An odour of fruit juice and bitter taste
- A salty odour and taste
- An odour of *Jasminum sambac* (L.) Aiton (Oleaceae) flower and producing a burning sensation when urinating

4. Fire-wind associated diabetes which includes two types and the urine is characterised by:

- An odour of cow urine and astringent taste
- An odour of *Santalum album* L. (Santalaceae) wood and peppery taste

5. Water associated diabetes which contains four types and the urine is characterised by:

- An odour of *Pandanus odorifer* (Forssk.) Kuntze (Pandanaceae) flower-cow manure-lemon-blood and sweet taste

6. Water-fire associated diabetes which includes four types and the urine is characterised by:

- An odour of *Magnolia champaca* (L.) Baill. ex Pierre (Magnoliaceae) flower
- A taste like *Syzygium cumini* (L.) Skeels (Myrtaceae) fruit
- A bad odour and a bitter-sour taste as well as ants gathering around the urine
- An odour of slaked lime (calcium hydroxide) and producing a burning sensation (similar to the one caused by lime (calcium oxide) when urinating

7. Water-wind associated diabetes which contains four types and the urine is characterised by:

- A strong odour and sour taste (Sithamparthanuppillai, 1982).

2.9.4. Complications of diabetes

Diabetes complications in SM incorporate lower abdominal pain, tiredness after urinating, flatulence, increased deficiency in sperm secretion, sperm in urine, general body weakness, loss of appetite, abscess formation, diarrhoea, unconsciousness, and death (Sithamparthanuppillai, 1982).

2.10. Level of scientific evidence available for plant species

TM is to a great extent not accepted by biomedical practitioners because traditional medicinal preparations have limited scientific evidence. For traditional medicinal preparations or medicinal plants to be accepted by biomedical practitioners, scientific evidence such as the safety and efficacy of the preparations are essential (Lemonnier et al., 2017; Wright et al., 2007). Equally, the existing data on preparation safety needs to be assessed. There are some benefits of grouping the levels of scientific evidence available for each plant species. Through this it will be possible to identify plant species that could be of interest for further study.

As in previous studies, the plants used in TM were categorised based on the traditional and scientific evidence available. For example, in a study conducted by de Montellano (1975), the plant species were classified based on information as plant species recognised botanically and the phytochemicals isolated. The findings of this study suggested to use both the traditional and modern knowledge to assess the effectiveness of the plant species utilised in TM.

Another study, by Heinrich et al. (1992) determined that the majority of the plant species reported to treat gastrointestinal illnesses in an ethnobotanical survey already had scientific evidence. Furthermore, Edwards et al. (2015) also classified common medicinal plants according to the maximum level of scientific evidence currently available in each.

In order to accept TM preparations within the modern health care practice, an assessment of potential toxic effects is essential. Toxicity can be split into intrinsic and extrinsic. Intrinsic toxicity can occur at either a normal dose or in the event of an overdose. The extrinsic toxicity can occur due to the contamination of preparations with microorganisms, heavy metals, pesticides, fertilizers, wrongly processed materials, and the addition of the wrong ingredients (Zhang et al., 2012) or accidental or intentional adulterations.

An example of intrinsic toxicity is seen with the aristolochic acids (aristolochic acid I and II) the principle toxic phytochemicals identified in plant species from the Aristolochiaceae. Aristolochic acid I and II cause direct damage to human epithelial kidney cells (HEK293) (Bakhiya et al., 2009). In a more recent study, aristolochic acids containing herbal preparations consumed by patients in South Korea had Fanconi syndrome (a kidney tubule function disorder) and severe kidney injuries (Ban et al., 2018). They are similarly toxic to other parts of the body (stomach and glomerular) (Kumar V. et al., 2003). Moreover, chronic administration of high dose of these compounds can lead to tubular epithelial cell death, urothelial cancer, damage to DNA, tubulointerstitial fibrosis, and renal failure (Debelle et al., 2008; Li et al., 2010).

Chapter 3

Materials and methods

3.1. Plants historically used to treat diabetes in Sri Lankan Siddha Medicine

3.1.1. Sri Lankan Siddha Medicine historical documents

There are several SM historical documents originally written and compiled in Tamil in SL. Still, they are all currently not accessible. On the other hand, some of the historical documents currently used as textbooks in Sri Lankan universities in the Bachelor of SM and Surgery (BSMS) degree are widely available and easily accessible. These textbooks are considered to be standardised Siddha historical documents and they form the basis of SM knowledge for SM graduates. This study, because of that, utilised these textbooks to obtain the information about historical antidiabetic Sri Lankan Siddha preparations. The three SM historical documents used were:

1. Pararasaseharam (Fifth Part) (*பரராசசேகரம்* (*ஐந்தாம் பாகம்*) - Pararaasaseharam (Ainthaam Paaham)): This document was compiled under King Pararaasaseharan (*பரராசசேகரன்*) between 1478 and 1519. It was initially printed as a book in 1935 by Ponniapillai, I. in Mallaaham and reprinted in 2003 by Sripathy Sarma, P. and published by Niyanthree Publication in Nallur, Jaffna, SL. (Anonymous, 2003).
2. Seharaasasehara Treatment (*செகராசசேகர வைத்தியம்* - Seharaasasehara Vaiththiyam): Contents of this document were compiled under King Seharaasaseharan (*செகராசசேகரன்*) between 1380 and 1414. It was first printed in 1927 by Ponniapillai, I. and reprinted in 2000 by the Provincial Department of Indigenous Medicine, Ministry of Health Eastern and Northern Provinces. (Anonymous, 2000).
3. Siddha Medicinal Procedure (*சித்த ஔடத செய்முறை* - Siththa Audatha Seimurai): This book was compiled by Ponniah, S.M. and Sabapathipillai, I. in 1980 and published by the Department of Ayurveda, Ministry of Health and Indigenous Medicine. (Ponniah and Sabapathipillai, 1980).

Only Anonymous (2003) and Anonymous (2000) contain both information about the symptoms and causes of diabetes as well as information on the preparations. On the other hand, Ponniah and Sabapathipillai (1980) only consists of information about the preparations. Only Sri Lankan origin preparations were considered in this study, consequently, a few preparations mentioned in Ponniah and Sabapathipillai (1980) were excluded because they were stated as Indian origin.

3.1.2. Plant species stated in the Sri Lankan Siddha Medicine historical documents

Causes, signs and symptoms, and antidiabetic preparations were written in the form of verses in ancient Tamil in the historical documents Anonymous (2000; 2003). These verses were translated to modern Tamil and the names of the plant species were confirmed by Dr. Pholtan R Rajamanoharan (an SM graduate, community Siddha medical officer, planning officer at the Planning Unit, Provincial Department of Indigenous Medicine, and in charge of the Provincial Herbal Garden in Trincomalee). Ponniah and Sabapathipillai (1980) only comprises historical Sri Lankan and Indian SM antidiabetic preparations written in modern Tamil. It is important to note that there might be some inconsistencies in the plant species names mentioned in the historical documents and current botanical identification. The exact botanical identification was based on the information available in the historical documents only. All the plant species stated in the historical documents are presented in Appendix A.

3.2. Plants contemporarily used to treat diabetes in Sri Lankan Siddha Medicine

3.2.1. Ethnobotanical study region

An ethnobotanical survey was conducted with SEHs residing in the Eastern Province of SL to obtain information about the plants they use to treat diabetes. The Eastern Province is one of the nine Provinces in SL and it consists of three districts (Batticaloa, Ampara, and Trincomalee) (Figure 3.1). The Eastern Province covers an area of 9,996 km^2 and it falls in the dry climatic zone (DCSSL, 2011). The major language spoken is Tamil and the total population is 1.6 million and is mainly made up of Sri Lankan Tamil (40%) followed by Sri

Lankan Moor (37%), Sinhalese (23%), and Indian Tamil (0.5%). The significant vegetation types identified in Eastern Province include dry mixed evergreen, grasslands, riverine, and mangrove forests (Dittus, 1985; Erdelen, 1988).

Figure 3.1 Map of the study region. Source: https://en.wikipedia.org/wiki/Eastern_Province,_Sri_Lanka

3.2.2. Ethical approval for the research

Research ethical approval was obtained from the UCL Research Ethics Committee (9141/001) on 13.06.2016 before conducting the interviews in SL. The purpose of this study and the informed consent sheet were read to each SEH before beginning the interview. The interviews were carried out only after receiving verbal consent from each SEH. SEHs participated voluntarily in this study. On top of that, they were free to withdraw at any point of the interview and no compensation was provided for participating in the interview.

This study was conducted after recognising the relevant obligations under the Convention on Biological Diversity United Nations (2011). The protocol had not been signed or ratified yet by SL on 23.09.2018 (at the time of writing this chapter). However, the UK ratified it on 22.02.2016 (https://www.cbd.int/abs/nagoya-protocol/signatories/, accessed on 23.09.2018). The right to authorship and use of the traditional knowledge of all informants was preserved. Still, using this information, except in scientific publications requires permission from the traditional owners of this knowledge. No permission is required by the government to collect and preserve plant material samples within SL. This ethnobotanical survey was started prior to the publication of the ConsEFS statement of best practice in ethnopharmacological research Heinrich et al. (2018). In spite of this, the ethnobotanical survey undertaken as part of this study has followed the guidelines outlined in Heinrich et al. (2018).

3.2.3. Ethnobotanical data collection and interviews

The ethnobotanical survey was conducted from 1st July to September 2016. I personally conducted the interviews with the SEHs and Dr. Pholtan R. Rajamanoharan was also present during all the interviews. The interviews were carried out in Tamil and the SEHs referred to the plant species using the Tamil names.

So far, 92 SEHs have registered with the Ayurveda Medical Council in the Eastern Province (AMCSL, 2018). The participants were actively chosen by Dr. Pholtan R. Rajamanoharan from the database of the registered SEHs. Furthermore, permissions and appointments were obtained verbally from each SEH by Dr. Pholtan R. Rajamanoharan through telephone calls. All the interviews were conducted in SEHs' homes. Anyhow, some of the SEHs who have provided permissions to participate in the survey were not able to participate in this study at the end due to unforeseen personal circumstances, while other SEHs directly refused to take part in this study. Accordingly, only 33 SEHs participated in this study. Of those who participated, six of them mentioned that they do not carry out any treatment for diabetes. On that account, they were excluded from this study. Interviews were conducted using a questionnaire which includes semi-structured questions (Appendix D). The questions focused on the social and demographic data (the gender, age, years of practice, and plant species currently utilised to treat diabetes) and interviews with each SEH lasted for a minimum of 15 minutes.

3.2.4. Scientific plant species names

Scientific names of the plant species stated in the historical documents and reported by the SEHs were obtained from Sugathadasa et al. (2008). They were then taxonomically validated using electronic databases like The Plant List (2013) and the Royal Botanic Gardens, Kew, Medicinal Plant Names Services (2016).

3.2.5. Voucher specimens and plant identification

Only plant species reported by the SEHs in the ethnobotanical survey were collected as voucher specimens. Priority was given to the plant species commonly available and cultivated in the Eastern Province. Fieldwork to collect plant part samples was conducted between September 2016 and June 2017. This is the ideal period for collecting flower and fruit specimens of most of the reported plant species. Collected plant samples were identified and confirmed by Dr. Pholtan R. Rajamanoharan. Herbarium specimens were prepared and deposited in the Herbarium of the Provincial Herbal Garden, Trincomalee for future reference. Voucher specimen numbers are indicated where applicable, in Table 5.2.

Voucher specimens of the five plant species collected to identify the compound(s) which cause α-glucosidase inhibition were also deposited at the Provincial Herbal Garden, namely VSAA2014 (*A. aspera*), VSIA2014 (*I. aquatica*), VSCG2014 (*C. grandis*), VSMM2014 (*M. maderaspatana*), and VSAH2014 (*A. heterophyllus*).

3.2.6. Ethnobotanical data analysis

The plant species documented from both historical documents and the ethnobotanical survey were categorised as being either food or medicinal plants, based on the local use in the Eastern Province by myself and Dr. Pholtan R. Rajamanoharan as well as using published works such as Rajapaksha (1998), Sugathadasa et al. (2008), and Jayaweera (2006, 1982, 1981, 1980).

3.2.7. Comparison of the historical and contemporary use of plants

The plant species mentioned in the historical documents were compared with the species reported by the SEHs in the ethnobotanical survey. Further, plant species which were reported to treat diabetes in the other ethnobotanical surveys carried out in the other regions include Jaffna (Rajamanoharan, 2014) and Vavuniya (Rajamanoharan, 2016) where SM is practised in SL were compared.

3.2.8. The assessment of the currently available scientific evidence

Initially, electronic databases (Web of Science, Scopus, and PubMed) were used to identify the relevant published scientific evidence of the documented plant species. The majority of the results obtained using Scopus, and PubMed were similar to the results obtained using Web of Science. On the other hand, full texts of some of the results those appeared on Scopus and PubMed were not available and accessible online. Thus, the relevant published scientific evidence was identified using a Web of Science search which looked at from 1900 to September 2017. The Web of Science database contains the following collections: Web of Science Core Collection (containing the world's leading scholarly books, journals, and proceedings from 1900 - present), BIOSIS Citation Index (an extensive index comprising biomedical and life sciences research from 1926 – present), Current Contents Connect (containing a comprehensive table of contents of leading scholarly journals from 1998 - present), Data Citation Index (covers the data sets of international discovery research from 1994 - present), Derwent Innovations Index (containing world patent index from 1994 - present), KCI-Korean Journal Database (covering scholarly literature originally published in Korea from 1980 - present), MEDLINE® (The U.S. National Library of Medicine® which is the primary database of life sciences, containing published literature from 1950 - present), Russian Science Citation Index (covering core Russian academic articles from 2005 - present), and SciELO Citation Index (containing leading open access journals published in countries involing Spain, Portugal, South Africa, and Latin America from 1997 - present). Hence, the feature "All Databases" was chosen to obtain the most comprehensive results across all the above-mentioned databases.

The quality of an academic journal article was determined by giving priority to works published by leading scholarly publishers such as Elsevier, Springer, Taylor & Francis, and Wiley-Blackwell (Wischenbart, 2015). The other factors as the number of citations made, authors of the article (background, number of articles published, etc.), and the date of the publication were considered as the quality check for the articles, which are not published by the leading scholarly publishers.

The plant species mentioned in American Herbal Pharmacopoeia (2011), Brendler (2010), European Medicines Agency (2009), Upton et al. (2016) and World Health Organization Monographs on Selected Medicinal Plants – Volumes 1 to 4 (1999; 2004; 2007; 2009) were excluded from the literature search. This was because the plant species stated in these works were globally distributed and scientifically very well studied.

Taxonomically validated plant species names (both genus and species names) were typed inside a double quotation mark (" ") when performing the primary search. In addition, synonyms (where applicable) and the same spellings of the scientific names as shown in The Plant List (2013) and Royal Botanic Gardens, Kew, Medicinal Plant Names Services (2016) were utilised in the search. The results were then refined using the term diabet* for the secondary search. Only antidiabetic pharmacological and clinical studies associated with reducing blood glucose levels and the inhibitory activity of enzymes (α-amylase and α-glucosidase) were considered for scientific evidence. Studies of diabetic complications were excluded from the searches.

3.3. The α-glucosidase inhibitory activity and the identification of the α-glucosidase inhibitory compound from the selected plant species

3.3.1. Fieldwork and sample collection

More than one different sample is required to conduct the metabolite profiling technique to identify the active compounds from plant sources (Wen et al., 2010). Hence, it was dicided to collect a plant species from different geographical sites in this work. A fieldwork was carried out to collect and preserve the selected plant samples between June and September 2014 from various locations throughout SL. The plant species were identified and then the chosen part was carefully collected. The collected plant species were confirmed by Dr. Pholtan R.S. Rajamanoharan. After collection, the fresh plant material was placed in a water-soaked paper pile to provide water to the fresh material and stop drying without ventilation. The paper pile was then placed in a hard paper bag and this bag was placed inside a plastic bag. The plant material was removed from the plastic bag and it was placed on paper that had been laid on the floor. It was shade dried at room temperature in a ventilated room during the summer period in Batticaloa, Eastern Province, SL. *A. aspera* samples were shade dried for four weeks while the rest of the plant species materials were shade dried for two weeks. Further, only *A. aspera* and *A. heterophyllus* materials were cut into small pieces before packing. Each dried plant material was packed separately in a sealed plastic bag and stored at room temperature. Finally, approximately 40 samples each weighing between 3 to 5 g, of each plant species, was available for study.

The official permit for transporting the collected plant materials to the UK from SL was obtained at the National Plant Quarantine Service (a part of the Ministry of Agriculture, SL) situated at the Colombo International Airport. The permit was issued after the samples were examined by experts in the lab of this department. Following from this, the plant samples were sent to the UK by fast courier service. On arrival to the UK, the samples were kept at room temperature, though, once they got to London, they were left in a freezer at – 20 °C for 48 hours to prevent the spread of pests and the other microorganisms. After this, they were transferred to a normal refrigerator to stop production of microorganisms like fungi.

3.3.2. Experimental

3.3.2.1. Chemicals

α-Glucosidase type I (*Saccharomyces cerevisiae*, lyophilised powder), Acarbose, and p-nitrophenyl α-D-glucopyranoside (PNPG) were purchased from Sigma-Aldrich Co. (St. Louis, MO).

3.3.2.2. Sample extraction

The dried plant materials were ground using a laboratory blender (Model 7009S, Waring® Laboratory Science, Torrington, CT) and sifted using a sieve of mesh (0.78 cm). Preliminary screening of the α-glucosidase inhibitory activity was conducted for the sample which had the greatest weight among the samples collected for each plant species. Solvents such as hexane, chloroform, ethyl acetate, acetone, methanol, and water were used to produce extracts which were then tested to determine which of them caused maximum inhibition of α-glucosidase. The extraction method utilised was based on that by Trinh et al. (2016). Briefly, 1 g of powdered dried plant material was mixed with 10 ml of solvent and vortexed for 1 minute. After which it was sonicated for 30 minutes. The mixture was then left at room temperature (25 °C) for 24 hours. The extracted solution was filtered using Whatman No. 1 filter paper and dried under pressure using a rotary evaporator (BUCHI Rotavapor®) at 40 °C until a concentrated mixture was obtained. The aqueous extracts were then obtained by freeze-drying the extracted water solutions.

Only one extract (out of 30) exhibited maximum α-glucosidase inhibition at the highest concentration (200 µg/ml) in the preliminary screening and was chosen for further study. Based on this observation, the same solvent was used for the production of extracts for all the collected samples of that particular plant species. The α-glucosidase inhibitory activity of all the samples was then studied in detail.

3.3.2.3. α-Glucosidase inhibition assay

The α-glucosidase inhibition assay was carried out in a similar way to that carried out Fujita et al. (2015). Briefly, 100 µl of 1.0 U/ml of yeast α-glucosidase solution was prepared in 0.1 M phosphate buffer (pH 6.9) and added to 50 µl of the different concentrations of plant extract (for example, 200, 100, 50, 25, 12.5, 6.25 µg/ml) in a 96-well plate to determine the IC_{50} value. The various plant extracts were completely dissolved in DMSO, apart from the aqueous extracts. The maximum amount of DMSO utilised was 1% for the highest concentration plant extract (200 µg/ml) and less than 1% for the other concentrations. The mixtures were then incubated at 25 °C for 10 minutes. Following from this, 50 µl of 5 mM p-nitrophenyl-α-D-glucopyranoside solution prepared in 0.1 M phosphate buffer (pH 6.9) was added into each well at specified time intervals. The absorbance of each well was recorded at 405 nm using a microplate reader, then the 96-well plate was incubated again at 25 °C for a further 5 minutes and the absorbance recorded at 405 nm. The phosphate buffer (50 µl of 0.1 M) was used as a negative control and Acarbose was utilised as a positive control. P-nitrophenyl-α-D-glucopyranoside is used as the substrate for α-glucosidase in this assay. P-nitrophenol is produced during the enzymatic hydrolysis of p-nitrophenyl-α-D-glucopyranoside.

$$\text{p-nitrophenyl-}\alpha\text{-D-glucopyranoside} \xrightarrow{\alpha\text{-Glucosidase}} \text{Product + p-nitrophenol}$$

The percentage inhibition of the extracts was calculated using the following formula:

$$\%\ \text{Inhibition} = \frac{\Delta\text{Absorption (Negative control)} - \Delta\text{Absorption (Sample)}}{\Delta\text{Absorption (Negative control)}}$$

Each concentration of the sample was added to three wells (triplicate) of the 96-well plate and the experiment was repeated at least three times.

3.3.2.4. Statistical analysis of α-glucosidase inhibition

The mean, standard deviation, and standard errors were calculated using Microsoft Excel 2016 (Redmond, WA) and the IC_{50} values were calculated using GraphPad Prism 7 (La Jolla, CA). Further, the one-way Analysis of Variance (ANOVA) test followed by the Tukey Test Honest Significant Difference test was carried out using IBM SPSS Statistics 24 (Armonk, NY).

3.3.2.5. Sample preparation for ^{1}H Nuclear Magnetic Resonance Spectra

Deuterated methanol (CD_3OD) (1 ml) was added to 200 mg of dried plant material in and vortexed for one minute after which it was sonicated for 30 minutes and left for 24 hours. The sample was then centrifuged at 13,000 rpm for 15 minutes and 800 µl of the supernatant was transferred into an NMR sample tube for NMR spectroscopy analysis. A Bruker Avance 400 MHz NMR spectrometer was utilised to obtain ^{1}H NMR spectra at 25 °C with 64 scans.

3.3.2.6. Data reduction and statistical analysis of ^{1}H Nuclear Magnetic Resonance Spectra

The Mnova 9.0.1 – Mestrelab (Santiago de Compostela, Spain) was used for the data reduction of the NMR spectra. The solvent (CD_3OD) peak at 3.31 ppm was utilised as a reference solvent peak and it was aligned to the NMR spectrum of each sample. Then the solvent peak regions (3.28 – 3.40 and 4.50 – 5.00 ppm) were excluded in each spectrum. Then the 0.00 to 9.00 ppm region was binned with a 0.04 ppm bucket width, which provided 216 buckets. Then the binned data was normalised to a total area of 100. Finally, MetaboAnalyst (http://www.metaboanalyst.ca, Quebec, Canada) was used to perform OPLS-DA.

3.3.2.7. Compounds isolated from selected plant families

The Web of Science (Philadelphia, PA), SciFinder® (Columbus, OH), and an online version of Dictionary of Natural Products (Boca Raton, FL) were utilised to identify the compounds isolated from Moraceae family. Even so, only the compounds that have had their ^{1}H NMR spectra produced in deuterated methanol were considered.

Chapter 4

Plants historically used to treat diabetes in Sri Lankan Siddha Medicine

4.1. Materials and methods

4.1.1. Documentation of traditional medicinal knowledge

Traditional medicinal knowledge involves diagnosis methods and use of ingredients (e.g. medicinal plants) in the traditional medicinal preparations. As mentioned before, this knowledge is usually kept as a secret by the traditional healers and only passed on to the next generation. Nevertheless, this knowledge can also be documented and written to make it publicly available. Anyway, documenting traditional medicinal knowledge is a complicated procedure, which is necessary to document the knowledge in a suitable way (Abbott, 2014).

There are some advantages and disadvantages of documenting traditional medicinal knowledge. The advantages like conservation of the knowledge for future generations to provide the access to develop TM use and encourage the commercialisation of traditional medicinal products. The disadvantages like the revelation of the knowledge to third parties and traditional healers will have restricted access and control to their knowledge (Abbott, 2014).

Traditional medicinal historical documents are used to document historical ethnopharmacological information while ethnopharmacological surveys are employed to record modern information to make it publicly available. Both documentation methods have some benefits and drawbacks. One benefit of historical documentation is that they form the foundation for modern documentation. Another benefit is historical documents contain very detailed ethnopharmacological information. The drawback of using historical documents is plant species cannot be confirmed directly by a person.

The advantage of modern documentation is the plant species can be confirmed directly by the participants in the ethnopharmacological surveys. One disadvantage of modern documentation is only the plant species currently used are documented. Hence, the basis of the plant use and the time when the plants currently utilised were involved were unknown. Another disadvantage is the data collected in modern documentation is limited because the traditional healers are not willing to reveal all the information they have.

Both historical and modern information is very useful in documenting ethnopharmacological information, because comparison studies can be carried out to investigate the changes and continuity of plant use in both methods, as well as fill the gaps created by the drawbacks of both methods. The recent surveys of antidiabetic plants have been published for several countries like India (Vidyasagar and Siddalinga, 2013), South Africa (Davids et al., 2016), Nigeria (Salihu Shinkafi et al., 2015), Mexico (Andrade-Cetto and Heinrich 2005), Turkey (Durmuşkahya and Öztürk, 2013), and China (Guo et al., 2017).

4.2. Results and discussion

4.2.1. Comparison of diabetes concepts in biomedicine and Siddha Medicine

There are some similarities and differences between the concepts (definition, causes, types, diagnosis, treatment, and complications) of diabetes. One of the similarities is that diabetes is considered as a polyuria associated condition. Biomedicine defines diabetes as being “excessive secretion of sweet urine”. On the other hand, SM defines diabetes as “passing foamy urine, like a pearl of fresh honey in the water”. Moreover, both medicines consider diabetes as an incurable disease. In addition, there are some common diabetes symptoms mentioned in both, including frequent urination, excessive thirst, blurred vision, weight loss, body odour, and insomnia. Another similarity between the two is that pills are orally administered during treatment. Diet management is also recommended in both biomedicine and SM in the diabetes treatment.

The causes of diabetes in SM differ from those of biomedicine. Consumption of animal fat-rich diets and social behaviours are considered as being the causes of diabetes in SM (Chapter 2). Despite that, biomedicine considers diabetes as being caused by the changes in the human body (Chapter 2). Besides, diabetes is grouped into three types in biomedicine whereas, it is classified into 24 types in SM. Another difference is diabetes diagnosed by various blood tests in biomedicine, while in SM the diagnosis is based on the diagnosis has based the odour and taste of the urine in SM. Apart from pills, other oral preparations (e.g. decoctions, powders, and diets) and topical preparations (e.g. oils and creams) are used in SM whereas insulin injections are the main route of drug administration in biomedicine (Anonymous, 2000).

Biomedicine medications are known to cause several unwanted adverse side effects in which potential side effects of SM are undocumented. Additionally, as SM treatments are individual, it is assumed that they cause less or no side effects, in spite of that, there is no scientific evidence for this claim.

4.2.2. Historical antidiabetic Sri Lankan Siddha Medicine preparations

A total of 60 antidiabetic preparations were identified from the Sri Lankan SM historical documents. Information about the ingredients (either scientific or English name), the amount utilised (converted to metric units from Tamil units where applicable), preparation methods, and dosages are presented in Appendix B. These preparations are not only used to treat diabetes. They are also utilised to treat several other disorders which are not related to diabetes. Apart from the 60 antidiabetic preparations mentioned, there are many other preparations used to treat all 20 types of polyuria associated conditions. However, this project specifically focused on those preparations that were specifically utilised in the treatment of diabetes.

Historical document, Anonymous (2003) contains the largest number of antidiabetic preparations followed by Anonymous (2000), and Ponniah and Sabapathipillai (1980). Both oral (pills, powders, decoctions, diets, and oils/creams) and topical (oils/creams) preparations were used to treat diabetes. The most common type of preparation was the pill (accounting for almost two-thirds of the treatments), followed by powder, cream, decoction, diet, and oil. The Pittu (பிட்டு) is a common diet in SL consumed for breakfast and dinner and rice flour is generally utilised to prepare it. While, other grain flours such as *Vigna mungo* (L.) Hepper and *Eleusine coracana* (L.) Gaertn. are used to prepare it. It is important to note that the preparations 4, 5, 6, and 7 are not commonly prepared for meals. Preparations 44 (Santhanaathiyennai - *சந்தனாதியெண்ணெய்*), 46 (Piramehachchanthanaathiyennai - *பிரமேகச்சந்தனாதியெண்ணெய்*), and 47 (Neerilivuchchanthanaathiyennai - *நீரிழிவுச்சந்தனாதியெண்ணெய்*) are the only three topical preparations stated in the historical documents (Appendix B).

The main components of the ingredients in the Sri Lankan antidiabetic preparations were plants, animal parts (comprising marine organisms), and inorganic substances (minerals and metals). The most common ingredient across the different preparations was plants, being found in approximately 97% of the preparations. This highlights the importance of plants in antidiabetic Sri Lankan Siddha preparations. Out of the 60 preparations, it was found that approximately two-thirds of them were made up entirely of plants. Preparation 41 (Piramehakkulihai - *பிரமேகக்குளிகை*) comprises of only animal ingredients and preparation 42 (Piramehakkulihai - *பிரமேகக்குளிகை*) contains only animal and inorganic ingredients. Preparations 16 (Salakkalichchalpalavukkum kaimarunthu - *சலக்கழிச்சல்பலவுக்கும் கைமருந்து*) and 53 (*தூள்* – Thool) incorporate only a single (one botanical) ingredient. A combination of all types of ingredients utilised in 13 preparations. Preparation 46 (Piramehachchanthanaathiyennai - *பிரமேகச்சந்தனாதியெண்ணெய்*) consists the highest number of ingredients (64) including 54 plant species in 40 families. The majority of the decoctions only prepared using plant ingredients. Anyway, preparation 50 is made using both inorganic substances and plant materials. The same plant part (bark) of different plant species used in preparation 49 (Kudineer - *குடிநீர்*). Besides, different parts of one plant species (*Senna auriculata*) utilised as the only ingredients in preparation 24 (Salakkalichchalpalavukkum kaimarunthu - *சலக்கழிச்சல்பலவுக்கும் கைமருந்து*) (Appendix B).

Adjuvants (honey, decoctions, and buttermilk, etc.) were usually consumed with antidiabetic Sri Lankan SM preparations. SM hospitals and SEHs only provide the SM preparations, although, they do not provide the adjuvants that would usually accompany them when consumed. The adjuvants prepared by the patients where applicable. It is recommended to avoid certain diets while taking some preparations to achieve better treatment results. For example, bitter and sour foods and fish should be avoided while administering preparation 14 (Suravappidippaanundai - சுவறப்பிடிப்பாணுண்டை) (Appendix B).

4.3. Plants used in the historical antidiabetic Sri Lankan Siddha Medicine preparations

The scientific name, family, Tamil name, part used, preparation, and source of 171 plant species in 73 families utilised in the antidiabetic Sri Lankan SM preparations are presented in Appendix A. The most commonly used plant species is *Senna auriculata* and the largest number of taxa are from the Fabaceae family. The plant parts including leaf, seed, bark, stem, root, fruit, flower, rhizome, and wood are utilised in the antidiabetic preparations and the seeds were the most commonly utilised part. The majority of the documented plant species used as food plants in SL. They are economically important, generally cultivated, and part of the wider Sri Lankan culture. Some examples of well-known and widely utilised food plants: *Allium sativum*, *Curcuma longa*, *Piper cubeba*, *P. nigrum, Saccharum officinarum*, *Zingiber officinale* and *Tamarindus indica*; fruits: *Anacardium occidentale*, *Cocos nucifera, Phoenix dactylifera*, *Ph. pusilla, Punica granatum, Artocarpus heterophyllus*, *Musa* × *paradisiaca,* and *Syzygium cumini*; green leaves: *Alternanthera sessilis*, *Ipomoea aquatica*, *Rivea ornata*, *Coccinia grandis*, *Mukia maderaspatana*, and *Murraya koenigii*; spices: *Cinnamomum verum, Myristica fragrans, Elettaria cardamomum,* and *Syzygium aromaticum*; grains: *Oryza sativa, Sesamum indicum, Vigna mungo, Cajanus cajan, Eleusine coracana, Panicum sumatrense,* and *Paspalum scrobiculatum* (Rajapaksha, 1998).

Most of the plants historically used to treat diabetes in Sri Lankan SM also have various other uses such as in Saiva (religious) rituals (*Elaeocarpus tuberculatus, Myroxylon balsamum, Cinnamomum cappara-coronde, Aegle marmelos, Santalum album*, and *Curcuma aromatica*), in cosmetics (*Crocus sativus, Chrysopogon zizanioides,* and *Santalum album*), in hygiene (*Ficus* *benghalensis* and *Azadirachta indica*), as an artefact (*Acacia chundra*), for manufacturing handicrafts (*Bambusa bambos, Cocos nucifera,* and *Borassus flabellifer*), textile production (*Gossypium arboretum*), incense (*Myroxylon balsamum* and *Santalum album*), and as medicine utilised for other conditions in SL (*Justicia adhatoda*, *Acorus calamus*, *Terminalia chebula*, *Ricinus communis*, *Vitex negundo*, *Coscinium fenestratum*, and *Aloe vera*) (Jayaweera, 2006, 1982, 1981, 1980). On top of that, *Cinnamomum cappara-coronde* was the only plant species endemic to SL (Sugathadasa et al., 2008).

There is only a mini review of plants utilised to treat diabetes in Indian SM currently available. This work was conducted by Parthiban et al. (2014) and identified 20 plant species from a historical Siddha Pharmacology document called Gunavagadam (குணவாடகம்). Yet, 16 out of 20 plant species were identified in Sri Lankan SM historical documents. For instance, *Terminalia arjuna, S. cumini, M. koenigii, C. grandis*, *Holarrhena pubescens*, and *Euphorbia hirta*. On the other hand, plant species like *Gymnema sylvestre, Helicteres isora, Hibiscus cannabinus*, and *Smilax china* were not mentioned in the Sri Lankan SM antidiabetic preparations.

Remarkably, almost all preparations contained either toxic plant species or plant species that belong to families containing many toxic plant species as ingredients in the antidiabetic preparations. According to Roth et al. (2012) and Harborne et al (1996), 49% of various parts of reviewed plant species (60 out of 123) may cause acute or chronic toxicity, posing the risk of teratogenicity and cancerogenicity, as well as allergic reactions (e.g. *Abrus precatorius*, *Strychnos potatorum*, *Aconitum heterophyllum*, *Hyoscyamus reticulatus*, and *Cycas circinalis*). Though, toxicity is also depending on the plant parts used as well as the dose administrated. Additionally, a toxicity assessment of the plants employed in antidiabetic Sri Lankan SM preparations is beyond the scope of this work.

4.4. Animal ingredients used in antidiabetic Sri Lankan Siddha Medicine preparations

Nearly, one-third of the antidiabetic preparations contain animal ingredients. Male deer musk (produced in a glandular sac in the lower abdomen), deer horn, civet musk (secreted in the anal scent glands), rhinoceros horn, cow gallstone and urine, human colostrum (foremilk), ant egg, *Coccus lacca* (Shellac – a resin excreted by the females of the lac insect) were utilised. Out of these different ingredients, cow gallstone was the most frequently utilised ingredient. In addition, marine organisms (pearl and red coral) were used in some of the preparations. Deer horn utilised in a calx form. Some of the ingredients as rhinoceros horn is rare and it will be unavailable in the future. It is also illegal to trade, possess, and use it.

4.5. Inorganic substances used in antidiabetic Sri Lankan Siddha Medicine preparations

Approximately, half of the antidiabetic preparations contain inorganic ingredients like metals (mercury, arsenic, iron, silver, gold, zinc, sulphur, and lead). Apart from metals, some of them contain minerals, including rock salt, borax, cinnabar, biotite (black mica), saltpetre (potassium nitrate), Roche alum, graphite, beryl, asbestos, gypsum, stibnite (contains antimony sulphide), mica (aluminium silicate), magnetite, and sulphur. Magnetite is the most frequently utilised inorganic substance. Noticeably, many of these inorganic substances are highly poisonous. For example, mercury, arsenic, etc. Silver and gold were used in a calx form and borax, cinnabar, and graphite were utilised in a purified form.

Some studies have evaluated the toxicity of some inorganic substances utilised in TMs. For instance, biotite is used in several antidiabetic preparations. In a study performed by Srinivasa et al. (2010), biotite ash when utilised with different drug vehicle did not show any systemic toxicity. In another study carried out by Vardhini et al. (2010), there was no genotoxicity exhibited in both an *in vivo* micronucleus assay and comet assay in Wistar rats of both genders. ‘Detoxification procedures’ are carried out for the inorganic substances while formulating the preparations. For example, the toxic properties of mica were removed during the preparation steps (Wijenayake et al., 2014). Still, these practices are a major concern and toxicological risks need to be clearly addressed.

4.6. Amounts and dosages used in Sri Lankan Siddha Medicine

Tamil units are utilised to measure the weights and volumes of the ingredients and doses in Sri Lankan SM. However, some of the Tamil units have been standardised to the equivalent metric units. In Sri Lankan SM historical documents, the measurements were stated in both standardised and non-standardised Tamil units. The standard Tamil units such as Palam (*பலம்*, 1 *பலம்* = 40 g), Panaavidai/Kaasidai (*பணாவிடை/காசிடை*, 1 *பணாவிடை* = 488 g), Kalanju (*கழஞ்சு*, 1 *கழஞ்சு* = 5 g), size of a louse (*பேன்பிடிப்பிரமாணம்* – Penpidippiramaanam = 1.25 mg), and size of an *Areca catechu* L. seed (*பாக்களவு* – Paakkalavu = 5 g) are used to measure the weights. Whereas, Marakkaal (*மரக்கால்*, 1 *மரக்கால்* = 1200 ml), Naali (*நாழி*, 1 *நாழி* = 600 ml), Kalam (*கலம்*, 1 *கலம்* = 57.6 l) and Koththu (*கொத்து*, 1 *கொத்து* = 150 ml) are utilised to measure the volumes of liquids. Likewise, non-standardised Tamil units like one handful (*பிடி* – Pidi), size of a small coconut (*சிறு தேங்காயளவு* – Siru Thengaaiyalavu), as required (*தேவையானளவு* – Thevaiyaanavalavu), and lemon size (*எலுமிச்சங்காயளவு* – Elumichchangkaayalavu) are used.

There is a great disadvantage when using the non-standardised Tamil units because, it would lead to inconsistency in the preparation methods and doses due to anatomical variations (hand size: from one person to the next; one region to the other: lemon size, the size of a small coconut etc.). Therefore, it is recommended to standardise the non-standardised units into metric units. On top of that, encourage the SM preparation manufacturers like SEHs and patients to use the exact amounts of ingredients during the manufacturing procedures and recommended dosages.

Chapter 5

Results and discussion

Plants contemporarily used to treat diabetes in Sri Lankan Siddha Medicine

5.1. Socio-demographic characteristics of the Siddha empirical healers who participated in the ethnopharmacological survey

Initially, 33 SEHs residing in the Eastern Province of SL were approached, although, six of them stated that they do not practise or produce any treatment for diabetes. They were, therefore, excluded from this study. The remaining 27 SEHs who are currently treating diabetes were interviewed for this study. The majority of participants were men and of the 27 who participated, it was found that most were aged between 61 and 70. Additionally, the majority of the SEHs had 41 – 50 years of experience practicing SM (Table 5.1).

Table 5.1 Demographics of the Siddha empirical healers who participated in this study (n = 27)

Category	Number of Siddha empirical healers	Percentage / %
Gender		
Male	25	93
Female	2	7
Age group		
21 - 30	0	0
31 - 40	6	22
41 - 50	0	0
51 - 60	0	0
61 - 70	17	63
71 - 80	3	11
81 - 90	1	4
90 - 100	0	0

Category	Number of Siddha empirical healers	Percentage / %
Years practicing Siddha Medicine		
1 - 10	1	4
11 - 20	5	19
21 - 30	0	0
31 - 40	0	0
41 - 50	17	63
51 - 60	3	11
60 - 70	1	4
Total	27	100

5.2. Diagnosis methods currently employed by Siddha empirical healers to diagnose diabetes

This study relies on the self-reporting information by the SEHs on their practice. In this investigation, the SEHs mentioned that they only use pulse reading (one of the eight diagnostic methods mentioned in Chapter 2) with a combination of symptoms recognised by SM as being linked to diabetes (stated in Chapter 2) to diagnose the illness.

5.3. The number of diabetic patients seen by a Siddha empirical healer

According to the information provided by the SEHs, on average, 12 diabetics are seen by an SEH per week. Nonetheless, they did not show any written evidence of the number of patients consulting them. Besides, they did not have any information on how many of the patients are returning for regular consultations and how many are visiting for the first time.

5.4. Contemporary antidiabetic Sri Lankan Siddha Medicine preparations

None of the SEHs wanted to reveal any information about the antidiabetic preparations such as the names, ingredients used, the dosage, and the units utilised. Yet, SEHs have stated that they prepare the antidiabetic preparations by themselves in their homes by buying and collecting the majority of the ingredients. The rare ingredients are provided by the Ayurvedic Drug Corporation at a reduced cost. The SEHs usually provide a one-month preparation to each patient and the patients paid for their consultation and treatment costs, usually in cash to them.

5.5. Types of ingredients currently used in the antidiabetic preparations

Remarkably, the SEHs who participated in this study reported that they only use botanical ingredients (one of the three types of the ingredients mentioned in the Sri Lankan SM historical documents in Chapter 4) in the antidiabetic preparations.

5.6. Plant species reported by the Siddha empirical healers

Overall, 88 plant species from 46 families were documented in this study (Table 5.2). *Syzygium cumini* was the most cited species (cited by 21 SEHs) followed by *Gymnema sylvestre*, *Artocarpus heterophyllus*, *Salacia reticulata*, and *Achyranthes aspera*. The largest number of reported taxa are from the Fabaceae family. The leaves were cited as the most frequently utilised plant part followed by fruits, whole plants, roots, and barks. Furthermore, the majority of the plants documented in this study were South Asian medicinal plants (*Withania somnifera, Typhonium trilobatum, Tribulus terrestris, Toddalia asiatica,* and *Tinospora sinensis*) followed by food plants (*A. aspera, Borassus flabellifer, Cinnamomum verum, Eleusine coracana,* and *Limonia acidissima*). Still, based on the study by Sugathadasa et al. (2008), none of the reported plant species is endemic to SL.

As mentioned before, the SEHs participated in this study were aged between 31 to 90 years, with a varying number of years of experience (1 to 70 years). In spite of this variation in both age and experience, all the participants reported using a combination of all types of plant species. In addition, there was no significant difference in the plant species reported by those aged under 40 and those aged over 70.

Remarkably, one-third of the plant species reported in this study had not been previously recorded either in the antidiabetic preparations of Sri Lankan SM historical documents or in the other ethnobotanical surveys carried out in the regions of SL where SM is practised. For instance, *Sesbania grandiflora* and *Pedalium murex* were reported for the first time in this study as ingredients in SM antidiabetic preparations in SL. At the same time, there was a strong overlap between the plant species reported by the SEHs and stated in the historical SM documents. For example, *Ficus racemosa* and *Salacia reticulata* were documented in both studies. Since these textbooks are employed in the university SM curriculum, this indicates that both written records (Leonti, 2011) and verbal communication form the basis of the plant species used. The most frequently utilised species in this study (*S. cumini*) was used in the antidiabetic preparations in the historical documents. *Senna auriculata* had been the most frequently stated plant species in the historical preparations (Sathasivampillai et al., 2017), although, only five SEHs in this work, consider it to be a useful plant in the antidiabetic preparations.

Table 5. 2 Reported plant species used to treat diabetes in Siddha Medicine in Eastern Province (n = 27)

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Abutilon indicum (L.) Sweet #	Malvaceae	துத்தி (Thuththi)	Whole plant	3
Achyranthes aspera L. (VS001)	Amaranthaceae	நாயுருவி (Naayuruvi)	Whole plant	11
Aegle marmelos (L.) Corrêa (VS002) #$	Rutaceae	வில்வை (Vilvai)	Bark, fruit	7
Aerva lanata (L.) Juss. (VS003) @	Amaranthaceae	தேங்காய்ப்பூக்கீரை (Thengaaippookkeerai)	Whole plant	2
Allium sativum L. #$	Amaryllidaceae	வெள்ளை வெங்காயம் (Vellai vengaayam)	Bulb	3

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Alternanthera sessilis (L.) R.Br. ex DC. (VS004)	Amaranthaceae	பொன்னாங்காணி (Ponnaangkaani)	Leaf	2
Anacardium occidentale L. (VS005) #$	Anacardiaceae	முந்திரிகை (Munthirihai)	Fruit	1
Andrographis paniculata (Burm.f.) Nees (VS006) #$@	Acanthaceae	சிரியாள்நங்கை (Siriyaalnangai)	Whole plant	3
Anethum graveolens L. #$	Apiaceae	சதகுப்பை (Sathahuppai)	Seed	1
Aristolochia bracteolata Lam. #@	Aristolochiaceae	ஆடுதின்னாப்பாலை (Aaduthinnaappaalai)	Whole plant	1
Artocarpus heterophyllus Lam. (VS007)	Moraceae	பலா (Palaa)	Mature leaf	13
Averrhoa carambola L. #@	Oxalidaceae	தமரத்தை (Thamaraththai)	Fruit	1

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Azadirachta indica A.Juss. (VS008) #$	Meliaceae	வேம்பு (Vembu)	Bark, tender leaf	4
Bacopa monnieri (L.) Wettst. #$@	Plantaginaceae	பிராம்மி (Piraammi)	Leaf	1
Basella alba L. (VS009) @	Basellaceae	பசளி (Pasali)	Leaf	3
Boerhavia diffusa L.	Nyctaginaceae	சாரணை (Saaranai)	Leaf	2
Borassus flabellifer L.	Arecaceae	பனை (Panai)	Fruit	2
Calotropis procera (Aiton) Dryand. #@	Asclepiadaceae	வெள்ளெருக்கு (Vellerukku)	Root	1
Cardiospermum halicacabum L. (VS010) #	Sapindaceae	முடக்கொத்தான் (Mudakkoththaan)	Leaf	5

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Carica papaya L. (VS011) #$@	Caricaceae	பப்பாசி (Pappaasi)	Leaf	3
Cassia fistula L. (VS012) #$	Fabaceae	கொன்றை (Kondrai)	Bark	1
Catharanthus roseus (L.) G.Don (VS013) #$@	Apocynaceae	பட்டி (Patti)	Root	1
Cheilocostus speciosus (J.Koenig) C.D.Specht (VS014)	Costaceae	வெண்கோட்டம் (Venkottam)	Rhizome	3
Chrysopogon zizanioides (L.) Roberty	Poaceae	இலாமிச்சை (Ilaamichchai)	Root	1
Cinnamomum verum J.Presl $	Lauraceae	கறுவா (Karuvaa)	Bark, leaf	1
Coccinia grandis (L.) Voigt (VS015) #	Cucurbitaceae	கொவ்வை (Kovvai)	Leaf	9
Coriandrum sativum L. #$@	Apiaceae	கொத்தமல்லி (Koththamalli)	Seed	5

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Coscinium fenestratum (Goetgh.) Colebr. *	Menispermaceae	மரமஞ்சள் (Maramanjal)	Stem	4
Crateva adansonii DC. @	Capparaceae	மாவிலங்கு (Maavilangu)	Bark	1
Cuminum cyminum L. #$	Apiaceae	சிறுஞ்சீரகம் (Sirunjcheeraham)	Fruit	5
Curcuma longa L. #$	Zingiberaceae	மஞ்சள் (Manjal)	Rhizome	5
Cyanthillium cinereum (L.) H.Rob. (VS016)	Asteraceae	சீதேவியார் செங்கழுநீர் (Seetheviyaar sengkaluneer)	Whole plant	2
Cynodon dactylon (L.) Pers. (VS017) #$@	Poaceae	அறுகு (Aruhu)	Whole plant	3

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Dregea volubilis (L.f.) Benth. ex Hook.f. (VS018) @	Asclepiadaceae	பெருகுறிஞ்சா (Perukurinjaa)	Leaf	4
Eclipta prostrata (L.) L. (VS019)	Asteraceae	கரிசலாங்கண்ணி (Karisalaangkanni)	Whole plant	3
Elettaria cardamomum (L.) Maton #$	Zingiberaceae	ஏலம் (Elam)	Fruit	5
Eleusine coracana (L.) Gaertn.	Poaceae	குரக்கன் (Kurakkan)	Seed	1
Evolvulus nummularius (L.) L. (VS020) @	Convolvulaceae	வெள்ளை விட்டுணுகிராந்தி (Vellai vittunukiraanthi)	Whole plant	1
Ferula assa-foetida L. #$	Apiaceae	பெருங்காயம் (Perungkaayam)	Resin	1
Ficus benghalensis L. (VS021)	Moraceae	ஆல் (Aal)	Bark	2

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Ficus racemosa L. (VS022) #	Moraceae	அத்தி (Aththi)	Bark	2
Ficus religiosa L. (VS033)	Moraceae	அரசு (Arasu)	Bark	3
Foeniculum vulgare Mill. #$	Apiaceae	பெருஞ்சீரகம் (Perunjcheeraham)	Fruit	2
Gymnema sylvestre (Retz.) R.Br. ex Sm. (VS024) $@	Apocynaceae	சிறுகுறிஞ்சா (Sirukurinjaa)	Leaf, root	18
Hygrophila auriculata (Schumach.) Heine *	Acanthaceae	நீர்முள்ளி (Neermulli)	Leaf	4
Illicium verum Hook.f. $@	Schisandraceae	அன்னாசிப்பூ (Annaasippoo)	Fruit	1
Indigofera aspalathoides DC. @	Fabaceae	சிவானார்வேம்பு (Sivanaarvembu)	Whole plant	2

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Indigofera tinctoria L.	Fabaceae	அவுரி (Avuri)	Root	2
Ipomoea aquatica Forssk. (VS025)	Convolvulaceae	வள்ளல் (Vallal)	Leaf	4
Kaempferia galanga L. #	Zingiberaceae	கச்சோலம் (Kachcholam)	Rhizome	2
Limonia acidissima Groff (VS026) #	Rutaceae	விளாத்தி (Vilaaththi)	Fruit	2
Merremia emarginata (Burm. f.) Hallier f. @	Convolvulaceae	பூமிசக்கரை (Poomisakkarai)	Rhizome	3
Mesua ferrea L.	Calophyllaceae	சிறுநாகம் (Sirunaaham)	Flower	2
Momordica charantia L. (VS027) #$@	Cucurbitaceae	பாகல் (Paahal)	Fruit, leaf	3
Mukia maderaspatana (L.) M.Roem. (VS028) #	Cucurbitaceae	மொசுமொசுக்கை (Mosumosukkai)	Leaf	6

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Murraya koenigii (L.) Spreng. (VS029) #$	Rutaceae	கறிவேம்பு (Karivembu)	Leaf	10
Myristica fragrans Houtt. #	Myristicaceae	சாதிக்காய் (Saathikkaai)	Leaf, mace	3
Nigella sativa L. #$	Ranunculaceae	கருஞ்சீரகம் (Karunjcheeraham)	Seed	2
Ocimum tenuiflorum L. (VS030) $@	Lamiaceae	கருந்துளசி (Karunthulasi)	Whole plant	3
Oryza sativa L. (VS031) $	Poaceae	நெல் (Nel)	Seed	4
Passiflora edulis Sims (VS032) $@	Passifloraceae	கொடித்தோடை (Kodiththodai)	Leaf	2
Pavetta indica L. #@	Rubiaceae	பாவட்டை (Paavattai)	Leaf	2

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Pedalium murex L. @	Pedaliaceae	ஆனைநெருஞ்சில் (Aanainerunjil)	Whole plant	2
Phyllanthus emblica L. (VS033) $	Phyllanthaceae	நெல்லி (Nelli)	Fruit, root	8
Piper longum L. (VS034) $	Piperaceae	திப்பிலி (Thippili)	Fruit	2
Piper nigrum L. $	Piperaceae	மிளகு (Milahu)	Fruit	2
Pongamia pinnata (L.) Pierre (VS035) *#@	Fabaceae	புங்கு (Pungu)	Root	3
Salacia reticulata Wight (VS036)	Celastraceae	கடலிறாஞ்சி (Kadaliraanji)	Bark	12

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Scoparia dulcis L.	Plantaginaceae	காட்டுக்கொத்தமல்லி (Kaattukkoththamalli)	Leaf	1
Senna auriculata (L.) Roxb. (VS037)	Fabaceae	ஆவாரை (Aavaarai)	Bark, flower, leaf, root, seed	5
Senna sophera (L.) Roxb. (VS038)	Fabaceae	பொன்னாவரை (Ponnaavarai)	Flower	2
Sesbania grandiflora (L.) Pers. (VS039) @	Fabaceae	அகத்தி (Ahaththi)	Leaf	3
Setaria italica (L.) P.Beauv. @	Poaceae	தினை (Thinai)	Seed	2
Stereospermum chelonoides (L.f.) DC.	Bignoniaceae	பாதிரி (Paathiri)	Root	2

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Syzygium aromaticum (L.) Merr. & L.M.Perry $	Myrtaceae	கராம்பு (Karaambu)	Flower bud	4
Syzygium cumini (L.) Skeels (VS040)	Myrtaceae	நாவல் (Naaval)	Bark, root, seed	21
Terminalia arjuna (Roxb. ex DC.) Wight & Arn. (VS041) $	Combretaceae	மருது (Maruthu)	Bark	1
Terminalia bellirica (Gaertn.) Roxb. (VS042) $	Combretaceae	தான்றி (Thaandri)	Fruit	2
Terminalia chebula Retz. $	Combretaceae	கடுக்காய் (Kadukkaai)	Fruit	5
Thespesia populnea (L.) Sol. ex Corrêa (VS043) *#	Malvaceae	பூவரசு (Poovarasu)	Bark	1
Tinospora sinensis (Lour.) Merr. $	Menispermaceae	சீந்தில் (Seenthil)	Stem	1

Scientific name, voucher specimen identification	Family	Tamil name	Part used	Number of times cited
Toddalia asiatica (L.) Lam. $@	Rutaceae	மிளகரணை (Milaharanai)	Root	1
Trachyspermum roxburghianum (DC.) H. Wolff #	Apiaceae	ஓமம் (Omam)	Fruit	3
Tribulus terrestris L. (VS044) #$	Zygophyllaceae	நெருஞ்சில் (Nerunjchil)	Whole plant	1
Trigonella foenum-graecum L. #$	Fabaceae	வெந்தயம் (Venthayam)	Seed	6
Typhonium trilobatum (L.) Schott @	Araceae	காட்டுக்கருணை (Kaattukkarunai)	Rhizome	1
Withania somnifera (L.) Dunal #$	Solanaceae	அமுக்கிராய் (Amukkiraai)	Rhizome	4
Zingiber officinale Roscoe $	Zingiberaceae	இஞ்சி (Inji)	Rhizome	4

* Rare (threatened) plant species based on IUCN (2018) - Red List of Threatened Species

$ Very well studied and globally distributed plant species based on American Herbal Pharmacopoeia (2011), Brendler (2010), European Medicines Agency (2009), Upton et al. (2016) and World Health Organization Monographs on Selected Medicinal Plants – Volumes 1 to 4 (1999; 2004; 2007; 2009) which were excluded from antidiabetic scientific evidence analysis

@ Plant species had not been reported in either antidiabetic preparations in Sri Lankan SM historical documents or ethnobotanical surveys carried out in SM practicing regions in SL

Toxic plant species based on Roth et al. (2012) and Harborne et al (1996)

Eight plant species were recorded previously to treat diabetes in the Northern Province. Seven species were reported in Vavuniya and only *Scoparia dulcis* was recorded in Jaffna (Rajamanoharan, 2014; 2016). The species like *Momordica charantia* and *G. sylvestre* were reported in both Eastern and Northern Provinces. Likewise, species such as *Andrographis paniculata* and *Toddalia asiatica* had only been reported in the Eastern Province. Interestingly, the most frequently mentioned species in this study (*S. cumini*) and cited in historical documents (*S. auriculata)* had not been recorded in the Northern Province (Rajamanoharan, 2014, 2016; Sathasivampillai et al., 2017). Additionally, as mentioned in the previous chapter, species including *S. auriculata, C. grandis, Trigonella foenum-graecum*, and *S. cumini* were mentioned in an Indian SM historical document. Though, species like *Smilax china, Terminalia arjuna*, *Acacia chundra,* and *Hibiscus cannabinus* utilised in Indian SM had not been mentioned by the SEHs in this study (Parthiban et al., 2014).

The toxicity studies of the plant extracts and herbal preparations play a very important role in assessing the safety and efficacy of drug purposes. Some species (e.g. *Aristolochia bracteolate*) are clearly toxic (Michl et al. 2016) and their use cannot be endorsed.

Chapter 6

Results and discussion

The antidiabetic scientific evidence available for plants used to treat diabetes in Sri Lankan Siddha Medicine

No antidiabetic scientific evidence is available for the antidiabetic preparations mentioned in the historical documents (Appendix B). As stated in the previous chapter, the SEHs did not reveal any information on the antidiabetic preparations they use. Due to this lack of background information, the pharmacological and clinical studies which are related to the antidiabetic activity of the individual plant species utilised in these preparations, as well as plant species reported by the SEHs, were reviewed to identify the relevant literature. Information like scientific name, family, level of scientific evidence, plant part used, active compound / extract, bioassay / model used, concentration / dose, duration, and references presented in Appendix C.

A total of 48 plant species (28%) mentioned in the historical documents (Appendix A) and 39 plant species (44%) reported by the SEHs (Chapter 5) were globally distributed and very well studied (as mentioned in 3.10. The assessment of the currently available scientific evidence and these plant species marked as $ in Appendix A and Table 5.2). Consequently, these plant species were excluded from further analysis. The remaining 123 out of the initial 171 plant species (72%) mentioned in the historical documents and 49 out of 88 plant species (56%) reported in the ethnobotanical survey were further assessed to identify the scientific evidence. Four levels of scientific evidence were established based on either the bioassay or model used to study the antidiabetic activity of the plant species:

1. Plants with no scientific evidence available
2. *In vitro* evidence and active compounds identified
3. *In vivo* evidence and active compounds identified
4. Clinical evidence and active compounds identified

6.1. Plants with no scientific evidence available

Approximately 41% (51 out of 123) of plant species historically utilised and 27% (13 out of 49) of plant species currently reported to have no scientific evidence of antidiabetic activity like *Lannea coromandelica*, *Piper cubeba*, *Trachyspermum roxburghianum, Phoenix pusilla,* and *Saccharum officinarum*. Some plant species were stated in several antidiabetic historical preparations and reported by many of the SEHs while, no scientific evidence was found to corroborate their antidiabetic activities. These plant species are suited for future studies to determine both their antidiabetic activity as well as potential toxicity. For example, *Pavetta indica*, *Crateva adansonii, Evolvulus nummularius, Pedalium murex,* and *Kaempferia galangal, Limonia acidissima, Nymphaea pubescens, Hyoscyamus reticulatus, Aconitum heterophyllum, Cinnamomum cappara-coronde, Cissampelos pareira, Mesua ferrea*, and *Acacia chundra.*

6.2. *In vitro* evidence and active compounds identified

α- Glucosidase, β-glucosidase, and α-amylase inhibitory, and glycogen synthesis bioassays were employed to investigate the antidiabetic activity in *in vitro* studies (Appendix C). It was found that the α-glucosidase inhibitory bioassay was the most frequently used among the reviewed *in vitro* studies.

Only 7 out of 123 plant species (6%) stated in the historical documents and 2 out of 49 plant species (4%) reported by the SEHs were found to have *in vitro* evidence. For instance*, Anacyclus pyrethrum*, *Setaria italica, Bambusa bambos*, *Mukia maderaspatana,* and *Gossypium arboretum.* Among them, *Abrus precatorius* has the has the most *in vitro* evidence to support its antidiabetic properties.

Active compounds had been only identified from *A. precatorius* and *Dichrostachys cinerea.* Three compounds were isolated from 50% methanol extract of *A. precatorius* leaves namely, lupenone, 24- methylenecycloartenone, and luteolin. These compounds exhibited α-amylase inhibitory activity with IC_{50} 31 µM, 0.6 mM, and 3.1 mM respectively (Yonemoto et al., 2014). It is of interest that the active compounds in the other plant species that have been shown to have *in vitro* activity are also identified. This can then be taken further and *in* *vivo* tests performed in animal models to provide more evidence regarding their antidiabetic properties.

6.3. *In vivo* evidence and active compounds identified

T1D (Alloxan- and Streptozotocin-induced diabetic) and T2D (diabetic dyslipidaemia [db/db], Kyoji Kondo A^y/a [KKAy], and high fat fed) (see Glossary for descriptions of these models) animal models were employed to study the antidiabetic activity (King and Bowe, 2016; King, 2012) (Appendix C). The majority of the studies were carried out in T1D (Streptozotocin-induced diabetic) models rather than T2D models. Still, as mentioned before in Chapter 2, the majority of the people have T2D. Hence, it is recommended to use more T2D models to study the antidiabetic activity of the plant extracts and active compounds in the future.

The most of the plant species both historically and currently used have *in vivo* evidence. A total of 59 out of 123 of the plant species (48%) historically utilised and 29 out of 49 of the plant species (59%) currently reported in the ethnobotanical survey have been studied up to this level, like *Tamarindus indica*, *Thespesia populnea, Ficus religiosa, Phyllanthus amarus, Alpinia galanga, Coccinia grandis*, *Sesbania grandiflora*, *Cardiospermum halicacabum,* and *Coscinium fenestratum. Syzygium cumini* has been studied the most frequently in *in vivo* models.

The antidiabetic compounds isolated from the species, including *Acorus calamus, Areca catechu, Cheilocostus speciosus, Plumbago zeylanica, Eclipta prostrata, Senna auriculata, Ficus benghalensis, Myristica fragrans, Syzygium cumini, Averrhoa carambola,* and *Scoparia dulcis.* The majority of the antidiabetic compounds (5) identified in *Oroxylum indicum.* In T1D models, β-amyrin palmitate (50 µg/kg) isolated from *Hemidesmus indicus* root when orally administered to Streptozotocin- and Alloxan-induced diabetic rats for 15 days, was able to reduce the blood glucose level to normal level. It was noted that β-amyrin palmitate was blocking glucose entering the intestine as one of its mechanisms of action (Nair et al., 2014). Costunolide (5 mg/kg) isolated from *C. speciosus* roots was orally administered to Streptozotocin-induced diabetic rats daily for 30 days. This treatment significantly reduced the blood glucose, total cholesterol, and triglyceride concentrations. Further, it was observed that the levels of plasma insulin, serum protein, and tissue glycogen were elevated. It is believed that costunolide may have induced insulin secretion in the pancreas (Eliza et al., 2009b). In another study carried out by Venkatachalam et al. (2013), 2-(3-acetoxy-4,4,14-trimethylandrost- 8-en-17-yl) (5 mg/kg) identified in *S. auriculata* flowers was orally administered to Alloxan-induced diabetic rats for 15 days. After 15 days, it was observed to decrease the blood glucose levels.

In T2D models, macelingan (10 mg/kg) isolated from *Myristica fragrans* seed kernel orally administrated to db/db mouse for 14 days reduced the elevated serum glucose, free fatty acid levels, and triglycerides concentrations. It was noticed that macelingan improved the insulin and glucose tolerance in the mice (Han et al., 2008).

Toxicity of the active extracts and compounds investigated further in some studies. For instance, 8000 mg/kg of both aqueous and methanol extracts obtained from *Achyranthes aspera* whole plant orally administered to Alloxan-induced diabetic rabbits for 7 days. This study revealed that this dose was nontoxic with no adverse side effects (Akhtar M. and Iqbal, 1991). In another study carried out by Kumar A. et al. (2008), mycaminose (2000 mg/kg) identified from *Syzygium cumini* mature seeds was administered to Streptozotocin-induced diabetic rats for 14 days and was found to be nontoxic.

The antidiabetic compounds should be identified in the rest of the plant species have *in vivo* evidence and they should be further studied in clinical trials. Plant species such as *Borassus flabellifer, Alternanthera sessilis, Ipomoea aquatica,* and *Senna sophera* were found to be the potential candidates for clinical studies because they are commonly available and widely consumed food plants in SL

6.4. Clinical evidence and active compounds identified

T1D and T2D patients were employed to investigate the antidiabetic activity at this level. However, most of the studies involved T2D patients (Appendix C). A sum of 6 out of 123 plant species (5%) mentioned in the historical documents and 5 out of 49 plant species (10%) reported by the SEHs were found to have clinical scientific evidence for treating diabetes (e.g. *Cyanthillium cinereum*, *Salacia reticulata, Ficus racemosa*, *Artocarpus heterophyllus,* and *Eleusine coracana*).

F. racemosa bark aqueous extract (1200 g/d) orally administered to T2D patients (18 men and 12 women) for one month showed a 15% reduction of fasting and 22% reduction of postprandial blood glucose levels (Ahmed et al., 2011). However, the authors did not state whether or not this clinical trial was a controlled trial. In another study, *F. racemosa* bark extract (100 mg twice a day) was administered orally to diabetics (25 male and 25 female) for 15 days and was found to reduce fasting and after breakfast serum glucose concentrations in both male and female participants. Moreover, renal and liver toxicity examinations revealed normal functions, thereby, this extract seems to be safe (Gul-E-Rana et al., 2013). A study carried out by Radha and Amrithaveni (2009), 2 g of *S. reticulata* bark powder was orally administered to 30 T2D subjects for 90 days. On the 90^{th} day, the blood tests revealed that there was a significant reduction in the blood glucose and lipid concentrations. Anyway, this study did not mention the toxicity outcomes.

Diabetes is a chronic disorder, thus, chronic clinical studies would provide more accurate results. There was a chronic study conducted by Bin Sayeed et al. (2013) for a preparation (6 g/day) containing *C. cinereum* root (as well as other unspecified ingredients) orally administrated for 6 months to 24 T2D sufferers (who had had the disease for more than 6 months). The results showed that there was a significant reduction in the blood glucose, triglyceride, haemoglobin A1C, and cholesterol concentrations. Yet, the dose used was very high. Besides, it was not reported how much *C. cinereum* root was present in the preparation. That being so, it seems appropriate to validate the data in additional clinical studies. A chronic toxicity study did not show any toxic effect of this dose for renal and liver functions.

Antidiabetic compounds (β-sitosterol, stigmasterol, and lanosterol) were only identified in the *F. racemosa* (Kushwaha et al., 2015). Anyhow, these compounds have not been studied in the clinical trials. On that account, the active compounds of the other plant species have clinical evidence should be identified and studied in further *in vitro* bioassays, *in vivo* models, and clinical trials.

Chapter 7

The α-glucosidase inhibitory activity and the identification of the α-glucosidase inhibitory compound from the selected plant species

As metabolite profiling using the Nuclear Magnetic Resonance (NMR) spectra and Orthogonal Partial Least Square - Discriminant Analysis (OPLS-DA) model has several advantages over the other techniques and also shown successful outcomes in identifying the active compounds in the plant extracts (see below), this approach was used as a part of a strategy to potentially identify α-glucosidase inhibitors from the extracts of a particular plant species grown in different geographical regions and under different ecological conditions by studying the correlation between the α-glucosidase inhibitory activity and the compounds present. The metabolite profiling technique is based on a statistical analysis of spectra data. Moreover, the variation of the phytochemical composition in the extracts causes the variation of a pharmacological activity. Hence, rather than using a single sample extract, a number of different sample extracts were used in metabolite profiling to study the variation of phytochemical composition (Liland, 2011). The sample size (number of samples) is an important factor which affects the quality of study involving statistical analysis. On that account, using a large number of samples in an investigation give more accurate outcomes, identify the outliers, and provide small margin error. On the other hand, a small sample size leads to inconclusive outcomes (Lenth, 2012). Therefore, a single sample cannot be utilised to conduct metabolite profiling technique to identify the α-glucosidase inhibitory compounds. Also, OPLS-DA is a supervised Multivariate Data Analysis (MVDA) method which requires a few groups of samples to conduct and identify the major contributors (NMR spectra signals) which are causing the separations between these groups. In other words, a particular extract of a single plant sample (one sample) cannot be used to group into a few groups. In this study, the samples were categorised as higher, moderate, and lower α-glucosidase inhibitory groups, consequently, at least three different samples were required to carry out this approach. Henceforward, several samples of a particular plant species were collected from the different geographical sites to conduct metabolite profiling to obtain more accurate results (statistically) by comparing the NMR spectra signals and identify the α-glucosidase inhibitory compound/s in this study.

7.1. Materials and methods

7.1.1. The identification of α-glucosidase inhibitory compounds from plants

7.1.1.1. Metabolite profiling

The bioactivities of a plant extract are caused by the compounds present within it. Bioassay-guided isolation is the most common technique used to identify bioactive compounds from plant extracts. There are some advantages and disadvantages of using this technique. The main advantage is that it can be utilised to identify novel bioactive compounds (Weller, 2012). On the other hand, when using this technique, the bioactive compounds can be destroyed during the isolation process. Thus, the bioactivity of the compounds can be lost before isolation. In addition, the concentration of an active compound can be reduced when using column chromatographic techniques, because the active compound is spread over several fractions (Strömstedt et al., 2014).

Metabolite profiling is used to study the comprehensive chemicals present in biological samples and their association between either a specific pharmacological activity or compound class (Yuliana et al., 2011). This reveals the major differences between the compounds and pharmacological activity, which could be related to chemical profiles (Wolfender et al., 2009). It is widely utilised in the following disciplines: Phytochemistry (Mandrone et al., 2017), chemotaxonomy (Sarrou et al., 2017), quality control (Agapouda et al., 2017), and clinical chemistry (Qian et al., 2017). Biological functional modification is caused by pathophysiological alterations, genetic changes, or challenges with external environment can be also assessed using metabolite profiling (Dunn et al., 2008). There are some benefits of this technique compared to bioassay-guided isolation technique. Metabolite profiling method is a quantitative, reproducible, and straightforward technique. It is a rapid way to identify the active compounds in a crude plant extract (Wang et al., 2004). Even so, the major drawback of this technique is that it is unable to predict unknown compounds present in the plant extract (Wen et al., 2010). Contemporarily, metabolite profiling combined with pharmacological activity approach is preferred over the traditional bioassay-guided isolation technique in drug discovery projects (Wolfender et al., 2015).

NMR spectroscopy is widely used to study the plant extracts in the metabolite profile (Kim et al., 2010). Non-interfering chemical structure investigations of compounds in cell suspensions, crude natural extracts, *in vivo* analysis of entire organisms, and undamaged tissues are studied by employing NMR spectroscopy. NMR spectroscopy provides distinct and individual spectra for every compound (Verpoorte et al., 2007). There are some advantages of NMR spectroscopy over the other analytical spectroscopy techniques. One of the advantages of NMR spectroscopy is the outstanding reproducibility (Colquhoun, 2007). Additionally, NMR spectroscopy can be utilised to identify novel compounds from extracts. The sample preparation procedure is straightforward (Verpoorte et al., 2007). The limitations of NMR spectroscopy include lower sensitivity, compounds with lower concentration often not being detectable, and signal overlapping (Holmes et al., 2006; Safer et al., 2011).

MVDA is a statistical based method employed to analyse the data obtained from more than one sample (CAMO, 2015) and this technique used to interpret the NMR spectroscopy measurements in metabolite profiling (Bylesjö et al., 2006; Wiklund et al., 2008). A regression, association between two data sets can be studied using MVDA, where the X component is the chemical profile and the Y component is the bioactivity (Sussulini, 2017). The OPLS-DA is a supervised method widely utilised to observe the association between the metabolite profile and bioactivity (Eriksson et al., 2013). The bioactive compounds are identified by recognising the NMR signals responsible for the separation between the high and low bioactive sample groups. OPLS-DA method is more appropriate than other the MVDA techniques such as Principle Component Analysis (PCA) when it comes to metabolite profiling, because OPLS-DA is a supervised method, the data can be categorised into groups before carrying out the MVDA. On the other hand, PCA is an unsupervised MVDA technique (Kang et al., 2008).

The combination of ^{1}H NMR spectroscopy with bioactivity and OPLS-DA has provided successful outcomes in previous studies. The bioactive compounds suvanine, halisulfate 1, and halisulfate 3 - 5 (sesterterpenes) which exhibited adenosine A1 receptor binding activity were identified from crude extracts of marine sponges (*PsammociniaII*) using NMR spectroscopy and OPLS-DA (Ali et al., 2013). Another example, Yuliana et al. (2013) correspondingly identified two flavonoid derivatives (hydroxy-panduratin and pinocembrine) responsible for adenosine A1 receptor binding activity from crude rhizome extract of *Boesenbergia rotunda* (L.) Mansf. (Zingiberaceae).

7.1.2. Selected plant species used for the α-glucosidase inhibitory activity and the identification α-glucosidase inhibitory compounds in this study

When selecting the plant species to study for α-glucosidase inhibitory activity, initially the plant species which are very well scientifically studied and commonly distributed around the world which marked in Appendix A and Table 5.2 were excluded. For example, garlic and ginger. After that, rare (threatened) and toxic plant species (see Appendix A and Table 5.2) were also omitted. Then from the remaining plant species (based on a systematic search of the scientific literature), antidiabetic active compounds had been identified were excluded. Then, species had no reports on α-glucosidase inhibitory activity were included. Plant species which are widely distributed throughout SL and easily accessible were prioritised. Plant parts of the species (used in the antidiabetic preparations) which are available throughout the year, easier to collect, and easier to preserve were considered. For instance, plant parts such as root, bark, flower, seed, and fruit of plant species which are used in the antidiabetic preparations were excluded and specifically leaves (including trees) and whole plants of herbaceous plants were included. Finally, the following five plant species were chosen for this study: *Achyranthes aspera* L. (whole plant), *Ipomoea aquatica* Forssk. (leaf), *Coccinia grandis* (L.) Voigt (leaf), *Mukia maderaspatana* (L.) M.Roem. (leaf), and *Artocarpus heterophyllus* Lam. (mature leaf). Yet, these selected plant species showed antidiabetic activities in various models (mostly in *in vivo* models) and there might be the other pharmacological mechanisms of action accountable for the antidiabetic activity of these selected plant species. For instance, *Senna auriculata* (Appendix C) flowers showed antidiabetic activities in various bioassays and *in vivo* models. Consequently, this study was aimed to study the α-glucosidase inhibitory activity and identify the α-glucosidase inhibitory compounds from one of these selected plants.

7.1.2.1. *Achyranthes aspera* L.

Achyranthes aspera (Figure 7.1) is a weed that belongs to the Amaranthaceae family. It is called Naayuruvi (நாயுருவி) in Tamil (SM) and is found in the tropical regions of the world (e.g. Africa, America, Asia, Australia, and Europe) (de Lange et al., 2004; Prain, 1963; Hooker, 1885). It is a food plant in Eastern SL. The common food dish for lunch is prepared using the stems and leaves (before flowering). *A. aspera* is likewise commonly used in TMs around the world (Fikru et al., 2012; Pai et al., 2010; Shibeshi et al., 2006). In Sri Lankan SM, the whole plant is utilised in antidiabetic preparations Kaareeya sinthooram (preparation 32) and Neerilivukku vanga senthooram (preparation 56) (Appendix B).

There are some pharmacological studies carried out in various experimental models using *A. aspera.* It exhibited anti-inflammatory (Khuda et al., 2014; Vetrichelvan and Jegadeesan, 2003), antiarthritic (Gokhale et al., 2002), abortifacient (Pakrashi and Bhattacharya, 1977), antifertility (Prakash, 1986; Varshney et al., 1986; Wadhwa et al., 1986), cancer chemopreventive (Chakraborty et al., 2002), antioxidant (Upadhya et al., 2015), antifungal, antibacterial (Khuda et al., 2015), and wound-healing effects (Barua et al, 2012) in several studies.

A. apsera has *in vivo* antidiabetic scientific evidence. The extract of dried stem and leaf (80% ethanol) at a dose of 200 mg/kg per day when orally administrated to Alloxan-induced diabetic rats for 2 weeks caused a significant decrease in the fasting blood glucose levels. The results observed were better than the positive control (Metformin®) utilised in this study (Talukder et al., 2012). Another study carried out by Akhtar and Iqbal (1991), using both aqueous and methanol extracts of the shade-dried whole plant (4000 mg/kg) involved oral administration to normal and Alloxan-induced diabetic rats. After 4 hours, it was noticed that blood glucose concentration was lowered to normal levels. Furthermore, toxicity study carried out during this study showed that an orally administered dose of 8000 mg/kg showed no toxic effects even after 7 days of treatment.

Figure 7. 1 *Achyranthes aspera* sample collected at Anaipanthy Pillaiyar Temple, Puliyantheevu, Batticaloa

Several compounds have been isolated from *A. aspera* including the betulinic acid (Pai et al., 2014), ecdysterone, linolenic acid, oleic acid, palmitic acid, stearic acid (Chakrabarti et al., 2012), betaine (Mehta et al., 2011), oleanolic acid (Mehta et al., 2010), strigmasta-5, 22-dien-3-beta-ol, trans-13-docasenoic acid, n-hexacosanyl n-decaniate, n-hexacos-17-enoic acid and n-hexacos-11-enoic acid, and n-hexacos-14-noic acid (Sharma S.K.R et al., 2009).

7.1.2.2. ***Ipomoea aquatica*** **Forssk.**

Ipomoea aquatica (Figure 7.2) is a perennial creeper and belongs to the Convolvulaceae family. It is called Vallal (வள்ளல்) in Tamil (SM). This species is generally found in Africa, Australia, and Asia (Edie and Ho, 1969). *I. aquatica* is a common food plant in SL and its leaves and stems are used to cook. *I. aquatica* leaves are utilised as an ingredient in Neerilivuchchanthanaathiyennai (preparation 47) (Appendix B) in Sri Lankan SM to treat diabetes.

Pharmacological studies show that *I. aquatica* possesses antioxidant (Bhalodi et al., 2008), anti-inflammatory and antibacterial (Dhanasekaran et al., 2010), antiulcer (Sivaraman and Muralidaran, 2008), hypolipidemic (Sivaraman, 2010), and diuretic (Mamun et al., 2003) activities.

Figure 7. 2 *Ipomoea aquatica* sample collected in Vavunatheevu, Batticaloa

Past literature shows that there is currently *in vivo* evidence regarding the antidiabetic properties of *I. aquatica*. An aqueous extract of the leaves was prepared using a dose of 3300 mg starting material /kg. This extract was orally administered to glucose challenged Wistar rats. After 2 hours, it was observed that the elevated blood glucose was lowered to a normal concentration. This effect was equivalent to the effect caused by the positive control used (15 mg/kg of Tolbutamide) (Malalavidhane et al. 2001). In another study carried out by Malalavidhane et al. (2000) in SL, an extract was prepared by boiling 3400 mg/kg of leaves of *I. aquatica.* This extract was orally administered to glucose challenged healthy rats. The results revealed that there was a 33% reduction in the blood glucose concentrations after 2 hours. In a further experiment, fresh leaves and stems (3400 mg/kg) were orally administered to Streptozotocin-induced diabetic rats for 1 week and blood tests showed that there was a significant reduction in fasting blood glucose concentration (Malalavidhane et al. 2003).

Compounds including aquaterin I – XI (Fan et al., 2014), violaxanthin, lutein, β-carotene (Fu et al., 2011), 7-O-beta-D-glucopyranosyl-dihydroquercetin-3-O-α-D-glucopyranoside (Prasad et al., 2005), 1-hexadecanoylpyrrolidine, 1-(14-methylhexadecanoyl)pyrrolidine, 1-octadecanoylpyrrolidine (Tofern et al., 1999), α-carotene, β-carotene, lutein, zeaxanthin, antheraxanthin, flavoxanthin, auroxanthin, luteoxanthin, neoxanthin (Wills and Rangga, 1996), pheophytin a, chlorophyll a, chlorophyll b, and lutein epoxide (Chen and Chen, 1992) have been isolated from *I. aquatica*.

7.1.2.3. *Coccinia grandis* (L.) Voigt

Coccinia grandis (Figure 7.3) is a climber and belongs to the Cucurbitaceae family. It is called Kovvai (*கொவ்வை*) in Tamil (SM) and found throughout Asia, Africa, Australia and Oceania, Caribbean and Southern USA (Muniappan et al., 2009). *C. grandis* leaves are used for both food and medicinal purposes in SL. The leaves are utilised to prepare dishes as Sothy (*சொதி*) (a traditional soup made with coconut milk, turmeric powder, green chilies, onions, and fenugreek) and Sambal (*சம்பல்*) (a salad prepared with fresh green leaves mixed with green chilies, onions, salt, and pepper) in the Eastern, Northern, and Central SL. These dishes are also used as medicine to treat diabetes in the Eastern and Northern SL (Rajapaksha, 1998). Sri Lankan SM historical documents mention that *C. grandis* leaves are utilised in Neerilivuchchanthanaathiyennai (preparation 47) (Appendix B) to treat diabetes. *C. grandis* has been shown to have bioactivities such as anticancer (Bhattacharya et al., 2011), antioxidant (Umamaheswari and Chatterjee, 2008), and anti-inflammatory (Deshpande et al., 2011) properties.

There is currently *in vivo* scientific evidence showing that *C. grandis* has antidiabetic activity. In one study, an aqueous extract (750 mg/kg) prepared from leaves, dried at 40 °C was orally administered to Streptozotocin-induced diabetic rats for 30 days. Blood tests revealed a decrease in the blood glucose levels. It was additonally observed that insulin secretion in the β-cells was increased (Attanayake et al., 2015). In another study, again 750 mg/kg aqueous extract of leaves was orally administered to Alloxan-induced diabetic rats. Blood tests carried out after 4 hours showed reduced blood sugar levels compared to the positive control Glibenclamide (0.50 mg/kg). In the acute toxicity study, it was revealed that there were no adverse effects when an aqueous extract of *C. grandis* leaves (2000 mg/kg) was administered orally for 2 days (Attanayake et al., 2013). Some compounds, includ ing taraxerol (Gantait et al., 2010), palmitic acid, stearic acid, oleic acid, linoleic acid, α-tocopherol, γ-tocopherol, and β-carotene (Sadou et al., 2007) have been isolated from this species.

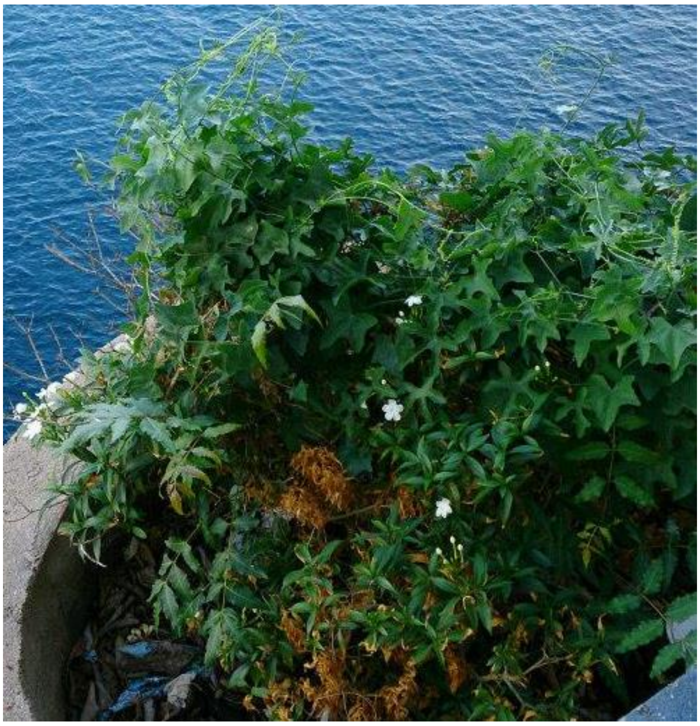

Figure 7. 3 *Coccinia grandis* sample collected at Thirukonecharam Temple, Trincomalee

7.1.2.4. *Mukia maderaspatana* (L.) M. Roem.

Mukia maderaspatana (Figure 7.4) is also a climber and belongs to the Cucurbitaceae family. It is called Mosumosukkai (மொசுமொசுக்கை) in Tamil

(SM) and it is distributed throughout most of the tropical zones in the world, incorporating Australia and Oceania (FZ, 2016). *M. maderaspatana* leaves are used for both food and medicinal purposes in SL. Leaves are utilised to prepare dishes like Sothy and Sambal (see section 1.12.3. *Coccinia grandis* (L.) Voigt) in SL. These food preparations are used to treat coughs (Rajapaksha, 1998). They are utilised in Neerilivuchchanthanaathiyennai (preparation 47) to treat diabetes in Sri Lankan SM (Appendix B).

Figure 7. 4 *Mukia maderaspatana* sample collected in Batharamulla, Colombo

Antimicrobial (Dhanaraj et al., 2012), gastroprotective (Gomathy et al., 2015), and antioxidant (Petrus and Bhuvaneshwari, 2012), activities of *M. maderaspatana* have been observed in past pharmacological studies. There is currently only one *in vitro* antidiabetic study for *M. maderaspatana.* The methanol extract of a shade-dried whole plant (0.25 mg/ml) was able to inhibit gluconeogenesis in a rat liver slice assay (Srilatha and Ananda, 2014). Compounds like 7-O-β-D-glucopyranosyl-6-C-β-D-glucopyranosylluteolin, 8-C-β-D-glucopyranosylapigenin, 6-C-β-D-glucopyranosylapigenin, 7-O-β-D-glucopyranosyl-6-C-β-D-glucopyranosylapigenin, 8-C-β-D-glucopyranosylluteolin, and 6-C-β-D-glucopyranosylluteolin (Petrus and

Bhuvaneshwari, 2012) have been identified and isolated from various parts of *M. maderaspatana*.

7.1.2.5. ***Artocarpus heterophyllus*** **Lam.**

Artocarpus heterophyllus (Figure 7.5) belongs to the Moraceae family and is referred to as Palaa (*பலா*) in Tamil (SM). It is commonly distributed in Asia, Australia, Africa, North and South America (Morton and Dowling,1987). The mature leaves of *A. heterophyllus* are utilised as both cattle food and medicine in SL. The decoction made by boiling mature leaves in water is consumed to treat diabetes (Jayaweera, 1982). Mature leaves are used as an ingredient in Neerilivuchchanthanaathiyennai (preparation 47) (Appendix B).

Figure 7. 5 *Artocarpus heterophyllus* sample collected in Peradeniya Royal Botanical Gardens, Lake Drive, Peradeniya, Kandy

Pharmacological studies show that *A. heterophyllus* has antiproliferative (Zheng et al., 2014) and anti-inflammatory (Wei et al., 2005) activities. In addition, clinical studies have shown that this species has antidiabetic properties. One such study utilised fresh mature leaves clinical evidence for treating diabetes. Fresh mature leaves (20 000mg/kg of starting plant material) which were then boiled in water and a 110 ml decoction orally administered to 10 normal and 10 T2D people. After 2 hours blood glucose levels had returned to the normal level (Fernando et al., 1991).

An ethanol extract of shade-dried leaves (100 mg/kg body weight) was orally administered to Alloxan-induced diabetic rats for 7 days. The results showed a decrease in the fasting blood sugar level. Glibenclamide (2.5 mg/kg) was utilised as a positive control in this study. Also, toxicity studies showed that when a dose of up to 5000 mg/kg was administered orally over a 7-day period there was no mortality (Okonkwo et al., 2015). In another study, 70% ethanol extract and n-butanol extract of the air-dried leaves (200 mg/kg) was orally administrated to Streptozotocin-induced diabetic rats for 10 days. The results show that there was a significant reduction in fasting blood glucose from 200 to 56 mg% and increased the insulin level in the blood from 10.8 to 19.5 µU/ml. These observed results were more effective than the positive control (Glibenclamide, 600 µg/kg) (Omar et al., 2011). In a study carried out by Chackrewarthy et al. (2010), the ethyl acetate fraction of dichloromethane extract of the fresh mature leaves (20 mg/kg) was orally administered to Streptozotocin-induced diabetic rats for 5 weeks. It was observed that plasma glucose levels were lowered by 39%.

An *in vitro* study conducted by Kotowaroo et al. (2006), the aqueous extract of the dried leaves (1000 µl/ml) exhibited inhibition of α-amylase while using starch as a substrate. In another study, the aqueous seed extract showed 87.52% antiglycation activity (Shakthi Deve et al., 2014). *A. heterophyllus* has pytochemicals including artoheterone A, artoheterone B, artocarpanone, β-carotene, lutein, lycopene, β-cryptoxanthin, flavokawain A, gemichalcone A, cyanomaclurin, dihydromorin, sakuranetin, naringenin, artocarpanone, isosinensetin, norartocarpetin, artonin Y, artoindonesianin S, artopeden A, artonin A, artonin F, morusin, artocarpin, cycloheterophyllin, isocyclomulberrin, and cyclocommunol (Ren et al., 2015; Ruiz-Montanez et al., 2015) all of which have been isolated.

7.2. Results and discussion

7.2.1. The α-glucosidase inhibitory activity of selected plant species

The mean percentage (n = 3) of the preliminary α-glucosidase inhibitory activity of the 30 extracts from the five selected plant species presented in Table 7.1. The methanol extract from mature *Artocarpus heterophyllus* leaves exhibited the highest α-glucosidase inhibitory activity (99.93 ± 0.01 %) at the highest concentration tested (200 µg/ml). Hence, all the collected methanol extract of mature *A. heterophyllus* leaf samples were studied further in this work. Additionally, there was no previous α-glucosidase inhibitory activity data available for all the selected plant species to compare to the results obtained in this study.

Table 7.1 α-Glucosidase inhibitory activity of the extracts of selected plant species and the positive control (Acarbose)

Plant species, extract, and Acarbose	α-Glucosidase inhibition / %
Achyranthes aspera	
Hexane	35.98 ± 0.79
Chloroform	23.82 ± 0.84
Ethyl acetate	19.29 ± 0.83
Acetone	17.34 ± 0.61
Methanol	8.76 ± 0.07
Aqueous	0.00
Artocarpus heterophyllus	

Plant species, extract, and Acarbose	α-Glucosidase inhibition / %
Hexane	0.00
Chloroform	6.51 ± 0.15
Ethyl acetate	25.13 ± 1.24
Acetone	39.36 ± 1.72
Methanol	99.93 ± 0.01
Aqueous	52.09 ± 2.58
Coccinia grandis	
Hexane	0.00
Chloroform	0.00
Ethyl acetate	7.72 ± 0.36
Acetone	12.16 ± 0.49
Methanol	12.66 ± 0.52
Aqueous	39.40 ± 1.48
Ipomoea aquatica	
Hexane	12.36 ± 0.34
Chloroform	15.93 ± 0.86
Ethyl acetate	17.41 ± 0.94
Acetone	32.55 ± 1.72
Methanol	41.02 ± 1.58
Aqueous	0.00

Plant species, extract, and Acarbose	α-Glucosidase inhibition / %
Mukia maderaspatana	
Hexane	18.47 ± 0.21
Chloroform	9.04 ± 0.23
Ethyl acetate	5.14 ± 0.20
Acetone	0.00
Methanol	0.00
Aqueous	0.00
Acarbose / µg/ml	
200	98.48 ± 0.28
175	88.74 ± 0.51
150	53.96 ± 0.54
125	10.48 ± 0.75
100	8.07 ± 0.30
75	5.54 ± 0.12

% α-Glucosidase inhibition values are presented as mean ± SD (n = 3)

7.2.2. The α-glucosidase inhibitory activity of collected samples of mature *Artocarpus heterophyllus* leaves

It was observed that the inhibitory activity of *A. heterophyllus* extracts on α-glucosidase was dose-dependent. The IC_{50} is the concentration of an inhibitor needed to provide 50% inhibition. On top of that, it is a scale used to determine the effectiveness of an inhibitor (Sittampalam et al., 2004). The IC_{50} values of

38 samples were found to compare the α-glucosidase inhibitory activity (Table 7.2). Samples with higher IC_{50} values had lower α-glucosidase inhibitory activity and vice versa.

It was found that the IC_{50} values varied significantly and were between 7.56 to 185.03 µg/ml depending on the extract utilised. The different metabolite composition and concentration can cause a variation of the bioactivities of biological samples (Oliver et al., 1998). It seems that the metabolite concentration is causing the variation of the α-glucosidase inhibitory activity observed in this study. This is discussed further below (7.3. Identifying the α-glucosidase inhibitory compounds).

Sample 32 collected from Nuwara Eliya (wet zone, 1416 m elevation, and red-yellow podzol soil) exhibited the greatest α-glucosidase inhibitory activity with IC_{50} of 7.56 µg/ml while, sample 15 collected from Kandy (also wet zone, at 586 m elevation, and reddish-brown latosol soil) had the lowest α-glucosidase inhibitory activity with IC_{50} of 185.03 µg/ml. This clearly shows that the α-glucosidase inhibitory activity varies with the geographical sites. Still, the mean IC_{50} value was 21.65 µg/ml for 38 samples. Acarbose was used as a positive control in this study had IC_{50} of 149.81 ± 0.95 µg/ml (~ 150 µg/ml). This value was previously reported by Lordan et al. (2013) (150 µg/ml) and Fujita et al. (2015) (152 µg/ml). The graph of α-glucosidase inhibition versus concentration is presented in Figure 7.6. The outcomes of the α-glucosidase inhibitory activity exhibit that the mature *A. heterophyllus* leaves are more effective in inhibiting α-glucosidase enzyme compared to Acarbose. For instance, samples had the higher α-glucosidase inhibitory activity.

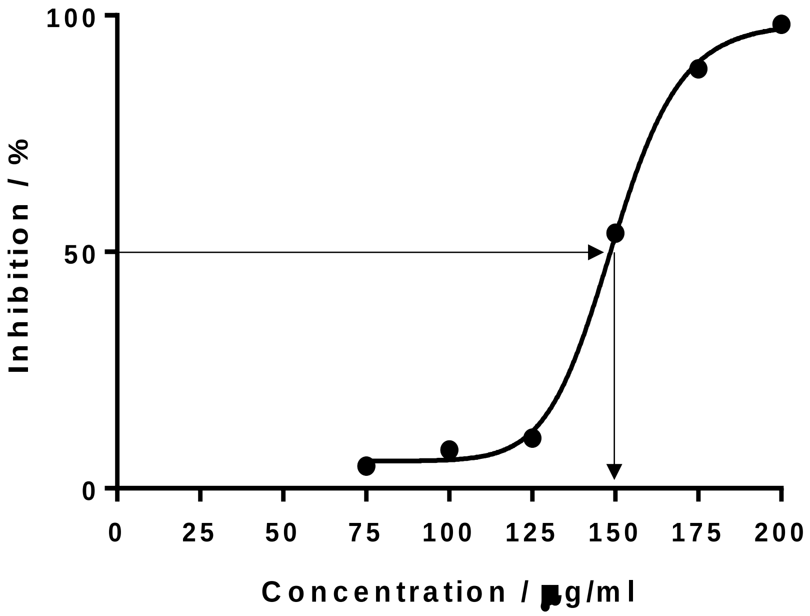

Figure 7. 6 Graph of α-glucosidase inhibition versus concentrations used of Acarbose

All the samples were grouped into three groups based on their IC_{50} values: lower (greater than IC_{50} of 31.65 µg/ml), moderate (mean ± 10 µg/ml, in the range of IC_{50} from 11.65 to 31.65 µg/ml), and higher (less than IC_{50} of 11.65 µg/ml) α-glucosidase inhibitory activity. The majority of the samples (23) had moderate, 12 samples showed higher, and three samples showed lower α-glucosidase inhibitory activities.

Table 7.2 The geographical information and the IC_{50} values of α-glucosidase inhibitory activity of 38 samples and Acarbose

Sample	Location	Latitude / °N	Longitude / °E	Climate zone	Elevation / m	Soil type	IC_{50} / µg/ml
1	Anaipanthy Pillaiyar Temple, Batticaloa	7.70846	81.69324	Dry	18	Regosol and alluvium	14.55 ± 0.38
2	88 Lake Road No. 2, Batticaloa	7.70549	81.69353	Dry	9	Regosol and alluvium	14.51 ± 0.43
3	Thiruchendur Muruhan Temple, Batticaloa	7.72152	81.7149	Dry	10	Regosol and alluvium	11.37 ± 0.41
4	Old Rest House Road, Batticaloa	7.71820	81.70016	Dry	10	Regosol and alluvium	16.91 ± 1.22
5	Mullamunai, Batticaloa	7.67844	81.60082	Dry	10	Regosol and alluvium	9.67 ± 0.47
6	Pandiruppu, Ampara	7.42597	81.81467	Dry	3	Regosol and alluvium	9.57 ± 0.51
7	Kalmunai, Ampara	7.42131	81.82225	Dry	10	Regosol and alluvium	9.73 ± 0.63

Sample	Location	Latitude / °N	Longitude / °E	Climate zone	Elevation / m	Soil type	IC_{50} / µg/ml
8	Muthiyagana Raja Buddhist Temple, Badulla	6.98431	81.06157	Intermediate	667	Red yellow podzol	46.25 ± 2.76
9	Muthiyagana Raja Buddhist Temple, Badulla	6.98412	81.06089	Intermediate	667	Red yellow podzol	56.69 ± 2.83
10	Battaramulla, Colombo	6.89979	79.91831	Wet	8	Red yellow podzol	11.37 ± 0.91
11	Jawatte Road, Colombo	6.89975	79.86647	Wet	13	Red yellow podzol	26.16 ± 1.56
12	Kacheri Road, Hambantota	6.12289	81.12663	Dry	17	Regosol and alluvium	11.94 ± 0.49
13	Yogarswamihal Ninaivalayam, Jaffna	9.65302	80.03865	Dry	10	Regosol and alluvium	14.37 ± 0.48
14	Chavakachcheri, Jaffna	9.66012	80.16342	Dry	11	Regosol and alluvium	25.08 ± 1.19

Sample	Location	Latitude / °N	Longitude / °E	Climate zone	Elevation / m	Soil type	IC_{50} / µg/ml
15	Kurinji Kumaran Temple, Kandy	7.25746	80.60336	Wet	586	Reddish brown latosol	185.03 ± 9.25
16	Pallekele, Kandy	7.27924	80.70378	Intermediate	468	Reddish brown latosol	13.26 ± 0.93
17	Peradeniya, Kandy	7.28078	80.62067	Wet	490	Reddish brown latosol	12.79 ± 0.92
18	Peradeniya, Kandy	7.28067	80.61979	Wet	491	Reddish brown latosol	15.20 ± 0.60
19	Church of Ceylon, Kilinochchi	9.38829	80.40776	Dry	28	Reddish brown	15.17 ± 1.25
20	Wathhimi Road, Kurunegala	7.48973	80.36666	Intermediate	135	Red yellow podzol	18.28 ± 0.97
21	Maliga Pitiya Stadium, Kurunegala	7.49089	80.36657	Intermediate	127	Red yellow podzol	10.48 ± 0.09

Sample	Location	Latitude / °N	Longitude / °E	Climate zone	Elevation / m	Soil type	IC_{50} / µg/ml
22	Kachcheri Road, Kurunegala	7.49132	80.3667	Intermediate	126	Red yellow podzol	22.40 ± 1.24
23	Dambulla, Matale	7.87089	80.64993	Dry	162	Reddish brown	8.83 ± 0.72
24	Matale Muthumariamman Temple, Matale	7.47205	80.62441	Wet	358	Reddish brown latosol	24.62 ± 1.07
25	Bandarapola, Matale	7.45020	80.67085	Wet	659	Reddish brown latosol	18.21 ± 0.94
26	Bandarapola, Matale	7.44975	80.68097	Wet	768	Reddish brown latosol	23.28 ± 1.16
27	Thiruketheecharam, Mannar	8.95114	79.96023	Dry	5	Solodised solonetz and solonchaks	26.59 ± 1.56
28	Dondra, Matara	5.92090	80.59259	Wet	14	Red yellow podzol	29.13 ± 0.64
29	Dondra, Matara	5.92248	80.58974	Wet	17	Red yellow podzol	15.14 ± 1.12

Sample	Location	Latitude / °N	Longitude / °E	Climate zone	Elevation / m	Soil type	IC_{50} / µg/ml
30	Kathirhamam Muruhan Temple, Monaragala	6.41846	81.33376	Dry	48	Reddish brown	16.30 ± 1.23
31	Kataragama, Monaragala	6.41418	81.32979	Dry	48	Reddish brown	11.91 ± 0.97
32	Nallathanniya, Nuwara Eliya	6.82145	80.50596	Wet	1416	Red yellow podzol	7.56 ± 0.67
33	Nallathanniya, Nuwara Eliya	6.82548	80.52180	Wet	1257	Red yellow podzol	7.62 ± 0.19
34	Mulgama, Nuwara Eliya	6.82601	80.52692	Wet	1235	Red yellow podzol	11.30 ± 0.57
35	Thirukonecharam Temple, Trincomalee	8.58096	81.24425	Dry	34	Reddish brown	19.98 ± 0.34

Sample	Location	Latitude / °N	Longitude / °E	Climate zone	Elevation / m	Soil type	IC_{50} / µg/ml
36	St. Antony's Church, Trincomalee	8.57215	81.23327	Dry	10	Reddish brown	13.20 ± 0.70
37	Rambaikulam, Vavuniya	8.73390	80.50737	Dry	100	Reddish brown	10.14 ± 0.57
38	Kovilkulam, Vavuniya	8.74211	80.50886	Dry	102	Reddish brown	8.17 ± 0.14
NA	Acarbose	NA	NA	NA	NA	NA	149.81 ± 0.95

IC_{50} values are presented as mean ± SD (n = 3)

NA: Not applicable

Table 7.3 Mean of the IC_{50} values for *Artocarpus heterophyllus* based on the climate zones, topography, and soil types

Category	Minimum / µg/ml	Maximum / µg/ml	Mean / µg/ml	Number of samples
IC_{50} value				
Low (Higher inhibition)	7.56	11.37	9.65*	3
Moderate (Moderate inhibition)	11.91	29.13	18.22*	23
High (Lower inhibition)	46.25	185.03	95.99*	12
Climate zone				
Dry	8.17	26.59	14.10	19
Intermediate	10.48	56.69	27.89	6
Wet	7.56	185.03	29.80	13
Topography region / elevation				
Coastal (0 - 30 m)	9.57	29.13	16.43	17
Plain (31 - 200 m)	8.17	22.40	13.52	9
Highland (above 200 m)	7.56	185.03	35.15	12
Soil type				
Red-yellow podzol	7.56	56.69	21.87	12
Reddish-brown	8.17	19.98	12.96	8

Category	Minimum / µg/ml	Maximum / µg/ml	Mean / µg/ml	Number of samples
Reddish-brown latosol	12.79	185.03	41.77	7
Regosol and alluvium	9.57	25.08	13.77	10

* Significant at $p < 0.01$

The correlation between the α-glucosidase inhibitory activity and the physical environmental factors such as climatic condition, topography (elevation), and soil types observed are discussed further. The samples were collected in all three climate zones (dry, intermediate, and wet) in SL. Remarkably, samples collected from the wet zone had both the highest (sample 32) and the lowest (sample 15) α-glucosidase inhibitory activities. The majority of the samples were collected from the dry (19 samples) followed by the wet (13 samples), and finally the intermediate (6 samples) zones (Table 7.3). The samples collected from the dry zone had the lowest mean IC_{50} value (14.10 µg/ml) followed by, the intermediate (27.89 µg/ml), and the wet zone samples (29.80 µg/ml). These results suggest that samples collected from the dry zone had the highest α-glucosidase inhibitory activity while those from the wet zone had the least inhibitory activity. As a result, it seems that there was a direct relationship between the α-glucosidase inhibitory activity and the climatic conditions.

The samples collected from three types of main topographies of SL (coastal, plain, and highland regions). The greatest number of samples (17 samples) was collected from the coastal region followed by the highland (12 samples), and plain (9 samples) regions. Again, remarkably samples collected from the highland region had both the highest (sample 32) and the lowest (sample 15) α-glucosidase inhibitory activities in this study. The plain region samples had the lowest mean IC_{50} value (13.52 µg/ml) followed by, the coastal (16.43 µg/ml), and highland (35.15 µg/ml) regions samples. Which probably seems that there was no direct correlation between the elevation (topography) and the α-glucosidase inhibitory activity of methanol extracts of mature *A. heterophyllus* leaves.

The majority of mature *A. heterophyllus* leaf samples were collected from the red-yellow podzol soil (12 samples) followed by the regosol and alluvium (10 samples), reddish-brown (8 samples), reddish-brown latosol (7 samples), and solodised-solonetz and solonchaks (1 sample) soils. The sample 32 which had the highest α-glucosidase inhibitory activity in this study and was collected from the red-yellow podzol soil whereas sample 15 had the lowest α-glucosidase inhibitory activity was collected from the reddish-brown latosol soil. The reddish-brown soil samples had the mean greatest α-glucosidase inhibitory activity (IC_{50}

of 12.96 µg/ml) followed by the regosol and alluvium (IC_{50} of 13.77 µg/ml), red-yellow podzol (IC_{50} of 21.87 µg/ml), and reddish-brown latosol (IC_{50} of 41.77 µg/ml). Only one sample was collected from the solodised solonetz and solonchaks soil (sample 27 from Mannar) and was found to have an IC_{50} of 26.59 µg/ml.

Even though, the α-glucosidase inhibitory activity of mature *A. heterophyllus* leaves has not been studied before. Mature *A. heterophyllus* leaves were previously studied in *in vivo* models and a clinical study conducted to evaluate its antidiabetic effects (see 7.1.2.5. *Artocarpus heterophyllus* Lam.). There might be the other pharmacological mechanisms responsible for the antidiabetic activity of mature *A. heterophyllus* leaves. Consequently, additional pharmacological and clinical investigations should be carried out. This study reveals that the antidiabetic activity of methanol extracts of mature *A. heterophyllus* leaves is linked to the α-glucosidase inhibitory activity.

7.2.3. Identifying the α-glucosidase inhibitory compounds

Three sample groups were established (higher, moderate, and lower α-glucosidase inhibitory activities) and used to identify the α-glucosidase inhibitory compound by using multivariate statistical analysis (OPLS-DA statistical model) of ^{1}H NMR spectra. The score plot of the OPLS-DA model is illustrated in Figure 7.7. The T score [1] and Orthogonal T score [1] showed 17.7% and 36.4% variability respectively. Further, a significant separation was observed between the higher, moderate, and lower α-glucosidase inhibitory active sample groups. Sample 32 had the highest α-glucosidase inhibitory activity followed by samples 33 and 38. These three samples were clearly grouped in the higher inhibition group (red). In addition, the rest of the samples had the higher α-glucosidase inhibitory activity (samples 3, 5, 6, 21, 23, 34, and 37) were clustered with the higher inhibition group while overlapping with the moderate inhibition group (blue). Sample 15 had the lowest α-glucosidase inhibitory activity followed by, the samples 9 and 8. All these three samples were clustered in the lower inhibition group while samples 9 and 8 were overlapped with the moderate inhibition group (green). Likewise, it was observed that sample 15 was located further away from all the other samples. On top of that, there was one outlier identified in this model, sample 22 had moderate α-glucosidase inhibitory activity and was located closer to sample 15. This seems to be a strong correlation between the α-glucosidase inhibitory activity and the chemical composition variation in this study.

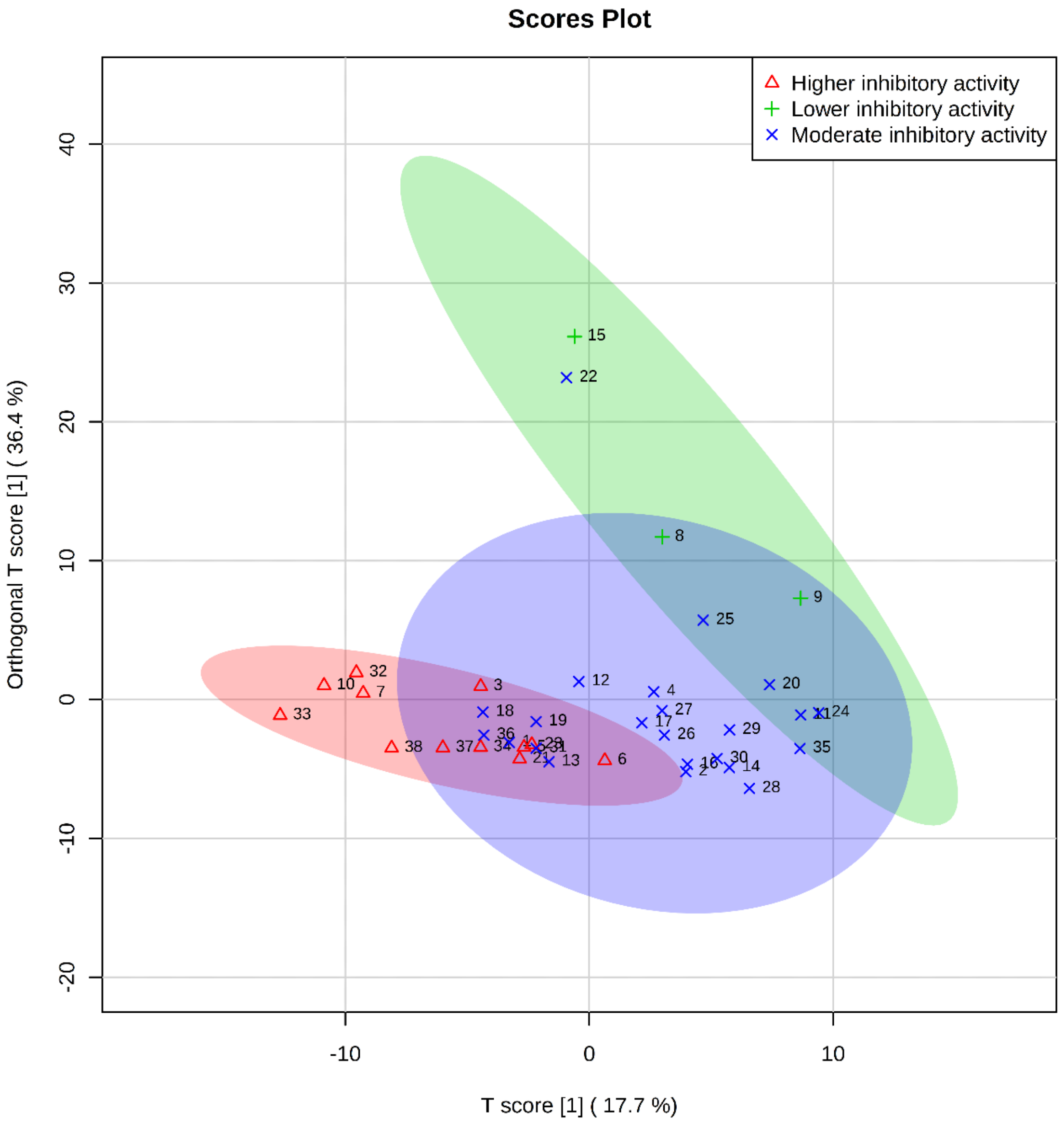

Figure 7.7 Orthogonal Partial Least Square - Discriminant Analysis score plot of the lower, moderate, and higher α-glucosidase inhibitory activity groups of mature *A. heterophyllus* leaf samples

The s-plot for the OPLS-DA model was used to identify the most relevant buckets contributing to the variation between the lower, moderate, and higher α-glucosidase inhibition sample groups (Figure 7.8). The s-plot revealed that 1.72, 1.92, 1.96, 1.28, and 1.44 ppm and 4.44, 4.32, 9.00, 6.84, and 8.40 ppm buckets were the major contributors to the chemical compostion variation between the higher and lower α-glucosidase inhibition groups.

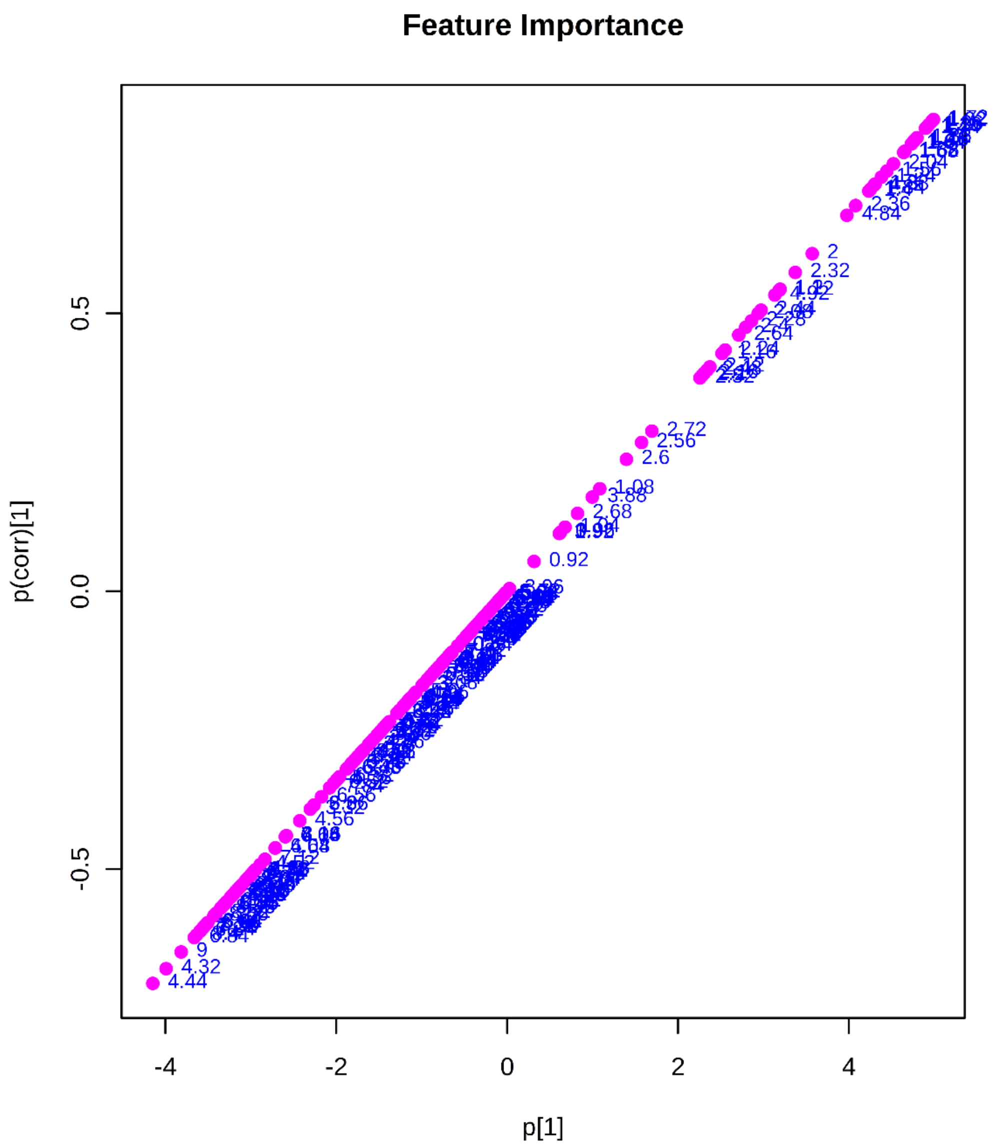

Figure 7.8 The s-plot analysis representing the major contributors of ^{1}H NMR spectra signals for the separations between the higher, moderate, and lower α-glucosidase inhibition groups

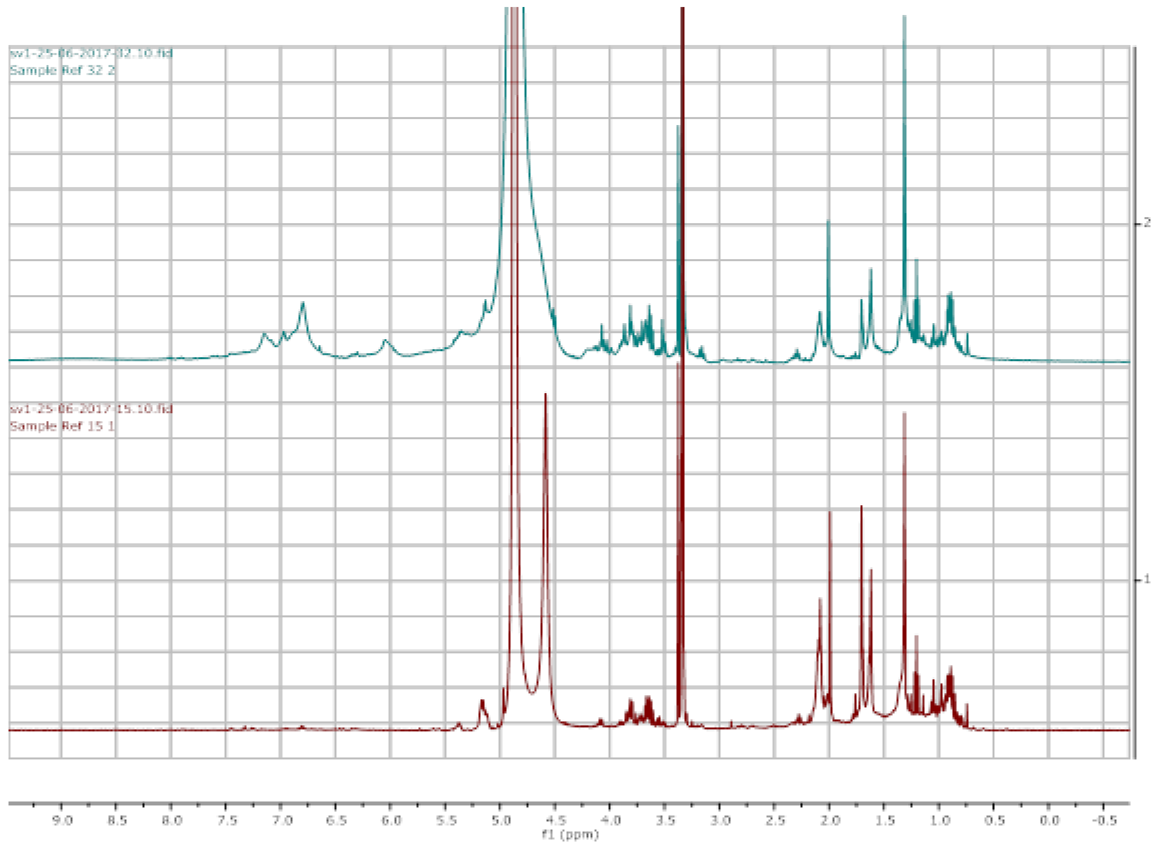

Figure 7.9 The ^{1}H NMR spectra of the samples had the highest (sample 32, above) and the lowest (sample 15, below) α-glucosidase inhibitory activities

The intensities of the NMR spectrum signals are directly proportional to the concentrations of the compounds present in the samples. Therefore, the compounds with higher concentrations will provide stronger signals with higher intensities, while, the compounds with less concentration will provide weaker signals with lower intensities (Mo and Raftery, 2008). As mentioned before, external factors affect the metabolite concentration in the biological samples (Oliver et al., 1998). Accordingly, environmental (external) factors such as climates, elevations, and soil types could be responsible for the variation in the metabolite concentrations in this study.

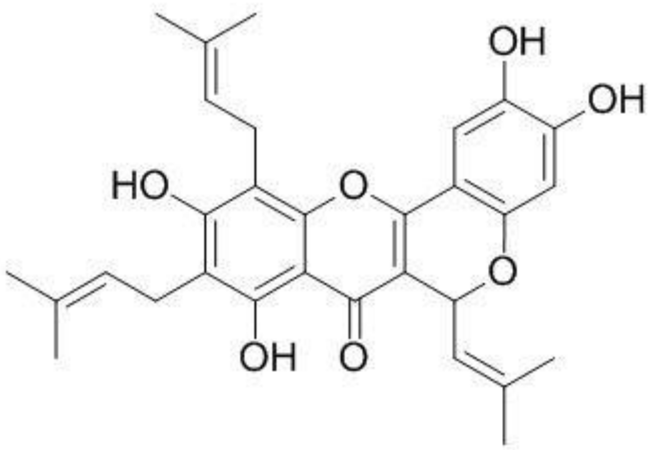

Figure 7.10 Chemical structure of Artoheterophyllin B

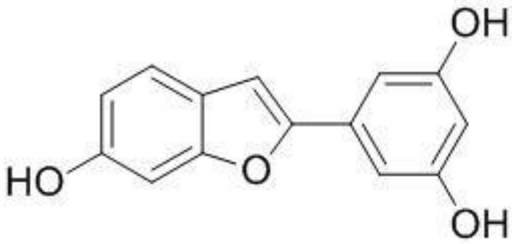

Figure 7.11 Chemical structure of Moracin M

^1H NMR spectra, performed in the methanol-d_4 solvent, of the compounds isolated from Moraceae family plant species were compared to the major buckets contributing to the separations in the OPLS-DA model. The major contributing buckets (6.84 and 1.72) matched with the corresponding ^1H NMR spectrum signals of Artoheterophyllin B (a flavonoid) (Figure 7.10) which was isolated from the methanol extract of *A. heterophyllus* twigs (Zheng et al., 2009) and Moracin M (also a flavonoid) (Figure 7.11) which had been isolated from the ethanol extract of *A. heterophyllus* leaves (Wang X. et al., 2017). Both compounds give NMR spectrum signals at 6.84 ppm, while the signals below 2 ppm (1.72 ppm) are very likely due to the aliphatic protons present in Artoheterophyllin B. Therefore, it is likely that Artoheterophyllin B is responsible for the higher α-glucosidase inhibitory activity of mature *A. heterophyllus* leaves.

Even so, no studies have been performed so far to determine the antidiabetic activity of Artoheterophyllin B. Thus, another chemical analytical technique such as Liquid Chromatography-Mass Spectrometry (LC-MS) should be utilised to confirm this. In addition, further phytochemical and pharmacological analysis should be carried out to identify the other α-glucosidase inhibitory compounds present in mature *A. heterophyllus* leaves.

Chapter 8

Conclusion

8.1. Findings and limitations

The findings of this Ph.D. research incorporate four parts. The first part is to identify and document the plant species mentioned in the Sri Lankan SM historical documents to treat diabetes (Chapter 4). The second part encompasses an ethnobotanical survey carried out in the Eastern Province of SL with SEHs to identify and document the plant species currently used to treat diabetes with a key aim being to prevent this knowledge from disappearing in the future. Additionally, the plant species recorded in the ethnobotanical survey were compared with the plant species documented in the historical documents in order to understand continuity and the change in the treatment of diabetes (Chapter 5). The third part assessed the current scientific evidence available using relevant published studies on antidiabetic activity for the majority of the plant species documented from both the historical documents and the ethnobotanical survey to provide a basis for future pharmacological and phytochemical studies (Chapter 6). In the final part, a metabolomics approach was utilised to assess the activity of a species on α-glucosidase as a target. An α-glucosidase inhibitor from a selected plant species was identified tentatively using a metabolomic profiling approach employing NMR spectroscopy and OPLS-DA (Chapter 7).

In the nutshell, the aims and objectives of this Ph.D. project have been achieved, despite the fact that there were some limitations identified in this work. The findings of this work contribute the new knowledge to ethnopharmacology, pharmacognosy, and medicinal plant research more broadly.

As stated in Chapter 2, SM is one of the TMs practised in SL and it is the main TM for Tamils. Ayurveda is the TM mostly practised in SL, followed by SM (Sivasanmugarajah, 2001). Comparatively, the majority of the published works regarding plants and preparations utilised in TM in SL were based on Ayurveda, for example, Kankanamalage et al. (2015) and Thabrew et al. (2001). In addition, a couple of ethnobotanical surveys had been carried out in the SM practising areas (Rajamanoharan 2014, 2016). There was only one study which assessed the plants used to treat diabetes in an Indian SM historical document (Parthiban et al., 2014). Therefore, this Ph.D. project systematically assessed and documented the importance of the historical and current Sri Lankan SM diabetes treatments and the plant species utilised in the preparations. This information was made publicly available also to prevent its disappearance in the future. Furthermore, since this information is now available in the public domain, it will be possible to be established this knowledge based on SM (Chapters 4 and 5).

Three Sri Lankan SM historical documents (used as university textbooks) were utilised to obtain information about the historical diabetes treatments in this investigation. In this respect, these documents revealed that there were considerable overlap between the symptoms utilised in biomedicine and SM to describe diabetes (Chapter 4). Since other historical documents could not be involved, more Sri Lankan SM historical documents currently available and accessible could have been identified and included in this study to obtain more details of diabetes and its treatments.

The ethnobotanical survey with the SEHs showed that they have great knowledge about diagnosing and treating diabetes. Moreover, they have expertise in plant species identifications, collections, preservations, and SM pharmacological skills (Chapter 5).

Only a minority of SEHs (one-third of currently registered) participated in this ethnobotanical survey (Chapter 5). Generally, some of the SEHs interviewed were not willing to reveal the most of the plant species they use to prepare the antidiabetic preparations. Much effort was put into this study to obtain the information presented in this work. Thus, more SEHs could have been covered in this investigation to obtain more information about current diabetes treatments. However, it was not possible to compare the preparations historically and currently utilised, as none of the SEHs revealed the names of the preparations they use.

The duration of the ethnobotanical survey was relatively short (three months) (Chapter 5), due to visa restriction in SL and only a limited time and funding were available to conduct this research. Because of that, this might have limited the number of species and other information obtained.

SM has been used for hundreds of years, which has numerous beneficial impacts including affordability and being easily accessible. Apart from these advantages, certainly there are other disadvantages as well in which ingredients (rhinoceros horn and rare plant species) are difficult to obtain and in some cases illegal to handle (Chapter 4 and Appendix B).

SM is less well-known to the Western world than the other TMs such as Ayurveda and Unani practised in SL. Most of the SM literature in Tamil has not been translated (Thas, 2008). Inversely, historical diabetes treatments in Sri Lankan SM have been translated and made publicly available in this project (Chapter 2 and Appendix B) considerably contributed towards SM. Anyhow, this study had only covered a part of the many facets of SM. For instance, a wide range of ingredients utilised in the preparations and the unique SM urine examination (Chapter 2) show that there is a great wealth of empirical knowledge in SM.

The historical documents contained almost exclusively preparations with a large number of diverse ingredients (Appendix B), hence, the principal active ingredient is unknown in such complex preparations. Untangling these complex preparations will remain an enormous challenge for the future.

Plants were the most important and commonly used ingredients in the antidiabetic preparations (Chapter 4 and Appendix B). Currently, SEHs are using only botanical ingredients in antidiabetic preparations. Further, more plant species were recorded in the historical documents than the ethnobotanical survey, which simply linked to the detailed analysis of the two parts of this research, with less information available for the current uses. There were continuity and some changes observed between the historical plant species and currently utilised. For example, the plant species currently utilised are mostly based on historical knowledge while presently no animal ingredients and inorganic substances are utilised.

Several pure metals and minerals were used in the historical preparations (Appendix B). This shows the wealth of chemistry knowledge in SM. Nevertheless, the procedures utilised to purify and convert metals and minerals were not mentioned for the antidiabetic preparations analysed in this work.

One of the main reasons for avoiding animal ingredients and inorganic substances at present by the SEHs may be due to the three-decade civil war in SL which ended in 2009. This war severely affected the Eastern and Northern Provinces, due to the limited supply of inorganic substances and animal ingredients during this period, they might have stopped using them. Still, during the interviews, the SEHs did not state the reasons for currently avoiding these ingredients. One can speculate why such information was not provided, and it is not possible to decide whether this is in fact linked to the inorganic substances no longer being utilised or an unwillingness to report their use. In general, it appeared that the information about these ingredients used as medicines are much more limited and may well deserve further research regarding their current potential benefits (if they exist) and risks. This should comprise epidemiological studies on the use of such preparations.

The literature search using electronic database revealed that the majority of the plant species had some *in vivo* scientific evidence and several plant species had no scientific evidence (Chapter 6). Overall, as one would expect, the information is very limited, most of the pharmacological studies carried out in T1D models. Yet, as stated above, approximately 90% of diabetics suffer from T2D (Holman et al., 2015). Therefore, further investigations of plant extracts and phytochemicals should be conducted in T2D related *in vivo* models in the future. The plants for which have no scientific evidence available may be potential candidates for further studies on antidiabetic activities.

None of the 60 preparations documented in this study have scientific evidence that could be used to assess potential therapeutic benefits. Even so, considerable pharmacological and clinical information of the individual plant species extracts are currently available, hence, it was not possible to assess the scientific evidence of the historical complex preparations.

Several full texts of the scientific evidence identified using Scopus and PubMed electronic databases were not available (Chapter 3), whereas only the abstracts of these works were available. The reason for this might be the journals discontinued by the publisher. Reviewed the scientific evidence required full texts to obtain more information about the studies. More broadly, this part of the study relies only on the published evidence and the quality of the studies utilised. Apparently, concerns have been raised about the reproducibility of clinical studies and this is not possible in such a review (Mullane et al., 2015; Mullane and Williams, 2015). Also, there were some problems identified. The pharmacological and clinical studies reviewed were often methodologically problematic for other reasons (e.g. unrealistic high doses, poor general design, etc.). Diabetes is a chronic illness thus the studies could have been conducted for a longer period to study the pharmacological effects. In the future, more rigorous experimental approaches will be needed to study the antidiabetic activity of the plant extracts and compounds. In many cases, the chemistry of the plant species was known relatively well. In further steps, observational and ideally intervention studies are essential.

Plant extracts contain mixtures of active, partly active, and inactive compounds. The bioactivity of a plant extract is not dependent on a single compound, as a result, due to this complexity, results from bioactivity assessments are often not reproducible (Heinrich, 2010). For instance, metabolomics techniques linked with *in vitro* or *in vivo* screening for bioactivity and toxicity can be used for a better phytochemical characterisation of plant extracts. Besides, several different samples of one plant species are required to conduct the metabolite profiling technique. Apart from this, as stated in Chapter 7, there are more advantages employing bioassay-guided isolation technique than metabolite profiling technique to identify the active compounds from plant extracts, like less time consumption to carry out this technique and identification of the synergetic effects of compounds (Wang et al., 2004). On that account, it was decided to employ the metabolite profiling approach to identify the α-glucosidase inhibitory compounds from mature *A. heterophyllus* leaf samples (Chapter 7).

In this study, 38 mature *A. heterophyllus* leaf samples had been collected from different geographical sites to conduct metabolite profiling. Again, a larger number of mature *A. heterophyllus* leaf samples could have been collected to study the α-glucosidase inhibitory activity to obtain more details of the α-glucosidase inhibitory compounds (Chapter 7).

α-Glucosidase inhibitory activities of selected plant species were conducted to create new scientific evidence in terms of evidence-based TM (Chapter 7). However, among the five selected plant species, only mature *A. heterophyllus* leaves showed a strong α-glucosidase inhibitory activity. Accordingly, all the collected samples of this species were studied in detail. Due to the time constraint in this Ph.D. research, all the other samples of the selected plant species had not been studied.

There was a huge variation of the α-glucosidase inhibitory activity of the mature *A. heterophyllus* leaf samples collected from different locations in SL (Chapter 7). Due to time and funding constraints, the initial idea of using the metabolomic analysis as a starting point to identify which compounds could be responsible for the activity could not be followed up in more detail. Although, a geographical comparison could still be completed. As stated before, the variation of the metabolite composition in the biological samples is caused by the physiological condition, interaction with other creatures, and genetic modification. In addition, the variation of metabolite concentrations is likewise caused by external factors such as physical environmental conditions (climate, elevations, and soil types) (Oliver et al., 1998). Based on the details of the environmental conditions of the geographical sites of each sample, there was an association between the α-glucosidase inhibitory activity and climatic conditions and phytochemical composition variability of crude methanol extracts of mature *A. heterophyllus* leaves. On the other hand, there was no association observed between the α-glucosidase inhibitory activity and elevation (Chapter 7). This study similarly suggests that several different samples of the same species should be collected and used for preliminarily screening to study a bioactivity. Afterward, further pharmacological and phytochemical studies should be conducted on the sample that showed the best bioactivity. Further, this finding suggests the geographical site to collect more potential mature *A. heterophyllus* leaves which can be utilised to prepare SM preparations.

The sample had the best α-glucosidase inhibitory activity (sample 32, IC_{50} of 7.56 µg/ml) was nearly 20 times more effective than the positive control (Acarbose, IC_{50} of 149.81 µg/ml) used in this study. It is a potential source for the natural α-glucosidase inhibitor (Chapter 7). *A. heterophyllus* is one of the most common plant species found in SL and which is easily obtainable with less or no cost, thus, after further research, this extract could be utilised as an inexpensive α-glucosidase inhibitor and affordable by the most people with diabetes in SL. Further studies required to be carried out to make use of this.

There were some drawbacks of using NMR spectroscopy like lower sensitivity (Safer et al., 2011) (Chapter 7). Despite that, a combination of NMR spectra and OPLS-DA technique revealed that Artoheterophyllin B might be responsible for the α-glucosidase inhibitory activity (Chapter 7). Anyhow, another analytical technique which is more sensitive than NMR spectroscopy, to give an example, Liquid Chromatography-Mass Spectrometry (LC-MS) could have been employed to confirm this outcome.

At present, the number of people relying on the biomedicine is increasing than TMs. Consequently, there is a potential risk to SM in the future because there are more biomedical hospitals than SM hospitals in the areas where SM mostly practised in SL. For example, there are 58 biomedical and 12 SM state-owned hospitals in the Eastern Province (MFSL, 2016). This clearly shows that the majority of the Tamil population are currently relying on biomedicine than SM in the Eastern Province. In addition, SM is currently more suitable for non-emergency treatments (AYUSH, 2018). At present, some of the patients are not benefiting from the treatments provided by the SEHs, on that account, the patients are losing the trust in the SEHs, treatments provided by them, and SM.

This is due to the inconsistent in the preparations provided by the SEHs (Sivasanmugarajah, 2001). These potential risks can be overcome by creating more scientific evidence for the SM preparations and implementing the recommendations provided below.

8.2. Future works

In the future, this work should be expanded to cover all currently available and accessible published SM books are written in SL to gain more information about diabetes treatments including the plants used in the preparations. On top of that, the same information can be obtained from the Indian SM historical documents and published books. A comparative study can be carried out between the diabetes treatments in Sri Lankan and Indian SM.

Ethnobotanical surveys should be carried out with SEHs residing in the Northern Province to record the useful plant species utilised by them before this knowledge disappears in the future. This information will provide the whole list of plants currently utilised to treat diabetes in Sri Lankan SM and more traditional SM information which is not available in the printed documents. Again, a comparative study would be highly desirable to identify the continuity and change between the treatments.

Additional pharmacological, phytochemical, and toxicity studies should be carried out to the mature *A. heterophyllus* leaf sample which showed the best α-glucosidase inhibitory activity. If this extract showed less or no side effects than currently available biomedical drugs, then it can be developed further and marketed for an affordable price in SL. On the other hand, α-glucosidase inhibitory compounds from this extract should be identified and the potential active compounds should be studied in T2D *in vivo* models and clinical trials.

Last but not least, this work will build the foundation for a more rigorous study in the future of antidiabetic Sri Lankan SM preparations and the plants utilised. It is also providing new opportunities to discover the best α-glucosidase inhibitory active extract and novel active compounds in drug discovery programs.

8.3. Recommendations beyond the immediate scope of this study

Based on the most of the aims and objectives (Chapter 1) achieved in this Ph.D. study, the following recommendations for the policy and practice and research needs were also identified. All these policies cannot be implemented immediately, nevertheless, they can be included in the practice in the future. The identified recommendations are discussed below:

8.3.1. For research and development

The following recommendations focusing on scientific aspects such as research methods, sample selections for future pharmacological, phytochemical, and toxicity studies are recommended:

1. Scientific investigations should be conducted to study the interactions, side effects, and complications caused by taking both biomedical drugs and SM preparations to treat diabetes.

2. Freeze-dried, fresh juices of the same plant part materials used in the SM preparations are recommended to use in the future pharmacological studies where fresh materials are available and easily obtainable.

8.3.2. For policy and practice

From the policy and practice perspective recommendations focus on how to further develop policies and for implementing best practice:

1. The Sri Lankan government needs to develop a strategy for advising the SEHs, biomedical doctors, and the population about the potential uses and safety of the plants. Additionally, awareness should be raised regarding potential interactions, side effects, and complications caused by taking both biomedical drugs and SM preparations to treat diabetes.

2. Sri Lankan government should identify the SEHs not currently on their register with the Ministry of Indigenous Medicine should be enlisted.

3. Despite claims that the preparations produced by the state Siddha preparations manufacturers are consistent, the Sri Lankan Ministry of Indigenous Medicine should introduce new, stricter regulation for registering the names of the preparations as well as, for example, their preparation methods,

ingredients and amounts utilised, storage conditions, and shelf-life of preparation produced by the SEHs. SEHs who are not willing to reveal such essential information should be barred from registering and practising SM. Moreover, regulatory procedures should be carried out to identify and exclude toxic substances from such preparations. For example, *Aristolochia* species like *A. bracteolate* clearly cannot be endorsed as a phytomedicine (Michl et al., 2016). Most notably, many of the inorganic substances are clearly not suitable (a topic not covered in detail in this study) because of their level of toxicity, many of these ingredients must be withdrawn in the future (toxic plant species have been marked in Appendix A and Table 5.2).

4. Tamil quantitative units which have not been standardised should be standardised by converting into metric units (4.6. Amounts and dosages used in Sri Lankan Siddha Medicine).

5. Currently, a Sri Lankan SM pharmacopeia is not available, thus, it is recommended to develop and publish such a legally binding document in the near future incorporating SM and Ayurvedic herbal medical substances.

6. Some plant species are rare and those species should be a focus of future research and cultivation strategies developed to prevent their disappearance in the future (these plant species have been marked in Appendix A and Table 5.2).

Finally, this Ph.D. project focused on the importance of assessing the historical TM documents and ethnobotanical survey to identify, document, and compare the change and continuity between the historical and contemporary TM treatments especially for diabetes. In addition, identifying an α-glucosidase inhibitory compound from plant extracts employing metabolomic profiling technique. This procedure can be utilised in the future antidiabetic medicinal plant researches.

References

Abbott, R., 2014. Documenting Traditional Medical Knowledge (SSRN Scholarly Paper No. ID 2406649). Rochester, NY: Social Science Research Network.

Abesundara, K. J., Matsui, T., and Matsumoto, K., 2004. α-Glucosidase inhibitory activity of some Sri Lanka plant extracts, one of which, *Cassia auriculata*, exerts a strong antihyperglycemic effect in rats comparable to the therapeutic drug Acarbose. J. Agric. Food Chem. 52, 2541 – 2545.

Abuelgassim, A.O., 2013. Effect of *Acacia Nilotica* fruit extract on serum glucose and lipid concentrations in Alloxan-induced diabetic rats. Pak. J. Biol. Sci. 16, 1398 – 402.

ADA (American Diabetes Association), 2016. Diagnosing diabetes and learning about prediabetes. Available at: http://www.diabetes.org/diabetes-basics/diagnosis/ [Accessed July 28, 2017].

Adisakwattana, S., Pudhom, K., Yibchok-Anun, S., 2009. Influence of the methanolic extract from *Abutilon indicum* leaves in normal and Streptozotocin-induced diabetic rats. Afr. J. Biotechnol. 8.

Agapouda, A., Booker, A., Kiss, T., Hohmann, J., Heinrich, M., Csupor, D., 2017. Quality control of *Hypericum perforatum* L. analytical challenges and recent progress. J. Pharm. Pharmacol.

Agrawal, R., Sethiya, N.K., Mishra, S.H., 2013. Antidiabetic activity of alkaloids of *Aerva lanata* roots on Streptozotocin-Nicotinamide induced type-II diabetes in rats. Pharm. Biol. 51, 635 – 642.

Ahmad, M., Prawez, S., Sultana, M., 2014. Anti-hyperglycemic, anti-hyperlipidemic and antioxidant potential of alcoholic extract of *Sida cordifolia* (areal part) in Streptozotocin-induced-diabetes in Wistar rats. Proceedings of the Indian National Science Academy Part B Biological Sciences Conference 84, 397 - 405.

Ahmad, M., Zaman, F., Sharif, T., Ch, M.Z., 2008. Antidiabetic and hypolipidemic effects of aqueous methanolic extract of *Acacia nilotica* pods in Alloxan-induced diabetic rabbits. Scand. J. Lab. Anim. Sci. 35, 29 – 34.

Ahmad, M.M., Shaikh, M.U.D., 1989. Improvement in glucose tolerance by *Caralluma tuberculata, Acacia Nilotica*, and *Papaver somniferum*. Pak. J. Zool. 21, 325 – 332.

Ahmed, F., Hudeda, S., Urooj, A., 2011. Antihyperglycemic activity of *Ficus racemosa* bark extract in type 2 diabetic individuals. J. Diabetes 3, 318 – 319.

Ahmed, F., Urooj, A., 2010a. *In vitro* studies on the hypoglycaemic potential of *Ficus racemosa* stem bark. J. Sci. Food Agric. 90, 397 – 401.

Ahmed, F., Urooj, A., 2010b. Effect of *Ficus racemosa* stem bark on the activities of carbohydrate hydrolysing enzymes: an *in vitro* study. Pharm. Biol. 48, 518–523.

Ajiboye, A.T., Asekun, O.T., Familoni, O.B., 2016. The role of plant natural products in diabetes drug discovery and development: A report with focus on Nigerian biodiversity. Presented at the World Congress on Clinical Trials in Diabetes, BioScientifica.

Akhtar, M.S., Iqbal, J., 1991. Evaluation of the hypoglycaemic effect of *Achyranthes aspera* in normal and Alloxan-diabetic rabbits. J. Ethnopharmacol. 31, 49–57.

Akhtar, M.S., Khan, M.A., Malik, M.T., 2002. Hypoglycaemic activity of *Alpinia galanga* rhizome and its extracts in rabbits. Fitoterapia 73, 623–628.

Akinlolu, A.A., Salau, B.A., Ekor, M., Otulana, J., 2015. *Musa sapientum* with exercises attenuates hyperglycaemia and pancreatic islet cells degeneration in Alloxan-diabetic rats. J. Intercult. Ethnopharmacol. 4, 202–207.

Ali, K., Iqbal, M., Yuliana, N.D., Lee, Y.J., Park, S., Han, S., Lee, J.W., Lee, H.S., Verpoorte, R., Choi, Y.H., 2013. Identification of bioactive metabolites against adenosine A1 receptor using NMR-based metabolomics. Metabolomics 9, 778–785.

Alrheam, A.I.A.A., Saad-Al Shehri, Z., 2015. Ethanopharmacological study of the aqueous, chloroform, ethanol leaves extracts and latex of *Calotropis procera* in diabetic rats. Biomed. Res. Ther. 2, 396–401.

AMCSL (Ayurvedic Medical Council, Sri Lanka), 2018. Siddha Professionals. Available at: http://www.ayurvedicmedicoun.gov.lk/web/index.php?option=com_amcprofessionals&view=amcprofessionals&Itemid=170&lang=en [Accessed August 4, 2018].

American Herbal Pharmacopoeia®, 2017. AHP-Verified™ Botanical Reference Materials. Available at: http://www.herbal-ahp.org/documents/BRM-CRS%20List/AHP-BRM%20Website%20List%20Order%208.28.18.pdf [Accessed August 24, 2017].

Andrade-Cetto, A., Heinrich, M., 2005. Mexican plants with hypoglycaemic effect used in the treatment of diabetes. J. Ethnopharmacol. 99, 325–348.

Anonymous, 2000. Seharaasasehara Treatment (*செகராசசேகர வைத்தியம்* - Seharaasasehara Vaiththiyam). Jaffna: Provincial Department of Indigenous Medicine, Ministry of Health Eastern and Northern Provinces. [In Tamil].

Anonymous, 2003. Pararasaseharam (Fifth Part) (*பரராசசேகரம் (ஐந்தாம் பாகம்)* - Pararaasaseharam (Ainthaam Paaham)). Nallur: Niyanthree Publication. [In Tamil].

Anonymous, 2015. Saiva Knowledge 10 (*சைவநெறி* 10 - Saiva Neri 10) Colombo: Educational Publications Department Inc. [In Tamil].

Arulmozhi, D.K., Kurian, R., Veeranjaneyulu, A., Bodhankar, S.L., 2007. Antidiabetic and antihyperlipidemic effects of *Myristica fragrans* in animal models. Pharmcol. Biol. 45, 64–68.

Arunachalam, K., Parimelazhagan, T., 2013. Antidiabetic activity of *Ficus amplissima* Smith. bark extract in Streptozotocin induced diabetic rats. J. Ethnopharmacol. 147, 302-310.

Arungarinathan, G., McKay, G.A., Fisher, M., 2011. Drugs for diabetes: part 4 Acarbose. Br. J. Cardiol. 18, 78–81.

Asad, M., Munir, T.A., Afzal, N., 2011. *Acacia nilotica* leave extract and Glyburide: Comparison of Fasting Blood Glucose, Serum Insulin, beta-Thromboglubulin Levels and Platelet Aggregation in Streptozotocin Induced Diabetic Rats. J. Pak. Med. Assoc. 61, 247–251.

Asad, M., Munir, T.A., Farid, S., Aslam, M., Shah, S.S., 2015. Duration effect of *Acacia nilotica* leaves extract and glibenclamide as hypolipidaemic and hypoglycaemic activity in Alloxan induced diabetic rats. J. Pak. Med. Assoc. 65, 1266-70.

Attanayake, A.P., Jayatilaka, K., Pathirana, C., Mudduwa, L.K.B., 2015. Antihyperglycemic activity of *Coccinia grandis* (L.) Voigt in Streptozotocin induced diabetic rats. Indian J. Tradit. Know. 14, 376–381.

Attanayake, A.P., Jayatilaka, K.A.P.W., Pathirana, C., Mudduwa, L.K.B., 2013. Study of antihyperglycemic activity of medicinal plant extracts in Alloxan induced diabetic rats. Anc. Sci. Life. 32, 193–8.

AYUSH (The Department of Ayurveda, Yoga and Naturopathy, Unani, Siddha, and Homoeopathy), 2018. Introduction and Origin of Siddha Medicine. Available at: http://www.indianmedicine.nic.in/index2.asp?slid=36&sublinkid=23&lang=1. [Accessed February 28, 2018].

Babish, J.G., Pacioretty, L.M., Bland, J.S., Minich, D.M., Hu, J., Tripp, M.L., 2010. Antidiabetic screening of commercial botanical products in 3T3-L1 adipocytes and db/db mice. J. Med. Food. 13, 535–547.

Badole, S., Patel, N., Bodhankar, S., Jain, B., Bhardwaj, S., 2006. Antihyperglycemic activity of aqueous extract of leaves of *Cocculus hirsutus* (L.) Diels in Alloxan-induced diabetic mice. Indian J. Pharmacol. 38, 49–53.

Bailey, C.J., Day, C., 1989. Traditional Plant Medicines as Treatments for Diabetes. Diabetes Care 12, 553–564.

Bailey, C.J., Tahrani, A.A., Barnett, A.H., 2016. Future glucose-lowering drugs for type 2 diabetes. Lancet Diabetes Endocrinol. 4, 350–359.

Bakhiya, N., Arlt, V.M., Bahn, A., Burckhardt, G., Phillips, D.H., Glatt, H., 2009. Molecular evidence for an involvement of organic anion transporters (OATs) in aristolochic acid nephropathy. Toxicology 264, 74–79.

Balasubramanian, T., Lal, M.S., Sarkar, M., Chatterjee, T.K., 2009. Antihyperglycemic and antioxidant activities of medicinal plant *Stereospermum suaveolens* in Streptozotocin-induced diabetic rats. J. Diet Suppl. 6, 227–251.

Ban, T.H., Min, J.W., Seo, C., Kim, D.R., Lee, Y.H., Chung, B.H., Jeong, K.H., Lee, J.W., Kim, B.S., Lee, S.H., Choi, B.S., Han, J.S., Yang, C.W., 2018. Update of aristolochic acid nephropathy in Korea. Korean J. Intern. Med. 33, 961–969.

Barua, C.C., Talukdar, A., Begum, S.A., Pathak, D.C., Sarma, D.K., Borah, R.S., Gupta, A., 2012. *In vivo* wound-healing efficacy and antioxidant activity of *Achyranthes aspera* in experimental burns. Pharm. Biol. 50, 892–899.

Bavarva, J.H., Narasimhacharya, A.V.R.L., 2008. Antihyperglycemic and hypolipidemic effects of *Costus speciosus* in Alloxan induced diabetic rats. Phytother. Res. 22, 620–626.

Belhekar, S.N., Chaudhari, P.D., Saryawanshi, J.S., Mali, K.K., Pandhare, R.B., 2013. Antidiabetic and antihyperlipidemic effects of *Thespesia populnea* fruit pulp extracts on Alloxan-induced diabetic rats. Indian J. Pharm. Sci. 75, 217–221.

Bhalodi, M., Shukla, S., Saluja, A.K., 2008. *In vitro* antioxidant activity of the flowers of *Ipomoea aquatica* Forsk. Pharmacogn. Mag. 4, 16.

Bhandari, U., Ansari, M.N., 2008b. Antihyperglycemic activity of aqueous extract of *Embelia ribes* Burm in Streptozotocin-induced diabetic rats. Indian J. Exp. Biol. 46, 607–613.

Bhandari, U., Ansari, M.N., 2009. Ameliorative effect of an ethanol extract of *Embelia ribes* fruits on Isoproterenol-induced cardiotoxicity in diabetic rats. Pharm. Biol. 47, 669–674.

Bhandari, U., Chaudhari, H.S., Khanna, G., 2013. Antidiabetic effects of *Embelia ribes* extract in high fat diet and low dose Streptozotocin-induced type 2 diabetic rats. Front. Life Sci. 7, 186-196.

Bhandari, U., Jain, N., Ansari, M.N., Pillai, K.K., 2008a. Beneficial effect of *Embelia ribes* ethanolic extract on blood pressure and glycosylated hemoglobin in Streptozotocin-induced diabetes in rats. Fitoterapia 79, 351–355.

Bhandari, U., Jain, N., Pillai, K.K., 2007. Further studies on antioxidant potential and protection of pancreatic beta-cells by *Embelia ribes* in experimental diabetes. Exp. Diabetes Res. 2007, 15803.

Bhandari, U., Kanojia, R., Pillai, K.K., 2002. Effect of ethanolic extract of *Embelia ribes* on dyslipidemia in diabetic rats. Int. J. Exp. Diabetes Res. 3, 159–62.

Bhaskara Rao, R., Murugesan, T., Sinha, S., Saha, B. P., Pal, M., and Mandal, S. C., 2002. Glucose lowering efficacy of *Ficus racemosa* bark extract in normal and Alloxan diabetic rats. Phytother. Res. 16, 590–592.

Bhat, M., Zinjarde, S.S., Bhargava, S.Y., Kumar, A.R., Joshi, B.N., 2011. Antidiabetic Indian plants: A good source of potent amylase inhibitors. J. Evid. Based Complementary Altern. Med. Med. 2011, 810207.

Bhattacharya, B., Pal, P., Lalee, A., Mal, D.K., Samanta., A., 2011. *In vivo* and *in vitro* anticancer activity of *Coccinia grandis* (L.) Voigt. (Family: Cucurbitaceae) on Swiss albino mice. J. Pharm. Res. 4, 567-569.

Bhavsar, C.J., Talele, G.S., 2013. Potential anti-diabetic activity of *Bombax ceiba*. Bangladesh J. Pharmacol. 8, 102-106.

Bhuyan, Z.A., Rokeya, B., Masum, N., Hossain, S., Mahmud, I., 2010. Antidiabetic Effect of *Syzygium cumini* L. Seed on Type 2 Diabetic Rats. Dhaka Univ. J. Biol. Sci. 19, 157–164.

Bin Sayeed, M.S., Mostofa, A.G.M., Ferdous, F.M.T.I., Islam, M.S., 2013. A randomized, placebo-controlled, crossover study of an herbal preparation containing *Vernonia cinerea* in the treatment of type 2 diabetes. J. Altern. Complementary Med. 19, 767–771.

Bischoff, H., Puls, W., Karause, H.P., Schutt, S., and Thomas, G., 1985. Pharmacological properties of the novel glucosidase inhibitors BAY m 1099 (Miglitol) and BAY o 1248. Diabetes Res. Clin. Prac. 1, 53-62.

Biswas, A., Chatterjee, S., Chowdhury, R., Sen, S., Sarkar, D., Chatterjee, M., Das, J., 2012. antidiabetic effect of seeds of *Strychnos Potatorum* Linn. in a Streptozotocin-induced model of diabetes. Acta Pol. Pharm. 69, 939–943.

Bopp, A., De Bona, K.S., Belle, L.P., Moresco, R.N., Moretto, M.B., 2009. *Syzygium cumini* inhibits adenosine deaminase activity and reduces glucose levels in hyperglycaemic patients. Fundam. Clin. Pharmacol. 23, 501–507.

Boucher, B., Ewen, S., Stowers, J., 1994. Betel nut (*Areca catechu*) consumption and the induction of glucose-intolerance in adult Cd1 mice and in their F1 and F2 offspring. Diabetologia 37, 49–55.

Brendler, T., 2010. African Herbal Pharmacopoeia. Port Louis: Association for African Medicinal Plants Standards.

Bruno, G., Runzo, C., Cavallo-Perin, P., Merletti, F., Rivetti, M., Pinach, S., Novelli, G., Trovati, M., Cerutti, F., Pagano, G., Piedmont Study Group for Diabetes Epidemiology, 2005. Incidence of type 1 and type 2 diabetes in adults aged 30-49 years: the population-based registry in the province of Turin, Italy. Diabetes Care 28, 2613–2619.

Bylesjö, M., Rantalainen, M., Cloarec, O., Nicholson, J.K., Holmes, E., Trygg, J., 2006. OPLS discriminant analysis: combining the strengths of PLS-DA and SIMCA classification. J. Chemom. 20, 341–351.

CAMO (CAMO Software AS), 2015. Multivariate Data Analysis. Available at: http://www.camo.com/multivariate_analysis.html [Accessed April 25, 2017].

Cazarolli, L.H., Kappel, V.D., Pereira, D.F., Moresco, H.H., Brighente, I.M.C., Pizzolatti, M.G., Silva, F.R.M.B., 2012. Anti-hyperglycaemic action of apigenin-6-C-β-fucopyranoside from *Averrhoa carambola*. Fitoterapia 83, 1176–1183.

CDCP (Centres for Disease Control and Prevention), 2017. About Diabetes. Available at: https://www.cdc.gov/diabetes/basics/diabetes.html [Accessed October 4, 2017].

Chackrewarthy, S., Thabrew, M.I., Weerasuriya, M.K.B., Jayasekera, S., 2010. Evaluation of the hypoglycaemic and hypolipidemic effects of an ethyl acetate fraction of *Artocarpus heterophyllus* (Jack) leaves in Streptozotocin-induced diabetic rats. Pharmacogn. Mag. 6, 186–190.

Chakrabarti, R., Srivastava, P.K., Kundu, K., Khare, R.S., Banerjee, S., 2012. Evaluation of immunostimulatory and growth promoting effect of seed fractions of *Achyranthes aspera* in common carp *Cyprinus carpio* and identification of active constituents. Fish Shellfish Immunol. 32, 839–843.

Chakraborty, A., Brantner, A., Mukainaka, T., Nobukuni, Y., Kuchide, M., Konoshima, T., Tokuda, H., Nishino, H., 2002. Cancer chemopreventive activity of *Achyranthes aspera* leaves on *Epstein-Barr* virus activation and two-stage mouse skin carcinogenesis. Cancer Lett. 177, 1–5.

Chaudhari, H.S., Bhandari, U., Khanna, G., 2013. *Embelia ribes* extract reduces high fat diet and low dose Streptozotocin-induced diabetic nephrotoxicity in rats. Excli. J. 12, 858–871.

Chee, B.J., Pauliena, M.B.S., Rasadah, M.A., Muhajir, H., 2007. Insulinotropic property of some tropical plant extracts on insulin secreting cell lines. J. Trop. For. Sci. 19, 119–120.

Chen, B., Chen, Y., 1992. Determination of Carotenoids and Chlorophylls in Water Convolvulus (*Ipomoea aquatica*) by Liquid-Chromatography. Food Chem. 45, 129–134.

Chudiwal, A.K., Jain, D.P., Jain, K.S., Singhai, A.K., Somani, R.S., 2008. Antidiabetic potential of rhizomes of *Alpinia galanga* in Alloxan-induced diabetic rats. Indian J. Pharmacol. 40, 171–171.

Colquhoun, I.J., 2007. Use of NMR for metabolic profiling in plant systems. J. Pestic. Sci. 32, 200–212.

Convention on Biological Diversity United Nations, 2011. Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity. Available at: https://www.cbd.int/abs/doc/protocol/nagoya-protocol-en.pdf [Accessed September 23, 2018].

Dahake, A.P., Chakma, C.S., Chakma, R.C., Bagherwal, P., 2010. Antihyperglycemic activity of methanolic extract of *Madhuca longifolia* bark. Diabetol. Croat. 39, 3–8.

Daisy, P., Eliza, J., Ignacimuthu, S., 2008. Influence of *Costus speciosus* (Koen.) Sm. rhizome extracts on biochemical parameters in Streptozotocin-induced diabetic rats. J. Health Sci. 54, 675–681.

Davids, D., Gibson, D., Johnson, Q., 2016. Ethnobotanical survey of medicinal plants used to manage High Blood Pressure and Type 2 Diabetes Mellitus in Bitterfontein, Western Cape Province, South Africa. J. Ethnopharmacol. 194, 755–766.

DCSSL (Department of Census & Statistics, Sri Lanka), 2011. Area of Sri Lanka by Province and District. Available at: http://www.statistics.gov.lk/Abstract2011/CHAP1/AB1-1.pdf [Accessed August 24, 2017].

DCSSL (Department of Census and Statistics Sri Lanka), 2017. Population and Housing. Available at: http://www.statistics.gov.lk/page.asp?page=Population%20and%20Housing [Accessed April 29, 2018].

de Lange, P.J., Scofield, R.P., Greene, T., 2004. *Achyranthes aspera* (Amaranthaceae), a new indigenous addition to the flora of the Kermadec Islands group. N. Z. J. Bot. 42, 167–173.

de Montellano, B.O., 1975. Empirical Aztec Medicine. Sci. 188, 215–220.

Debelle, F.D., Vanherweghem, J.-L., Nortier, J.L., 2008. Aristolochic acid nephropathy: a worldwide problem. Kidney Int. 74, 158–169.

Debnath, T., Radhakrishnan, R., Murugananthan, G., Talwar, S., K, N., 2013. Hypoglycaemic effects of alcoholic root extract of *Borassus flabellifer* (Linn.) in normal and diabetic rats. Pak. J. Pharm. Sci. 26, 673–679.

DeFronzo, R.A., Ferrannini, E., Zimmet, P., Alberti, G., 2015. International Textbook of Diabetes Mellitus. New Jersey: John Wiley & Sons.

Deshmukh, T., Yadav, B.V., Badole, S.L., Bodhankar, S.L., Dhaneshwar, S.R., 2008. Antihyperglycemic activity of alcoholic extract of *Aerva lanata* (L.) AL Juss. Ex JA Schultes leaves in Alloxan-induced diabetic mice. J. Appl. Biomed. 6, 81–87.

Deshpande, S.V., Patil, M. J., Daswadkar, S.C., Suralkar, U., Agarwal, A., 2011. A study on anti-inflammatory activity of the leaf and stem extract of *Coccinia grandis* Vioght. Int. J. Appl. Biol. Pharm. Technol. 2, 247-250.

Dhanabal, S.P., Sureshkumar, M., Ramanathan, M., Suresh, B., 2005. Hypoglycaemic effect of ethanolic extract of *Musa sapientum* on Alloxan-induced diabetes mellitus in rats and its relation with antioxidant potential. J. Herb. Pharmacother. 5, 7–19.

Dhanaraj, T.S., Murugaiah, K., Jegadeesan, M., 2012. Antimicrobial activity of ethanol extract of *Mukia maderaspatana* (L.) M. Roemer. J. Pure Appl. Microbiol. 6, 451-454.

Dhanasekaran, S., Palayan, M., Kumar, S.S., 2010. Evaluation of anti-microbial and anti-inflammatory activity of methanol leaf extract of *Ipomoea aquatica* Forsk. Res. J. Pharm. Biol. Chem. Sci. 1, 258–264.

Dikshit, P., Shukla, K., Tyagi, M.K., Garg, P., Gambhir, J.K., Shukla, R., 2012. Antidiabetic and antihyperlipidemic effects of the stem of *Musa sapientum* Linn. in Streptozotocin-induced diabetic rats. J. Diabetes 4, 378–385.

Dittus, W.P.J., 1985. The Influence of Cyclones on the Dry Evergreen Forest of Sri Lanka. Biotropica 17, 1–14.

DMSL (Department of Meteorology Sri Lanka), 2016. Climate of Sri Lanka. Available at:

http://www.meteo.gov.lk/index.php?option=com_content&view=article&id=94&Itemid=310&lang=en [Accessed April 29, 2018].

Dunn, W.B., 2008. Current trends and future requirements for the mass spectrometric investigation of microbial, mammalian and plant metabolomes. Phys. Biol. 5, 011001.

Durmuşkahya, C., Öztürk, M., 2013. Ethnobotanical survey of medicinal plants used for the treatment of diabetes in Manisa, Turkey. Sains Malaysiana 42, 1431–1438.

Edo, A.E., Eregie, A., Adediran, O.S., Ohwovoriole, A.E., 2011. Glycaemic response to some commonly eaten fruits in type 2 diabetes mellitus. West Afr. J. Med. 30, 94–8.

Edwards, S.E., Rocha, I. da C., Williamson, E.M., Heinrich, M., 2015. Phytopharmacy: An Evidence-Based Guide to Herbal Medicinal Products. New Jersey: John Wiley & Sons.

Eleazu, C.O., Iroaganachi, M., Eleazu, K.C., 2013. Ameliorative potentials of cocoyam (*Colocasia esculenta* L.) and unripe plantain (*Musa paradisiaca* L.) on the relative tissue weights of Streptozotocin-induced diabetic rats. J. Diabetes Res. 2013, 160964.

Eleazu, C.O., Okafor, P., 2015. Use of unripe plantain (*Musa paradisiaca*) in the management of diabetes and hepatic dysfunction in Streptozotocin-induced diabetes in rats. Interv. Med. Appl. Sci. 7, 9–16.

Eliza, J., Daisy, P., Ignacimuthu, S., Duraipandiyan, V., 2009a. Antidiabetic and antilipidemic effect of eremanthin from *Costus speciosus* (Koen.) Sm., in STZ-induced diabetic rats. Chem. Biol. Interact. 182, 67–72.

Eliza, J., Daisy, P., Ignacimuthu, S., Duraipandiyan, V., 2009b. Normo-glycemic and hypolipidemic effect of costunolide isolated from *Costus speciosus* (Koen ex. Retz.) Sm. in Streptozotocin-induced diabetic rats. Chem. Biol. Interact. 179, 329–334.

Eliza, J., Rajalakshmi, M., Ignacimuthu, S.J., Daisy, P., 2011. Normalizing effects of *Costus speciosus* rhizome crude extracts and its fractions on diabetic complications in STZ-induced diabetic rats. Med. Chem. Res. 20, 1111–1118.

El-Toumy, S.A., Omara, E.A., Carlos, J., Bermejo, J., 2009. Phenolic metabolites from *Acacia nilotica* flowers and evaluation of antihyperglycemic effect of aqueous extract. Planta Med. 75, 1065–1066.

Erdelen, W., 1988. Forest ecosystems and nature conservation in Sri Lanka. Biol. Conserv. 43, 115–135.

Eriksson, L., Byrne, T., Johansson, E., Trygg, J., Vikström, C., 2013. Multi- and Megavariate Data Analysis Basic Principles and Applications. Umeå: Umetrics Academy.

Eskander, E.F., Jun, H.W., 1995. Hypoglycemic and hyperinsulinemic effects of some Egyptian herbs used for the treatment of diabetes mellitus (type II) in rats. Egypt. J. Pharm. Sci. 36, 331–342.

European Medicines Agency, 2009. European Medicines Agency's Committee on Herbal Medicinal Products. Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_lilisti/document_listing_000193.jsp. [Accessed February 29, 2016].

Evans, J.M., Newton, R.W., Ruta, D.A., MacDonald, T.M., Morris, A.D., 2000. Socio-economic status, obesity and prevalence of Type 1 and Type 2 diabetes mellitus. Diabetes Med. 17, 478–480.

Fan, B.Y., Gu, Y.C., He, Y., Li, Z.R., Luo, J.G., Kong, L.Y., 2014. Cytotoxic Resin Glycosides from *Ipomoea aquatica* and Their Effects on Intracellular Ca2+ Concentrations. J. Nat. Prod. 77, 2264–2272.

Farswan, M., Mazumder, P.M., Parcha, V., Upaganlawar, A., 2009. Modulatory Effect of *Syzygium cumini* seeds and its isolated compound on biochemical parameters in diabetic rats. Pharmacogn. Mag. 5, 127–133.

FDSL (Forest Department of Sri Lanka), 2017. Forest Cover. Available at: http://www.forestdept.gov.lk/index.php/en/# [Accessed February 14, 2018].

Feng X., 2003. Use of *Cassia sophera* Linn. and its extract with excellent blood glucose-lowering effect for treating and ameliorating symptoms of diabetes. Chinese Patent 1764466-A.

Fernando, M.R., Wickramasinghe, N., Thabrew, M.I., Ariyananda, P.L., Karunanayake, E.H., 1991. Effect of *Artocarpus heterophyllus* and *Asteracanthus longifolia* on glucose tolerance in normal human subjects and in maturity-onset diabetic patients. J. Ethnopharmacol. 31, 277–282.

Fikru, A., Makonnen, E., Eguale, T., Debella, A., Mekonnen, A.G., 2012. Evaluation of *in vivo* wound healing activity of methanol extract of *Achyranthes aspera* L. J. Ethnopharmacol. 143, 469–474.

Fu, H., Xie, B., Ma, S., Zhu, X., Fan, G., Pan, S., 2011. Evaluation of antioxidant activities of principal carotenoids available in water spinach (*Ipomoea aquatica*). J. Food Compos. Anal. 24, 288–297.

Fujita, A., Sarkar, D., Wu, S., Kennelly, E., Shetty, K., Genovese, M.I., 2015. Evaluation of phenolic-linked bioactives of camu-camu (*Myrciaria dubia* Mc. Vaugh) for antihyperglycemia, antihypertension, antimicrobial properties and cellular rejuvenation. Food Res. Int. 77, 194–203.

Funke, I., Melzig, M.F., 2006. Traditionally used plants in diabetes therapy: phototherapeutics as inhibitors of alpha-amylase activity. Rev. Bras. Farmacogn. 16, 1–5.

FZ (Flora of Zimbabwe), 2016. Species information: *Mukia maderaspatana*. Available at: http://www.zimbabweflora.co.zw/speciesdata/species.php?species_id=156990 [Accessed February 29, 2016].

Ganapaty, S., Nyamathulla, S., Vijay, K., 2006. Hypoglycaemic activity of aerial parts of *Cocculus hirrsutus* on Alloxan induced diabetes. Indian J. Nat. Prod. 22, 17–20.

Gandhi, G.R., Sasikumar, P., 2012. Antidiabetic effect of *Merremia emarginata* Burm. F. in Streptozotocin induced diabetic rats. Asian Pac. J. Trop. Biomed. 2, 281–286.

Gantait, A., Sahu, A., Venkatesh, P., Dutta, P.K., Mukherjee, P.K., 2010. Isolation of Taraxerol from *Coccinia grandis*, and its Standardization. J. Planar Chromatogr. Mod. TLC 23, 323–325.

Gautam, B., Vadivel, V., Stuetz, W., Biesalski, H.K., 2012. Bioactive compounds extracted from Indian wild legume seeds: antioxidant and type II diabetes-related enzyme inhibition properties. Int. J. Food Sci. Nutr.63, 242–245.

Gayathri, M., Kannabiran, K., 2008. Hypoglycaemic activity of *Hemidesmus indicus* R. Br. on Streptozotocin-induced diabetic rats. Int. J. Diabetes Dev. Ctries. 28, 6–10.

Gayathri, M., Kannabiran, K., 2009. Effect of 2-hydroxy-4-methoxy benzoic acid from the roots of *Hemidesmus indicus* on Streptozotocin-induced diabetic rats. Indian J. Pharm. Sci. 71, 581–585.

Gokhale, A.B., Damre, A.S., Kulkarni, K.R., Saraf, M.N., 2002. Preliminary evaluation of anti-inflammatory and anti-arthritic activity of *S. lappa, A. speciosa* and *A. aspera.* Phytomedicine 9, 433–437.

Gomathy, G., Venkatesan, D., Palani, S., 2015. Gastroprotective potentials of the ethanolic extract of *Mukia maderaspatana* against indomethacin-induced gastric ulcer in rats. Nat. Prod. Res. 29, 2107–2111.

Gulati, V., Gulati, P., Harding, I.H., Palombo, E.A., 2015. Exploring the antidiabetic potential of Australian Aboriginal and Indian Ayurvedic plant extracts using cell-based assays. BMC Complementary Altern. Med. 15, 8.

Gul-E-Rana, Karim, S., Khurhsid, R., Saeed-Ul-Hassan, S., Tariq, I., Sultana, M., Rashid, A.J., Shah, S.H., Murtaza, G., 2013. Hypoglycaemic activity of *Ficus racemosa* bark in combination with oral hypoglycaemic drug in diabetic human. Acta Pol. Pharm. 70, 1045–1049.

Guo, J., Han, J., Wang, S., Liu, J., 2017. An ethnobotanical survey of medicinal plants used for the ailment of diabetes mellitus in Changzhi city of Shanxi province, China. Biomed. Res. 28, 1370–1377.

Gupta, S., Sharma, S.B., Prabhu, K.M., 2009a. Ameliorative effect of *Cassia auriculata* L. leaf extract on glycaemic control and atherogenic lipid status in Alloxan-induced diabetic rabbits. Indian J. Exp. Biol. 47, 974–980.

Gupta, S., Sharma, S.B., Prabhu, K.M., Bansal, S.K., 2009b. Protective role of *Cassia auriculata* leaf extract on hyperglycaemia-induced oxidative stress and its safety evaluation. Indian J. Biochem. Biophys. 46, 371–377.

Habtemariam, S., 2012. Identification of the antidiabetic and antihyperlipidemic principles of *Cassia auriculata*. Planta Med. 78, 1084–1084.

Halim, M.E., Misra, A., 2011. The effects of the aqueous extract of *Pterocarpus santalinus* heartwood and vitamin E supplementation in Streptozotocin-induced diabetic rats. J. Med. Plants Res. 5, 398–409.

Hamidreza, H., Heidari, Z., Shahraki, M., Moudi, B., 2010. A stereological study of effects of aqueous extract of *Tamarindus indica* seeds on pancreatic islets in Streptozotocin-induced diabetic rats. Pak. J. Pharm. Sci. 23, 427–34.

Han, K.L., Choi, J.S., Lee, J.Y., Song, J., Joe, M.K., Jung, M.H., Hwang, J.K., 2008. Therapeutic potential of peroxisome proliferators-activated receptor-alpha/gamma dual agonist with alleviation of endoplasmic reticulum stress for the treatment of diabetes. Diabetes 57, 737–745.

Hanhineva, K., Törrönen, R., Bondia-Pons, I., Pekkinen, J., Kolehmainen, M., Mykkänen, H., Poutanen, K., 2010. Impact of dietary polyphenols on carbohydrate metabolism. Int. J. Mol. Sci. 11, 1365–1402.

Harborne, J.B., 1996. Dictionary of Plant Toxins. Michigan: Wiley.

Harvey, A.L., 2010. Plant natural products in antidiabetic drug discovery. Curr. Org. Chem. 14, 1670–1677.

Hatapakki, B.C., Suresh, H.M., Bhoomannavar, V., Shivkumar, S.I., 2005. Effect of *Cassia auriculata* Linn flowers against Alloxan-induced diabetes in rats. J. Nat. Rem. 5, 132–136.

Heinrich, M., 2010. Ethnopharmacology in the 21st Century – Grand Challenges. Front. Pharmacol. 1, 8.

Heinrich, M., Lardos, A., Leonti, M., Weckerle, C., Willcox, M., with the ConSEFS advisory group, 2018. Best practice in research: Consensus Statement on Ethnopharmacological Field Studies - ConSEFS. J. Ethnopharmacol. 211, 329–339.

Heinrich, M., Rimpler, H., Barrera, N.A., 1992. Indigenous phytotherapy of gastrointestinal disorders in a lowland Mixe community (Oaxaca, Mexico): ethnopharmacologic evaluation. J. Ethnopharmacol. 36, 63–80.

Hemmati, M., Zohoori, E., Mehrpour, O., Karamian, M., Asghari, S., Zarban, A., Nasouti, R., 2015. Antiatherogenic potential of jujube, saffron and barberry: anti-diabetic and antioxidant actions. Excli. J. 14, 908–915.

Holman, N., Young, B., Gadsby, R., 2015. Current prevalence of Type 1 and Type 2 diabetes in adults and children in the UK. Diabetes Med. 32, 1119–1120.

Holmes, E., Tang, H., Wang, Y., Seger, C., 2006. The assessment of plant metabolite profiles by NMR-based methodologies. Planta Med. 72, 771–785.

Huang, P.L., Chi, C.W, Liu, T.Y., 2013. Areca nut procyanidins ameliorate Streptozocin-induced hyperglycaemia by regulating gluconeogenesis. Food Chem. Toxicol. 55, 137–143.

IDF (International Diabetes Federation), 2014. IDF Diabetes Atlas. Available at: https://www.idf.org/diabetesatlas. [Accessed February 29, 2016].

IDF (International Diabetes Federation), 2015. IDF Diabetes Atlas. Available at: https://www.idf.org/diabetesatlas. [Accessed February 29, 2016].

IDF (International Diabetes Federation), 2017. IDF Diabetes Atlas. Available at: http://diabetesatlas.org/IDF_Diabetes_Atlas_8e_interactive_EN/ [Accessed September 7, 2018].

Im, R., Mano, H., Matsuura, T., Nakatani, S., Shimizu, J., Wada, M., 2009. Mechanisms of blood glucose-lowering effect of aqueous extract from stems of Kothala himbutu (*Salacia reticulata*) in the mouse. J. Ethnopharmacol. 121, 234–240.

IUCN (International Union for Conservation of Nature and Natural Resources), 2016. Sri Lanka. Available at: https://www.iucn.org/asia/countries/sri-lanka [Accessed August 24, 2018].

IUCN (International Union for Conservation of Nature and Natural Resources), 2018. The IUCN Red List of Threatened Species. Available at: https://www.iucnredlist.org/ [Accessed November 01, 2018].

Jaber, H., Baydoun, E., EL-Zein, O., Kreydiyyeh, S.I., 2013. Antihyperglycemic effect of the aqueous extract of banana infructescence stalks in Streptozotocin-induced diabetic rats. Plant Foods Hum. Nutr. 68, 83–89.

Jahan, I.A., Nahar, N., Mosihuzzaman, M., Rokeya, B., Ali, L., Azad Khan, A.K., Makhmur, T., Iqbal Choudhary, M., 2009. Hypoglycaemic and antioxidant activities of *Ficus racemosa* Linn. fruits. Nat. Prod. Res. 23, 399–408.

Jain, S., Bhatia, G., Barik, R., Kumar, P., Jain, A., Dixit, V.K., 2010. Antidiabetic activity of *Paspalum scrobiculatum* Linn. in Alloxan induced diabetic rats. J. Ethnopharmacol. 127, 325–328.

Jana, K., Chatterjee, K., Ali, K.M., De, D., Bera, T.K., Ghosh, D., 2012. Antihyperglycemic and antioxidative effects of the hydro-methanolic extract of the seeds of *Caesalpinia bonduc* on Streptozotocin-induced diabetes in male albino rats. Pharmacogn. Res. 4, 57–62.

Jarald, E.E., Joshi, S.B., Jain, D.C., 2008. Antidiabetic activity of flower buds of *Michelia champaca* Linn. Indian J. Pharmacol. 40, 256–260.

Jarald, E.E., Joshi, S.B., Jain, D.C., 2010. Antidiabetic activity of extracts and fraction of *Cassia auriculata* Linn. J. Nat. Rem. 10, 17–26.

Jayaweera, D.M.A., 1980. Medicinal plants (Indigenous and exotic) used in Ceylon: Acanthaceae - Burseraceae. Colombo: National Science Council of Sri Lanka.

Jayaweera, D.M.A., 1981. Medicinal Plants (Indigenous and Exotic) Used in Ceylon: Flacourtiaceae - Lythraceae. Colombo: National Science Council of Sri Lanka.

Jayaweera, D.M.A., 1982. Medicinal Plants (Indigenous and Exotic) Used in Ceylon: Magndaceae - Rubiaceae. Colombo: National Science Council of Sri Lanka.

Jayaweera, D.M.A., 2006. Medicinal Plants (Indigenous and Exotic) Used in Ceylon: Rutaceae - Zygophyllaceae. Colombo: National Science Council of Sri Lanka.

Jia, W., Gao, W., Tang, L., 2003. Antidiabetic herbal drugs officially approved in China. Phytother. Res. 17, 1127–1134.

Juvekar, A.R., Halade, G.V., 2006. Hypoglycaemic activity of Cassia auriculata in neonatal Streptozotocin-induced non-insulin dependent diabetes mellitus in rats. J Nat. Rem. 6, 14–18.

Kang, J., Choi, M.Y., Kang, S., Kwon, H.N., Wen, H., Lee, C.H., Park, M., Wiklund, S., Kim, H.J., Kwon, S.W., Park, S., 2008. Application of a ^{1}H nuclear magnetic resonance (NMR) metabolomics approach combined with orthogonal projections to latent structure-discriminant analysis as an efficient tool for discriminating between Korean and Chinese herbal medicines. J. Agric. Food Chem. 56, 11589–11595.

Kankanamalage, T.N.M., Dharmadasa, R.M., Abeysinghe, D.C., Wijesekara, R.G.S., 2014. A survey on medicinal materials used in traditional systems of medicine in Sri Lanka. J. Ethnopharmacol. 155, 679-691.

Kar, A., Choudhary, B.K., Bandyopadhyay, N.G., 2003. Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in Alloxan diabetic rats. J. Ethnopharmacol. 84, 105–108.

Karan, S.K., Pal, D., Mishra, S.K., Mondal, A., 2013. Antihyperglycemic effect of *Vetiveria zizanioides* (L.) Nash root extract in Alloxan-induced diabetic rats. Asian J. Chem. 25, 1555–1557.

Karthic, K., Kirthiram, K.S., Sadasivam, S., Thayumanavan, B., Palvannan, T., 2008. Identification of alpha-amylase inhibitors from *Syzygium cumini* Linn seeds. Indian J. Exp. Biol. 46, 677–680.

Kasiviswanath R., Ramesh A., Kumar K.E., 2005. Hypoglycaemic and antihyperglycemic effect of *Gmelina asiatica* Linn. in normal and in Alloxan-induced diabetic rats. Biol. Pharm. Bull. 4, 729 – 732.

Kaushik, P., Kaushik, D., Yadav, J., Pahwa, P., 2013. Protective effect of *Alpinia galanga* in STZ induced diabetic nephropathy. Pak. J. Biol. Sci. 16, 804–11.

Kazeem, M.I., Abimbola, S.G., Ashafa, A.O.T., 2013. Inhibitory potential of *Gossypium arboreum* leaf extracts on diabetes key enzymes, alpha-amylase and alpha-glucosidase. Bangladesh J. Pharmacol. 8, 149–155.

Kazeem, M.I., Mayaki, A.M., Ogungbe, B.F., Ojekale, A.B., 2016. *In vitro* studies on *Calotropis procera* leaf extracts as inhibitors of key enzymes linked to diabetes mellitus. Iran J. Pharm. Res. 15, 37–44.

Khuda, F., Iqbal, Z., Khan, A., Zakiullah, Shah, W.A., Shah, Y., Ahmad, L., Hassan, M., Khan, A., Khan, A., 2015. Antibacterial and antifungal activities of leaf extract of *Achyranthes aspera* (Amaranthaceae) from Pakistan. Pak. J. Pharm. Sci. 28, 1797–1800.

Khuda, F., Iqbal, Z., Khan, A., Zakiullah, Shah, Y., Ahmad, L., Nasir, F., Hassan, M., Ismail, Shah, W.A., 2014. Evaluation of anti-inflammatory activity of selected medicinal plants of Khyber Pakhtunkhwa, Pakistan. Pak. J. Pharm. Sci. 27, 365–368.

Kim, H.K., Choi, Y.H., Verpoorte, R., 2010. NMR-based metabolomic analysis of plants. Nat. Protoc. 5, 536–549.

Kim, J.S., Hyun, T.K., Kim, M.J., 2011. The inhibitory effects of ethanol extracts from sorghum, foxtail millet and proso millet on α-glucosidase and α-amylase activities. Food Chem. 124, 1647–1651.

Kirana, H., Agrawal, S.S., Srinivasan, B.P., 2009. Aqueous extract of *Ficus religiosa* Linn. reduces oxidative stress in experimentally induced type 2 diabetic rats. Indian J. Exp. Biol. 47, 822–826.

Kirana, H., Jali, M.V., Srinivasan, B.P., 2011. The study of aqueous extract of *Ficus religiosa* Linn. on cytokine TNF-α in type 2 diabetic rats. Pharmacogn. Res. 3, 30–34.

Kondeti, V.K., Badri, K.R., Maddirala, D.R., Thur, S.K.M., Fatima, S.S., Kasetti, R.B., Rao, C.A., 2010. Effect of *Pterocarpus santalinus* bark, on blood glucose, serum lipids, plasma insulin and hepatic carbohydrate metabolic enzymes in Streptozotocin-induced diabetic rats. Food Chem. Toxicol. 48, 1281–1287.

Kotowaroo, M.I., Mahomoodally, M.F., Gurib-Fakim, A., Subratty, A.H., 2006. Screening of traditional antidiabetic medicinal plants of Mauritius for possible alpha-amylase inhibitory effects *in vitro*. Phytother. Res. 20, 228–231.

Krisanapun, C., Lee, S.H., Peungvicha, P., Temsiririrkkul, R., and Baek, S. J., 2011. Antidiabetic activities of *Abutilon indicum* (L.) Sweet are mediated by enhancement of adipocyte differentiation and activation of the GLUT1 promoter. J. Evid. Based Complementary Altern. Med. 1–9.

Krisanapun, C., Lee, S.H., Peungvicha, P., Temsiririrkkul, R., Baek, S.J., 2010. Antidiabetic activities of *Abutilon indicum* Sweet mediated by enhancement PPAR gamma and activation of the GLUT1 promoter. Faseb J. 24.

Krisanapun, C., Peunpicha, P., Temsirifirkkul, R., Wongkrajang, Y., 2009. Aqueous extract of *Abutilon indicum* Sweet inhibits glucose absorption and stimulates insulin secretion in rodents. Nutr. Res. 29, 579–587.

Kulkarni, C.R., Joglekar, M.M., Patil, S.B., Arvindekar, A.U., 2012. Antihyperglycemic and antihyperlipidemic effect of *Santalum album* in Streptozotocin-induced diabetic rats. Pharm. Biol. 50, 360–365.

Kulkarni, Y.A., Veeranjaneyulu, A., 2013. Effects of *Gmelina arborea* extract on experimentally induced diabetes. Asian Pac. J. Trop. Med. 6, 602–608.

Kumar, A., Ilavarasan, R., Deecaraman, M., Aravindan, P., Padmanabhan, N., Krishan, M.R.V., 2013. Antidiabetic activity of *Syzygium cumini* and its isolated compound against Streptozotocin-induced diabetic rats. J. Med. Plants Res. 2, 246–249.

Kumar, A., Ilavarasan, R., Jayachandran, T., Deecaraman, M., Aravindan, P., Padmanabhan, N., Krishan, M.R.V., 2008. Antidiabetic activity of *Syzygium cumini* and its isolated compound against Streptozotocin-induced diabetic rats. J. Med. Plants Res. 2, 246–249.

Kumar, A., Lingadurai, S., Shrivastava, T.P., Bhattacharya, S., Haldar, P.K., 2011. Hypoglycemic activity of *Erythrina variegata* leaf in Streptozotocin-induced diabetic rats. Pharm. Biol. 49, 577–582.

Kumar, M., Gautam, M.K., Singh, A., Goel, R.K., 2013. Healing effects of *Musa sapientum* var. *paradisiaca* in diabetic rats with co-occurring gastric ulcer: cytokines and growth factor by PCR amplification. BMC Complementary Altern. Med. 13, 305.

Kumar, S., Kumar, D., Deshmukh, R.R., Lokhande, P.D., More, S.N., Rangari, V.D., 2008. Antidiabetic potential of *Phyllanthus reticulatus* in Alloxan-induced diabetic mice. Fitoterapia 79, 21–23.

Kumar, V., Poonam, Prasad, A.K., Parmar, V.S., 2003. Naturally occurring aristolactams, aristolochic acids, and dioxoaporphines and their biological activities. Nat. Prod. Rep. 20, 565–583.

Kumar, V.K., Lalitha, K.G., 2014. In vitro study on α-amylase inhibitory activity of an Ayurvedic medicinal plant, *Anacyclus pyrethrum* DC root. Indian J. Pharmacol. 46, 350–351.

Kumar, V.L., Padhy, B.M., 2011. Protective effect of aqueous suspension of dried latex of *Calotropis procera* against oxidative stress and renal damage in diabetic rats. Biocell 35, 63–69.

Kunyanga, C.N., Imungi, J.K., Okoth, M.W., Biesalski, H.K., Vadivel, V., 2011. Flavonoid content in ethanolic extracts of selected raw and traditionally processed indigenous foods consumed by vulnerable groups of Kenya: antioxidant and type II diabetes-related functional properties. Int. J. Food Sci. Nutr. 62, 465–473.

Kunyanga, C.N., Imungi, J.K., Okoth, M.W., Biesalski, H.K., Vadivel, V., 2012. Total phenolic content, antioxidant and antidiabetic properties of methanolic extract of raw and traditionally processed Kenyan indigenous food ingredients. Food Sci. Technol. 45, 269–276.

Kushwaha, P.S., Raj, V., Singh, A.K., Keshari, A.K., Saraf, S.A., Mandal, S.C., Yadav, R.K., Saha, S., 2015. Antidiabetic effects of isolated sterols from *Ficus racemosa* leaves. RSC Adv. 5, 35230–35237.

Kwon, Y.I.I., Vattem, D.A., Shetty, K., 2006. Evaluation of clonal herbs of Lamiaceae species for management of diabetes and hypertension. Asia Pac. J. Clin. Nutr. 15, 107–118.

Latha, M., and Pari, L., 2003. Effect of an aqueous extract of *Scoparia dulcis* on blood glucose, plasma insulin and some polyol pathway enzymes in experimental rat diabetes. Braz. J. Med. Biol. Res. 37, 577–586.

Latha, M., Pari, L., 2003. Antihyperglycemic effect of *Cassia auriculata* in experimental diabetes and its effects on key metabolic enzymes involved in carbohydrate metabolism. Clin. Exp. Pharmacol. Physiol. 30, 38–43.

Latha, M., Pari, L., Ramkumar, K. M., Rajaguru, P., Suresh, T., and Dhanabal, T., 2009. Antidiabetic effects of scoparic acid D isolated from *Scoparia dulcis* in rats with Streptozotocin-induced diabetes. Nat. Prod. Res. 23, 1528–1540.

Latha, M., Pari, L., Sitasawad, S., and Bhonde, R., 2004. Insulin-secretagogue activity and cytoprotective role of the traditional antidiabetic plant *Scoparia dulcis* (Sweet Broomweed). Life Sci. 75, 2003–2014.

Lemonnier, N., Zhou, G.-B., Prasher, B., Mukerji, M., Chen, Z., Brahmachari, S.K., Noble, D., Auffray, C., Sagner, M., 2017. Traditional Knowledge-based Medicine: A review of history, principles, and relevance in the present context of P4 systems medicine. Prog. Preventive Med. 2, e0011.

Lemus, M., Ramos, Y., Liscano, A., D' Armas, H., 2013. Effect of aqueous extract of *Phyllanthus niruri* (Euphorbiaceae), in diabetic rats. Rev. Cient-Fac De Cien. Vet. 23, 11–18.

Lenth, V.R., 2012. Some Practical Guidelines for Effective Sample Size Determination. Am. Stat. 55, 2001.

Leonti, M., 2011. The future is written: impact of scripts on the cognition, selection, knowledge and transmission of medicinal plant use and its implications for ethnobotany and ethnopharmacology. J. Ethnopharmacol. 134, 542–555.

Li, J., Wei, X., Xie, Q., Hoa Pham, T.T., Wei, J., He, P., Jiao, Y., Xu, X., Giang Nguyen, T.H., Wen, Q., Huang, R., 2016. Protective Effects of 2-Dodecyl-6-Methoxycyclohexa-2,5 -Diene-1,4-Dione Isolated from *Averrhoa Carambola* L. (Oxalidaceae) Roots on High-Fat Diet-Induced Obesity and Insulin Resistance in Mice. Cell. Physiol. Biochem. 40, 993–1004.

Li, J., Zhang, Liang, Jiang, Z., Shu, B., Li, F., Bao, Q., Zhang, Luyong, 2010. Toxicities of aristolochic acid I and aristololactam I in cultured renal epithelial cells. Toxicol. In Vitro 24, 1092–1097.

Liu, I.M., Liou, S.S., Lan, T.W., Hsu, F.L., Cheng, J.T., 2005. Myricetin as the active principle of *Abelmoschus moschatus* to lower plasma glucose in Streptozotocin-induced diabetic rats. Planta Med. 71, 617–621.

Liu, Y.X., Si, M.M., Lu, W., Zhang, L.X., Zhou, C.X., Deng, S.L., Wu, H.S., 2015. Effects and molecular mechanisms of the antidiabetic fraction of *Acorus calamus* L. on GLP-1 expression and secretion *in vivo* and *in vitro*. J. Ethnopharmacol. 166, 168–175.

Lordan, S., Smyth, T.J., Soler-Vila, A., Stanton, C., Ross, R.P., 2013. The α-amylase and α-glucosidase inhibitory effects of Irish seaweed extracts. Food Chem. 141, 2170–2176.

Madhavan, V., Joshi, R., Murali, A., Yoganarasimhan, S.N., 2007. Antidiabetic activity of *Curculigo orchioides* root tuber. Pharm. Biol. 45, 18–21.

Madhavan, V., Murali, A., Lalitha, D.S., Yoganarasimhan, S., 2015. Studies on antihyperglycemic effect of *Euphorbia antiquorum* L. root in diabetic rats. J. Intercult. Ethnopharmacol. 4, 308–313.

Maiti, R., Das, U.K., Ghosh, D., 2005. Attenuation of hyperglycaemia and hyperlipidaemia in Streptozotocin-induced diabetic rats by aqueous extract of seed of *Tamarindus indica*. Biol. Pharm. Bull. 28, 1172–1176.

Maiti, R., Jana, D., Das, U.K., Ghosh, D., 2004. Antidiabetic effect of aqueous extract of seed of *Tamarindus indica* in Streptozotocin-induced diabetic rats. J. Ethnopharmacol. 92, 85–91.

Malalavidhane, S., Wickramasinghe, S., Jansz, E.R., 2001. An aqueous extract of the green leafy vegetable *Ipomoea aquatica* is as effective as the oral hypoglycaemic drug Tolbutamide in reducing the blood sugar levels of Wistar rats. Phytother. Res. 15, 635–637.

Malalavidhane, T.S., Wickramasinghe, S., Jansz, E.R., 2000. Oral hypoglycemic activity of *Ipomoea aquatica*. J. Ethnopharmacol. 72, 293–298.

Malalavidhane, T.S., Wickramasinghe, S., Perera, M.S.A., Jansz, E.R., 2003. Oral hypoglycaemic activity of *Ipomoea aquatica* in Streptozotocin-induced diabetic Wistar rats. Phytother. Res. 17, 1098–1100.

Mallick, C., Chatterjee, K., Guhabiswas, M., Ghosh, D., 2007. Antihyperglycemic effects of separate and composite extract of root of *Musa paradisiaca* and leaf of *Coccinia indica* in Streptozotocin-induced diabetic male Albino rat. Afr. J. Tradit. Complementary Altern. Med. 4, 362–371.

Mamun, M.M., Billah, M.M., Ashek, M.A., Ahasan, M.M., Hossain, M.J., Sultana, T., 2003. Evaluation of diuretic activity of *Ipomoea aquatica* (Kalmisak) in mice model study. J. Med. Sci. 3, 395–400.

Mandal, S., Barik, B., Mallick, C., De, D., Ghosh, D., 2008. Therapeutic effect of ferulic acid, an ethereal fraction of ethanolic extract of seed of *Syzygium cumini* against Streptozotocin-induced diabetes in male rat. Methods Find. Exp. Clin. Pharmacol. 30, 121–128.

Mandrone, M., Scognarniglio, M., Fiorentino, A., Sanna, C., Cornioli, L., Antognoni, F., Bonvicini, F., Poli, F., 2017. Phytochemical profile and alpha-glucosidase inhibitory activity of Sardinian *Hypericum scruglii* and *Hypericum hircinum*. Fitoterapia 120, 184–193.

Marles, R.J., Farnsworth, N.R., 1995. Antidiabetic plants and their active constituents. Phytomedicine 2, 137–189.

Matsui, T., Ogunwande, I.A., Abesundara, K.J.M., Matsumoto, K., 2006. Antihyperglycemic Potential of Natural Products. Mini Rev. Med. Chem. 6, 349–356.

Mehta, F.A., Patel, B.G., Pandya, S.S., Ahir, K.B., 2010. Densitometric HPTLC method for analysis of oleanolic acid in *Achyranthes aspera* L. J. Planar Chromatogr. Mod. TLC 23, 289–292.

Mehta, F.A., Patel, B.G., Pandya, S.S., Ahir, K.B., 2011. High-Performance Thin-Layer Chromatographic Analysis of betaine in alcohol extracts of *Achyranthes aspera* L. Planar Chromatogr. Mod. TLC 24, 136–139.

MFSL (Ministry of Finance - The Treasury of Sri Lanka), 2017. Annual Report 2017. Available at: http://www.treasury.gov.lk/documents/10181/12870/2017.pdf/2bce4f3d-ebde-4409-b2b5-c8a0801b3edc [Accessed August 24, 2018].

MFSL (Ministry of Finance - The Treasury of Sri Lanka), 2016. General Information – 2016: Ministries, Departments and State-Owned Enterprise. Available at: http://www.treasury.gov.lk/documents/10181/388145/General+Information+2016/ae1c2b15-3c0d-4178-ab07-3671a489df00 [Accessed August 24, 2018].

Michl, J., Kite, G.C., Wanke, S., Zierau, O., Vollmer, G., Neinhuis, C., Simmonds, M.S.J., Heinrich, M., 2016. LC-MS- and (1)H NMR-Based metabolomic analysis and *in vitro* toxicological assessment of 43 *Aristolochia* Species. J. Nat. Prod. 79, 30–37.

Mo, H., Raftery, D., 2008. Solvent signal is an NMR concentration reference. Anal. Chem. 80, 9835–9839.

Morton, J.F., Dowling, C.F., 1987. Fruits of Warm Climates. Miami: J.F. Morton.

Mosihuzzaman, M., Nahar, N., Ali, L., Rokeya, B., Khan, A.K., Nur-E-Alam, M., Nandi, R.P., 1994. Hypoglycaemic effects of three plants from Eastern Himalayan belt. Diabetes Res. 26, 127–138.

Mullane, K., Enna, S.J., Piette, J., Williams, M., 2015. Guidelines for manuscript submission in the peer-reviewed pharmacological literature. Biochem. Pharmacol. 97, 225–235.

Mullane, K., Williams, M., 2015. Unknown unknowns in biomedical research: does an inability to deal with ambiguity contribute to issues of irreproducibility? Biochem. Pharmacol. 97, 133–136.

Muniappan, R., Reddy, G.V.P, Raman, A., 2009. *Coccinia grandis* (L.) Voigt (Cucurbitaceae). In: Biological Control of Tropical Weeds using Arthropods. Cambridge, UK: Cambridge University Press.

Murthy, B.K., Nammi, S., Kota, M.K., Rao, R.V.K., Rao, N.K., Annapurna, A., 2004. Evaluation of hypoglycemic and antihyperglycemic effects of *Datura metel* (Linn.) seeds in normal and Alloxan-induced diabetic rats. J. Ethnopharmacol. 91, 95–98.

Nahar, L., Nasrin, F., Zahan, R., Haque, A., Haque, E., Mosaddik, A., 2014. Comparative study of antidiabetic activity of *Cajanus cajan* and *Tamarindus indica* in Alloxan-induced diabetic mice with a reference to in vitro antioxidant activity. Pharmacogn. Res. 6, 180–7.

Nair, S.A., Sabulal, B., Radhika, J., Arunkumar, R., Subramoniam, A., 2014. Promising anti-diabetes mellitus activity in rats of beta-amyrin palmitate isolated from *Hemidesmus indicus* roots. Eur. J. Pharmacol. 734, 77–82.

Nam, J., Choi, H., 2008. Effect of butanol fraction from *Cassia tora* L. seeds on glycaemic control and insulin secretion in diabetic rats. Nutr. Res. Pract. 2, 240–6.

Nampoothiri, S.V., Philip, R.M., Kankangi, S., Kiran, C.R., Menon, A.N., 2015. Essential oil composition, α-amylase inhibition and antiglycation potential of *Curcuma aromatica* Salisb. J. Essent. Oil-Bear. Plants 18, 1051–1058.

Narayansami V., 1975. Introduction to the Siddha System of Medicine. Chennai: Anandam Research Institute of Siddha Medicine.

Natarajan, V., Arul Gnana Dhas, A.S., 2013. Effect of active fraction isolated from the leaf extract of *Dregea volubilis* Linn. Benth. on plasma glucose concentration and lipid profile in Streptozotocin-induced diabetic rats. Springerplus 2, 394.

National Institute of Siddha, Chennai, India, 2018. About Siddha Medicine. Available at: http://nischennai.org/siddhamedicine.html [Accessed February 4, 2018].

Nearing, M., 1985. The green pharmacy. Herbal medicines in modern usage. International Development Research Centre Rep. 14, 10–11.

Neto, L., Mário, C., de Vasconcelos, C.F., Thijan, V.N., Caldas, G.F., Araújo, A.V., Costa-Silva, J.H., Amorim, E.L., Ferreira, F., de Oliveira, A.F., 2013. Evaluation of antihyperglycemic activity of *Calotropis procera* leaves extract on Streptozotocin-induced diabetes in Wistar rats. Rev. Bras. Farmacogn. 23, 913–919.

Nisha, P., Mini, S., 2013. Flavonoid rich ethyl acetate fraction of *Musa paradisiaca* inflorescence down-regulates the Streptozotocin induced oxidative stress, hyperglycaemia and mRNA levels of selected inflammatory genes in rats. J. Funct. Foods 5, 1838–1847.

Noor Shahida, A., Wong, T.W., Choo, C.Y., 2009. Hypoglycemic effect of quassinoids from *Brucea javanica* (L.) Merr (Simaroubaceae) seeds. J. Ethnopharmacol. 124, 586–591.

Okoli, C.O., Ibiam, A.F., Ezike, A.C., Akah, P.A., Okoye, T.C., 2010. Evaluation of antidiabetic potentials of *Phyllanthus niruri* in Alloxan diabetic rats. Afr. J. Biotechnol. 9, 248–259.

Okoli, C.O., Obidike, I.C., Ezike, A.C., Akah, P.A., Salawu, O.A., 2011. Studies on the possible mechanisms of antidiabetic activity of extract of aerial parts of *Phyllanthus niruri*. Pharm. Biol. 49, 248–255.

Okonkwo, C. C., Agu, C. V., Njoku, O. U., Abonyi, U., Victor, A., Anaduaka, E. G., et al., 2015. Hypoglycaemic and Hematinic properties of ethanol leaf extract of *Artocarpus heterophyllus* in Alloxan induced diabetic rats. Afr. J. Tradit., Complementary Altern. Med. 12, 144–148.

Olagunju, J.A., Kazeem, O.W., Oyedapo, O.O., 2000. Further studies on the mechanism of carbohydrate intolerance induced in the rat by an ethanolic root extract of *Plumbago zeylanica*. Pharm. Biol. 38, 362–366.

Oliveira, A.C.P., Endringer, D.C., Amorim, L. a. S., Das Gracas, M., Brandao, M.D.G., Coelho, M.M., 2005. Effect of the extracts and fractions of *Baccharis trimera* and *Syzygium cumini* on glycaemia of diabetic and non-diabetic mice. J. Ethnopharmacol. 102, 465–469.

Oliver, S.G., Winson, M.K., Kell, D.B., Baganz, F., 1998. Systematic functional analysis of the yeast genome. Trends Biotechnol. 16, 373–378.

Omar, H.S., El-Beshbishy, H.A., Moussa, Z., Taha, K.F., Singab, A.N.B., 2011. Antioxidant activity of *Artocarpus heterophyllus* Lam. (Jack fruit) leaf extracts: remarkable attenuations of hyperglycaemia and hyperlipidaemia in Streptozotocin-diabetic rats. Sci. World J. 11, 788–800.

Omara, E.A., Nada, S.A., Farrag, A.R.H., Sharaf, W.M., El-Toumy, S.A., 2012. Therapeutic effect of *Acacia nilotica* pods extract on Streptozotocin induced diabetic nephropathy in rat. Phytomedicine 19, 1059–1067.

Pai, S.R., Nimbalkar, M.S., Pawar, N.V., Patil, R.P., Dixit, G.B., 2010. Seasonal discrepancy in phenolic content and antioxidant properties from bark of *Nothapodytes nimmoniana* (Grah.) Mabb. Int. J. Pharm. Biol. Sci. 1, 1–17.

Pai, S.R., Upadhya, V., Hegde, H.V., Joshi, R.K., Kholkute, S.D., 2014. New report of triterpenoid betulinic acid along with oleanolic acid from *Achyranthes aspera* by Reversed-Phase-Ultra Flow Liquid Chromatographic analysis and confirmation Using High-Performance Thin-Layer Chromatographic and Fourier Transform-Infrared Spectroscopic techniques. Planar Chromatogr. Mod. TLC 27, 38–41.

Pakrashi, A., Bhattacharya, N., 1977. Abortifacient principle of *Achyranthes aspera* Linn. Indian J. Exp. Biol. 15, 856–858.

Panabokke, C.R., 1996. Soils and Agro-ecological Environments of Sri Lanka. Colombo: Natural Resources, Energy & Science Authority.

Pandey, M., Khan, A., 2002. Hypoglycaemic effect of defatted seeds and water-soluble fibre from the seeds of *Syzygium cumini* (Linn.) Skeels in Alloxan diabetic rats. Indian J. Exp. Biol. 40, 1178–1182.

Pandit, R., Phadke, A., Jagtap, A., 2010. Antidiabetic effect of *Ficus religiosa* extract in Streptozotocin-induced diabetic rats. J. Ethnopharmacol. 128, 462–466.

Panigrahi, G., Panda, C., Patra, A., 2016. Extract of *Sesbania grandiflora* ameliorates hyperglycaemia in high fat diet-Streptozotocin induced experimental diabetes mellitus. Scientifica 2016, 4083568.

Pari, L., and Latha, M., 2004. Antihyperglycemic effect of *Scoparia dulcis* effect on key metabolic enzymes of carbohydrate metabolism in Streptozotocin-induced diabetes. Pharm. Biol. 42, 570–576.

Pari, L., and Latha, M., 2005. Effect on lipid peroxidation in Streptozotocin diabetes. Gen. Physiol. Biophys. 24, 13–26.

Pari, L., and Satheesh, M., 2004. Antidiabetic effect of *Boerhavia diffusa* effect on serum and tissue lipids in experimental diabetes. J. Med. Food. 7, 472–476.

Pari, L., and Venkateswaran, S., 2002. Hypoglycaemic activity of *Scoparia dulcis* L. extract in Alloxan-induced hyperglycaemic rats. Phytother. Res. 16, 662–664.

Pari, L., Latha, M., 2006. Antihyperlipidemic effect of *Scoparia dulcis* (sweet broomweed) in Streptozotocin diabetic rats. J. Med. Food 9, 102–107.

Pari, L., Umamaheswari, J., 1999. Hypoglycaemic effect of *Musa sapientum* L. in Alloxan-induced diabetic rats. J. Ethnopharmacol. 68, 321–325.

Pari, L., Umamaheswari, J., 2000. Antihyperglycemic activity of *Musa sapientum* flowers: effect on lipid peroxidation in Alloxan diabetic rats. Phytother. Res. 14, 136–138.

Parthiban, P., Thillaivanan, S., Kanakavalli, K., Deporal, P., Chilambuselvi, P., Kalpana, A., 2014. A review on antidiabetic herbs in Siddha Medicine. Int. J. Pharm. Arch. 3, 338-345.

Parveen, R., Ahmad, M.M., 1994. Betal nuts (*Areca catechu*) consumption as an agent for diabetes mellitus. Pak. J. Zool. 26, 305–308.

Patel, D.K., Kumar, R., Prasad, S.K., 2011. Antidiabetic and in vitro antioxidant potential of *Hybanthus enneaspermus* (Linn) F. Muell in Streptozotocin-induced diabetic rats. Asian Pac. J. Trop. Biomed. 1, 316-322.

Patil, S.B., Ghadyale, V.A., Taklikar, S.S., Kulkarni, C.R., Arvindekar, A.U., 2011. Insulin secretagogue, alpha-glucosidase and antioxidant activity of some selected spices in Streptozotocin-induced diabetic rats. Plant Foods Hum. Nutr. 66, 85–90.

Patil, V.V., Sutar, N.G., Pimprikar, R.B., Patil, A.P., Chaudhari, R.Y., Patil, V.R., 2010. Antihyperglycemic and hypoglycaemic effect of *Ficus racemosa* leaves. J. Nat. Remedies 10, 11–16.

Perera, H.K.I., Premadasa, W.K.V.K., Poongunran, J., 2016. α-glucosidase and glycation inhibitory effects of *Costus speciosus* leaves. BMC Complementary Altern. Med. 16.

Perera, P.K., 2012. Current scenario of herbal medicine in Sri Lanka. Proceedings of the Speech presented at 4th Annual Herbal International Summit cum Exhibition on Medicinal & Aromatic Products, Spices and finished products (hi-MAPS), NSIC, Okhla Industrial Estate, New Delhi.

Petrus, A.J.A., Bhuvaneshwari, N., 2012. Antioxidant flavonoid metabolites of *Mukia maderaspatana* (L.) M. Roemer leaves. Asian J. Chem. 24, 1261–1267.

Pham, H.T.T., Huang, W., Han, C., Li, J., Xie, Q., Wei, J., Xu, X., Lai, Z., Huang, X., Huang, R., Wen, Q., 2017. Effects of *Averrhoa carambola* L. (Oxalidaceae) juice mediated on hyperglycaemia, hyperlipidaemia, and its influence on regulatory protein expression in the injured kidneys of Streptozotocin-induced diabetic mice. Am. J. Transl. Res. 9, 36–49.

Ponniah, S.M., Sabapathipillai, I., 1980. Siddha Medicinal Procedure (சித்த ஔடத செய்முறை - Siththa Audatha Seimurai). Jaffna: Department of Ayurveda, Ministry of Health & Indigenous Medicine. [In Tamil].

Prakash, A.O., 1986. Potentialities of some indigenous plants for antifertility activity. Int. J. Crude Drug Res. 24, 19–24.

Prasad, K.N., Divakar, S., Shivamurthy, G.R., Aradhya, S.M., 2005. Isolation of a free radical-scavenging antioxidant from water spinach (*Ipomoea aquatica* Forsk). J. Sci. Food Agric. 85, 1461–1468.

Prisilla, D.H., Balamurugan, R., Shah, H.R., 2012. Antidiabetic activity of methanol extract of *Acorus calamus* in STZ induced diabetic rats. Asian Pac. J. Trop. Biomed. 2, S941-S946.

Punitha, I.S.R., Rajendran, K., Shirwaikar, A., Shirwaikar, A., 2005. Alcoholic stem extract of *Coscinium fenestratum* regulates carbohydrate metabolism and improves antioxidant status in Streptozotocin-Nicotinamide induced diabetic rats. J. Evid. Based Complementary Altern. Med. 2, 375–381.

Qian, Y., Peng, Y., Shang, E., Zhao, M., Yan, L., Zhu, Z., Tao, J., Su, S., Guo, S., Duan, J., 2017. Metabolic profiling of the hepatotoxicity and nephrotoxicity of Ginkgolic acids in rats using Ultra-Performance Liquid Chromatography-High-Definition Mass Spectrometry. Chem. Biol. Interact. 273, 11–17.

Radha, R., Amrithaveni, M., 2009. Role of medicinal plant *Salacia reticulata* in the management of Type II Diabetic Subjects. Anc. Sci. Life 29, 14–16.

Rafiullah, M.R.M., Siddiqui, A.W., Mir, S.R., Ali, M., Pillai, K.K., Singh, S., 2006. Antidiabetic activity of some Indian medicinal plants. Pharm. Biol. 44, 95–99.

Raghavan, K.V., Rao, J.M., Rao, R.J., Tiwari, A.K., Yadav, J.S., 2005. Antioxidant from natural source. Patent: EP1572673A1.

Rahman, M.S., Rahman, M.Z., Begum, B., Chowdhury, R., Islam, S.N., Rashid, M.A., 2011. Antidiabetic principle from *Eclipta prostrata*. Latin Am. J. Pharm. 30, 1656–1660.

Rai, P.K., Jaiswal, D., Rai, N.K., Pandhija, S., Rai, A.K., Watal, G., 2009. Role of glycaemic elements of *Cynodon dactylon* and *Musa paradisiaca* in diabetes management. Lasers Med. Sci. 24, 761–768.

Raj, N., Nadeem, S., Jain, S., Raj, C., Nandi, K.C.P., 2011. Ameliorative Effects of *Alpinia calcarata* in Alloxan-Induced Diabetic Rats. Dig. J. Nanomater. Biostruct. 6, 991–997.

Rajamanoharan, P. R. S., 2014. An Ethnobotanical Survey of Medicinal Plants in Sillalai, Jaffna, Northern Province, Sri Lanka. Int. J. Herb. Med. 1, 22–30.

Rajamanoharan, P. R. S., 2016. Existence and Survey of Medicinal Plants of Thiru Palani Murugan Kovil, Asikulam, Vavuniya District, Northern Province, Sri Lanka. World J. Pharm. Res. 5.

Rajapaksha, U., 1998. Traditional Food Plants in Sri Lanka. Colombo: Hector Kobbekaduwa Agrarian Research and Training Institute.

Rajasekar, R., Manokaran, K., Rajasekaran, N., Duraisamy, G., Kanakasabapathi, D., 2014. Effect of *Alpinia calcarata* on glucose uptake in diabetic rats-an *in vitro* and *in vivo* model. J. Diabetes Metab. Disord. 13, 33–33.

Rajesh, M.S., Harish, M.S., Sathyaprakash, R.J., Shetty, A.R., Shivananda, T.N., 2009. Antihyperglycemic activity of the various extracts of *Costus speciosus* rhizomes. J. Nat. Remed. 9, 235–241.

Rajesh, R., Chitra, K., Paarakh, P.M., 2012. Anti hyperglycemic and antihyperlipidemic activity of aerial parts of *Aerva lanata* Linn Juss in Streptozotocin-induced diabetic rats. Asian Pac. J. Trop. Biomed. 2, S924–S929.

Raju, M.G., Reddy, T.H.S., 2017. Antidiabetic and hypolipidemic activity of methanolic extract of *Aristolochia bracteolata* on Streptozotocin-induced diabetic rat model. Int. J. Pharm. Sci. Res. 8, 1173.

Ramanathan, 2008. The Origin and Development of Siddha Medicine (*சித்த மருத்துவத்தின் தோற்றமும் வளர்ச்சியும்* – Siddha Maruththuvaththin Thotramum Valarchiyum) Jaffna: Kanagathaara. [In Tamil].

Randriamampionona, D., Rafamantanana, M., Rabemanantsoa, C., Rakotoniriana, F., Cheuk, K., Corbisier, A.M., Mahillon, J., Ratsima-Manga, S., El Jaziri, M., 2008. Ex situ conservation and clonal propagation of the malagasy *Syzygium cuminii*, an antidiabetic plant. Belgian J. Bot. 141, 14–20.

Rao, B.K., Giri, R., Kesavulu, M.M., Apparao, C., 2001. Effect of oral administration of bark extracts of *Pterocarpus santalinus* L. on blood glucose level in experimental animals. J. Ethnopharmacol. 74, 69–74.

Rao, J.M., Katragadda, S.B., Tiwari, A.K., Tatipaka, H.B., Pullela, V.S., Suryadevara, P.R., Sastry, B.S., Ali, A.Z., Yadav, J.S., 2007. Alpha glucosidase inhibitory active fraction of plant *Oroxylum indicum*, useful for treating post prandial hyperglycaemia, hyperglycaemia, diabetes mellitus, obesity and disease condition requiring hyperglycaemic control. Indian Patent 200600477.

Ren, G., Peng, J., Liu, A., Liang, J., Yuan, W., Wang, H., He, J., 2015. Structure elucidation and NMR assignments of two new flavanones from the roots of *Artocarpus heterophyllus*. Magn. Reson. Chem. 53, 872–874.

Riya, M.P., Antu, K.A., Pal, S., Chandrakanth, K.C., Anilkumar, K.S., Tamrakar, A.K., Srivastava, A.K., Raghu, K.G., 2015. Antidiabetic property of *Aerva lanata* (L.) Juss. ex Schult. is mediated by inhibition of alpha glucosidase, protein glycation and stimulation of adipogenesis. J. Diabetes 7, 548–561.

Rokeya, B., Ali, L., Banerjee, A., Khan, A.K.A., Mosihuzzaman, M., Moinuddin, S.M., Nahar, N., Chowdhury, N.S., Hannan, J.M.A., 1997. Insulin releasing effects of some pure compounds from *Hemidesmus indicus* on isolated rat islets. Diabetologia 40, A376–A376.

Roth, L., Daunderer, M., Kormann, K., 2012. Giftpflanzen - Pflanzengifte: Vorkommen, Wirkung, Therapie - allergische und phototoxische Reaktionen. Hamburg: Nikol Verlagsges. [In German].

Roy, S., Sehgal, R., Padhy, B.M., Kumar, V.L., 2005. Antioxidant and protective effect of latex of *Calotropis procera* against Alloxan-induced diabetes in rats. J. Ethnopharmacol. 102, 470–473.

Royal Botanic Gardens, Kew, 2016. Medicinal Plant Names Services. Available at: https://www.kew.org/science/data-and-resources/tools-and-services/medicinal-plant-names-services [Accessed January 4, 2017].

Ruiz-Montanez, G., Burgos-Hernandez, A., Calderon-Santoyo, M., Lopez-Saiz, C.M., Velazquez-Contreras, C.A., Navarro-Ocana, A., Ragazzo-Sanchez, J.A., 2015. Screening antimutagenic and antiproliferative properties of extracts isolated from Jackfruit pulp (*Artocarpus heterophyllus* Lam). Food Chem. 175, 409–416.

Sabu, M.C., Subburaju, T., 2002. Effect of *Cassia auriculata* Linn. on serum glucose level, glucose utilization by isolated rat hemidiaphragm. J. Ethnopharmacol. 80, 203–206.

Sadou, H., Sabo, H., Alma, M.M., Saadou, M., Leger, C.L., 2007. Chemical content of the seeds and physio-chemical characteristic of the seed oils from

Citrullus colocynthis, Coccinia grandis, Cucumis metuliferus and *Cucumis prophetarum* of Niger. Bull. Chem. Soc. Ethiop. 21, 323–330.

Safer, S., Cicek, S.S., Pieri, V., Schwaiger, S., Schneider, P., Wissemann, V., Stuppner, H., 2011. Metabolic fingerprinting of *Leontopodium* species (Asteraceae) by means of ^{1}H NMR and HPLC-ESI-MS. Phytochem. 72, 1379–1389.

Salihu Shinkafi, T., Bello, L., Wara Hassan, S., Ali, S., 2015. An ethnobotanical survey of antidiabetic plants used by Hausa-Fulani tribes in Sokoto, Northwest Nigeria. J. Ethnopharmacol. 172, 91–99.

Sangameswaran, B., Jayakar, B., 2007. Antidiabetic and spermatogenic activity of *Cocculus hirsutus* (L) Diels. Afr. J. Biotechnol. 6, 1212–1216.

Sangeetha, R., Vedasree, N., 2012. In vitro α-Amylase Inhibitory Activity of the Leaves of *Thespesia populnea*. ISRN Pharmacol. 2012, 515634.

Sarrou, E., Ganopoulos, I., Xanthopoulou, A., Masuero, D., Martens, S., Madesis, P., Mavromatis, A., Chatzopoulou, P., 2017. Genetic diversity and metabolic profile of *Salvia officinalis* populations: implications for advanced breeding strategies. Planta 246, 201–215.

Sathasivampillai, S.V., Rajamanoharan, P.R.S., Munday, M., Heinrich, M., 2017. Plants used to treat diabetes in Sri Lankan Siddha Medicine - An ethnopharmacological review of historical and modern sources. J. Ethnopharmacol. 198, 531–599.

Satyanarayana, K., Mangathayaru, V., Sreekanth, J., Venkateswarlu, V., Kokate, C.K., 2001. Studies on hypoglycaemic and cardiotonic effects of roots of *Cocculus hirsutus*. Indian J. Pharm. Sci. 63, 30–35.

Schoenfelder, T., Warmlin, C.Z., Manfredini, M.S., Pavei, L.L., Reus, J.V., Tristao, T.C., Fernandes, M.S., Costa-Campos, L., 2010. Hypoglycaemic and hypolipidemic effect of leaves from *Syzygium cumini* (L.) Skeels, Myrtaceae. in diabetic rats. Rev. Bras. Farmacogn. 20, 222–227.

Seetharam, Y.N., Chalageri, G., Setty, S.R., Bheemachar, 2002. Hypoglycaemic activity of *Abutilon indicum* leaf extracts in rats. Fitoterapia 73, 156–159.

Senaratna, L. K., 2001. A check list of the flowering plants of Sri Lanka. Colombo: National Science Foundation of Sri Lanka.

Shahani, S., Shahani, L., 2015. Use of insulin in diabetes: a century of treatment. Hong Kong Med. J. 21, 553–559.

Shahraki, M.R., Harati, M., Shahraki, A.R., 2011. Prevention of high fructose-induced metabolic syndrome in male Wistar rats by aqueous extract of *Tamarindus indica* seed. Acta Med. Iran. 49, 277–83.

Shahreen, S., Banik, J., Hafiz, A., Rahman, S., Zaman, A.T., Shoyeb, M.A., Chowdhury, M.H., Rahmatullah, M., 2012. Antihyperglycemic activities of leaves of three edible fruit plants (*Averrhoa carambola, Ficus hispida* and *Syzygium samarangense*) of Bangladesh. Afr. J. Tradit. Complementary Altern. Med. 9, 287–291.

Shakthi Deve, A., Sathish Kumar, T., Kumaresan, K., Rapheal, V.S., 2014. Extraction process optimization of polyphenols from Indian *Citrus sinensis* - as novel antiglycative agents in the management of diabetes mellitus. J. Diabetes Metab. Disord. 13, 11–11.

Shane-McWhorter, L., 2009. American Diabetes Association® Guide to Herbs and Nutritional Supplements. New York: McGraw-Hill.

Sharma, S.K., Vasudeva, N., Ali, M., 2009. A new aliphatic acid from *Achyranthes aspera* Linn. Roots. Indian J. Chem. Sect B-Org. Chem. Incl. Med. Chem. 48, 1164–1169.

Shibeshi, W., Makonnen, E., Zerihun, L., Debella, A., 2006. Effect of *Achyranthes aspera* L. on fetal abortion, uterine and pituitary weights, serum lipids and hormones. Afr. Health Sci. 6, 108–112.

Shinde, J., Taldone, T., Barletta, M., Kunaparaju, N., Hu, B., Kumar, S., Placido, J., Zito, S.W., 2008. Alpha-glucosidase inhibitory activity of *Syzygium cumini* (Linn.) Skeels seed kernel *in vitro* and in Goto-Kakizaki (GK) rats. Carbohydr. Res. 343, 1278–1281.

Shirwaikar, A., Rajendran, K., Punitha, I.S.R., 2005a. Antidiabetic activity of alcoholic stem extract of *Coscinium fenestratum* in Streptozotocin-nicotinamide induced type 2 diabetic rats. J. Ethnopharmacol. 97, 369–374.

Shirwaikar, A., Rajendran, K., Punitha, I.S.R., 2005b. Antihyperglycemic activity of the aqueous stem extract of *Coscinium fenestratum* in non-insulin dependent diabetic rats. Pharm. Biol. 43, 707–712.

Shodehinde, S.A., Ademiluyi, A.O., Oboh, G., Akindahunsi, A.A., 2015. Contribution of *Musa paradisiaca* in the inhibition of α-amylase, α-glucosidase and Angiotensin-I converting enzyme in Streptozotocin induced rats. Life Sci. 133, 8–14.

Shukla, S., Rai, P.K., Chatterji, S., Rai, N.K., Rai, A.K., Watal, G., 2012. LIBS based screening of glycaemic elements of *Ficus religiosa*. Food Biophys. 7, 43–49.

Si, M., Lou, J., Zhou, C.X., Shen, J.N., Wu, H.H., Yang, B., He, Q.J., Wu, H.S., 2010. Insulin releasing and alpha-glucosidase inhibitory activity of ethyl acetate fraction of *Acorus calamus* in *vitro* and *in vivo*. J. Ethnopharmacol. 128, 154–159.

Singh, J., Kakkar, P., 2013. Modulation of liver function, antioxidant responses, insulin resistance and glucose transport by *Oroxylum indicum* stem bark in STZ induced diabetic rats. Food Chem. Toxicol. 62, 722–731.

Singh, N., Gupta, M., 2007. Effects of ethanolic extract of *Syzygium cumini* (Linn) seed powder on pancreatic islets of Alloxan diabetic rats. Indian J. Exp. Biol. 45, 861–867.

Singh, N., Tyagi, D.S., Garg, V., Joneja, S., Agarwal, C.S., Asthana, A., 1990. Effect of long term feeding of different extracts of *Syzygium cumini* L seeds on Alloxan-induced diabetes in Albino rats. Agric. Biol. Res. 6, 80–88.

Sithamparthanuppillai, S., 1982. Disorder Explanation (*நோய் விளக்கம்* – Noi Vilakkam). Chennai: Siddha Medicine Book Research Centre. [In Tamil].

Sittampalam, G.S., Coussens, N.P., Brimacombe, K., Grossman, A., Arkin, M., Auld, D., Austin, C., Baell, J., Bejcek, B., Caaveiro, J.M.M., Chung, T.D.Y., Dahlin, J.L., Devanaryan, V., Foley, T.L., Glicksman, M., Hall, M.D., Haas, J.V., Inglese, J., Iversen, P.W., Kahl, S.D., Kales, S.C., Lal-Nag, M., Li, Z., McGee, J., McManus, O., Riss, T., Trask, O.J., Weidner, J.R., Wildey, M.J., Xia, M., Xu, X. (Eds.), 2004. Assay Guidance Manual. Bethesda (MD): Eli Lilly & Company and the National Centre for Advancing Translational Sciences.

Sivaraman, D., 2010. Hypolipidemic activity of *Ipomoea aquatica* Forsk. Leaf extracts on lipid profile in hyperlipidaemic rats. Int. J. Pharm. Biol. Arch. 1.

Sivaraman, D., Muralidaran, P., 2008. Antiulcerogenic evaluation of the ethanolic extract of water spinach (*Ipomoea aquatica* Forsk) in aspirin ulcerated rats. J. Pharm. Res. 1.

Sivasanmugarajah, 2001. The Siddha Pharmacy and Pharmacology (*சித்த மருந்தியலும் மருந்தாக்கவியலும்* – Siddha Marunthiyalum Marunthaakkaviyalum). Jaffna: Siddha Medical Development Society. [In Tamil].

Sivasanmugarajah, 2002. Principles of Siddha Medicine (*சித்த மருத்துவ மூலத்துவம்* – Siddha Maruththuva Moolathaththuvam). Jaffna: Siddha Medical Development Society. [In Tamil].

Sivasanmugarajah, S., 2000. Sri Lankan Siddha Medicine in 20th century (இருபதாம் நூற்றாண்டின் ஈழத்துச் சித்த மருத்துவம் – Irupathaam Nootraandil Eelaththuchchiththa Maruththuvam). Jaffna: Siddha Medicine Development Society. [In Tamil].

SLADC (Sri Lanka Ayurvedic Drugs Corporation), 2018. About SLADC. Available at: http://www.ayurvediccorp.gov.lk/web/index.php?option=com_content&view=article&id=1&Itemid=109&lang=en [Accessed February 14, 2018].

Sole, S.S., Srinivasan, B.P., 2012. Aqueous extract of tamarind seeds selectively increases glucose transporter-2, glucose transporter-4, and islets' intracellular calcium levels and stimulates beta-cell proliferation resulting in improved glucose homeostasis in rats with Streptozotocin-induced diabetes mellitus. Nutr. Res. 32, 626–636.

Song, M.Y., Bae, U.J., Lee, B. H., Kwon, K.B., Seo, E.A., Park, S.J., Kim, M.S., Song, H.J., Kwon, K.S., Park, J.W., Ryu, D.G., Park, B.H., 2010. *Nardostachys jatamansi* extract protects against cytokine-induced beta-cell damage and Streptozotocin-induced diabetes. World J. Gastroenterol. 16, 3249–3257.

Srilatha, B.R., Ananda, S., 2014. Antidiabetic effects of *Mukia maderaspatana* and its phenolics: an *in vitro* study on gluconeogenesis and glucose uptake in rat tissues. Pharm. Biol. 52, 597–602.

Srilatha, B.R., Ananda, S., 2014. Antidiabetic effects of *Mukia maderaspatana* and its phenolics: An *in vitro* study on gluconeogenesis and glucose uptake in rat tissues. Pharm. Biol. 52, 597–602.

Srinivasa, A., Surekhaa, P.A., Kishorea, A.S., Srinivasana, M., Murthya, P.B., Reddy, N.P., 2010. Toxicity profiles of Abharak and Tamar bhasmas in different vehicles. J. of Herb. Med. and Toxicol. 4, 189–196.

Stephen E.S., 2005. Complementary and alternative medicine. Harrisons principles of internal medicine. 16th edn., New York: McGraw-Hill Medical.

Strömstedt, A.A., Felth, J., Bohlin, L., 2014. Bioassays in natural product research - strategies and methods in the search for anti-inflammatory and antimicrobial activity. Phytochem. Anal. 25, 13–28.

Subash Babu, P., Prabuseenivasan, S., Ignacimuthu, S., 2007. Cinnamaldehyde - a potential antidiabetic agent. Phytomedicine 14, 15–22.

Sugathadasa, K.S.S., Jeevandara, P.M., Devanarayana, A. and Pushpakumara, D.K.N.G., 2008. A Checklist of Medicinal Plants of Sri Lanka. Colombo: Bandaranaike Memorial Ayurvedic Research Institute.

Sundaram, R., Naresh, R., Shanthi, P., Sachdanandam, P., 2012. Antihyperglycemic effect of iridoid glucoside, isolated from the leaves of *Vitex negundo* in Streptozotocin-induced diabetic rats with special reference to glycoprotein components. Phytomedicine 19, 211–216.

Sunil, C., Duraipandiyan, V., Agastian, P., Ignacimuthu, S., 2012. Antidiabetic effect of plumbagin isolated from *Plumbago zeylanica* L. root and its effect on GLUT4 translocation in Streptozotocin-induced diabetic rats. Food Chem. Toxicol. 50, 4356–4363.

Surana, S.J., Gokhale, S.B., Jadhav, R.B., Sawant, R.L., Wadekar, J.B., 2008. Antihyperglycemic activity of various fractions of *Cassia auriculata* Linn. in Alloxan diabetic rats. Indian J. Pharm. Sci. 70, 227–229.

Sussulini, A., 2017. Metabolomics: From Fundamentals to Clinical Applications. New York: Springer.

Talukder, F.Z., Khan, K.A., Uddin, R., Jahan, N., Alam, M.A., 2012. *In vitro* free radical scavenging and antihyperglycemic activities of *Achyranthes aspera* extract in Alloxan-induced diabetic mice. Drug Discoveries Ther. 6, 298–305.

Tan, K.K., Kim, K.H., 2013. *Alternanthera sessilis* red ethyl acetate fraction exhibits antidiabetic potential on obese type 2 diabetic rats. Evid. Based Complementary Alternat. Med. 2013, 845172.

Teixeira, C.C., Weinert, L.S., Barbosa, D.C., Ricken, C., Esteves, J.F., Fuchs, F.D., 2004. *Syzygium cumini* (L.) skeels in the treatment of type 2 diabetes - Results of a randomized, double-blind, double-dummy, controlled trial. Diabetes Care 27, 3019–3020.

Thabrew, M.I., Senaratna, L., Samarawickrema, N., Munasinghe, C., 2001. Antioxidant potential of two polyherbal. preparations used in Ayurveda for the treatment of rheumatoid arthritis. J. Ethnopharmacol. 76, 285-291.

Thakur, M., Chauhan, N.S., Sharma, V., Dixit, V.K., Bhargava, S., 2012. Effect of *Curculigo orchioides* on hyperglycaemia-induced oligospermia and sexual dysfunction in male rats. Int. J. Impot. Res. 24, 31–37.

Thas, J.J., 2008. Siddha Medicine – background and principles and the application for skin diseases. Clin. Dermatol., 26, 62-78.

The Plant List, 2013. The Plant List. Available at: http://www.theplantlist.org/ [Accessed February 28, 2017].

Tofern, B., Mann, P., Kaloga, M., Jenett-Siems, K., Witte, L., Eich, E., 1999. Aliphatic pyrrolidine amides from two tropical *Convolvulaceous* species. Phytochem. 52, 1437–1441.

Trinh, B.T.D., Staerk, D., Jäger, A.K., 2016. Screening for potential α-glucosidase and α-amylase inhibitory constituents from selected Vietnamese plants used to treat type 2 diabetes. J. Ethnopharmacol. 186, 189–195.

Tripathi, A.K., Kohli, S., 2014. Pharmacognostical standardization and antidiabetic activity of *Syzygium cumini* (Linn.) barks (Myrtaceae) on Streptozotocin-induced diabetic rats. J. Complementary Integr. Med. 11, 71–81.

Umamaheswari, M., Chatterjee, T.K., 2008. *In vitro* antioxidant activities of the fractions of *Coccinia Grandis* L. leaf extract. Afr. J. Tradit., Complementary Altern. Med. 5, 61.

Upadhya, V., Pai, S.R., Hegde, H.V., 2015. Effect of method and time of extraction on total phenolic content in comparison with antioxidant activities in different parts of *Achyranthes aspera*. J. King Saud Univ. Sci. 27, 204–208.

Upton, R., Graff, A., Jolliffe, G., Länger, R., Williamson, E., 2016. American Herbal Pharmacopoeia: Botanical Pharmacognosy - Microscopic Characterization of Botanical Medicines. Florida: CRC Press.

Urooj, A., Rupashri, K., Puttaraj, S., 2006. Glycaemic responses to finger millet based Indian preparations in non-insulin dependent diabetic and healthy subjects. J. Food Sci. Technol. 43, 620–625.

Uthamaroyan, C.S., 1992. The History and Research of Siddha Medicine (தோற்றக்கிரம ஆராய்ச்சியும் சித்த மருத்துவ வரலாறும் - Thotra Kirama Araiachium Siddha Maruthuva Varalarum). Chennai: Tamil Nadu Government Siddha Medical Board. [In Tamil].

Vadivel, V., Nandety, A., Biesalski, H.K., 2011a. Antioxidant, free radical scavenging and type II diabetes-related enzyme inhibition properties of traditionally processed Jequirity bean (*Abrus precatorius* L.). Int. J. Food Sci. Technol. 46, 2505–2512.

Vadivel, V., Stuetz, W., Scherbaum, V., Biesalski, H.K., 2011b. Total free phenolic content and health relevant functionality of Indian wild legume grains: Effect of indigenous processing methods. J. Food Compos. Anal. 24, 935–943.

Vardhini, N.V., Sathya, T.N., Murthy, P.B., 2010. Assessment of genotoxic potential of herbomineral preparations- Bhasmas. Curr. Sci. 99, 1096–1100.

Varshney, M.D., Sharma, B.B., Gupta, D.N., 1986. Antifertility screening of plants Part II. Effect of ten indigenous plants on early and late pregnancy in albino rats. Comp. Physiol. Ecol. 11, 183– 189.

Vasant, R.A., Narasimhacharya, A.V.R.L., 2012. Ameliorative effect of tamarind leaf on fluoride-induced metabolic alterations. Environ. Health Preventative Med. 17, 484–493.

Veeramani, C., Al-Numair, K.S., Alsaif, M.A., Chandramohan, G., Al-Numair, N.S., Pugalendi, K.V., 2012. Protective effect of *Cardiospermum halicacabum* leaf extract on glycoprotein components on STZ-induced hyperglycaemic rats. Asian Pac. J. Trop. Med. 5, 939–944.

Veeramani, C., Pushpavalli, G., Pugalendi, K.V., 2008. Antihyperglycemic effect of *Cardiospermum halicacabum* Linn. leaf extract on STZ-induced diabetic rats. J. Appl. Biomed. 6, 19–26.

Veerapur, V.P., Prabhakar, K.R., Thippeswamy, B.S., Bansal, P., Srinivasan, K.K., Unnikrishnan, M.K., 2012. Antidiabetic effect of *Ficus racemosa* Linn. stem bark in high-fat diet and low-dose Streptozotocin-induced type 2 diabetic rats: A mechanistic study. Food Chem. 132, 186–193.

Venkatachalam, M., Singaravelu, G., Govindaraju, K., Jong S.A., 2013. PTP 1B inhibitory action of a phytochemical propanoic acid, 2-(3-acetoxy-4,4,14-trimethylandrost-8-en-17-yl). Curr. Sci. 105, 827.

Venkatesh, S., Kusuma, R., Sateesh, V., 2012. Antidiabetic activity of *Pandanus odoratissimus* root extract. Indian J. Pharm. Educ. Res. 46, 340-345.

Verma, R.K., Mishra, G., Singh, P., Jha, K.K., Khosa, R.L., 2015. Antidiabetic activity of methanolic extract of *Alpinia galanga* Linn. aerial parts in Streptozotocin induced diabetic rats. Ayu. 36, 91–95.

Verpoorte, R., Choi, Y.H., Kim, H.K., 2007. NMR-based metabolomics at work in phytochemistry. Phytochem. Rev. 6, 3–14.

Vetrichelvan, T., Jegadeesan, M., 2002. Anti-diabetic activity of alcoholic extract of *Aerva lanata* (L.) Juss. ex Schultes in rats. J. Ethnopharmacol. 80, 103–107.

Vetrichelvan, T., Jegadeesan, M., 2003. Effect of alcohol extract of *Achyranthes aspera* Linn. on acute and subacute inflammation. Phytother. Res. 17, 77–79.

Vidyasagar, G.M., Siddalinga, M.S.M., 2013. Medicinal plants used in the treatment of Diabetes mellitus in Bellary district, Karnataka. Indian J. Tradit. Know. 12.

Vijayakumar, M., Govindarajan, R., Rao, G.M.M., Rao, C.V., Shirwaikar, A., Mehrotra, S., Pushpangadan, P., 2006. Action of *Hygrophila auriculata* against Streptozotocin-induced oxidative stress. J. Ethnopharmacol. 104, 356–361.

Villaseñor, I.M., Lamadrid, M.R.A., 2006. Comparative anti-hyperglycemic potentials of medicinal plants. J. Ethnopharmacol. 104, 129–131.

Wadhwa, V., Singh, M.M., Gupta, D.N., Singh, C., Kamboj, V.P., 1986. Contraceptive and hormonal properties of *Achyranthes aspera* in rats and hamsters. Planta Med. 3, 231–233.

Wang, X.L., Di, X.X., Shen, T., Wang, S.Q., Wang, X.N., 2017. New phenolic compounds from the leaves of *Artocarpus heterophyllus*. Chin. Chem. Lett. 28, 37–40.

Wang, Y., Tang, H., Nicholson, J.K., Hylands, P.J., Sampson, J., Whitcombe, I., Stewart, C.G., Caiger, S., Oru, I., Holmes, E., 2004. Metabolomic strategy for the classification and quality control of phytomedicine: a case study of chamomile flower (*Matricaria recutita* L.). Planta Med. 70, 250–255.

Wei, B.L., Weng, J.R., Chiu, P.H., Hung, C.F., Wang, J.P., Lin, C.N., 2005. Antiinflammatory flavonoids from *Artocarpus heterophyllus* and *Artocarpus communis*. J. Agric. Food Chem. 53, 3867–3871.

Weller, M.G., 2012. A Unifying Review of Bioassay-Guided Fractionation, Effect-Directed Analysis and Related Techniques. Sensors (Basel) 12, 9181–9209.

Wen, H., Kang, S., Song, Y., Song, Y., Sung, S.H., Park, S., 2010. Differentiation of cultivation sources of *Ganoderma lucidum* by NMR-based metabolomics approach. Phytochem. Anal. 21, 73–79.

Weragoda, P.B., 1980. The traditional system of medicine in Sri Lanka. J. Ethnopharmacol. 2, 71–73.

Werner, W.L., Balasubramaniam, S., 1992. Structure and Dynamics of the Upper Montane Rain Forests of Sri Lanka, in: Tropical Forests in Transition, Advances in Life Sciences. Basel: Birkhäuser.

WHO (World Health Organization), 2017. Diabetes. Available at: http://www.who.int/news-room/fact-sheets/detail/diabetes [Accessed October 4, 2017].

Wijenayake, A., Pitawala, A., Bandara, R., Abayasekara, C., 2014. The role of herbometallic preparations in traditional medicine - a review on mica drug processing and pharmaceutical applications. J. Ethnopharmacol. 155, 1001–1010.

Wiklund, S., Johansson, E., Sjöström, L., Mellerowicz, E.J., Edlund, U., Shockcor, J.P., Gottfries, J., Moritz, T., Trygg, J., 2008. Visualization of GC/TOF-MS-based metabolomics data for identification of biochemically interesting compounds using OPLS class models. Anal. Chem. 80, 115–122.

Wills, R.B.H., Rangga, A., 1996. Determination of carotenoids in Chinese vegetables. Food Chem. 56, 451–455.

Wischenbart, R., 2015. The Global Ranking of the Publishing Industry 2015. Available at: http://www.wischenbart.com/upload/Global-Ranking-Publishing-Industry-2017_Table-of-Content.pdf [Accessed August 24, 2018]

Witters, L.A., 2001. The blooming of the French lilac. J. Clin. Invest. 108, 1105–1107.

Wolfender, J.L., Glauser, G., Boccard, J., Rudaz, S., 2009. MS-based plant metabolomic approaches for biomarker discovery. Nat. Prod. Commun. 4, 1417–1430.

Wolfender, J.L., Marti, G., Thomas, A., Bertrand, S., 2015. Current approaches and challenges for the metabolite profiling of complex natural extracts. J. Chromatogr. A, 1382, 136–164.

World Health Organization Monographs on Selected Medicinal Plants - Volume 1, 1999. Table of Contents. Available from: <http://apps.who.int/medicinedocs/en/m/abstract/Js14213e/>. [Accessed February 28, 2017].

World Health Organization Monographs on Selected Medicinal Plants - Volume 2, 2004. Table of Contents. Available from: <http://apps.who.int/medicinedocs/en/d/Js2200e/>. [Accessed February 28, 2017].

World Health Organization Monographs on Selected Medicinal Plants - Volume 3, 2007. Table of Contents. Available from: <http://apps.who.int/medicinedocs/en/m/abstract/Js14213e/>. [Accessed February 28, 2016].

World Health Organization Monographs on Selected Medicinal Plants - Volume 4, 2009. Table of Contents. Available from: <http://apps.who.int/medicinedocs/en/m/abstract/Js16713e/>. [Accessed February 28, 2017].

Wright, C.I., Van-Buren, L., Kroner, C.I., Koning, M.M.G., 2007. Herbal medicines as diuretics: a review of the scientific evidence. J. Ethnopharmacol. 114, 1–31.

Wu, H., Li, Y., Weng, L., Zhou, C., He, Q., Lou, Y., 2007. A fraction of *Acorus calamus* L. extract devoid of beta-asarone enhances adipocyte differentiation in 3T3-L1 cells. Phytother. Res. 21, 562–564.

Wu, H.S., Zhu, D.F., Zhou, C.X., Feng, C.R., Lou, Y.J., Yang, B., He, Q.J., 2009. Insulin sensitizing activity of ethyl acetate fraction of *Acorus calamus* L. *in vitro* and *in vivo*. J. Ethnopharmacol. 123, 288-92.

Yadav, S.K., Nagori, B.P., Desai, P.K., 2014. Pharmacological characterization of different fractions of *Calotropis procera* (Asclepiadaceae) in Streptozotocin induced experimental model of diabetic neuropathy. J. Ethnopharmacol. 152, 349–357.

Yeh, G.Y., Eisenberg, D.M., Kaptchuk, T.J., Phillips, R.S., 2003. Systematic review of herbs and dietary supplements for glycaemic control in diabetes. Diabetes Care 26, 1277–1294.

Yerima, M., Anuka, J.A., Salawu, O.A., Abdu-Aguye, I., 2014. Antihyperglycemic activity of the stem-bark extracts of *Tamarindus indica* L. on experimentally induced hyperglycemic and normoglycemic Wistar rats. Pak. J. Biol. Sci. 17, 414–8.

Yin, Z., Zhang, W., Feng, F., Zhang, Y., Kang, W., 2014. α-Glucosidase inhibitors isolated from medicinal plants. Food Sci. Hum. Wellness 3, 136–174.

Yonemoto, R., Shimada, M., Gunawan-Puteri, M.D.P.T., Kato, E., Kawabata, J., 2014. α-Amylase inhibitory triterpene from *Abrus precatorius* leaves. J. Agric. Food Chem. 62, 8411–8414.

Yoshino, K., Miyauchi, Y., Kanetaka, T., Takagi, Y., Koga, K., 2009. Anti-diabetic activity of a leaf extract prepared from *Salacia reticulata* in mice. Biosci. Biotechnol. Biochem. 73, 1096–1104.

Yuliana, N.D., Budijanto, S., Verpoorte, R., Choi, Y.H., 2013. NMR metabolomics for identification of adenosine A1 receptor binding compounds from *Boesenbergia rotunda* rhizomes extract. J. Ethnopharmacol. 150, 95–99.

Yuliana, N.D., Khatib, A., Choi, Y.H., Verpoorte, R., 2011. Metabolomics for bioactivity assessment of natural products. Phytother. Res. 25, 157–169.

Zaccardi, F., Webb, D.R., Yates, T., Davies, M.J., 2015. Pathophysiology of type 1 and type 2 diabetes mellitus: a 90-year perspective. Postgrad. Med. J. 2015-133281.

Zarmouh, M.M., Subramaniyam, K., Viswanathan, S., Kumar, P.G., 2010. Cause and effect of *Plumbago zeylanica* root extract on blood glucose and hepatic enzymes in experimental diabetic rats. Afr. J. Microbiol. Res. 4, 2674–2677.

Zhang, J., Wider, B., Shang, H., Li, X., Ernst, E., 2012. Quality of herbal medicines: challenges and solutions. Complementary Ther. Med. 20, 100–106.

Zheng, Z.P., Xu, Y., Qin, C., Zhang, S., Gu, X., Lin, Y., Xie, G., Wang, M., Chen, J., 2014. Characterization of antiproliferative activity constituents from *Artocarpus heterophyllus*. J. Agric. Food Chem. 62, 5519–5527.

Zhou, C.X., Qiao, D., Yan, Y.Y., Wu, H.S., Mo, J.X., Gan, L.S., 2012. A new antidiabetic sesquiterpenoid from *Acorus calamus*. Chin. Chem. Lett. 23, 1165–1168.

Appendix A

Table A.1. List of plant species used in historical antidiabetic Sri Lankan Siddha preparations

Scientific name	Family	Tamil name	Part used	Preparation	Source
Abelmoschus moschatus Medik. #	Malvaceae	தக்கோலம் (Thakkolam)	SE	44, 46, 47	PA
Abies spectabilis (D.Don) Mirb. *	Pinaceae	தாளிசபத்திரி (Thaalisapaththiri)	LE	9, 44	PA
Abrus precatorius L. #	Fabaceae	குன்றிமணி (Kundrimani)	RO	10, 43	PA
			RO	51	SV
			SE	11, 14, 17, 30, 1, 33	PA
Abutilon indicum (L.) Sweet #	Malvaceae	துத்தி (Thuththi)	RO	45	PA
			SE	1	PA
Acacia chundra (Rottler) Willd.	Fabaceae	கருங்காலி (Karungkaali)	BA	25	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			HE	29	PA
			RE	11, 34	PA
			RO	27	PA
Acacia leucophloea (Roxb.) Willd.	Fabaceae	வெள்வேல் (Velvel)	BA	13	PA
			RE	1, 11	PA
Acacia nilotica (L.) Delile	Fabaceae	கருவேல் (Karuvel)	BA	13, 34, 43, 45	PA
			BA	51, 56	SV
			RE	1, 11, 13, 17, 31, 35	PA
			TL	18	PA
Achyranthes aspera L.	Amaranthaceae	நாயுருவி (Naayuruvi)	WP	56	SV
			WP	32	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Aconitum heterophyllum Wall. ex Royle *#	Ranunculaceae	அதிவிடயம் (Athividayam)	RO	8, 9	PA
			RO	57, 59, 60	SA
			RO	55	SV
Acorus calamus L. #	Acoraceae	வசம்பு (Vasambu)	RH	10	PA
Aegle marmelos (L.) Corrêa #$	Rutaceae	வில்வை (Vilvai)	BA	19	PA
			RO	9, 44, 46, 47	PA
			RO	60	SA
Allium sativum L. #$	Amaryllidaceae	வெள்ளை வெங்காயம் (Vellai vengaayam)	BU	58	SA
Aloe vera (L.) Burm.f. #$	Xanthorrhoeaceae	கற்றாழை (Katraalai)	LE	10, 44, 47	PA
			LE	51	SV
			RO	53, 55	SV

Scientific name	Family	Tamil name	Part used	Preparation	Source
Alpinia calcarata (Haw.) Roscoe #	Zingiberaceae	சிற்றரத்தை (Sitraraththai)	RH RH	47 59, 60	PA SA
Alpinia galanga (L.) Willd. #	Zingiberaceae	பேரரத்தை (Peraraththai)	RH RH	44 60	PA SA
Alternanthera sessilis (L.) R.Br. ex DC.	Amaranthaceae	பொன்னாங்காணி (Ponnaangkaani)	LE LE WP	47 59 44, 46, 47	PA SA PA
Alysicarpus vaginalis (L.) DC.	Fabaceae	குதிரைவாலி (Kuthiraivaali)	WP	23	PA
Anacardium occidentale L. #$	Anacardiaceae	முந்திரிகை (Munthirihai)	FR FR	9 51	PA SV

Scientific name	Family	Tamil name	Part used	Preparation	Source
Anacyclus pyrethrum (L.) Lag. *	Asteraceae	அக்கராகாரம் (Akkaraahaaram)	RO	9, 12	PA
			RO	58, 59, 60	SA
Anethum graveolens L. #$	Apiaceae	சதகுப்பை (Sathahuppai)	SE	58	SA
Aquilaria agallocha Roxb. #	Thymelaeaceae	அகில் (Ahil)	WO	44	PA
Areca catechu L. #	Arecaceae	கமுகு (Kamuhu)	RE	9	PA
			SE	1	PA
			SE	51	SV
Artocarpus heterophyllus Lam.	Moraceae	பலா (Palaa)	ML	47	PA
Asparagus racemosus Willd. $	Asparagaceae	சாத்தாவாரி (Saaththaavaari)	LE	47	PA
			RH	9, 44, 46, 47	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Aucklandia lappa DC. [syn. *Saussurea lappa* (Decne.) C.B.Clarke] $	Asteraceae	கோட்டம் (Kottam)	RO	8, 9, 10, 43, 44, 46, 47	PA
Azadirachta indica A.Juss. #$	Meliaceae	வேம்பு (Vembu)	RE	1, 11, 34	PA
Bambusa bambos (L.) Voss	Poaceae	மூங்கில் (Moongil)	LE	29	PA
Boerhavia diffusa L.	Nyctaginaceae	மூக்கரட்டை (Mookkarattai)	TL	5	PA
Bombax ceiba L. #	Malvaceae	முள்ளிலவு (Mullilavu)	BA RE	45 45	PA PA
Borassus flabellifer L.	Arecaceae	பனை (Panai)	FR	12	PA
Cadaba fruticosa (L.) Druce #	Capparaceae	வீழி (Veeli)	LE	44, 47	PA
Caesalpinia bonduc (L.) Roxb.	Fabaceae	கழற்சி (Kalatchi)	TL	21	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Cajanus cajan (L.) Millsp. $	Fabaceae	துவரை (Thuwarai)	RO	46	PA
Cannabis sativa L. #$	Cannabaceae	கஞ்சா (Kanjaa)	LE	46	PA
			LE	55	SV
			LE	58	SA
			SE	57	SA
Cardiospermum halicacabum L. #	Sapindaceae	முடக்கொத்தான் (Mudakkoththaan)	WP	46	PA
Cassia fistula L. #$	Fabaceae	கொன்றை (Kondrai)	BA	10, 43	PA
			BA	25, 49	SV
			LE	11	PA
			RO	21	PA
Catunaregam spinosa (Thunb.) Tirveng.	Rubiaceae	மருக்காரை (Marukkaarai)	RO	27	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Cedrus deodara (Roxb. ex D.Don) G.Don $	Pinaceae	தேவதாரு (Thevathaaru)	WO	44, 46, 47	PA
			WO	59, 60	SA
Celastrus paniculatus Willd.	Celastraceae	வாலுளுவை (Vaaluluvai)	SE	58	SA
Centipeda minima (L.) A.Braun & Asch.	Asteraceae	மருக்கொழுந்து (Marukkolunthu)	WP	46	PA
Cheilocostus speciosus (J.Koenig) C.D.Specht [syn. *Costus speciosus* (J.Koenig) Sm.]	Costaceae	வெண்கோட்டம் (Venkottam)	RH	47	PA
			RO	57, 58, 60	SA
Chrysopogon zizanioides (L.) Roberty [syn. *Vetiveria zizanioides* (L.) Nash]	Poaceae	இலாமிச்சை (Ilaamichchai)	RO	44	PA
			RO	9	PA
			RO	46	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			RO	47	PA
Cinnamomum cappara-coronde Blume	Lauraceae	கற்பூரம் (Katpooram)	RE	8, 9, 44, 47	PA
			RE	60	SA
Cinnamomum verum J.Presl $	Lauraceae	கறுவா (Karuvaa)	BA	46	PA
			BA	59, 60	SA
Cissampelos pareira L.	Menispermaceae	மலைதாங்கி (Malaithaangi)	TL	4, 6	PA
			WP	16, 25, 26, 29	PA
Coccinia grandis (L.) Voigt #	Cucurbitaceae	கொவ்வை (Kovvai)	LE	47	PA
Cocculus hirsutus (L.) W.Theob.	Menispermaceae	கட்டுக்கொடி (Kattukkodi)	LE	34	PA
Cocos nucifera L. $	Arecaceae	தென்னை (Thennai)	FL	10, 11, 48	PA
			FR	44, 47	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			UF	36, 48	PA
Commiphora mukul (Hook. ex Stocks) Engl. $	Burseraceae	குக்கில் (Kukkil)	RE	35	PA
Cordia dichotoma G.Forst.	Boraginaceae	நறுவிலி (Naruvili)	BA	38, 45	PA
Coscinium fenestratum (Goetgh.) Colebr. *	Menispermaceae	மரமஞ்சள் (Maramanjal)	ST	11, 34, 27, 29	PA
Crocus sativus L. #$	Iridaceae	குங்குமம் (Kungkumam)	SI	44, 47	PA
			SI	58, 60	SA
Cuminum cyminum L. #$	Apiaceae	சீரகம் (Seeraham) / சிறுஞ்சீரகம் (Sirunjcheeraham)	FR	9, 8, 46	PA
			FR	55	SV
			FR	57, 59, 58, 60	SA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Curculigo orchioides Gaertn.	Hypoxidaceae	நிலப்பனை (Nilappanai)	RH	9, 11, 29, 46	PA
Curcuma aromatica Salisb. #	Zingiberaceae	கஸ்தூரி மஞ்சள் (Kasththoori manjal)	RH	11	PA
Curcuma longa L. #$	Zingiberaceae	மஞ்சள் (Manjal)	RH	13, 14, 28, 30	PA
Cyanthillium cinereum (L.) H.Rob. [syn. *Vernonia cinerea* (L.) Less.]	Asteraceae	சீதேவியார் செங்கழுநீர் (Seetheviyaar sengkaluneer)	WP	46	PA
Cycas circinalis L. *#	Cycadaceae	மதனகாமம் (Mathanakaamam)	FL	44	PA
Cyperus mitis Steud.	Cyperaceae	பெருங்கோரை (Perungkorai)	RH	46	PA
Cyperus rotundus L. $	Cyperaceae	கோரை (Korai)	RH	1, 7, 8, 9, 27, 47	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			RO	26	PA
Datura metel L. #	Solanaceae	ஊமத்தை (Oomaththai)	SE	12	PA
			SE	58	SA
			SE	55	SV
Dichrostachys cinerea (L.) Wight & Arn.	Fabaceae	விடத்தல் (Vidaththal)	TL	21	PA
Eclipta prostrata (L.) L.	Asteraceae	கரிசலாங்கண்ணி (Karisalaangkanni)	WP	1	PA
Elaeocarpus tuberculatus Roxb.	Elaeocarpaceae	உருத்திராட்சம் (Uruththiraatcham)	SE	60	SA
Elettaria cardamomum (L.) Maton #$	Zingiberaceae	ஏலம் (Elam)	FR	8, 9, 44, 46, 47	PA
			FR	57, 58, 59, 60	SA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			FR FR	55 47	SV PA
Eleusine coracana (L.) Gaertn.	Poaceae	குரக்கன் (Kurakkan)	SE	2, 3, 6	PA
Embelia ribes Burm.f.	Primulaceae	வாய்விடங்கம் (Vaaividangam)	SE	27	PA
Erythrina variegata L.	Fabaceae	முருக்கு (Murukku)	LE	47	PA
Erythroxylum monogynum Roxb.	Erythroxylaceae	செம்மணத்தி (Semmanaththi)	BA	13	PA
Euphorbia antiquorum L. #	Euphorbiaceae	கள்ளி (Kalli)	LA RO	54 39	SV PA
Euphorbia hirta L. #$	Euphorbiaceae	அம்மான் பச்சரிசி (Ammaan pachcharisi)	WP	37, 45	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Ferula assa-foetida L. #$	Apiaceae	பெருங்காயம் (Perungkaayam)	RE	58	SA
Ficus amplissima Sm.	Moraceae	இத்தி (Iththi)	BA	14	PA
Ficus benghalensis L.	Moraceae	ஆல் (Aal)	BA RO	14, 35 29	PA PA
Ficus racemosa L. #	Moraceae	அத்தி (Aththi)	BA BA LA	10, 13, 14, 43, 45, 46, 49, 51 45	PA SV PA
Ficus religiosa L.	Moraceae	அரசு (Arasu)	BA	14	PA
Foeniculum vulgare Mill. #$	Apiaceae	பெருஞ்சீரகம் (Perunjcheeraham)	FR FR	9 55	PA SV

Scientific name	Family	Tamil name	Part used	Preparation	Source
Gardenia crameri Tirveng.	Rubiaceae	கம்பி (Kambi)	RE	45	PA
Glycyrrhiza glabra L. #$	Fabaceae	அதிமதுரம் (Athimathuram)	RO	9, 44, 46, 47	PA
			RO	51	SV
			RO	57, 58, 59, 60	SA
Gmelina arborea Roxb.	Lamiaceae	பெருங்குமிழ் (Perungkumil)	RO	27	PA
Gmelina asiatica L.	Lamiaceae	நிலக்குமிழ் (Nilakkumil)	RO	46	PA
Gossypium arboreum L. #	Malvaceae	பருத்தி (Paruththi)	SE	17, 23, 31	PA
Gymnosporia emarginata (Willd.) Thwaites [syn. *Maytenus emarginata* (Willd.) Ding Hou]	Celastraceae	முட்புல்லாந்தி (Mutpullaanthy)	BA	45	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Hemidesmus indicus (L.) R. Br. ex Schult.	Apocynaceae	நன்னாரி (Nannaari)	RB	59	SA
			RO	8, 46, 47	PA
Holarrhena pubescens Wall. ex G.Don *	Apocynaceae	வெட்பாலை (Vetpaalai)	SE	44, 46, 47	PA
			SE	58	SA
Hybanthus enneaspermus (L.) F.Muell.	Violaceae	ஓரிதழ்த்தாமரை (Orithalththaamarai)	WP	46	PA
Hygrophila auriculata (Schumach.) Heine *	Acanthaceae	நீர்முள்ளி (Neermulli)	WP	1	PA
Hyoscyamus reticulatus L. #	Solanaceae	குரோசாணி ஓமம் (Kurosaani omam)	SE	8, 12, 44, 47	PA
			SE	57, 58	SA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Indigofera tinctoria L.	Fabaceae	அவுரி (Avuri)	LE	18	PA
Ipomoea aquatica Forssk.	Convolvulaceae	வள்ளல் (Vallal)	LE	47	PA
Ipomoea littoralis Blume	Convolvulaceae	தாளி (Thaali)	LE	47	PA
Justicia adhatoda L. [syn. *Adhatoda vasica* Nees] $	Acanthaceae	ஆடாதோடை (Aadaathodai)	RO	50	SA
Kaempferia galanga L. #	Zingiberaceae	கச்சோலம் (Kachcholam)	RH	44, 47	PA
Lannea coromandelica (Houtt.) Merr. [syn. *Odina wodier* Roxb.] #	Anacardiaceae	ஒதியம் (Othiyam)	BA	13, 45	PA
Limonia acidissima Groff #	Rutaceae	விளாத்தி (Vilaaththi)	FR RE	9 1, 13, 14, 33, 34, 35, 45	PA PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			RO	30, 31	PA
Madhuca longifolia (J.Koenig ex L.) J.F.Macbr.	Sapotaceae	இலுப்பை (Iluppai)	FL	1, 8	PA
			FL	58	SA
Magnolia champaca (L.) Baill. ex Pierre [syn. *Michelia champaca* L.] *	Magnoliaceae	செண்பகம் (Senpaham)	FL	9, 44, 46	PA
			FL	60	SA
Mesua ferrea L.	Calophyllaceae	சிறுநாகம் (Sirunaaham)	FL	44, 46, 47	PA
			FL	58, 60	SA
Mollugo cerviana (L.) Ser.	Molluginaceae	பற்படாகம் (Patpadaaham)	WP	46	PA
Moringa oleifera Lam. $	Moringaceae	முருங்கை (Murungai)	BA	20, 22, 28, 29, 30	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			LE	44	PA
			RE	1	PA
Mukia maderaspatana (L.) M.Roem. #	Cucurbitaceae	மொசுமொசுக்கை (Mosumosukkai)	LE	47	PA
Murraya koenigii (L.) Spreng. #$	Rutaceae	கறிவேம்பு (Karivembu)	LE	45	PA
			ST	29	PA
			RO	29	PA
Musa × *paradisiaca* L. [syn. *Musa* × *sapientum* L.]	Musaceae	வாழை (Vaalai)	FR	39	PA
			LE	18	PA
			RH	9	PA
Myristica fragrans Houtt. #	Myristicaceae	சாதிக்காய் (Saathikkaai)	LE	1, 9, 44, 46, 47	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			LE	57	SA
			MA	8, 12, 44, 47	PA
			MA	57, 58, 60	SA
			MA	53, 55	SV
			SE	1, 8, 9, 12, 44, 46, 47	PA
			SE	57, 58, 59, 60	SA
			SE	55	SV
Myroxylon balsamum (L.) Harms	Fabaceae	சாம்பிராணி (Saampiraani)	RE	55	SV
Nardostachys jatamansi (D.Don) DC. [syn. *Nardostachys grandiflora* DC] *#	Caprifoliaceae	சடாமாஞ்சில் (Sadaamaanjil)	RO	44, 46, 47	PA
Nelumbo nucifera Gaertn. $	Nelumbonaceae	தாமரை (Thaamarai)	RC	44, 46, 47	PA
			RH	9	PA
			RH	51	SV

Scientific name	Family	Tamil name	Part used	Preparation	Source
			SE	57	SA
Neopicrorhiza scrophulariiflora (Pennell) D.Y.Hong [syn. *Picrorhiza scrophulariiflora* Pennell] $	Plantaginaceae	கடுகுரோகிணி (Kaduhurohini)	RO	47	PA
			RO	58, 60	SA
			SE	44	PA
Nervilia concolor (Blume) Schltr. [syn. *Nervilia aragoana* Gaudich.]	Orchidaceae	ஓரிலைத்தாமரை (Orilaiththaamarai)	WP	59	SA
Nigella sativa L. #$	Ranunculaceae	கருஞ்சீரகம் (Karunjcheeraham)	SE	58, 60	SA
Nymphaea pubescens Willd. *	Nymphaeaceae	செங்கழுநீர் (Sengkaluneer)	RH	10,43, 44, 46, 47	PA
			RH	51	SV

Scientific name	Family	Tamil name	Part used	Preparation	Source
Oroxylum indicum (L.) Kurz	Bignoniaceae	வாகை (Vaahai)	RE	1	PA
Oryza sativa L. $	Poaceae	நெல் (Nel)	SE	2, 3, 4, 5, 7, 33	PA
			SE	52	SV
Pandanus odorifer (Forssk.) Kuntze [syn. *Pandanus odoratissimus* L.f.] *	Pandanaceae	தாழை (Thaalai)	FL	44, 47	PA
Panicum antidotale Retz.	Poaceae	கிருமிசத்துரு (Kirumisaththuru)	FR	58	SA
Panicum sumatrense Roth *	Poaceae	சாமை (Saamai)	SE	2	PA
Papaver somniferum L. #	Papaveraceae	அபின் (Abin)	LA	12, 37, 39, 40	PA
			LA	57, 58	SA
			LA	55	SV
Paspalum scrobiculatum L. *	Poaceae	வரகு (Varahu)	SE	2, 3	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Pavonia odorata Willd. #	Malvaceae	பேராமட்டி (Peraamatti)	RO	46	PA
Phoenix dactylifera L. $	Arecaceae	பேரீச்சை (Pereechchai)	FR	8, 9	PA
			FR	51	SV
Phoenix pusilla Gaertn.	Arecaceae	ஈச்சை (Eechchai)	FL	10, 46	PA
			UF	35	PA
Phyllanthus amarus Schumach. & Thonn.	Phyllanthaceae	கீழ்காய்நெல்லி (Keelkaainelli)	RO	45	PA
			WP	46	PA
Phyllanthus emblica L. $	Phyllanthaceae	நெல்லி (Nelli)	FR	8, 13, 14, 19, 26, 28, 29, 30, 34, 39, 46	PA
			FR	51, 55	SV
			RO	46	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Phyllanthus reticulatus Poir.	Phyllanthaceae	நீர்ப்பூலா (Neerppoolaa)	BA TL	14, 45 37	PA PA
Piper chuvya Hunter ex C.DC.	Piperaceae	செவ்வியம் (Sevviyam)	RO RO	58 26	SA PA
Piper cubeba L.f.	Piperaceae	வால்மிளகு (Vaalmilahu)	FR	58, 59, 60	SA
Piper longum L. $	Piperaceae	திப்பிலி (Thippili)	FR FR FR	44, 45, 46 58, 60 56	PA SA SV
Piper nigrum L. $	Piperaceae	மிளகு (Milahu)	FR FR FR	44, 45 60 53	PA SA SV

Scientific name	Family	Tamil name	Part used	Preparation	Source
Plectranthus hadiensis (Forssk.) Schweinf. ex Sprenger [syn. *Plectranthus zatarhendi* var. tomentosus (Benth.) Codd]	Lamiaceae	இருவேலி (Iruveli)	RO	44, 46, 47	PA
Plumbago zeylanica L.	Plumbaginaceae	கொடிவேலி (Kodiveli)	RB RO	11 26	PA PA
Pogostemon heyneanus Benth.	Lamiaceae	பச்சிலை (Pachchilai)	LE	44, 46, 47	PA
Pterocarpus santalinus L.f. *	Fabaceae	செஞ்சந்தனம் (Senjchanthanam)	WO	44, 46, 47	PA
Punica granatum L. #$	Lythraceae	மாதுளை (Maathulai)	FR RO	9, 45 35	PA PA
Rhus succedanea L. #	Anacardiaceae	கற்கடகசிங்கி (Katkadahasingi)	GA	9, 11	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Ricinus communis L. #$	Euphorbiaceae	ஆமணக்கு (Aamankku)	RO	46	PA
Rivea ornata Choisy	Convolvulaceae	முசுட்டை (Musuttai)	SE TL	35 21	PA PA
Rotheca serrata (L.) Steane & Mabb. [syn. *Clerodendrum serratum* (L.) Moon]	Lamiaceae	சிறுதேக்கு (Siruthekku)	RO	58, 60	SA
Rubia cordifolia L. $	Rubiaceae	மஞ்சிட்டி (Manjitti)	BU RO ST	46 44 44, 47	PA PA PA
Saccharum arundinaceum Retz.	Poaceae	பெருங்கரும்பை (Perungkarumbai)	ST	26	PA
Saccharum officinarum L.	Poaceae	கரும்பு (Karumbu)	ST ST	9, 45 51	PA SV

Scientific name	Family	Tamil name	Part used	Preparation	Source
Salacia reticulata Wight	Celastraceae	கடலிறாஞ்சி (Kadaliraanji)	BA	1, 10, 13, 14, 29, 34, 35, 43, 45	PA
			BA	49, 51	SV
			RO	46	PA
Santalum album L. *	Santalaceae	சந்தனம் (Santhanam)	WO	8, 9, 10, 44, 46, 47	PA
			WO	60	SA
			WO	51	SV
Senna auriculata (L.) Roxb. [syn. *Cassia auriculata* L.]	Fabaceae	ஆவாரை (Aavaarai)	BA	1, 8, 10, 13, 14, 19, 24, 35, 39, 43	PA
			BA	49	SV
			BA	57	SA
			FB	23	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			FL	8, 10, 24, 38	PA
			FL	57	SA
			LE	8, 11, 23	PA
			MR	51, 52	SV
			RB	23	PA
			RB	53	SV
			RO	8, 10, 24, 29	PA
			RO	51	SV
			RO	57	SA
			SE	1	PA
			SE	10, 12, 17, 19, 29, 30, 31, 34, 36, 39, 40, 48	PA
			SE	57	SA
			TL	1, 4, 5, 15, 18, 24	PA
			TL	57	SA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			UF	57	SA
			UF	8, 10, 24, 38	PA
			WP	20, 21, 34	PA
			WP	55	SV
Senna sophera (L.) Roxb. [syn. *Cassia sophera* L.]	Fabaceae	பொன்னாவரை (Ponnaavarai)	MS	3	PA
Senna tora (L.) Roxb. [syn. *Cassia tora* L.]	Fabaceae	ஊசித்தகரை (Oosiththaharai)	SE	44, 47	PA
Sesamum indicum L. $	Pedaliaceae	எள்ளு (Ellu)	MS	52	SV
			RO	9	PA
			SE	1, 5, 7, 18, 35, 39, 44, 46, 47	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Shorea robusta Gaertn *	Dipterocarpaceae	வெண்குந்திருக்கம் (Venkunthirukkam)	RE	47	PA
Sida cordifolia L. #	Malvaceae	சிற்றாமட்டி (Sitraamatti)	RO	44, 46, 47	PA
Solanum erianthum D. Don #	Solanaceae	கறிமுள்ளி (Karimulli)	SE	9	PA
Spermacoce hispida L.	Rubiaceae	நத்தைச்சூரி (Naththaichchoori)	SE	59	SA
Sterculia foetida L. #	Malvaceae	பூதவிருக்கம் (Poothavirukkam)	BA	46	PA
Stereospermum chelonoides (L.f.) DC. [syn. *Stereospermum suaveolens* (Roxb.) DC]	Bignoniaceae	பாதிரி (Paathiri)	RO	46	PA
Strychnos potatorum L.f. #	Loganiaceae	தேற்றான் (Thetraan)	SE	1, 11, 13, 14, 21, 23, 28, 29, 30, 33, 34, 35	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
			SE	60	SA
Symplocos racemosa Roxb.	Symplocaceae	வெள்ளிலோத்திரம் (Velliloththiram)	BA	27, 44	PA
Syzygium aromaticum (L.) Merr. & L.M.Perry $	Myrtaceae	கராம்பு (Karaambu)	FB	8, 9, 12, 15, 44, 46, 47	PA
			FB	58, 59, 60	SA
			FB	55	SV
Syzygium cumini (L.) Skeels	Myrtaceae	நாவல் (Naaval)	BA	34, 43	PA
			BA	49, 51	SV
			MB	50	SV
			TL	21	PA
Tamarindus indica L. *	Fabaceae	புளி (Puli)	SE	1, 9, 11, 21, 34	PA
			SE	54	SV

Scientific name	Family	Tamil name	Part used	Preparation	Source
Terminalia arjuna (Roxb. ex DC.) Wight & Arn. $	Combretaceae	மருது (Maruthu)	BA	34, 35, 45	PA
Terminalia bellirica (Gaertn.) Roxb. $	Combretaceae	தான்றி (Thaandri)	FR	9, 14, 26, 29, 30, 34, 46	PA
Terminalia chebula Retz. $	Combretaceae	கடுக்காய் (Kadukkaai)	FR	13, 14, 19, 26, 27, 28, 29, 30, 31, 46	PA
			FR	50	SV
			SE	9	PA
			SE	60	SA
			WP	46	PA
Thespesia populnea (L.) Sol. ex Corrêa *#	Malvaceae	பூவரசு (Poovarasu)	BA	13	PA
			RB	23	PA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Tinospora sinensis (Lour.) Merr. [syn. *Tinospora cordifolia* (Willd.) Miers] $	Menispermaceae	சீந்தில் (Seenthil)	ST	27, 44, 46, 47	PA
			ST	57	SA
			ST	59	SA
Trachyspermum roxburghianum (DC.) H. Wolff [syn. *Trachyspermum involucratum* (Roxb.) H. Wolff] #	Apiaceae	ஓமம் (Omam) / அசமதாகம் (Asamathaaham)	FR	8, 44	PA
			FR	55	SV
			FR	57, 58	SA
Tribulus terrestris L. #$	Zygophyllaceae	நெருஞ்சில் (Nerunjchil)	WP	46	PA
			RO	26	PA
Trigonella foenum-graecum L. #$	Fabaceae	வெந்தயம் (Venthayam)	SE	44, 46, 47	PA
			SE	59	SA

Scientific name	Family	Tamil name	Part used	Preparation	Source
Vigna mungo (L.) Hepper	Fabaceae	உழுந்து (Ulunthu)	SE	2	PA
Vitex negundo L.	Lamiaceae	நொச்சி (Nochchi)	LE	47	PA
			RO	44	PA
Withania somnifera (L.) Dunal #$	Solanaceae	அமுக்கிராய் (Amukkiraai)	RH	46	PA
Zingiber officinale Roscoe $	Zingiberaceae	இஞ்சி (Inji)	RH	35, 39, 40, 44, 45	PA
			RH	58, 59, 60	SA
			RH	51	SV
Ziziphus jujuba Mill. *#	Rhamnaceae	இலந்தை (Ilanthai)	LE	11	PA
			TL	14	PA
Ziziphus rugosa Lam. #	Rhamnaceae	துடரி (Thudari)	TL	21	PA

* Rare (threatened) plant species based on IUCN (2018) - Red List of Threatened Species

Toxic plant species based on Roth et al. (2012) and Harborne et al (1996)

$ Very well studied and globally distributed plant species based on American Herbal Pharmacopoeia (2011), Brendler (2010), European Medicines Agency (2009), Upton et al. (2016) and World Health Organization Monographs on Selected Medicinal Plants – Volumes 1 to 4 (1999; 2004; 2007; 2009)

Abbreviations

Part used

BA: bark, BU: bulb, FL: flower, FB: flower bud, FR: fruit, HE: heartwood, GA: gall, LA: latex, LE: leaf, MA: mace / aril, MB: mature bark, ML: mature leaf, MR: mature root, MS: mature seed, RB: root bark, RC: receptacle, RE: resin, RH: rhizome, RO: root, SE: seed, SI: stigma, ST: stem, TL: tender leaf, UF: unripe fruit, WO: wood, WP: whole plant

Preparation

1: *காந்தக்குளிகை* – Kaanthakkulihai; 2, 3: *தவிடு* – Thavidu; 4, 5, 6, 7: *பிட்டு* – Pittu; 8: *ஏலாதிச்சூரணம்* – Elaathichchooranam; 9: *ஏலாதிச்சஞ்சீவிச்சூரணம்* – Elaathichchancheevichchooranam; 10: பெரிய குளிகை - Periya kulihai; 11: மேகநாதக்குளிகை – Mehanaathakkulihai; 12: *கபாட சிந்தாமணிக்குளிகை* - Kapaada Sinthaamanikkulihai; 13: *அயக்காந்தக்குளிகை* – Ayakkaanthakkulihai; 14: *சுவறப்பிடிப்பாணுண்டை* – Suravappidippaanundai; 15, 16, 17, 18, 19, 20, 21, 22, 23, 24: *சலக்கழிச்சல்பலவுக்கும் கைமருந்து* - Salakkalichchalpalavukkum kaimarunthu; 25, 26, 27, 28, 29, 49, 50, 51: *குடிநீர்* – Kudineer; 30: *காந்தாயக்குளிகை* – Kaanthaayakkulihai; 31: வெள்ளைக்குன்றிமணிக்குளிகை – Vellaikkundrimanikkulihai; 32: *காரீய சிந்தூரம்* - Kaareeya sinthooram; 33: *மனோசிலைக்குளிகை* – Manosilaikkulihai; 34: *திரிலோகவடகம்* – Thirilohavadaham; 35, 36, 37, 38, 39, 40, 41, 42: *பிரமேகக்குளிகை* – Piramehakkulihai; 43: *நாவல்*

நெய் - Naaval ney; 44: *சந்தனாதியெண்ணெய்* – Santhanaathiyennai; 45: *வச்சிரசிந்தாமணி இரசாயனம்* - Vachchirasinthaamani irasaayanam; 46: *பிரமேகச்சந்தனாதியெண்ணெய்* – Piramehachchanthanaathiyennai; 47: *நீரிழிவுச்சந்தனாதியெண்ணெய்* – Neerilivuchchanthanaathiyennai; 48: *காந்தரசக்குளிகை* – Kaantharasakkulihai; 52, 53: *தூள்* – Thool; 54: *நீரிழிவுக்கு வங்கசெந்தூரம்* - Neerilivukku vangasenthooram; 55: *பிரமேக நீரிழிவுக்கு வெட்டுமாறன் தூள்* - Pirameha neerilivukku Vettumaaran thool; 56: *நீரிழிவுக்கு வங்க செந்தூரம்* - Neerilivukku vanga senthooram; 57: *அமுது சர்க்கரைச்சூரணம்* - Amuthu Sarkkaraichchooranam; 58: *நந்தீசுர சிந்தாமணி* - Nantheesura Sinthaamani; 59: *பூரணச்சந்திராதி மாத்திரை* - Pooranachchanthiraathi Maaththirai; 60: *மிருத்த சஞ்சீவினி மாத்திரை* - Miruththa Sanjeevini Maaththirai

Source

PA: Pararasaseharam (Fifth Part) (*பரராசசேகரம் (ஐந்தாம் பாகம்)*) - Pararaasaseharam (Ainthaam Paaham) (Anonymous, 2003), SV: Seharaasasehara Treatment (*செகராசசேகர வைத்தியம்* - Seharaasasehara Vaiththiyam) (Anonymous, 2000), SA: Siddha Medicinal Procedure (*சித்த ஔடத செய்முறை* - Siththa Audatha Seimurai) (Ponniah and Sabapathipillai, 1980).

Appendix B

Antidiabetic historical Sri Lankan Siddha Medicine preparations

1. Pararasaseharam (Fifth Part) (பரராசசேகரம் **(**ஐந்தாம் பாகம்**) - Pararaasaseharam (Ainthaam Paaham))**

This document contains 48 antidiabetic Sri Lankan Siddha preparations and the information of ingredient, amount, method, and dosage of each preparation are presented below.

1. காந்தக்குளிகை – Kaanthakkulihai (p. 10)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abutilon indicum (L.) Sweet	Seed	5 g
Acacia leucophloea (Roxb.) Willd.	Resin	5 g
Acacia nilotica (L.) Delile	Resin	5 g
Azadirachta indica A.Juss.	Resin	5 g
Borassus flabellifer L.	Fruit juice	As required
Cyperus rotundus L.	Rhizome	5 g
Eclipta prostrata (L.) L.	Whole plant juice	As required
Hygrophila auriculata (Schumach.) Heine	Whole plant	5 g
Limonia acidissima Groff	Resin	5 g

Scientific / English name	Processed botanical drug	Amount
Madhuca longifolia (J.Koenig ex L.) J.F.Macbr.	Flower juice	As required
Moringa oleifera Lam.	Resin	5 g
Myristica fragrans Houtt.	Seed	5 g
Myristica fragrans Houtt.	Leaf	5 g
Oroxylum indicum (L.) Kurz	Resin	5 g
Salacia reticulata Wight	Bark	5 g
Senna auriculata (L.) Roxb.	Seed	5 g
Senna auriculata (L.) Roxb.	Tender leaf	5 g
Senna auriculata (L.) Roxb.	Bark	5 g
Sesamum indicum L.	Seed	5 g
Strychnos potatorum L.f.	Seed	5 g
Tamarindus indica L.	Seed	5 g
Beryl	NA	5 g
Bitumen	NA	5 g
Buffalo curd	NA	5 g
Cinnabar	NA	5 g
Magnetite	NA	5 g
Mercury	NA	5 g
Purified graphite	NA	5 g

Scientific / English name	Processed botanical drug	Amount
Roche alum	NA	5 g
Rose water	NA	As required

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable.

Mix all the other ingredients except *Borassus flabellifer* fruit juice, *Madhuca longifolia* flower juice, rose water, *Eclipta prostrata* whole plant juice, and buffalo curd together.

Grind this mixture while adding *Borassus flabellifer* followed by *Madhuca longifolia* flower juice, rose water, *Eclipta prostrata* whole plant juice, and buffalo curd. Then make *Strychnos potatorum* L.f. (Loganiaceae) seed size tablets and dry them.

Dosage: One tablet morning and night after meals

2. தவிடு – Thavidu (p. 28)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Eleusine coracana (L.) Gaertn.	Seed	Equal amount
Oryza sativa L.	Seed	Equal amount

Scientific / English name	Processed botanical drug	Amount
Panicum sumatrense Roth	Seed	Equal amount
Paspalum scrobiculatum L.	Seed	Equal amount
Vigna mungo (L.) Hepper	Seed	Equal amount

Method

Pulverise all the ingredients separately into powder and mix them together. Open dry roast the mixture while stirring.

Dosage: one table spoon three times a day after meals

3. தவிடு – Thavidu (p. 28)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Senna sophera (L.) Roxb.	Mature seed	Equal amount
Eleusine coracana (L.) Gaertn.	Seed	Equal amount
Oryza sativa L.	Seed	Equal amount
Paspalum scrobiculatum L.	Seed	Equal amount

Method

Pulverise all the ingredients separately into powder and mix them together. Open dry roast the mixture while stirring.

Dosage: one table spoon three times a day after meals

4. பிட்டு - Pittu (p. 29)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Cissampelos pareira L.	Tender leaf	Equal amount
Oryza sativa L.	Open dry roasted seed flour	Equal amount
Senna auriculata (L.) Roxb.	Tender leaf	Equal amount

Method

Mix tender leaves of *Cissampelos pareira* and *Senna auriculata* together and add to open dry roasted rice flour. Then add hot water to the mixture and stir it to make small chunks. Open steam the mixture until observing the steam passing through it.

Dosage: Consume as food as required once a day either morning or night

5. பிட்டு - Pittu (p. 29)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Boerhavia diffusa L.	Tender leaf	Equal amount

Scientific / English name	Processed botanical drug	Amount
Oryza sativa L.	Open dry roasted seed flour	Equal amount
Sesamum indicum L.	Seed oil cake	Equal amount

Method

Mix *Boerhavia diffusa* tender leaf and sesame oil cake together and add to open roasted rice flour. Then add hot water to the mixture and stir it to make small chunks. Open steam the mixture until observing the steam passing through it.

Dosage: Consume as food as required once a day either morning or night

6. பிட்டு - Pittu (p. 29)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Cissampelos pareira L.	Tender leaf	Equal amount
Eleusine coracana (L.) Gaertn.	Open dry roasted seed flour	Equal amount
Oryza sativa L.	Open dry roasted seed flour	Equal amount
Senna auriculata (L.) Roxb.	Tender leaf	Equal amount

Method

Mix open roasted rice flour and *Eleusine coracana* seed flour together and add tender leaves of *Senna auriculata* and *Cissampelos pareira* to it. Then add hot water to the mixture and stir it to make small chunks. Open steam the mixture until observing the steam passing through it.

Dosage: Consume as food as required once a day either morning or night

7. பிட்டு - Pittu (p. 29)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Cyperus rotundus L.	Rhizome flour	Equal amount
Oryza sativa L.	Open dry roasted seed flour	Equal amount
Sesamum indicum L.	Puffed seed	Equal amount

Method

Mix *Cyperus rotundus* rhizome flour and *Sesamum indicum* seed puff together and add to open roasted rice flour. Then add hot water to the mixture and stir it to make small chunks. Open steam the mixture until observing the steam passing through it.

Dosage: Consume as food as required once a day either morning or night

8. ஏலாதிச்சூரணம் – Elaathichchooranam (p. 33)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Aconitum heterophyllum Wall. ex Royle	Root	Equal amount
Aucklandia lappa DC.	Root	Equal amount
Cinnamomum cappara-coronde Blume	Resin	Equal amount
Cuminum cyminum L.	Dried fruit	Equal amount
Cyperus rotundus L.	Rhizome	Equal amount
Elettaria cardamomum (L.) Maton	Dried fruit	Equal amount
Hemidesmus indicus (L.) R. Br. ex Schult.	Root	Equal amount
Hyoscyamus reticulatus L.	Seed	Equal amount
Madhuca longifolia (J. Koenig ex L.) J. F. Macbr.	Flower	Equal amount
Myristica fragrans Houtt.	Mace	Equal amount
Myristica fragrans Houtt.	Seed	Equal amount
Phoenix dactylifera L.	Fruit	Equal amount
Phyllanthus emblica L.	Fruit	Equal amount
Santalum album L.	Wood	Equal amount
Senna auriculata (L.) Roxb.	Leaf	Equal amount
Senna auriculata (L.) Roxb.	Flower	Equal amount
Senna auriculata (L.) Roxb.	Unripe fruit	Equal amount

Scientific / English name	Processed botanical drug	Amount
Senna auriculata (L.) Roxb.	Root	Equal amount
Senna auriculata (L.) Roxb.	Bark	Equal amount
Syzygium aromaticum (L.) Merr. & L.M. Perry	Flower bud	Equal amount
Trachyspermum roxburghianum (DC.) H. Wolff	Dried fruit	Equal amount
Dried cow gallstone	NA	Equal amount
Male deer musk	NA	Equal amount

Method

Sundry all the ingredients and pulverise or scrape or press or crush all the ingredients separately where applicable. Mix all the ingredients together and sift the mixture.

Dosage: 265 mg three times a day after meals

9. ஏலாதிச்சஞ்சீவிச்சூரணம் - Elaathichchancheevichchooranam (p. 34)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abies spectabilis (D. Don) Mirb.	Leaf	5 g
Aconitum heterophyllum Wall. ex Royle	Root	5 g
Aegle marmelos (L.) Corrêa	Root	5 g

Scientific / English name	Processed botanical drug	Amount
Anacardium occidentale L.	Fruit	5 g
Anacyclus pyrethrum (L.) Lag.	Root	5 g
Areca catechu L.	Resin	5 g
Areca catechu L.	Seed	5 g
Asparagus racemosus Willd.	Tuber	5 g
Aucklandia lappa DC.	Root	5 g
Chrysopogon zizanioides (L.) Roberty	Root	5 g
Cinnamomum cappara-coronde Blume	Resin	5 g
Cuminum cyminum L.	Dried fruit	5 g
Curculigo orchioides Gaertn.	Tuber	5 g
Cyperus rotundus L.	Rhizome	5 g
Elettaria cardamomum (L.) Maton	Dried fruit	5 g
Foeniculum vulgare Mill.	Dried fruit	5 g
Glycyrrhiza glabra L.	Root	5 g
Limonia acidissima Groff	Fruit	5 g
Magnolia champaca (L.) Baill. ex Pierre	Flower	5 g
Musa × *paradisiaca* L.	Rhizome	5 g
Myristica fragrans Houtt.	Seed	5 g
Myristica fragrans Houtt.	Leaf	5 g

Scientific / English name	Processed botanical drug	Amount
Nelumbo nucifera Gaertn.	Rhizome	5 g
Phoenix dactylifera L.	Fruit	5 g
Punica granatum L.	Fruit	5 g
Rhus succedanea L.	Gall	5 g
Saccharum officinarum L. jaggery	NA	65 g
Santalum album L.	Wood	5 g
Sesamum indicum L.	Root	5 g
Solanum erianthum D. Don	Seed	5 g
Syzygium aromaticum (L.) Merr. & L.M. Perry	Flower bud	5 g
Tamarindus indica L.	Seed	5 g
Terminalia bellirica (Gaertn.) Roxb.	Fruit pulp	5 g
Terminalia chebula Retz.	Seed	5 g
Asbestos	NA	5 g
Dried cow gallstone	NA	5 g
Male deer musk	NA	5 g
Roche alum	NA	5 g

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable. Mix all the ingredients together and add *Saccharum officinarum* jaggery (one third of the amount of powder) to the mixture. Preserve it.

Dosage: 265 mg three times a day after meals

10. பெரிய குளிகை - Periya kulihai (p. 40)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abrus precatorius L.	Root	30 g
Acorus calamus L.	Rhizome	30 g
Aloe vera (L.) Burm.f.	Dried pulp of leaf	30 g
Aucklandia lappa DC.	Root	30 g
Cassia fistula L.	Bark	30 g
Cocos nucifera L.	Flower	30 g
Ficus racemosa L.	Bark	30 g
Nymphaea pubescens Willd.	Rhizome	30 g
Phoenix pusilla Gaertn.	Flower	30 g
Salacia reticulata Wight	Bark	30 g
Santalum album L.	Wood	30 g

Scientific / English name	Processed botanical drug	Amount
Senna auriculata (L.) Roxb.	Bark	30 g
Senna auriculata (L.) Roxb.	Flower	30 g
Senna auriculata (L.) Roxb.	Root	30 g
Senna auriculata (L.) Roxb.	Seed	30 g
Senna auriculata (L.) Roxb.	Unripe fruit	30 g
Dried cow gallstone	NA	30 g
Gold	NA	30 g
Mica	NA	30 g
Pearl	NA	30 g
Red coral	NA	30 g
Reservior water	NA	As required
Roche alum	NA	30 g

Method

Pulverise or press or scrape or crush all the ingredients separately where applicable. Mix mica, roche alum, dried cow gallstone, pearl, red coral, gold, *Nymphaea pubescens* rhizome, roots of *Aucklandia lappa*, *Abrus precatorius* and *Senna auriculata*, *Aloe vera* dried pulp of leaf, *Santalum album* wood, flowers of *Phoenix pusilla*, *Cocos nucifera*, and *Senna auriculata*, seed and unripen fruit of *Senna auriculata*, barks of *Senna auriculata* and *Salacia reticulata* together.

Then mix *Ficus racemosa* bark and *Acorus calamus* rhizome together and pour reservoir water. Boil and filter it.

Grind previously prepared mixture while adding the decoction for three days. Finally make *Ficus racemosa* L. (Moraceae) fruit size tablets and shade dry.

Dosage: One tablet twice a day after meals

11. மேகநாதக்குளிகை – Mehanaathakkulihai (p. 41)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abrus precatorius L.	Seed	5 g
Acacia chundra (Rottler) Willd.	Resin	10 g
Acacia leucophloea (Roxb.) Willd.	Resin	10 g
Acacia nilotica (L.) Delile	Resin	10 g
Azadirachta indica A. Juss.	Resin	10 g
Cassia fistula L.	Leaf juice	As required
Cocos nucifera L.	Flower	10 g
Coscinium fenestratum (Goetgh.) Colebr.	Stem	10 g
Curculigo orchioides Gaertn.	Rhizome	10 g
Curcuma aromatica Salisb.	Rhizome	10 g

Scientific / English name	Processed botanical drug	Amount
Plumbago zeylanica L.	Root bark	10 g
Rhus succedanea L.	Gall	5 g
Senna auriculata (L.) Roxb.	Leaf juice	As required
Strychnos potatorum L.f.	Seed	5 g
Tamarindus indica L.	Seed outer skin	5 g
Ziziphus jujuba Mill.	Leaf juice	As required
Black tin powder	NA	30 g
Gypsum	NA	10 g
Mercury calx	NA	10 g
Mica	NA	20 g
Purified sulphur and arsenic	NA	50 g

Method

Pulverise or press or scrape or crush all the ingredients separately where applicable.

Mix mica, mercury calx, gypsum, black tin red powder, purified sulphur and arsenic, resins of *Acacia chundra*, *A. leucophloea*, *A. nilotica*, and *Azadirachta indica*, *Coscinium fenestratum* stem, *Plumbago zeylanica* root bark, rhizomes of *Curcuma aromatica* and *Curculigo orchioides*, *Cocos nucifera* flower, *Tamarindus indica* seed outer skin, seeds of *Abrus precatorius* and *Strychnos potatorum*, and

Rhus succedanea gall together and grind the mixture with *Senna auriculata* leaf juice for 3 days. Then grind with leaf juices of *Ziziphus jujuba* and *Cassia fistula* each per 3 days and make *Strychnos potatorum* seed size tablets. Shade dry them.

Dosage: One tablet twice a day after meals

12. கபாட சிந்தாமணிக்குளிகை - Kapaada Sinthaamanikkulihai (p. 42)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Anacyclus pyrethrum (L.) Lag.	Root	5 g
Areca catechu L.	Resin	5 g
Datura metel L.	Seed	2.5 g
Hyoscyamus reticulatus L.	Seed	5 g
Myristica fragrans Houtt.	Seed	5 g
Myristica fragrans Houtt.	Mace	5 g
Papaver somniferum L.	Latex	2.5 g
Senna auriculata (L.) Roxb.	Seed	55 g
Syzygium aromaticum (L.) Merr. & L. M. Perry	Flower bud	5 g
Asbestos	NA	5 g
Beryl	NA	5 g
Buffalo buttermilk	NA	10 ml

Scientific / English name	Processed botanical drug	Amount
Cinnabar	NA	5 g
Magnetite	NA	5 g
Roche alum	NA	5 g

Method

Pulverise or press or scrape or crush all the ingredients separately where applicable.

Mix all the other ingredients together except *Senna auriculata* seed and buffalo whey together. Lightly open dry roast *Senna auriculata* seed while stirring and add to the mixture. Grind the mixture while adding buffalo curd and make *Solanum torvum* Sw. (Solanaceae) fruit size tablets. Then shade dry them.

Dosage: One tablet twice a day after meals for 40 days

13. அயக்காந்தக்குளிகை - Ayakkaanthakkulihai (pp. 42, 43)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Acacia leucophloea (Roxb.) Willd.	Bark	400 g
Acacia nilotica (L.) Delile	Bark	400 g
Acacia nilotica (L.) Delile	Resin	Equal amount
Curcuma longa L.	Rhizome	Equal amount

Scientific / English name	Processed botanical drug	Amount
Erythroxylum monogynum Roxb.	Bark	400 g
Ficus racemosa L.	Bark	400 g
Lannea coromandelica (Houtt.) Merr.	Bark	400 g
Limonia acidissima Groff	Resin	Equal amount
Phyllanthus emblica L.	Fruit	Equal amount
Salacia reticulata Wight	Bark	400 g
Senna auriculata (L.) Roxb.	Bark	400 g
Strychnos potatorum L.f.	Seed	Equal amount
Terminalia chebula Retz.	Fruit pulp	Equal amount
Thespesia populnea (L.) Sol. ex Corrêa	Bark	400 g
Graphite	NA	Equal amount
Iron	NA	Equal amount
Magnetite	NA	Equal amount
Mercury	NA	Equal amount
Mica	NA	Equal amount
Water	NA	4800 ml

Method

Mix graphite and mercury together and melt the mixture. Then crush it.

Pulverise or press or scrape or crush all the other ingredients separately where applicable.

Mix crushed molten graphite and mercury mixture, iron, magnetite, mica, *Terminalia chebula* fruit pulp, *Phyllanthus emblica* fruit, *Strychnos potatorum* seed, *Curcuma longa* rhizome, resins of *Acacia nilotica* and *Limonia acidissima* together.

Mix barks of *Ficus racemose*, *Senna auriculata*, *Salacia reticulata*, *Acacia nilotica*, *A. leucophloea*, *Lannea coromandelica*, *Thespesia populnea* and *Erythroxylum monogynum* together. Pour water and boil it for 8 days.

Grind previously prepared mixture while adding the decoction and make *Areca catechu* L. (Arecaceae) seed size (5 g) tablets. Shade dry and crush them into powder.

Dosage: One tablet twice a day after meals

14. சுவறப்பிடிப்பாணுண்டை – Suravappidippaanundai (p. 12)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abrus precatorius L.	Seed	50 g
Curcuma longa L.	Rhizome	50 g
Ficus amplissima Sm.	Bark	3200 g

Scientific / English name	Processed botanical drug	Amount
Ficus benghalensis L.	Bark	3200 g
Ficus racemosa L.	Bark	3200 g
Ficus religiosa L.	Bark	3200 g
Limonia acidissima Groff	Resin	200 g
Phyllanthus emblica L.	Fruit	400 g
Phyllanthus reticulatus Poir.	Bark	160 g
Salacia reticulata Wight	Bark	800 g
Senna auriculata (L.) Roxb.	Bark	1600 g
Strychnos potatorum L.f.	Outer skin removed seed	50 g
Terminalia bellirica (Gaertn.) Roxb.	Fruit	400 g
Terminalia chebula Retz.	Fruit	400 g
Ziziphus jujuba Mill.	Tender leaf	80 g
Cow urine	NA	50 g
Graphite	NA	50 g
Human colostrum / foremilk	NA	50 g
Water	NA	9600 ml
Water	NA	4800 ml
Magnetite	NA	50 g

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable. Mix barks of *Ficus racemosa* L., *Ficus amplissima*, *Ficus benghalensis*, and *Ficus religiosa*, *Senna auriculata*, *Salacia reticulata*, and *Phyllanthus reticulatus* and *Ziziphus jujuba* tender leaf and pour 9600 ml water into the mixture. Then boil until reaching one eight of the initial volume.

Mix *Terminalia chebula*, fruits of *Phyllanthus emblica*, and *Terminalia bellirica* together and pour 4800 ml water into the mixture and boil until reaching one fourth of the initial volume. Add this decoction to previously prepared decoction and stir it. Then boil the decoction mixture and filter it.

Grind graphite with human colostrum. Pour cow urine to magnetite and boil it thoroughly. Mix ground graphite, boiled magnetite, *Curcuma longa* rhizome and seeds of *Abrus precatorius*, and *Strychnos potatorum* together and grind with previously prepared decoction mix. Then boil and add *Limonia acidissima* resin. Boil it again and make 5 g tablets. Finally, shade dry them.

Dosage: One tablet twice a day after meals

15. சலக்கழிச்சல்பலவுக்கும் கைமருந்து - Salakkalichchalpalavukkum kaimarunthu (p. 27)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Senna auriculata (L.) Roxb.	Tender leaf	Half handful
Syzygium aromaticum (L.) Merr. & L. M. Perry	Flower bud	5

Scientific / English name	Processed botanical drug	Amount
Buffalo buttermilk	NA	1200 ml
Dried cow gallstone	NA	244 g

Method

Pulverise all the ingredients separately and mix them together. Pour buffalo buttermilk into a clay pot and cover the pot mouth with a piece of cotton cloth. Place the ground mixture on the cloth and cover by placing another clay pot upside down on top of the pot with buttermilk. Then boil it. Finally grind the mixture with boiled buffalo buttermilk.

Dosage: 10 ml twice a day after meals for 21 days

16. *சலக்கழிச்சல்பலவுக்கும் கைமருந்து* - Salakkalichchalpalavukkum kaimarunthu (p. 27)

Ingredients

Scientific name	Processed botanical drug	Amount
Cissampelos pareira L.	Whole plant	As required

Method

Shade dry and pulverise *Cissampelos pareira* whole plant.

Dosage: As required three times a day after meals

17. ***சலக்கழிச்சல்பலவுக்கும் கைமருந்து*** **- Salakkalichchalpalavukkum kaimarunthu (p. 27)**

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abrus precatorius L.	Seed	5 g
Acacia nilotica (L.) Delile	Resin	20 g
Gossypium arboreum L.	Seed	15 g
Senna auriculata (L.) Roxb.	Seed	10 g
Buffalo buttermilk	NA	As required

Method

Pulverise all the ingredients separately and mix them together. Then grind the mixture with buffalo buttermilk.

Dosage: As required twice a day after meals

18. ***சலக்கழிச்சல்பலவுக்கும் கைமருந்து*** **- Salakkalichchalpalavukkum kaimarunthu (p. 27)**

Ingredients

Scientific / English name	Processed botanical drug	Amount
Acacia nilotica (L.) Delile	Tender leaf	Equal amount

Scientific / English name	Processed botanical drug	Amount
Indigofera tinctoria L.	Leaf	Equal amount
Musa × *paradisiaca* L.	Leaf	Equal amount
Senna auriculata (L.) Roxb.	Tender leaf	Equal amount
Sesamum indicum L. oil	NA	Equal amount
Magnetite	NA	As required

Method

Pulverise or press or crush all the other ingredients separately where applicable except *Musa* × *paradisiaca* leaf. Then mix them together. Wrap the mixture in a *Musa* × *paradisiaca* leaf and burn it in dried *Oryza sativa* L. (Poaceae) husk. Then grind it with sesame oil.

Dosage: As required twice a day after meals

19. *சலக்கழிச்சல்பலவுக்கும் கைமருந்து* - Salakkalichchalpalavukkum kaimarunthu (p. 27)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Aegle marmelos (L.) Corrêa	Bark	Equal amount
Phyllanthus emblica L.	Fruit	Equal amount
Senna auriculata (L.) Roxb.	Seed	Equal amount

Senna auriculata (L.) Roxb.	Bark	Equal amount
Terminalia chebula Retz.	Dried fruit	Equal amount
Buffalo buttermilk	NA	As required

Method

Pulverise all the other ingredients separately except *Phyllanthus emblica* fruit and mix them together. Pour buffalo buttermilk into *Phyllanthus emblica* fruit and macerate overnight. Then press all *Phyllanthus emblica* fruits and pour the solution into previously prepared powder. Dissolve it.

Dosage: As required twice a day before meals

20. *சலக்கழிச்சல்பலவுக்கும் கைமருந்து* - Salakkalichchalpalavukkum kaimarunthu (p. 27)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Moringa oleifera Lam.	Bark	Equal amount
Senna auriculata (L.) Roxb.	Whole plant	Equal amount
Honey	NA	Equal amount

Method

Grind both ingredients separately and mix them together. Grind the mixture with honey.

Dosage: As required twice a day after meals

21. சலக்கழிச்சல்பலவுக்கும் கைமருந்து - Salakkalichchalpalavukkum kaimarunthu (p. 27)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Caesalpinia bonduc (L.) Roxb.	Tender leaf	Equal amount
Cassia fistula L.	Root	Equal amount
Dichrostachys cinerea (L.) Wight & Arn.	Tender leaf	Equal amount
Rivea ornata Choisy	Tender leaf	Equal amount
Senna auriculata (L.) Roxb.	Whole plant	Equal amount
Strychnos potatorum L.f.	Seed	Equal amount
Syzygium cumini (L.) Skeels	Tender leaf	Equal amount
Tamarindus indica L.	Seed juice	Equal amount
Ziziphus rugosa Lam.	Tender leaf	Equal amount
Roche alum	NA	Equal amount

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable. Then mix them together and grind the mixture.

Dosage: As required three times a day after meals

22. ***சலக்கழிச்சல்பலவுக்கும் கைமருந்து*** **- Salakkalichchalpalavukkum kaimarunthu (p. 27)**

Ingredients

Scientific / English name	Processed botanical drug	Amount
Moringa oleifera Lam.	Bark	As required
Honey	NA	As required

Method

Pulverise *Moringa oleifera* bark and grind with honey.

Dosage: As required twice a day after meals

23. ***சலக்கழிச்சல்பலவுக்கும் கைமருந்து*** **- Salakkalichchalpalavukkum kaimarunthu (pp. 27, 28)**

Ingredients

Scientific name	Processed botanical drug	Amount
Alysicarpus vaginalis (L.) DC.	Whole plant	Half handful
Gossypium arboreum L.	Seed	One quatar handful
Senna auriculata (L.) Roxb.	Flower bud	Half handful

Scientific name	Processed botanical drug	Amount
Senna auriculata (L.) Roxb.	Leaf	Half handful
Senna auriculata (L.) Roxb.	Root bark	Half handful
Strychnos potatorum L.f.	Seed	One quater handful
Thespesia populnea (L.) Sol. ex Corrêa	Mature root bark	Half handful

Method

Pulverise or press all the ingredients separately where applicable. Then mix them together and grind the mixture.

Dosage: Lemon size three times a day after meals

24. சலக்கழிச்சல்பலவுக்கும் கைமருந்து - Salakkalichchalpalavukkum kaimarunthu (p. 28)

Ingredients

Scientific name	Processed botanical drug	Amount
Senna auriculata (L.) Roxb.	Bark	Equal amount
Senna auriculata (L.) Roxb.	Flower	Equal amount
Senna auriculata (L.) Roxb.	Root	Equal amount
Senna auriculata (L.) Roxb.	Tender leaf	Equal amount
Senna auriculata (L.) Roxb.	Unripe fruit	Equal amount

Method

Pulverise all the ingredients separately and mix them together.

Dosage: As required three times a day after meals

25. குடிநீர் – Kudineer (p. 30)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Acacia chundra (Rottler) Willd.	Bark	Equal amount
Cassia fistula L.	Bark	Equal amount
Cissampelos pareira L.	Whole plant	Equal amount
Water	NA	As required

Method

Mix all the ingredients and pour water into the mixture. Boil it until reaching one eighth of the initial volume.

Dosage: As required twice a day before meals

26. குடிநீர் – Kudineer (p. 30)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Cissampelos pareira L.	Whole plant	Equal amount
Cyperus rotundus L.	Root	Equal amount
Phyllanthus emblica L.	Fruit	Equal amount
Piper chuvya Hunter ex C. DC.	Root	Equal amount
Plumbago zeylanica L.	Root	Equal amount
Saccharum arundinaceum Retz.	Stem	Equal amount
Terminalia bellirica (Gaertn.) Roxb.	Fruit	Equal amount
Terminalia chebula Retz.	Fruit	Equal amount
Tribulus terrestris L.	Root	Equal amount
Water	NA	As required

Method

Mix all the ingredients and pour water into the mixture. Boil the mixture.

Dosage: As required twice a day before meals

27. குடிநீர் – Kudineer (p. 30)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Acacia chundra (Rottler) Willd.	Root	Equal amount
Catunaregam spinosa (Thunb.) Tirveng.	Root	Equal amount
Coscinium fenestratum (Goetgh.) Colebr.	Stem	Equal amount
Cyperus rotundus L.	Rhizome	Equal amount
Embelia ribes Burm.f.	Seed	Equal amount
Gmelina arborea Roxb.	Root	Equal amount
Symplocos racemosa Roxb.	Bark	Equal amount
Terminalia chebula Retz.	Fruit	Equal amount
Tinospora sinensis (Lour.) Merr.	Stem	Equal amount
Water	NA	As required

Method

Mix all the ingredients and pour water into the mixture. Boil the mixture.

Dosage: As required twice a day before meals

28. குடிநீர் – Kudineer (p. 30)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Curcuma longa L.	Rhizome	120 g
Moringa oleifera Lam.	Bark	160 g
Phyllanthus emblica L.	Fruit	80 g
Strychnos potatorum L.f.	Seed	40 g
Terminalia chebula Retz.	Fruit	200 g
Water	NA	As required

Method

Mix all the ingredients and pour water into the mixture. Boil it until reaching one eighth of the initial volume.

Dosage: As required twice a day before meals

29. குடிநீர் – Kudineer (p. 30)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Acacia chundra (Rottler) Willd.	Heartwood	Equal amount

Scientific / English name	Processed botanical drug	Amount
Bambusa bambos (L.) Voss	Leaf	Equal amount
Cissampelos pareira L.	Whole plant	Equal amount
Coscinium fenestratum (Goetgh.) Colebr.	Stem	Equal amount
Curculigo orchioides Gaertn.	Rhizome	Equal amount
Ficus benghalensis L.	Root	Equal amount
Moringa oleifera Lam.	Bark	Total amount of all the other ingredients
Murraya koenigii (L.) Spreng.	Stem	Equal amount
Murraya koenigii (L.) Spreng.	Root	Equal amount
Phyllanthus emblica L.	Fruit	Equal amount
Salacia reticulata Wight	Bark	Equal amount
Senna auriculata (L.) Roxb.	Seed	Equal amount
Senna auriculata (L.) Roxb.	Root	Equal amount
Strychnos potatorum L.f.	Seed	Equal amount
Terminalia bellirica (Gaertn.) Roxb.	Fruit	Equal amount
Terminalia chebula Retz.	Fruit	Equal amount
Water	NA	As required

Method

Mix all the ingredients and pour water into the mixture. Boil the mixture.

Dosage: As required twice a day before meals for seven days

30. காந்தாயக்குளிகை – Kaanthaayakkulihai

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abrus precatorius L.	Seed	25 g
Curcuma longa L.	Rhizome	25 g
Limonia acidissima Groff	Root	25 g
Moringa oleifera Lam.	Bark	50 g
Phyllanthus emblica L.	Fruit	25 g
Senna auriculata (L.) Roxb.	Seed	75 g
Strychnos potatorum L.f.	Seed	25 g
Terminalia bellirica (Gaertn.) Roxb.	Fruit	25 g
Terminalia chebula Retz.	Fruit	25 g
Graphite	NA	80 g
Magnetite	NA	25 g

Method

Mix fruits of *Terminalia chebula*, *Phyllanthus emblica*, and *Terminalia bellirica* and pour water into the mixture. Then boil it. Pulverise or crush all the other ingredients separately where applicable. Then mix them and grind with previously prepared decoction. Finally make 244 g size tablets.

Dosage: One tablet twice a day after meals

31. வெள்ளைக்குன்றிமணிக்குளிகை – Vellaikkundrimanikkulihai (p. 37)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abrus precatorius L.	Seed	Equal amount
Acacia nilotica (L.) Delile	Resin	Equal amount
Gossypium arboreum L.	Seed	Equal amount
Limonia acidissima Groff	Root	Equal amount
Senna auriculata (L.) Roxb.	Seed	Equal amount
Terminalia chebula Retz.	Fruit	Equal amount
Magnetite	NA	Equal amount
Water	NA	As required

Method

Pulverise *Terminalia chebula* fruit and pour water into it. Then boil it.

Open dry roast all the other ingredients separately while stirring. Pulverise or crush all the ingredients separately where applicable. Then mix and grind with previously prepared decoction. Make 244 g size tablets.

Dosage: One tablet twice a day after meals

32. காரீய சிந்தூரம் - Kaareeya sinthooram (p. 38)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Achyranthes aspera L.	Whole plant	160 g
Purified graphite	NA	160 g

Method

Pulverise both ingredients separately and mix. Then open dry roast the mixture while stirring until turning into red.

Dosage: As required twice a day after meals

33. மனோசிலைக்குளிகை – Manosilaikkulihai (p. 37)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abrus precatorius L.	Seed	30 g
Limonia acidissima Groff	Resin	50 g
Oryza sativa L.	Seed macerated water	As required
Oryza sativa L.	Seed	As required
Strychnos potatorum L.f.	Seed	30 g
Graphite	NA	80 g
Magnetite	NA	90 g
Mercury	NA	10 g
Red arsenic	NA	45 g

Method

Pulverise or crush all the ingredients except mercury separately where applicable. Then mix. Place the mixture as a heap on a cotton cloth and dig a hole on the middle of the heap (from the peak of the heap). Then pour mercury into the hole and wrap the mixture with the cloth. Tie it and macerate in *Oryza sativa* (rice) washed water for 4 days. On the fourth day grind the macerated mixture with *Oryza sativa* seed macerated water and make *Abrus precatorius* L. (Fabaceae) seed size (125 mg) tablets. Finally, shade dry them.

Dosage: One tablet twice a day after meals

34. திரிலோகவடகம் – Thirilohavadaham (p. 39)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Acacia chundra (Rottler) Willd.	Resin	40 g
Acacia nilotica (L.) Delile	Bark	4000 g
Azadirachta indica A. Juss.	Resin	40 g
Cocculus hirsutus (L.) W. Theob.	Leaf	4000 g
Coscinium fenestratum (Goetgh.) Colebr.	Stem outer skin	40 g
Limonia acidissima Groff	Resin	40 g
Phyllanthus emblica L.	Fruit	40 g
Salacia reticulata Wight	Bark	4000 g
Senna auriculata (L.) Roxb.	Whole plant	4000 g
Senna auriculata (L.) Roxb.	Seed	600 g
Strychnos potatorum L.f.	Seed	40 g
Syzygium cumini (L.) Skeels	Bark	4000 g
Tamarindus indica L.	Seed juice	40 g
Terminalia arjuna (Roxb. ex DC.) Wight & Arn.	Bark	4000 g
Terminalia bellirica (Gaertn.) Roxb.	Fruit	40 g
Iron	NA	40 g

Scientific / English name	Processed botanical drug	Amount
Magnetite	NA	40 g
Mercury	NA	40 g
Water	NA	115.2 l

Method

Mix *Senna auriculata* whole plant, barks of *Salacia reticulata*, *Syzygium cumini*, *Acacia nilotica*, and *Terminalia arjuna*, and *Cocculus hirsutus* leaf and pour water into the mixture. Then boil it until reaching to one eighth of initial volume and filter.

Pulverise or press or crush iron, magnetite, mercury, *Coscinium fenestratum* stem outer skin, *Tamarindus indica* seed juice, resins of *Limonia acidissima*, *Azadirachta indica*, and *Acacia chundra*, seeds of *Strychnos potatorum* and *Senna auriculata*, *Terminalia bellirica* and *Phyllanthus emblica* separately where applicable. Then mix them and grind the mixture with previously prepared decoction. Then boil the mixture and after cooled make *Areca catechu* L. (Arecaceae) seed size tablets. Finally, shade dry them.

Dosage: One tablet twice a day after meals

35. பிரமேகக்குளிகை – Piramehakkulihai (pp. 37, 38)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Acacia nilotica (L.) Delile	Resin	As required

Scientific / English name	Processed botanical drug	Amount
Commiphora mukul (Hook. ex Stocks) Engl.	Resin	As required
Ficus benghalensis L.	Bark	80 g
Limonia acidissima Groff	Resin	As required
Phoenix pusilla Gaertn.	Unripe fruit	80 g
Punica granatum L.	Root	80 g
Rivea ornata Choisy	Seed	As required
Salacia reticulata Wight	Bark	80 g
Senna auriculata (L.) Roxb.	Bark	80 g
Sesamum indicum L.	Seed	As required
Strychnos potatorum L.f.	Seed	As required
Terminalia arjuna (Roxb. ex DC.) Wight & Arn.	Bark	80 g
Zingiber officinale Roscoe	Rhizome	80 g
Graphite	NA	As required
Iron powder	NA	As required
Magnetite	NA	As required
Mercury	NA	As required
Red ochre	NA	As required
Stibnite	NA	As required
Sulphur	NA	As required

Scientific / English name	Processed botanical drug	Amount
Zinc	NA	As required

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable. Mix barks of *Ficus benghalensis*, *Salacia reticulata*, *Senna auriculata*, and *Terminalia arjuna*, *Punica granatum* root, *Phoenix pusilla* unripe fruit, and *Zingiber officinale* and pour water into the mixture. Then boil until reaching to one eighth of initial volume and filter.

Mix all the other ingredients together and grind the mixture with previously prepared decoction. Make *Punica granatum L.* (Lythraceae) seed size tablets and shade dry them.

Dosage: One tablet twice a day after meals

36. பிரமேகக்குளிகை – Piramehakkulihai (p. 38)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Cocos nucifera L.	Unripe fruit	10
Senna auriculata (L.) Roxb.	Seed	40 g
Buffalo buttermilk	NA	As required
Graphite	NA	8 g

Scientific / English name	Processed botanical drug	Amount
Magnetite	NA	8 g
Mercury	NA	8 g
Sulfur	NA	8 g

Method

Pulverise or scrape or press or crush all the other ingredients except buffalo buttermilk separately where applicable. Then mix them together and grind it with buffalo buttermilk. Make tablets and macerate them in buffalo buttermilk.

Dosage: As required twice a day after meals

37. பிரமேகக்குளிகை – Piramehakkulihai (p. 38)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Euphorbia hirta L.	Whole plant	1 Handful
Papaver somniferum L.	Latex	1952 g
Phyllanthus reticulatus Poir.	Tender leaf	Size of a small coconut
Buffalo buttermilk	NA	2400 ml

Method

Mix *Phyllanthus reticulatus* tender leaf and *Euphorbia hirta* whole plant mix together and close steam using buffalo buttermilk instead of water. Then add *Papaver somniferum* to it and grind the mixture. Then make *Caesalpinia bonduc* (L.) Roxb. (Fabaceae) seed size tablets and shade dry.

Dosage: One tablet twice a day after meals

38. பிரமேகக்குளிகை – Piramehakkulihai (p. 38)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Cordia dichotoma G.Forst.	Bark	Equal amount
Senna auriculata (L.) Roxb.	Flower	Equal amount
Senna auriculata (L.) Roxb.	Unripe fruit	Equal amount
Buffalo buttermilk	NA	As required
Buttermilk	NA	As required
Cow milk	NA	As required
Graphite	NA	20 g
Mercury	NA	80 g
Mercury	NA	20 g
Sulphur	NA	80 g

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable. Mix mercury (80 g), sulphur and *Cordia dichotoma* bark and pour cow milk into the mixture. Then boil the mixture. Melt graphite and mix with mercury (20 g). Mix *Senna auriculata* flower and unripe fruit together and close steam using buttermilk instead of water. Mix all three mixtures and grind with buffalo buttermilk. Make *Caesalpinia bonduc* (L.) Roxb. (Fabaceae) seed size tablets. Finally shade dry.

Dosage: One tablet twice a day after meals

39. பிரமேகக்குளிகை – Piramehakkulihai (p. 39)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Euphorbia antiquorum L.	Root	25 g
Musa × paradisiaca L.	Fruit	Equal amount
Papaver somniferum L.	Latex	Equal amount
Phyllanthus emblica L.	Fruit	25 g
Senna auriculata (L.) Roxb.	Seed	120 g
Senna auriculata (L.) Roxb.	Firewood	As required
Senna auriculata (L.) Roxb.	Seed	Equal amount
Sesamum indicum L. oil	Seed	Equal amount

Scientific / English name	Processed botanical drug	Amount
Zingiber officinale Roscoe	Rhizome	Equal amount
Graphite	NA	Equal amount
Honey	NA	Equal amount
Lead	NA	Equal amount
Magnetite	NA	25 g
Mercury	NA	Equal amount
Water	NA	Equal amount

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable. Mix magnetite, *Phyllanthus emblica* fruit, *Euphorbia antiquorum* root, and *Senna auriculata* seed in a rusted (reddish-yellow hydrated ferric oxides) bowl and pour *Sesamum indicum* oil while stirring. Then pour water (twice the amount of previously prepared mixture) into a clay pot and cover and tie a piece of cotton cloth on the mouth of the pot. Then place the mixture on the cloth and cover and tie the mixture with another piece of cotton cloth. Cover the covered mixture with another clay pot placing upside down and use *Senna auriculata* bark as firewood to boil the mixture until the whole water evaporates. Preserve the mixture in an oily container.

Dosage: 5 g twice a day after meals

40. பிரமேகக்குளிகை – Piramehakkulihai (p. 39)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Papaver somniferum L.	Latex	Equal amount
Senna auriculata (L.) Roxb.	Seed	As required
Zingiber officinale Roscoe	Rhizome	Equal amount
Graphite	NA	Equal amount
Honey	NA	As required
Lead	NA	Equal amount
Mercury	NA	Equal amount

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable. Melt lead and mix with all the other ingredients together. Then grind the mixture while adding honey and make *Solanum trilobatum* L. (Solanaceae) fruit size tablets.

Dosage: One tablet twice a day after meals

41. பிரமேகக்குளிகை – Piramehakkulihai (p. 39)

Ingredients

English name	Processed botanical drug	Amount
Ant egg	NA	As required
Buffalo milk	NA	As required
Milk	NA	As required

Method

Press ant egg and dry thoroughly. Then grind it with buffalo milk and leave it for a day. Grind it with milk and shade dry the mixture. Then grind and sift it.

Dosage: *Oryza sativa* L. (Poaceae) seed size three times a day

42. பிரமேகக்குளிகை – Piramehakkulihai (p. 39)

Ingredients

English name	Processed botanical drug	Amount
Ant egg	NA	As required
Orpiment	NA	As required

Method

Open dry roast ant egg and grind it. Then mix with purified arsenic trisulfide and grind the mixture.

Dosage: As required three times a day after meals

43. நாவல் நெய் - Naaval ney (pp. 44, 45)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abrus precatorius L.	Root	15 g
Acacia nilotica (L.) Delile	Bark	30 g
Aucklandia lappa DC.	Root	10 g
Cassia fistula L.	Bark	30 g
Ficus racemosa L.	Bark	30 g
Nymphaea pubescens Willd.	Rhizome	5 g
Salacia reticulata Wight	Bark	30 g
Senna auriculata (L.) Roxb.	Bark	30 g
Syzygium cumini (L.) Skeels	Bark	30 g
Ghee	NA	600 ml
Roche alum	NA	20 g

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable.

Mix barks of *Syzygium cumini*, *Ficus racemosa*, *Cassia fistula*, *Senna auriculata*, *Salacia reticulata*, and *Acacia nilotica*. Pour water to the mixture. Boil and add ghee. Then boil it again.

Mix *Nymphaea pubescens* rhizome, roots of *Aucklandia lappa* and *Abrus precatorius* and roche alum and grind with previously prepared mixture.

Dosage: Consume 5 g twice a day after meals

44. சந்தனாதியெண்ணெய் – Santhanaathiyennai (pp. 50, 51)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abelmoschus moschatus Medik.	Seed	30 g
Abies spectabilis (D. Don) Mirb.	Leaf	30 g
Aegle marmelos (L.) Corrêa	Root	240 g
Aloe vera (L.) Burm.f.	Leaf	3600 ml
Alpinia galanga (L.) Willd.	Rhizome	30 g
Alternanthera sessilis (L.) R.Br. ex DC.	Whole plant	3600 ml

Scientific / English name	Processed botanical drug	Amount
Aquilaria agallocha Roxb.	Wood	240 g
Asparagus racemosus Willd.	Rhizome juice	3600 ml
Aucklandia lappa DC.	Root	30 g
Cadaba fruticosa (L.) Druce	Leaf	3600 ml
Cedrus deodara (Roxb. ex D. Don) G. Don	Wood	30 g
Chrysopogon zizanioides (L.) Roberty	Root	240 g
Cinnamomum cappara-coronde Blume	Resin	As required
Cocos nucifera L.	Fruit water	3600 ml
Crocus sativus L.	Stigma	As required
Cycas circinalis L.	Flower	30 g
Elettaria cardamomum (L.) Maton	Dried fruit	30 g
Glycyrrhiza glabra L.	Root	30 g
Holarrhena pubescens Wall. ex G. Don	Seed	30 g
Hyoscyamus reticulatus L.	Seed	30 g
Kaempferia galanga L.	Rhizome	30 g
Magnolia champaca (L.) Baill. ex Pierre	Flower	30 g
Mesua ferrea L.	Flower	30 g
Moringa oleifera Lam.	Leaf juice	3600 ml
Myristica fragrans Houtt.	Leaf	30 g

Scientific / English name	Processed botanical drug	Amount
Myristica fragrans Houtt.	Mace	30 g
Myristica fragrans Houtt.	Seed	30 g
Nardostachys jatamansi (D. Don) DC.	Root	30 g
Nelumbo nucifera Gaertn.	Receptacle	240 g
Neopicrorhiza scrophulariiflora (Pennell) D. Y. Hong	Seed	30 g
Nymphaea pubescens Willd.	Rhizome	30 g
Pandanus odorifer (Forssk.) Kuntze	Flower	As required
Piper longum L.	Dried fruit	30 g
Piper nigrum L.	Dried fruit	30 g
Plectranthus hadiensis (Forssk.) Schweinf. ex Sprenger	Root	30 g
Pogostemon heyneanus Benth.	Leaf	30 g
Pterocarpus santalinus L.f.	Wood	30 g
Rubia cordifolia L.	Root	30 g
Rubia cordifolia L.	Stem	30 g
Santalum album L.	Wood	480 g
Senna tora (L.) Roxb.	Seed	30 g
Sesamum indicum L. oil	NA	7200 ml
Sida cordifolia L.	Root	240 g
Symplocos racemosa Roxb.	Bark	30 g

Scientific / English name	Processed botanical drug	Amount
Syzygium aromaticum (L.) Merr. & L. M. Perry	Flower bud	30 g
Tinospora sinensis (Lour.) Merr.	Stem	240 g
Trachyspermum roxburghianum (DC.) H. Wolff	Dried fruit	30 g
Trigonella foenum-graecum L.	Seed	30 g
Vitex negundo L.	Root juice	3600 ml
Zingiber officinale Roscoe	Dried rhizome	30 g
Bitumen	NA	30 g
Dried cow gallstone	NA	As required
Male deer musk	NA	As required
Stibnite	NA	30 g
Water	NA	4200 ml

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable.

Mix woods of *Aquilaria agallocha* and *Santalum album*, *Aegle marmelos* root, *Nelumbo nucifera* receptacle, *Tinospora sinensis* stem juice, roots of *Sida cordifolia* and *Chrysopogon zizanioides* together and pour water to the mixture. Boil and filter it.

Mix *Myristica fragrans* mace, rhizomes of *Kaempferia galanga*, *Alpinia galanga*, and *Nymphaea pubescens*, roots of *Nardostachys jatamansi* , *Plectranthus hadiensis*, *Rubia cordifolia*, *Glycyrrhiza glabra*, and *Aucklandia lappa*, flowers of *Cycas circinalis*, *Mesua ferrea*, and *Magnolia champaca*, dried fruits of *Elettaria cardamomum*, *Trachyspermum roxburghianum*, *Piper nigrum*, and *Piper longum*, leaves of *Pogostemon heyneanus*, *Myristica fragrans*, and *Abies spectabilis*, seeds of *Abelmoschus moschatus*, *Holarrhena pubescens*, *Hyoscyamus reticulatus*, *Trigonella foenum-graecum*, *Senna tora*, *Neopicrorhiza scrophulariiflora*, and *Myristica fragrans*, *Rubia cordifolia* stem, *Symplocos racemosa* bark, woods of *Cedrus deodara* and *Pterocarpus santalinus*, *Zingiber officinale* dried rhizome, *Syzygium aromaticum* flower bud, bitumen, and stibnite together and mix this mixture with previously prepared decoction. Macerate it.

Then mix *Alternanthera sessilis* whole plant juice, *Vitex negundo* root juice, *Asparagus racemosus* rhizome juice, leaf juices of *Aloe vera*, *Moringa oleifera*, and *Cadaba fruticose* and *Cocos nucifera* fruit water together and add this mixture and sesame oil to macerated mixture.

After that boil until reaching wax state and mix *Pandanus odorifer* flower, *Crocus sativus* stigma, *Cinnamomum cappara-coronde* resin, dried cow gallstone and male deer musk together. Then add to the boiled mixture before it cooled.

Dosage: Apply as required all over the body including head once a day and have a shower.

45. வச்சிரசிந்தாமணி இரசாயனம் - Vachchirasinthaamani irasaayanam (pp. 45, 46)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abutilon indicum (L.) Sweet	Root	400 g
Acacia nilotica (L.) Delile	Bark	400 g
Bombax ceiba L.	Bark	400 g
Bombax ceiba L.	Resin	400 g
Cordia dichotoma G. Forst.	Bark	400 g
Euphorbia hirta L.	Whole plant	400 g
Ficus racemosa L.	Bark	400 g
Ficus racemosa L.	Latex	400 g
Gardenia crameri Tirveng.	Resin	400 g
Gymnosporia emarginata (Willd.) Thwaites	Bark	400 g
Lannea coromandelica (Houtt.) Merr.	Bark	400 g
Limonia acidissima Groff	Resin	400 g
Murraya koenigii (L.) Spreng.	Leaf	4000 g
Murraya koenigii (L.) Spreng.	Leaf juice	2400 ml
Phyllanthus amarus Schumach. & Thonn.	Root	400 g
Phyllanthus reticulatus Poir.	Bark	400 g
Piper longum L.	Dried fruit	400 g

Scientific / English name	Processed botanical drug	Amount
Piper nigrum L.	Dried fruit powder	400 g
Punica granatum L.	Fruit juice	600 ml
Saccharum officinarum L. jaggery	NA	200 g
Salacia reticulata Wight	Bark	400 g
Terminalia arjuna (Roxb. ex DC.) Wight & Arn.	Bark	400 g
Zingiber officinale Roscoe	Dried rhizome	200 g
Bitumen	NA	20 g
Honey	NA	600 ml
Kerria lacca	NA	400 g
Mercury	NA	400 g
Mica	NA	200 g
Water	NA	230.4 l

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable.

Mix mercury, barks of *Ficus racemosa*, *Cordia dichotoma*, *Acacia nilotica*, *Salacia reticulata*, *Bombax ceiba*, *Terminalia arjuna*, *Gymnosporia emarginata*, *Phyllanthus reticulatus*, and *Lannea coromandelica*, roots of *Phyllanthus amarus, Abutilon indicum*, and

Euphorbia hirta, resins of *Bombax ceiba*, *Limonia acidissima*, *Bauhinia variegata*, and *Gardenia crameri* and *Kerria lacca*, *Zingiber officinale* dried rhizome, *Piper longum* dried fruit, and *Murraya koenigii* leaf. Pour water into the mixture and boil.

Then pour *Murraya koenigii* leaf juice and *Punica granatum* fruit juice into the mixture. Add *Piper nigrum* dried fruit powder, bitumen, mica, and *Saccharum officinarum* crushed jaggery. Pour honey and boil until reaching wax state.

Dosage: 1250 mg twice a day after meals for 40 days

46. பிரமேகச்சந்தனாதியெண்ணெய் – Piramehachchanthanaathiyennai (pp. 51, 52)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abelmoschus moschatus Medik.	Seed	15 g
Aegle marmelos (L.) Corrêa	Root	1 Handful
Alternanthera sessilis (L.) R.Br. ex DC.	Whole plant	1 Handful
Asparagus racemosus Willd.	Rhizome juice	600 ml
Aucklandia lappa DC.	Root	15 g
Cajanus cajan (L.) Millsp.	Root macerated water	600 ml
Cannabis sativa L.	Purified leaf	1 Handful
Cardiospermum halicacabum L.	Whole plant	1 Handful
Cedrus deodara (Roxb. ex D. Don) G. Don	Wood	15 g

Scientific / English name	Processed botanical drug	Amount
Cedrus deodara (Roxb. ex D. Don) G. Don	Wood	160 g
Centipeda minima (L.) A. Braun & Asch.	Whole plant	15 g
Chrysopogon zizanioides (L.) Roberty	Root	40 g
Cinnamomum verum J. Presl	Bark	15 g
Cuminum cyminum L.	Dried fruit	15 g
Curculigo orchioides Gaertn.	Rhizome	1 Handful
Cyanthillium cinereum (L.) H. Rob.	Whole plant	1 Handful
Cyperus mitis Steud.	Rhizome	1 Handful
Eclipta prostrata (L.) L.	Whole plant	1 Handful
Elettaria cardamomum (L.) Maton	Dried fruit	15 g
Ficus racemosa L.	Bark	15 g
Glycyrrhiza glabra L.	Root	15 g
Gmelina asiatica L.	Root	1 Handful
Hemidesmus indicus (L.) R. Br. ex Schult.	Root	1 Handful
Holarrhena pubescens Wall. ex G. Don	Seed	15 g
Hybanthus enneaspermus (L.) F. Muell.	Whole plant	1 Handful
Magnolia champaca (L.) Baill. ex Pierre	Flower	15 g
Mesua ferrea L.	Flower	15 g
Mollugo cerviana (L.) Ser.	Whole plant	1 Handful

Scientific / English name	Processed botanical drug	Amount
Myristica fragrans Houtt.	Leaf	15 g
Myristica fragrans Houtt.	Seed	15 g
Nardostachys jatamansi (D. Don) DC.	Root	15 g
Nelumbo nucifera Gaertn.	Receptacle juice	600 ml
Nymphaea pubescens Willd.	Rhizome	15 g
Pavonia odorata Willd.	Root	1 Handful
Phoenix pusilla Gaertn.	Flower	15 g
Phyllanthus amarus Schumach. & Thonn.	Whole plant	1 Handful
Phyllanthus emblica L.	Fruit	15 g
Phyllanthus emblica L.	Fruit juice	600 ml
Phyllanthus emblica L. macerated water	Root	600 ml
Piper longum L.	Dried fruit	15 g
Plectranthus hadiensis (Forssk.) Schweinf. ex Sprenger	Root	40 g
Pogostemon heyneanus Benth.	Leaf	15 g
Pterocarpus santalinus L.f.	Wood	40 g
Ricinus communis L.	Root	1 Handful
Rubia cordifolia L.	Bulb	15 g
Salacia reticulata Wight macerated water	Root	600 ml
Santalum album L.	Wood	160 g

Scientific / English name	Processed botanical drug	Amount
Sesamum indicum L. oil	Seed	As required
Sida cordifolia L.	Root	1 Handful
Sterculia foetida L.	Bark	15 g
Stereospermum chelonoides (L.f.) DC.	Root	1 Handful
Syzygium aromaticum (L.) Merr. & L. M. Perry	Dried flower bud	15 g
Terminalia bellirica (Gaertn.) Roxb.	Fruit	15 g
Terminalia chebula Retz.	Fruit	15 g
Tinospora sinensis (Lour.) Merr.	Stem	1 Handful
Tribulus terrestris L.	Whole plant	1 Handful
Trigonella foenum-graecum L.	Seed	15 g
Withania somnifera (L.) Dunal	Rhizome	1 Handful
Butter	NA	15 g
Civet musk	NA	30 g
Cow milk	NA	600 ml
Dried cow gallstone	NA	15 g
Kerria lacca macerated water	NA	600 ml
Water	NA	600 ml

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable.

Mix woods of *Santalum album*, *Cedrus deodara* (160 g), and *Pterocarpus santalinus* and pour water into the mixture. Then boil the mixture.

Mix *Phyllanthus emblica* fruit juice, *Cannabis sativa* purified leaf, macerated water of *Salacia reticulata*, *Phyllanthus emblica*, (600 ml) and *Cajanus cajan*, rhizomes of *Cyperus mitis*, *Asparagus racemosus*, *Curculigo orchioides*, and *Withania somnifera*, roots of *Gmelina asiatica*, *Ricinus communis*, *Sida cordifolia*, *Pavonia odorata*, *Hemidesmus indicus*, *Aegle marmelos*, *Stereospermum chelonoides*, *Plectranthus hadiensis*, and *Chrysopogon zizanioides*, *Tinospora sinensis* stem, whole plants of *Phyllanthus amarus*, *Tribulus terrestris*, *Cardiospermum halicacabum*, *Mollugo cerviana*, *Alternanthera sessilis*, *Cyanthillium cinereum*, *Hybanthus enneaspermus*, and *Eclipta prostrata*, *Nelumbo nucifera* receptacle juice, *Phoenix pusilla* fruit juice, *Kerria lacca* macerated water, and cow milk and pour water into the mixture. Then boil the mixture. Then mix this decoction with previously prepared decoction and pour sesame oil.

After that mix barks of *Sterculia foetida*, *Ficus racemosa*, and *Cinnamomum verum*, *Syzygium aromaticum* bud, *Rubia cordifolia* bulb, dried fruits of *Cuminum cyminum*, *Elettaria cardamomum* and *Piper longum*, flowers of *Mesua ferrea* and *Magnolia champaca*, fruits of *Phyllanthus emblica* (15 g), *Terminalia chebula*, and *Terminalia bellirica* leaves of *Pogostemon heyneanus* and *Myristica fragrans*, *Nymphaea pubescens* rhizome, roots of *Glycyrrhiza glabra*, *Nardostachys jatamansi* , and *Aucklandia lappa*, seeds of *Trigonella foenum-graecum*, *Holarrhena pubescens*, *Myristica fragrans*, *Abelmoschus moschatus*, *Centipeda minima* whole plant, *Cedrus deodara* wood (15 g), and butter and add to the decoction mixture. Grind and filter it. Finally sprinkle dried cow gallstone and civet musk and preserve.

Dosage: Apply as required all over the body (from head to toe) once a day and have a shower

47. நீரிழிவுச்சந்தனாதியெண்ணெய் – Neerilivuchchanthanaathiyennai (pp. 54, 55, 56)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abelmoschus moschatus Medik.	Seed	30 g
Aegle marmelos (L.) Corrêa	Root	240 g
Aloe vera (L.) Burm.f.	Leaf juice	3600 ml
Alpinia calcarata (Haw.) Roscoe	Rhizome	30 g
Alternanthera sessilis (L.) R.Br. ex DC.	Whole plant	240 g
Alternanthera sessilis (L.) R.Br. ex DC.	Leaf juice	3600 ml
Artocarpus heterophyllus Lam.	Mature leaf	30 g
Asparagus racemosus Willd.	Rhizome	240 g
Asparagus racemosus Willd.	Leaf juice	3600 ml
Aucklandia lappa DC.	Root	240 g
Cadaba fruticosa (L.) Druce	Leaf juice	3600 ml
Cedrus deodara (Roxb. ex D. Don) G. Don	Wood	30 g
Cheilocostus speciosus (J. Koenig) C. D. Specht	Root	30 g
Chrysopogon zizanioides (L.) Roberty	Root	240 g

Scientific / English name	Processed botanical drug	Amount
Chrysopogon zizanioides (L.) Roberty	Root	30 g
Cinnamomum cappara-coronde Blume	Resin	As required
Coccinia grandis (L.) Voigt	Leaf juice	3600 ml
Cocos nucifera L.	Tender fruit water	7200 ml
Crocus sativus L.	Stigma	30 g
Crocus sativus L.	Stigma	As required
Cyperus rotundus L.	Rhizome	240 g
Cyperus rotundus L.	Rhizome	30 g
Elettaria cardamomum (L.) Maton	Dried fruit	30 g
Erythrina variegata L.	Leaf juice	3600 ml
Glycyrrhiza glabra L.	Root	30 g
Hemidesmus indicus (L.) R. Br. ex Schult.	Root	240 g
Holarrhena pubescens Wall. ex G. Don	Seed	30 g
Hyoscyamus reticulatus L.	Seed	30 g
Ipomoea aquatica Forssk.	Leaf	30 g
Ipomoea littoralis Blume	Leaf juice	3600 ml
Kaempferia galanga L.	Rhizome	30 g
Mesua ferrea L.	Flower	30 g
Mukia maderaspatana (L.) M. Roem.	Leaf	30 g

Scientific / English name	Processed botanical drug	Amount
Myristica fragrans Houtt.	Leaf	30 g
Myristica fragrans Houtt.	Mace	30 g
Myristica fragrans Houtt.	Seed	30 g
Nardostachys jatamansi (D. Don) DC.	Root	30 g
Nelumbo nucifera Gaertn.	Receptacle	240 g
Neopicrorhiza scrophulariiflora (Pennell) D. Y. Hong	Root	30 g
Nymphaea pubescens Willd.	Rhizome	30 g
Pandanus odorifer (Forssk.) Kuntze	Flower petal	As required
Plectranthus hadiensis (Forssk.) Schweinf. ex Sprenger	Root	30 g
Pogostemon heyneanus Benth.	Leaf	30 g
Pterocarpus santalinus L.f.	Wood	30 g
Rubia cordifolia L.	Stem	30 g
Santalum album L.	Wood	240 g
Santalum album L.	Wood	30 g
Senna tora (L.) Roxb.	Seed	30 g
Sesamum indicum L. oil	Seed	7200 ml
Shorea robusta Gaertn	Resin	30 g
Sida cordifolia L.	Root	240 g
Syzygium aromaticum (L.) Merr. & L. M. Perry	Dried flower bud	30 g

Scientific / English name	Processed botanical drug	Amount
Tinospora sinensis (Lour.) Merr.	Stem	240 g
Trigonella foenum-graecum L.	Seed	30 g
Vitex negundo L.	Leaf juice	3600 ml
Bitumen	NA	30 g
Civet musk	NA	30 g
Cow milk	NA	30 g
Dried cow gallstone	NA	30 g
Male deer musk	NA	30 g
Water	NA	As required

Method

Pulverise or scrape or press or crush all the ingredients separately where applicable.

Mix roots of *Sida cordifolia*, *Aucklandia lappa*, *Chrysopogon zizanioides* (240 g), *Aegle marmelos*, and *Hemidesmus indicus*, rhizomes of *Asparagus racemosus* and *Cyperus rotundus* (240 g), *Santalum album* wood (240 g), *Alternanthera sessilis* whole plant, *Tinospora sinensis* stem, *Nelumbo nucifera* receptacle and pour water into the mixture. Boil until reaching one eighth of the initial volume.

Mix *Cocos nucifera* tender fruit water, *Sesamum indicum* oil, and leaf juices of *Coccinia grandis*, *Ipomoea littoralis*, *Alternanthera sessilis*, *Asparagus racemosus*, *Aloe vera*, *Cadaba fruticosa*, *Erythrina variegata*, and *Vitex negundo* and pour into the previously prepared decoction.

Mix bitumen, *Syzygium aromaticum* dried flower bud, *Elettaria cardamomum* dried fruit, *Mesua ferrea* flower, leaves of *Ipomoea aquatica*, *Mukia maderaspatana*, Myristica *fragrans* and *Pogostemon heyneanus*, *Artocarpus heterophyllus* mature leaf, *Myristica fragrans* mace, *Shorea robusta* resin, rhizomes of *Kaempferia galanga*, *Nymphaea pubescens*, *Alpinia calcarata*, and *Cyperus rotundus* (30 g), roots of *Chrysopogon zizanioides* (30 g), *Nardostachys jatamansi*, *Cheilocostus speciosus*, *Plectranthus hadiensis*, *Neopicrorhiza scrophulariiflora*, and *Glycyrrhiza glabra*, seeds of *Myristica fragrans*, *Abelmoschus moschatus*, *Hyoscyamus reticulatus*, *Trigonella foenum-graecum*, *Holarrhena pubescens*, and *Senna tora*, *Rubia cordifolia* stem, *Crocus sativus* stigma (30 g), and woods of *Santalum album* (30 g), *Cedrus deodara*, and *Pterocarpus santalinus* and mix with previously prepared decoction.

Blend with cow milk until reaching mustard seed particle size and spread *Pandanus odorifer* flower petals over it. Then filter it.

Mix male deer musk, dried cow gallstone, and civet musk, *Cinnamomum cappara-coronde* resin, and *Crocus sativus* stigma and add to the filtered mixture. Mix while stirring.

Dosage: Apply as required all over the body (from head to toe) once a day and have a shower

48. காந்தரசக்குளிகை – Kaantharasakkulihai (p. 36)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Cocos nucifera L.	Flower	40 g
Cocos nucifera L.	Unripe fruit	4
Senna auriculata (L.) Roxb.	Seed	40 g
Buffalo buttermilk	NA	As required
Magnetite	NA	40 g
Mercury	NA	80 g

Method

Mix all the other ingreadients except buffalo buttermilk. Then grind the mixture with buffalo buttermilk and make 244 g size tablets. Finally shade dry.

Dosage: One tablet twice a day after meals

2. Seharaasasehara Treatment (செகராசசேகர வைத்தியம் - Seharaasasehara Vaiththiyam)

Seharaasasehara Treatment has 8 preparations used to treat diabetes in Sri Lankan Siddha Medicine. Details information of these preparations are described further.

49. குடிநீர் - Kudineer (vs 25; p. 205)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Cassia fistula L.	Bark	30 g
Ficus racemosa L.	Bark	30 g
Salacia reticulata Wight	Bark	30 g
Senna auriculata (L.) Roxb.	Bark	30 g
Syzygium cumini (L.) Skeels	Bark	30 g
Water	NA	As required

Method

Macerate all the ingredients in water overnight and filter. Then boil it.

Dosage: As required twice a day before meals

50. குடிநீர் – Kudineer (vss 30, 31; p. 205)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Syzygium cumini (L.) Skeels	Mature bark	100 g
Magnetite	NA	50 g
Reservoir water	NA	1200 ml

Method

Pulverise *Syzygium cumini* mature bark and crush magnetite. Mix both of them together and pour reservoir water. Finally boil thoroghly until the whole water evaporates.

Dosage: As required twice a day after meals

51. குடிநீர் – Kudineer (vss 32, 33; p. 205)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Abrus precatorius L.	Root	Equal amount
Acacia nilotica (L.) Delile	Bark	Equal amount
Aloe vera (L.) Burm.f.	Dried leaf pulp	Equal amount

Scientific / English name	Processed botanical drug	Amount
Anacardium occidentale L.	Fruit	Equal amount
Areca catechu L.	Seed	Equal amount
Ficus racemosa L.	Bark	Equal amount
Glycyrrhiza glabra L.	Root	Equal amount
Nelumbo nucifera Gaertn.	Rhizome	Equal amount
Nymphaea pubescens Willd.	Rhizome	Equal amount
Phoenix dactylifera L.	Fruit	Equal amount
Phyllanthus emblica L.	Dried fruit	Equal amount
Saccharum officinarum L. jaggery	NA	As required
Salacia reticulata Wight	Bark	Equal amount
Santalum album L.	Wood	Equal amount
Senna auriculata (L.) Roxb.	Root	Equal amount
Syzygium cumini (L.) Skeels	Bark	Equal amount
Terminalia chebula Retz.	Dried fruit	Equal amount
Zingiber officinale Roscoe	Dried rhizome	Equal amount
Water	NA	As required

Method

Mix all the ingredients together and pour water to the mixture. Then boil it.

Dosage: As required twice a day before meals

52. தூள் – Thool (vs 40; p. 205)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Senna auriculata (L.) Roxb.	Mature root	Equal amount
Sesamum indicum L.	Mature seed	Equal amount
Oryza sativa L.	Seed	Equal amount

Method

Pulverise all the ingredients separately and mix them together.

Dosage: 625 mg three times a day after meals

53. தூள் – Thool (vs 41; p. 207)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Senna auriculata (L.) Roxb.	Root bark	5 g

Method

Pulverise *Senna auriculata* root.

Dosage: 625 mg three times a day after meals

54. நீரிழிவுக்கு வங்கசெந்தூரம் - Neerilivukku vangasenthooram (vss 43, 44; pp. 207, 208)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Euphorbia antiquorum L.	Latex	5 g
Tamarindus indica L.	Seed skin	5 g
Tin	NA	5 g

Method

Mix tin with *Euphorbia antiquorum* latex and melt it by heating. Grind *Tamarindus indica* seed skin and mix it with previously prepared mixture. Place into a clay pot and place another clay pot (as a lid to cover the pot) on top the clay pot with mixtures. Place this set up in a furnace and burn it. Once cooled the powder would appear as red.

Dosage: 1.25 mg twice a day after meals

55. பிரமேக நீரிழிவுக்கு வெட்டுமாறன் தூள் - Pirameha neerilivukku Vettumaaran thool (vs 45; p. 208)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Aconitum heterophyllum Wall. ex Royle	Root	5 g
Cannabis sativa L.	Purified leaf	5 g
Cuminum cyminum L.	Dried fruit	5 g
Datura metel L.	Seed	5 g
Elettaria cardamomum (L.) Maton	Dried fruit	5 g
Foeniculum vulgare Mill.	Dried fruit	5 g
Myristica fragrans Houtt.	Mace	5 g
Myristica fragrans Houtt.	Seed	5 g
Myroxylon balsamum (L.) Harms	Resin	5 g
Papaver somniferum L.	Latex	5 g
Phyllanthus emblica L.	Dried fruit	5 g
Piper longum L.	Dried fruit	5 g
Senna auriculata (L.) Roxb.	Whole plant	5 g
Syzygium aromaticum (L.) Merr. & L. M. Perry	Flower bud	5 g
Trachyspermum roxburghianum (DC.) H. Wolff	Dried fruit	5 g
Bitumen	NA	5 g
Magnetite	NA	5 g

Method

Pulverise and sift all the ingredients separately. Then mix them together.

Dosage: 5 g three times a day after meals

56. நீரிழிவுக்கு வங்க செந்தூரம் - Neerilivukku vanga (vs 42; p. 207)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Acacia nilotica (L.) Delile	Bark	Equal amount
Achyranthes aspera L.	Whole plant	Equal amount
Aloe vera (L.) Burm.f.	Root	Equal amount
Piper nigrum L.	Dried fruit	Equal amount
Tin	NA	Equal amount

Method

Mix tin and *Aloe vera* (L.) Burm.f. root together and burn the mixture. Then pulverise all the other ingredients separately and mix them together. Finally add previously burnt ash into this mixture and open dry roast while stirring.

Dosage: As required twice a day after meals

3. சித்த ஔடத செய்முறை - Siththa Audatha Seimurai – Siddha Medicinal Procedure

This source contains 4 antidiabetic preparations of Sri Lankan SM.

57. அமுது சர்க்கரைச்சூரணம் (ஏட்டுப்பிரதி) - Amuthu Sarkkaraichchooranam (Ettuppirathi) (p. 14)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Aconitum heterophyllum Wall. ex Royle	Root	25 g
Cannabis sativa L.	Seed	6.25 g
Cheilocostus speciosus (J. Koenig) C. D. Specht	Root	25 g
Cuminum cyminum L.	Dried fruit	25 g
Elettaria cardamomum (L.) Maton	Dried fruit	25 g
Glycyrrhiza glabra L.	Root	25 g
Hyoscyamus reticulatus L.	Seed	25 g
Myristica fragrans Houtt.	Leaf	25 g
Myristica fragrans Houtt.	Mace	25 g
Myristica fragrans Houtt.	Seed	25 g
Nelumbo nucifera Gaertn.	Seed	100
Papaver somniferum L.	Latex	6.25 g
Senna auriculata (L.) Roxb.	Bark	25 g

Scientific / English name	Processed botanical drug	Amount
Senna auriculata (L.) Roxb.	Flower	25 g
Senna auriculata (L.) Roxb.	Root	25 g
Senna auriculata (L.) Roxb.	Seed	25 g
Senna auriculata (L.) Roxb.	Tender leaf	25 g
Senna auriculata (L.) Roxb.	Unripe fruit	25 g
Syzygium aromaticum (L.) Merr. & L.M. Perry	Flower bud	25 g
Tinospora sinensis (Lour.) Merr.	Stem	1500 g
Trachyspermum roxburghianum (DC.) H. Wolff	Dried fruit	25 g
Civet musk	NA	6.25 g
Male deer musk	NA	6.25 g

Method

Pulverise *Senna auriculata* bark, *Syzygium aromaticum* flower bud, dried fruits of *Cuminum cyminum*, *Trachyspermum roxburghianum* and *Elettaria cardamomum*, *Senna auriculata* flower, *Myristica fragrans* leaf, *Myristica fragrans* mace, roots of *Cheilocostus speciosus*, *Glycyrrhiza glabra*, *Senna auriculata*, and *Aconitum heterophyllum*, seeds of *Senna auriculata*, *Myristica fragrans*, *Nelumbo nucifera*, and *Hyoscyamus reticulatus*, and tender leaf and unripen fruit of *Senna auriculata* separately and mix them together.

Then pulverise male deer musk, civet musk, *Papaver somniferum* resin, *Cannabis sativa* seed, and *Tinospora sinensis* stem together and mix with previously prepared mixture. Finally grind the mixture.

Dosage: 125 – 250 g twice a day after meals

58. நந்தீசுர சிந்தாமணி (சுதேச வைத்திய ஔடதத்திரட்டு) - Nantheesura Sinthaamani (Suthesa Vaithiya Audathaththirattu) (p. 20)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Allium sativum L.	Bulb	5 g
Anacyclus pyrethrum (L.) Lag.	Root	5 g
Anethum graveolens L.	Seed	5 g
Cannabis sativa L.	Purified leaf	5 g
Celastrus paniculatus Willd.	Seed	5 g
Cheilocostus speciosus (J. Koenig) C.D.Specht	Root	5 g
Crocus sativus L.	Stigma	5 g
Cuminum cyminum L.	Dried fruit	5 g
Datura metel L.	Seed	5 g
Elettaria cardamomum (L.) Maton	Dried fruit	5 g
Ferula assa-foetida L.	Resin	5 g
Glycyrrhiza glabra L.	Root	5 g
Holarrhena pubescens Wall. ex G. Don	Seed	5 g
Hyoscyamus reticulatus L.	Seed	10 g

Scientific / English name	Processed botanical drug	Amount
Madhuca longifolia (J. Koenig ex L.) J. F. Macbr.	Flower	5 g
Mesua ferrea L.	Flower	5 g
Myristica fragrans Houtt.	Mace	5 g
Myristica fragrans Houtt.	Seed	5 g
Neopicrorhiza scrophulariiflora (Pennell) D. Y. Hong	Root	5 g
Nigella sativa L.	Seed	5 g
Panicum antidotale Retz.	Dried fruit	5 g
Papaver somniferum L.	Purified latex	5 g
Piper chuvya Hunter ex C. DC.	Root	5 g
Piper cubeba L.f.	Fruit	5 g
Piper longum L.	Dried fruit	5 g
Rotheca serrata (L.) Steane & Mabb.	Root	5 g
Syzygium aromaticum (L.) Merr. & L. M. Perry	Flower bud	5 g
Trachyspermum roxburghianum (DC.) H. Wolff	Dried fruit	5 g
Zingiber officinale Roscoe	Rhizome	5 g
Purified Arsenic	NA	5 g
Purified borax	NA	5 g
Purified cinnabar	NA	5 g
Purified magnetite	NA	5 g

Scientific / English name	Processed botanical drug	Amount
Rock salt	NA	5 g

Method

Pulverise or scrape or press or crack all the ingredients separately where applicable and mix them together. Finally, open dry roast the mixture seven times, while stirring.

Dosage: One tablet twice a day after meals

59. பூரணச்சந்திராதி மாத்திரை (இருபாலைச்செட்டியார் வைத்திய விளக்கம்) Pooranachchanthiraathi Maaththirai (Irupaalaichchettiyar Vaiththiya Vilakkam) (p. 41)

Ingredients

Scientific / English name / English name	Processed botanical drug	Amount
Aconitum heterophyllum Wall. ex Royle	Root	5 g
Alpinia calcarata (Haw.) Roscoe	Rhizome	5 g
Alternanthera sessilis (L.) R.Br. ex DC.	Leaf juice	500 ml
Anacyclus pyrethrum (L.) Lag.	Root	5 g
Cedrus deodara (Roxb. ex D. Don) G. Don	Wood	5 g
Cinnamomum verum J. Presl	Bark	5 g
Cuminum cyminum L.	Dried fruit	5 g

Scientific / English name / English name	Processed botanical drug	Amount
Elettaria cardamomum (L.) Maton	Dried fruit	5 g
Glycyrrhiza glabra L.	Root	5 g
Hemidesmus indicus (L.) R. Br. ex Schult.	Root bark	5 g
Myristica fragrans Houtt.	Seed	5 g
Nervilia concolor (Blume) Schltr.	Whole plant	5 g
Piper cubeba L.f.	Dried fruit	5 g
Spermacoce hispida L.	Seed	5 g
Syzygium aromaticum (L.) Merr. & L. M. Perry	Flower bud	5 g
Tinospora sinensis (Lour.) Merr.	Stem juice	500 ml
Trigonella foenum-graecum L.	Seed	5 g
Zingiber officinale Roscoe	Dried rhizome	5 g
Beryl	NA	80 g
Rhinoceros horn	NA	160 g

Method

Pulverise or scrape or press or crack all the ingredients separately where applicable and mix them together except *Tinospora sinensis* stem, *Alternanthera sessilis* leaf, and *Hybanthus enneaspermus* whole plant.

Grind the mixture with *Tinospora sinensis* stem juice for a day followed by *Alternanthera sessilis* leaf juice, and *Hybanthus enneaspermus* whole plant juice each per day. Finally make *Solanum trilobatum L.* (Solanaceae) fruit size tablets and dry them.

Dosage: One tablet twice a day after meals

60. மிருத்த சஞ்சீவினி மாத்திரை (இருபாலைச்செட்டியார் வைத்திய விளக்கம்) - Miruththa Sanjeevini Maaththirai (Irupaalaichchettiyaar Vaiththiya Vilakkam) (pp. 47, 48)

Ingredients

Scientific / English name	Processed botanical drug	Amount
Aconitum heterophyllum Wall. ex Royle	Root	5 g
Aegle marmelos (L.) Corrêa	Root	5 g
Alpinia calcarata (Haw.) Roscoe	Rhizome	5 g
Alpinia galanga (L.) Willd.	Rhizome	5 g
Anacyclus pyrethrum (L.) Lag.	Root	5 g
Cedrus deodara (Roxb. ex D. Don) G. Don	Wood	5 g
Cheilocostus speciosus (J. Koenig) C. D. Specht	Root	5 g
Cinnamomum cappara-coronde Blume	Resin	5 g
Cinnamomum verum J. Presl	Bark	5 g
Cinnamomum verum J. Presl	Bark	5 g

Scientific / English name	Processed botanical drug	Amount
Crocus sativus L.	Stigma	5 g
Cuminum cyminum L.	Seed	5 g
Elaeocarpus tuberculatus Roxb.	Seed	5 g
Elettaria cardamomum (L.) Maton	Dried fruit	5 g
Glycyrrhiza glabra L.	Root	5 g
Justicia adhatoda L.	Root	60 g
Magnolia champaca (L.) Baill. ex Pierre	Flower	5 g
Mesua ferrea L.	Flower	5 g
Myristica fragrans Houtt.	Mace	5 g
Myristica fragrans Houtt.	Seed	5 g
Neopicrorhiza scrophulariiflora (Pennell) D. Y. Hong	Root	5 g
Nigella sativa L.	Seed	5 g
Piper cubeba L.f.	Dried fruit	5 g
Piper longum L.	Dried fruit	5 g
Piper nigrum L.	Dried fruit	5 g
Rotheca serrata (L.) Steane & Mabb.	Root	5 g
Santalum album L.	Wood	5 g
Strychnos potatorum L.f.	Seed	5 g
Syzygium aromaticum (L.) Merr. & L. M. Perry	Flower bud	5 g

Scientific / English name	Processed botanical drug	Amount
Terminalia chebula Retz.	Seed	5 g
Zingiber officinale Roscoe	Dried rhizome	5 g
Deer horn calx	NA	5 g
Dried cow gallstone	NA	5 g
Gold calx	NA	5 g
Purified	NA	5 g
Purified cinnabar	NA	50 g
Purified pearl	NA	5 g
Red coral	NA	5 g
Rhinoceros horn	NA	5 g
Rock salt	NA	5 g
Silver calx	NA	5 g
Water	NA	

Method

Pulverise or scrape or press or crack all the other ingredients separately where applicable and mix the ingredients together except roots of *Aegle marmelos* and *Justicia adhatoda*, *Piper longum* dried fruit, *Magnolia champaca* flower, barks of *Cinnamomum verum* and *Santalum album*, and purified cinnabar.

Pour water to *Justicia adhatoda* root and boil it until reaching one eighth of the initial volume. Grind previously prepared mixture with this decoction for a day followed by decoctions of *Piper longum* dried fruit, *Aegle marmelos* root, *Magnolia champaca* flower, and *Santalum album* bark per day.

Then add purified cinnabar to the ground mixture and grind it with *Cinnamomum verum* bark decoction for 12 hours. Finally make *Vigna radiata* (L.) R. Wilczek (Fabaceae) seed size tablets and shade dry them.

Dosage: One tablet twice a day after meals

Note: If this preparation taken with appropriate adjuvant, dead could be alive.

Appendix C

Pharmacology studies of reviewed plants

Table C.1. Detailed information of pharmacological and clinical studies of reviewed plants

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Abelmoschus moschatus Medik.	Malvaceae	*In vivo*	AE	Myricetin	SID	1 mg/kg	30 min	Liu I.M. et al. (2005)
Abrus precatorius L.	Fabaceae	*In vitro*	LE	Lupenone	AAI	31 µM	NA	Yonemoto et al. (2014)
		In vitro	LE	24-methylenecycloartenone	AAI	0.6 mM	NA	Yonemoto et al. (2014)
		In vitro	LE	Luteolin	AAI	3.1 mM	NA	Yonemoto et al. (2014)
		In vitro	LE	50% Methanol	AAI	NS	NA	Yonemoto et al. (2014)
		In vitro	SE	Methanol	AAI	1 mg/ml	NA	Vadivel et al. (2011a)
		In vitro	SE	Methanol	AAI	1 mg/ml	NA	Vadivel et al. (2011a)
		In vitro	SE	Methanol	AGI	1 mg/ml	NA	Vadivel et al. (2011a)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vitro	SE	Methanol	AAI	NS	NA	Vadivel et al. (2011b)
		In vitro	SE	Methanol	AGI	1 mg/ml	NA	Vadivel et al. (2011b)
Abutilon indicum (L.) Sweet	Malvaceae	*In vivo*	LE	99.5% Methanol	NOR, SID	500 mg/kg	2 h	Adisakwattana et al. (2009)
		In vivo	LE	Aqueous	NOR	400 mg/kg	4 h	Seetharam et al. (2002)
		In vivo	LE, TW, RO	Ethanol	NOR	400 mg/kg	4 h	Krisanapun et al. (2011)
		In vivo	LE, TW, RO	Aqueous	SID	NS	2 week	Krisanapun et al. (2010)
		In vivo	LE, TW, RO	Aqueous	NOR, SID	0.5 g/kg	30 min	Krisanapun et al. (2009)
		In vitro	LE	99.5% Methanol	AGI	2.45 mg/ml	NA	Adisakwattana et al. (2009)
Acacia leucophloea (Roxb.) Willd.	Fabaceae	*In vivo*	FL	70% Methanol	AID	25 mg/kg	21 d	El-Toumy et al. (2009)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	NS	NS	AID	1.5 mg/100 g bw	16 d	Eskander and Jun (1995)
		In vitro	SE	Phenol	AAI	148.7 µg/mg	NA	Gautam et al. (2012)
		In vitro	SE	Phytic acid	AAI	8.8 µg/mg	NA	Gautam et al. (2012)
		In vitro	SE	L-Dopa	AAI	239.7 µg/mg	NA	Gautam et al. (2012)
		In vitro	SE	Methanol	AAI	NS	NA	Vadivel et al. (2011b)
		In vitro	SE	Methanol	AGI	1 mg/ml	NA	Vadivel et al. (2011b)
Acacia nilotica (L.) Delile	Fabaceae	*In vivo*	BA	NS	db/db	100 mg/kg	7 d	Babish et al. (2010)
		In vivo	BA	Aqueous	AID	2 ml /200 g bw	NS	Ahmad M.M. and Shaikh (1989)
		In vivo	BA	Aqueous	GLD	2 ml /200 g bw	NS	Ahmad M.M. and Shaikh (1989)
		In vivo	FR	Methanol	NOR	200 mg/kg	3 week	Abuelgassim (2013)
		In vivo	LE	80% Methanol	AID	400 mg/kg	2, 3 week	Asad et al. (2015)
		In vivo	LE	80% Methanol	SID	300 mg/kg	3 week	Asad et al. (2011)
		In vivo	PO	30% Methanol	SID	150 mg/kg	60 d	Omara et al. (2012)
		In vivo	PO	75% Methanol	AID	400 mg/kg	1 month	Ahmad M. et al. (2008)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vitro	HE	NS	3T3-L1 adipocytes	50 µg/ml	2 d	Babish et al. (2010)
Achyranthes aspera L.	Amaranthaceae	*In vivo*	LE, ST	80% Ethanol	AID	200 mg/kg	2 week	Talukder et al. (2012)
		In vivo	WP	Aqueous	AID	4 g/kg	4 h	Akhtar and Iqbal (1991)
		In vivo	WP	Methanol	AID	4 g/kg	4 h	Akhtar and Iqbal (1991)
		In vivo	WP	NA	NOR	2 g/kg	4 h	Akhtar and Iqbal (1991)
Acorus calamus L.	Acoraceae	*In vivo*	RA	Ethanol	db/db	100 mg/kg	3 week	Wu H. et al. (2007)
		In vivo	RA	Ethanol	NOR	200 mg/kg	1 h	Si et al. (2010)
		In vivo	RA	Ethanol	GLD	400 mg/kg	1 h	Si et al. (2010)
		In vivo	RA	Ethanol	AMY	100 mg/kg	30 min	Si et al. (2010)
		In vivo	RA	70% Ethanol	db/db	100 mg/kg	5 week	Liu Y.X. et al. (2015)
		In vivo	RA	70% Ethanol	SID	100 mg/kg	4 week	Liu Y.X. et al. (2015)
		In vivo	RA	70% Ethanol	DIO	100 mg/kg	2 week	Liu Y.X. et al. (2015)
		In vivo	RH	Methanol	SID	200 mg/kg	21 d	Prisilla et al. (2012)
		In vitro	RA	Ethanol	AGI	0.41 µg/ml	NA	Si et al. (2010)
		In vitro	RA	Ethanol	L6 rat skeletal muscle cell	12.5 µg/ml	NA	Wu H.S. et al. (2009)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vitro	RH	1β,5α-guiane-4β,10α-diol-6one	HepG2 cell	1 µg/ml	NA	Zhou C.X. et al. (2012)
Aerva lanata (L.) Juss.	Amaranthaceae	*In vivo*	AE	50% Ethanol	AID	500 mg/kg	2 week	Vetrichelvan and Jegadeesan (2002)
		In vivo	AE	Methanol, Aqueous	SID	200 mg/kg	2 week	Rajesh R. et al. (2012)
		In vivo	LE	Ethanol	AID	400 mg/kg	28 d	Deshmukh et al. (2008)
		In vivo	RO	Methanol	SNI	10 mg/kg	2 week	Agrawal et al. (2013)
		In vivo	WP	70% Ethanol	SID	500 mg/kg	300 min	Riya et al. (2015)
		In vitro	WP	70% Ethanol	AGR	108.7 µg/ml	NA	Riya et al. (2015)
		In vitro	WP	Ethyl acetate	AGR	208.04 µg/ml	NA	Riya et al. (2015)
		In vitro	WP	70% Ethanol	AGI	81.76 µg/ml	NA	Riya et al. (2015)
		In vitro	WP	Ethyl acetate	AGI	108.23 µg/ ml	NA	Riya et al. (2015)
Alpinia calcarata (Haw.) Roscoe	Zingiberaceae	*In vivo*	RH	Ethanol	SID	200 mg/kg	30 d	Rajasekar et al. (2014)
		In vivo	RH	Ethanol	AID	100 mg/kg/d	21 d	Raj et al. (2011)
		In vitro	RH	Ethanol	RHE	NS	NA	Rajasekar et al. (2014)
		In vitro	RH	Ethanol	AGI	50 µl/ml	NA	Rajasekar et al. (2014)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Alpinia galanga (L.) Willd.	Zingiberaceae	*In vitro*	AE	Methanol	SID	200 mg/kg	21 d	Verma et al. (2015)
		In vivo	RH	Ethanol	SID	200 mg/kg	40 d	Kaushik et al. (2013)
		In vivo	RH	Ethanol	AID	200 mg/kg	2 week	Chudiwal et al. (2008)
		In vivo	RH	Ethanol	GID	200 mg/kg	2 week	Chudiwal et al. (2008)
		In vivo	RH	Methanol	AID	3, 4 g/kg	6 h	Akhtar M.S. et al. (2002)
		In vivo	RH	Aqueous	AID	4 g/kg	6 h	Akhtar M.S. et al. (2002)
Alternanthera sessilis (L.) R.Br. ex DC.	Amaranthaceae	*In vivo*	AE	95% Ethanol	FID	250 mg/kg	2 week	Tan and Kim (2013)
		In vivo	AE	95% Ethanol	SID	250 mg/kg	2 week	Tan and Kim (2013)
Anacyclus pyrethrum (L.) Lag.	Asteraceae	*In vitro*	RO	Ethanol	AAI	29.25 µg/ml	NA	Kumar V.K. and Lalitha (2014)
Areca catechu L.	Arecaceae	*In vivo*	HW	Ethanol	SID	250 mg/kg	24 h	Parveen and Ahmad (1994)
		In vivo	HW	Ethanol	NGL	250 mg/kg	24 h	Parveen and Ahmad (1994)
		In vivo	HW	Aqueous	NGL	250 mg/kg	24 h	Parveen and Ahmad (1994)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	HW	Aqueous	SID	250 mg/kg	24 h	Parveen and Ahmad (1994)
		In vivo	NS	Ethyl acetate	NOR	500 mg/kg	2 h	Boucher et al. (1994)
		In vivo	NS	Ethyl acetate	AID	250 mg/kg	7 d	Boucher et al. (1994)
		In vivo	SE	Procyanidin	SID	1 mg/ml	5 week	Huang et al. (2013)
Aristolochia bracteolata Lam.	Aristolochiaceae	*In vivo*	WP	Methanol	SID	200 mg/kg	28 d	Raju and Reddy (2017)
Artocarpus heterophyllus Lam.	Moraceae	Clinical	ML	Aqueous	NOR, DIA	20 g/kg (starting material)	1 h	Fernando et al. (1991)
		In vivo	LE	Ethanol	AID	100 mg/kg	7 d	Okonkwo et al. (2015)
		In vivo	LE	70% Ethanol, n-butanol	SID	200 mg/kg	10 d	Omar et al. (2011)
		In vitro	LE	Aqueous	AAI	1000 µl/ml	NA	Kotowaroo et al. (2006)
		In vivo	ML	Dichloromethane	SID	20 mg/kg	5 week	Chackrewarthy et al. (2010)
		In vitro	SE	Aqueous	AGL	NS	NA	Shakthi Deve et al. (2014)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Averrhoa carambola L.	Oxalidaceae	*In vivo*	FR	NA	SID	25 mg/kg	21 d	Pham et al. (2017)
		In vivo	LE	Methanol	GLD	400 mg/kg	1 h	Shahreen et al. (2012)
		In vivo	LE	Apigenin-6-C-(2''-O-α-rhamnopyranosyl)-β-fucopyranoside	NOR	20 mg/kg	180 min	Cazarolli et al. (2012)
		In vivo	LE	Apigenin-6-C-β-fucopyranoside	NOR	20 mg/kg	180 min	Cazarolli et al. (2012)
		In vivo	RO	2-dodecyl-6-methoxycycyclohexa-2,5-1,4-dione	HFD	12.5 mg/kg	16 week	Li et al. (2016)
Bambusa bambos (L.) Voss	Poaceae	*In vitro*	NS	NS	3T3-L1 adipocytes	50 µg/ml	NA	Babish et al. (2010)
Boerhavia diffusa L.	Nyctaginaceae	*In vivo*	LE	Aqueous	AID	200 mg/kg	4 week	Pari and Satheesh (2004)
Bombax ceiba L.	Malvaceae	*In vivo*	BA	Ethyl acetate	SID	600 mg/kg	21 d	Bhavsar and Talele (2013)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Borassus flabellifer L.	Arecaceae	*In vivo*	RO	Ethanol	AID	NS	1 week	Debnath et al. (2013)
		In vivo	RO	Ethanol	NOR	100 mg/kg	7 d	Debnath et al. (2013)
Caesalpinia bonduc (L.) Roxb.	Fabaceae	*In vivo*	SE	60% Methanol	SID	250 mg/kg	21 d	Jana et al. (2012)
Calotropis procera (Aiton) Dryand.	Asclepiadaceae	*In vivo*	LA	NA	AID	100 mg/kg	31 d	Roy et al. (2005)
		In vivo	LE	Aqueous	SID	200 mg/kg	15 d	Alrheam and Saad-Al Shehri (2015)
		In vivo	LE	Chloroform	SID	200 mg/kg	15 d	Alrheam and Saad-Al Shehri (2015)
		In vivo	LE	Ethanol	SID	200 mg/kg	15 d	Alrheam and Saad-Al Shehri (2015)
		In vivo	LA	NA	SID	200 mg/kg	15 d	Alrheam and Saad-Al Shehri (2015)
		In vivo	LA	Aqueous	AID	100 mg/kg	90 d	Kumar V. and Padhy (2011)
		In vivo	LE	Ethanol	SID	300 mg/kg	4 week	Neto et al. (2013)
		In vivo	RO	Methanol	SID	100 mg/kg	42 d	Yadav et al. (2014)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vitro	LE	Aqueous	AGI	3.25 mg/ml	NA	Kazeem et al. (2016)
		In vitro	LE	Ethanol	AAI	7.80 mg/ml	NA	Kazeem et al. (2016)
Cardiospermum halicacabum L.	Sapindaceae	*In vivo*	LE	Ethanol	SID	200 mg/kg	45 d	Veeramani et al. (2008, 2012)
Cheilocostus speciosus (J.Koenig) C.D.Specht	Costaceae	*In vivo*	RH	Costunolide, eremanthin	SID	20 mg/kg	NS	Eliza et al. (2011)
		In vivo	RH	Hexane	SID	250 mg/kg	60 d	Daisy et al. (2008); Eliza et al. (2011)
		In vivo	RH	Aqueous	SID	200 mg/kg	240 min	Rajesh M. et al. (2009)
		In vivo	RH	Eremanthin	SID	20 mg/kg	60 d	Eliza et al. (2009a)
		In vivo	RH	Ethyl acetate, methanol	SID	400 mg/kg	60 d	Daisy et al. (2008)
		In vivo	RH	NA	NOR	NS	30 min	Mosihuzzaman et al. (1994)
		In vivo	RO	95% Ethanol	SID	400 mg/kg	4 week	Ali et al. (2014)
		In vivo	RO	Costunolide	SID	5 mg/kg	30 d	Eliza et al. (2009b)
		In vivo	RO	95% Ethanol	AID	300 mg/kg	4 week	Bavarva and Narasimhacharya (2008)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vitro	LE	Methanol	AAI	67.5 µg/ml	NA	Perera, H.K.I., et al. (2016)
		In vitro	LE	Methanol	AGI	5.88 mg/ml	NA	Perera, H.K.I., et al. (2016)
Chrysopogon zizanioides (L.) Roberty	Poaceae	*In vivo*	RO	Ethanol	AID	100 mg/kg	28 d	Karan et al. (2013)
Coccinia grandis (L.) Voigt	Cucurbitaceae	*In vivo*	LE	Aqueous	SID	0.75 g/kg	30 d	Attanayake et al. (2015)
		In vivo	LE	Aqueous	AID	0.75 g/kg	4 h	Attanayake et al. (2013)
Cocculus hirsutus (L.) W.Theob.	Menispermaceae	*In vivo*	AE	Methanol	SID	400 mg/kg	15 d	Sangameswaran and Jayakar (2007)
		In vivo	AE	Methanol	AID	NS	NS	Ganapaty et al. (2006)
		In vivo	LE	Aqueous	AID	250 mg/kg	6 h	Badole et al. (2006)
		In vivo	LE	Aqueous	NOR	1000 mg/kg	30 min	Badole et al. (2006)
		In vivo	RO	Methanol	AID	NS	NS	Satyanarayana et al. (2001)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Coscinium fenestratum (Goetgh.) Colebr.	Menispermaceae	*In vivo*	ST	Ethanol	SNI	500 mg/kg	12 d	Punitha et al. (2005)
		In vivo	ST	Ethanol	SNI	NS	12 d	Shirwaikar et al. (2005a)
		In vivo	ST	99% Chloroform	NOR, SID	250 mg/kg	5 d	Shirwaikar et al. (2005b)
Curculigo orchioides Gaertn.	Hypoxidaceae	*In vivo*	RH	Aqueous	SID	100 mg/kg	28 d	Thakur et al. (2012)
		In vivo	RT	90% Ethanol	AID	500 mg/kg	7 d	Madhavan et al. (2007)
		In vivo	RT	Aqueous	AID	500 mg/kg	7 d	Madhavan et al. (2007)
		In vitro	RH	Ethanol	3T3-L1 cell	214.73 µg/ml	NA	Gulati et al. (2015)
		In vitro	WO	Ethanol	3T3-L1 cell	171.45 µg/ml	NA	Gulati et al. (2015)
Curcuma aromatica Salisb.	Zingiberaceae	*In vitro*	RH	Dichloromethane	AAI	8.97 µl/ml	NA	Nampoothiri et al. (2015)
Cyanthillium cinereum (L.) H.Rob.	Asteraceae	Clinical	RO	NA	T2D	6 g/d (preparation contains unknown amount)	6 month	Bin Sayeed et al. (2013)
Datura metel L.	Solanaceae	*In vivo*	SE	NA	NOR, AID	25 mg/kg	8 h	Murthy et al. (2004)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Dichrostachys cinerea (L.) Wight & Arn.	Fabaceae	*In vitro*	ST	(−)-mesquitol	AGI	32 μM	NA	Raghavan (2004)
Dregea volubilis (L.f.) Benth. ex Hook.f.	Asclepiadaceae	*In vivo*	LE	Ethanol	SID	200 mg/kg	210 min	Natarajan and Arul Gnana Dhas (2013)
Eclipta prostrata (L.) L.	Asteraceae	*In vivo*	WP	Eclalbasaponin II	AID	10 mg/kg	7 d	Rahman et al. (2011)
		In vivo	WP	Methanol	AID	300 mg/kg	7 d	Rahman et al. (2011)
Eleusine coracana (L.) Gaertn.	Poaceae	Clinical	NS	NA	T1D, NOR	NS	30 min	Urooj et al. (2006)
		In vitro	SE	NA	AGI	NS	NA	Kunyanga et al. (2012)
		In vitro	SE	Methanol	AGI	NS	NA	Kunyanga et al. (2012)
		In vitro	SE	50% Ethanol	AGI	NS	NA	Kunyanga et al. (2011)
		In vitro	SE	NS	AGI	NS	NA	Kunyanga et al. (2011)
Embelia ribes Burm.f.	Primulaceae	*In vivo*	FR	70% Ethanol	FDI and SID	100 mg/kg	21 d	Bhandari et al. (2013); Chaudhari et al. (2013)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	FR	Ethanol	SID	200 mg/kg	40 d	Bhandari and Ansari (2009)
		In vivo	FR	Ethanol	SID	100 mg/kg	6 week	Bhandari et al. (2008a)
		In vivo	FR	Aqueous	SID	100 mg/kg	40 d	Bhandari and Ansari (2008b)
		In vivo	FR	90% Ethanol	SID	100 mg/kg	40 d	Bhandari et al. (2007)
		In vivo	FR	90% Ethanol	SID	200 mg/kg	20 d	Bhandari et al. (2002)
Erythrina variegata L.	Fabaceae	*In vivo*	LE	95% Methanol	SID	900 mg/kg	21 d	Kumar A. et al. (2011)
Euphorbia antiquorum L.	Euphorbiaceae	*In vivo*	RO	95% Ethanol	FRF	200 mg/kg	21 d	Madhavan et al. (2015)
		In vivo	RO	Aqueous	FRF	200 mg/kg	21 d	Madhavan et al. (2015)
Ficus amplissima Sm.	Moraceae	*In vivo*	BA	Methanol	GLD	50 mg/kg	1 h	Arunachalam and Parimelazhagan (2013)
		In vivo	BA	Methanol	NOR	50 mg/kg	3 h	Arunachalam and Parimelazhagan (2013)
		In vivo	BA	Methanol	SID	50 mg/kg	21 d	Arunachalam and Parimelazhagan (2013)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Ficus benghalensis L.	Moraceae	*In vivo*	SB	95% Ethanol	AID	250 mg/kg twice a d	1 week	Kar et al. (2003)
Ficus racemosa L.	Moraceae	Clinical	BA	Aqueous	T2D	1.2 g/d	1 month	Ahmed et al. (2011)
		In vivo	BA	Aqueous	AID, NOR	200 mg/kg	1 month	Bhaskara Rao et al. (2002)
		In vivo	FR	80% Ethanol	SID	1.25 g/kg bw per 10 ml water	60 min	Jahan et al. (2009)
		In vivo	FR	80% Ethanol	NOR	1.25 g/kg bw per 10 ml water	60 min	Jahan et al. (2009)
		In vivo	LE	β-sitosterol, stigmasterol, lanosterol	SID	100 mg/kg	7 d	Kushwaha et al., (2015)
		In vivo	LE	80% Ethanol	NOR, AID	100, 200, 300 mg/kg bw	6 h	Patil V.V. et al. (2010)
		In vivo	SB	95% Ethanol	FDI, SID	200, 400 mg/kg	2 week	Veerapur et al. (2012)
		In vitro	BA	NA	AAI	NS	NA	Ahmed and Urooj (2010a)
		In vitro	BA	NA	AGI	280 µg/ml	NA	Ahmed and Urooj (2010a)
		In vitro	BA	NA	BGI	212 µg/ml	NA	Ahmed and Urooj (2010a)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vitro	BA	NS	AAI	NS	NA	Ahmed and Urooj (2010a)
		In vitro	BA	NS	AGI	259 µg/ml	NA	Ahmed and Urooj (2010a)
		In vitro	BA	NS	BGI	223 µg/ml	NA	Ahmed and Urooj (2010a)
		In vitro	SB	95% Ethanol	RHE	100 µg/ml	NA	Veerapur et al. (2012)
		In vitro	SB	Aqueous	GD A	5 mmol/l	NA	Ahmed and Urooj (2010b)
Ficus religiosa L.	Moraceae	*In vivo*	BA	Aqueous	SID	200 mg/kg	4 week	Kirana et al. (2011)
		In vivo	BA	Aqueous	SID, GLD	50 mg/kg	21 d	Pandit et al. (2010)
		In vivo	BA	Aqueous	SID	100 mg/kg	4 week	Kirana et al. (2009)
		In vivo	LE	Aqueous	SID	300 mg/kg	2 h	Shukla et al. (2012)
Gmelina arborea Roxb.	Lamiaceae	*In vivo*	BA	Aqueous	AID	1 g/kg	4 h	Attanayake et al. (2013)
		In vivo	BA	Aqueous	SID	250 mg/kg	28 d	Kulkarni Y.A. and Veeranjaneyulu (2013)
Gmelina asiatica L.	Lamiaceae	*In vivo*	RO	95% Ethanol	NOR, AID	100 mg/kg	6 h	Kasiviswanath et al. (2005)
Gossypium arboreum L.	Malvaceae	*In vitro*	LE	Aqueous	AAI	10.10 mg/ml	NA	Kazeem et al. (2013)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vitro	LE	Acetone	AGI	2.75 mg/ml	NA	Kazeem et al. (2013)
Hemidesmus indicus (L.) R. Br. ex Schult.	Apocynaceae	*In vivo*	RO	β-amyrin palmitate	AID	50 µg/kg	15 d	Nair et al. (2014)
		In vivo	RO	β-amyrin palmitate	GLD	50 µg/kg	15 d	Nair et al. (2014)
		In vivo	RO	β-amyrin palmitate	SID	50 µg/kg	20 d	Nair et al. (2014)
		In vivo	RO	2-hydroxy-4-methoxy benzoic acid	SID	500 µg/kg	7 week	Gayathri and Kannabiran (2009)
		In vivo	RO	Aqueous	SID	500 mg/kg	12 week	Gayathri and Kannabiran (2008)
		In vivo	RO	Aqueous	GLD	500 mg/kg	12 week	Gayathri and Kannabiran (2008)
		In vivo	RO	Ethanol	NOR	NS	NS	Rokeya et al. (1997)
		In vivo	RO	Ethanol	T1D	NS	NS	Rokeya et al. (1997)
		In vivo	RO	Ethanol	T2D	NS	NS	Rokeya et al. (1997)
Hybanthus enneaspermus (L.) F.Muell.	Violaceae	*In vivo*	WP	Ethanol	SID	250 mg/kg	21 d	Patel et al. (2011)
Hygrophila auriculata (Schumach.) Heine	Acanthaceae	*In vivo*	AE	50% Ethanol	SID	100 mg/kg	3 week	Vijayakumar et al. (2006)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Ipomoea aquatica Forssk.	Convolvulaceae	*In vivo*	EP	Aqueous	GLU challenged	3.4 g/kg	2 h	Malalavidhane et al. (2000)
		In vivo	EP	Aqueous	GLU challenged	3.3 g/kg	2 h	Malalavidhane et al. (2001)
		In vivo	LE, ST	NA	SID	3.4 g/kg	1 week	Malalavidhane et al. (2003)
Madhuca longifolia (J.Koenig ex L.) J.F.Macbr.	Sapotaceae	*In vivo*	BA	Methanol	NOR	100 mg/kg	30 min	Dahake et al. (2010)
		In vivo	BA	Methanol	GLD	100 mg/kg	12 d	Dahake et al. (2010)
		In vivo	BA	Methanol	SID	100 mg/kg	NS	Dahake et al. (2010)
Magnolia champaca (L.) Baill. ex Pierre	Magnoliaceae	*In vivo*	FB	Aqueous	GLD	400 mg/kg	1 h	Jarald et al. (2008)
		In vivo	FB	Ethanol	GLD	400 mg/kg	1 h	Jarald et al. (2008)
		In vivo	FB	Ethanol	AID	200 mg/kg	7 d	Jarald et al. (2008)
		In vivo	FB	Petroleum ether	GLD	400 mg/kg	1 h	Jarald et al. (2008)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Merremia emarginata (Burm. f.) Hallier f.	Convolvulaceae	*In vivo*	NS	Methanol	SID	100 mg/kg	28 d	Gandhi and Sasikumar (2012)
Mukia maderaspatana (L.) M.Roem.	Cucurbitaceae	*In vitro*	WP	Methanol	Rat liver slice	0.25 mg/ml	NS	Srilatha and Ananda (2014)
Musa × *paradisiaca* L.	Musaceae	Clinical	FR	NA	T2D	5 g	1 week	Edo et al. (2011)
		In vivo	FL	Ethanol	AID	200 mg/kg	8 d	Dhanabal et al. (2005)
		In vivo	FL	Chloroform	AID	0.25 g/kg bw	30 d	Pari and Umamaheswari (2000)
		In vivo	FL	Chloroform	AID	0.25 g/kg	30 d	Pari and Maheswari (1999)
		In vivo	FR	NA	NGL	500 mg/kg bw	4 h	Rai et al. (2009)
		In vivo	IN	Methanol	SID	200 mg/kg bw/d	60 d	Nisha and Mini (2013)
		In vivo	IS	Aqueous	SID	50, 75 g/l	7 d	Jaber et al. (2013)
		In vivo	RO	60% Methanol	SID	80 mg/100 g bw/d	14 d	Mallick et al. (2007)
		In vivo	ST	Lyophilized juice	SID	50 mg/kg	4 week	Dikshit et al. (2012)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	SU	70% Methanol	AID	5, 10 mg/kg	21 d	Akinlolu et al. (2015)
		In vivo	UF	NA	SID	65 mg/kg bw	12 d	Eleazu and Okafor (2015)
		In vivo	UF	NA	SID	NS	1 d	Shodehinde et al. (2015)
		In vivo	UF	NA	SID	NS	21 d	Eleazu et al. (2013)
		In vivo	UF	Ethanol	SID	100 mg/kg/d	10 d	Kumar M. et al. (2013)
Myristica fragrans Houtt.	Myristicaceae	*In vivo*	FR	50% Ethanol	CID	150 mg/kg	7 d	Arulmozhi et al. (2007)
		In vivo	SK	Macelingan	db/db	10 mg/kg	14 d	Han et al. (2008)
		In vitro	MA	Methanol	AGI	0.85 mg/ml	NA	Patil S.B. et al. (2011)
		In vitro	LE	Methanol	Insulin secreting BRIN-BD11 cell	1.731 µg/l	NS	Chee et al. (2007)
Nardostachys jatamansi (D.Don) DC.	Caprifoliaceae	*In vivo*	HR	Aqueous	SID	125 mg/kg	3 d	Song et al. (2010)
Oroxylum indicum (L.) Kurz	Bignoniaceae	*In vivo*	SB	50% Ethanol	SNI	250 mg/kg	28 d	Singh J. and Kakkar (2013)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	SB	Oroxylin A	AGI	25.90 µg/ml	NA	Rao J.M. et al. (2007)
		In vivo	SB	Chrysin	AGI	57.59 µg/ml	NA	Rao J.M. et al. (2007)
		In vivo	SB	Methoxy chrysin	AGI	95 µl/ml	NA	Rao J.M. et al. (2007)
		In vivo	SB	Oroxyloside methyl ester	AGI	97.31 µg/ml	NA	Rao J.M. et al. (2007)
		In vivo	SB	Baiclain	AGI	38.71 µg/ml	NA	Rao J.M. et al. (2007)
		In vivo	SB	Acetone	AGI	84 µg/ml	NA	Rao J.M. et al. (2007)
		In vivo	SB	Acetone	AGI	124 µg/ml	NA	Rao J.M. et al. (2007)
		In vivo	SB	50% Ethanol	BSA	2.10 µg/ml	NA	Singh J. and Kakkar (2013)
Pandanus odorifer (Forssk.) Kuntze	Pandanaceae	*In vivo*	RO	80% Ethanol	AID	150 mg/kg	10 d	Venkatesh et al. (2012)
Papaver somniferum L.	Papaveraceae	*In vivo*	SE	Aqueous	AID, GLD	2 ml /200 g	NS	Ahmad M.M. and Shaik (1989)
Paspalum scrobiculatum L.	Poaceae	*In vivo*	SE	Ethanol	AID	500 mg/kg	15 d	Jain et al. (2010)
Phyllanthus amarus Schumach. & Thonn.	Phyllanthaceae	*In vivo*	AE	98% Methanol	AID	100 mg/kg	25 d	Okoli et al. (2011)
		In vivo	AE	Methanol	NGL	200 mg/kg	1 h	Okoli et al. (2010)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	AE	Methanol	AID	200 mg/kg	28 d	Okoli et al. (2010)
		In vivo	NS	Aqueous	AID	200 mg/kg	45 d	Lemus et al. (2013)
		In vivo	TL	95% Ethanol	AID	300 mg/kg	4 week	Bavarva and Narasimhacharya (2007)
		In vitro	AE	98% Methanol	AAI	2.15 mg/ml	NA	Okoli et al. (2011)
		In vitro	AE	99% Methanol	AGI	0.2 mg/ml	NA	Okoli et al. (2011)
Phyllanthus reticulatus Poir.	Phyllanthaceae	*In vivo*	LE	Petroleum ether, Ethanol	AID	1000 mg/kg	21 d	Kumar S. et al. (2008)
Plumbago zeylanica L.	Plumbaginaceae	*In vivo*	RO	Plumbagin	SID	15 mg/kg	28 d	Sunil et al. (2012)
		In vivo	RO	70% Ethanol	SID	100 mg/kg	42 d	Zarmouh et al. (2010)
		In vivo	RO	Ethanol	NOR	400 mg/kg	30 d	Olagunju et al. (2000)
Pterocarpus santalinus L.f.	Fabaceae	*In vivo*	BA	95% Ethanol	SID	150 mg/kg	45 d	Kondeti et al. (2010)
		In vivo	BA	95% Ethanol	AID	0.25 g/kg	7 h	Rao B.K. et al. (2001)
		In vivo	HE	Aqueous	SID	250 mg/kg	16 week	Halim and Misra (2011)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Salacia reticulata Wight	Celastraceae	Clinical	BA	NA	T2D	2 g/d	90 d	Radha and Amrithaveni (2009)
		In vivo	LE	Aqueous	SID	1 mg	NS	Yoshino et al. (2009)
		In vivo	LE	Aqueous	MAL loaded	1 mg	30 min	Yoshino et al. (2009)
		In vivo	LE	Aqueous	SUC loaded	1 mg	30 min	Yoshino et al. (2009)
		In vivo	ST	Aqueous	KK-Ayd	4.5 mg dry matter/10 ml water	4 week	Im et al. (2009)
		In vitro	LE	Aqueous	AGI	31 µg/ml	NA	Yoshino et al. (2009)
		In vitro	LE	Aqueous	AGI	13 µg/ml	NA	Yoshino et al. (2009)
Santalum album L.	Santalaceae	*In vivo*	NS	Petroleum ether	SID	10 µl/kg twice a d	60 d	Kulkarni C.R. et al. (2012)
Scoparia dulcis L.	Plantaginaceae	*In vivo*	LE	Aqueous	AID	0.45 g/kg	45 d	Pari and Venkateswaran (2002)
		In vivo	NS	Methanol	SID	200 mg/kg	21 d	Mishra et al. (2013)
		In vivo	NS	Aqueous	SID	50 mg/kg	3 week	Pari and Latha (2004)
		In vivo	WP	Scoparic acid D	SID	20 mg/kg	15 d	Latha et al. (2009)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	WP	Aqueous	SID	200 mg/kg	15 d	Latha et al. (2004)
		In vivo	WP	Aqueous	SID	200 mg/kg	3 week	Pari and Latha (2005)
		In vivo	WP	Aqueous	SID	200 mg/kg	6 week	Latha and Pari, (2003); Pari and Latha, (2006)
		In vitro	NS	Methanol	AGI	80.35 µg/ml	NA	Mishra et al. (2013)
Senna auriculata (L.) Roxb.	Fabaceae	*In vivo*	FL	2-(3-acetoxy-4,4,14-trimethylandrost-8-en-17-yl)	AID	5 mg/kg	15 d	Venkatachalam et al. (2013)
		In vivo	FL	Chloroform	GLD	400 mg/kg	2 h	Jarald et al. (2010)
		In vivo	FL	Ethanol	AID	200 mg/kg	7 d	Jarald et al. (2010)
		In vivo	FL	Ethanol	AID	200 mg/kg	7 d	Jarald et al. (2010)
		In vivo	FL	Chloroform	Fasted NOR	400 mg/kg	30 min	Jarald et al. (2010)
		In vivo	FL	50% Methanol	AID	0.20 g/kg	8 d	Surana et al. (2008)
		In vivo	FL	90% Ethanol	AID	250 mg/kg	1 h	Hatapakki et al. (2005)
		In vivo	FL	Methanol	NOR	4.9 mg/kg	30 min	Abesundara et al. (2004)
		In vivo	FL	Methanol	NOR	5 mg/kg	60 min	Abesundara et al. (2004)
		In vivo	FL	Aqueous	SID	0.45 g/kg	30 d	Latha and Pari (2003)
		In vivo	LE	Aqueous	SID	400 mg/kg	5 h	Gupta et al. (2009a)
		In vivo	LE	Aqueous	SID	100 mg/kg	21 d	Gupta et al. (2009b)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	LE	Aqueous	AID	400 mg/kg	3 d	Gupta et al. (2009c)
		In vivo	LE	50% Ethanol	NOR	200 mg/kg	4 h	Sabu and Subburaju (2002)
		In vivo	LE	50% Ethanol	AID	200 mg/kg	3 d	Sabu and Subburaju (2002)
		In vivo	WP	95% Ethanol	SID	400 mg/kg	28 d	Juvekar and Halade (2006)
		In vivo	WP	Aqueous	SID	250 mg/kg	28 d	Juvekar and Halade (2006)
		In vitro	FL	Methanol	AGI	0.196 mg/ml	NA	Venkatachalam et al. (2013)
		In vitro	FL	Methanol	AGI	0.023 mg/ml	NA	Abesundara et al. (2004)
		In vitro	LE	50% Ethanol	RHE	25 mg/ml	NA	Sabu and Subburaju (2002)
		In vitro	NS	Kaempferol-3-*O*-rutinoside	AGI	NS	NA	Habtemariam (2012)
		In vitro	NS	Kaempferol-3-*O*-rutinoside	PLI	NS	NA	Habtemariam (2012)
Senna sophera (L.) Roxb.	Fabaceae	*In vivo*	SE	Aqueous	DIA	2 g	2 week	Feng (2003)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
Senna tora (L.) Roxb.	Fabaceae	*In vivo*	SE	85% Methanol	NOR	20 mg/100 g bw	30 min	Nam and Choi (2008)
Sesbania grandiflora (L.) Pers.	Fabaceae	*In vivo*	LE	Methanol	HFD and SID	200 mg/kg	28 d	Panigrahi et al. (2016)
Setaria italica (L.) P.Beauv.	Poaceae	*In vitro*	SE	70% Ethanol	AGI	1.1 µg/ml	NA	Kim et al. (2011)
Sida cordifolia L.	Malvaceae	*In vivo*	AE	Ethanol	SID	400 mg/kg	28 d	Ahmad M. et al. (2014)
Stereospermum chelonoides (L.f.) DC.	Bignoniaceae	*In vivo*	BA	95% Ethanol	SID	200 mg/kg	14 d	Balasubramanian et al. (2009)
Strychnos potatorum L.f.	Loganiaceae	*In vivo*	SE	NA	SID	100 mg/kg	12 week	Biswas et al. (2012)
Syzygium cumini (L.) Skeels	Myrtaceae	*In vivo*	BA	NS	SID	500 mg/kg	21 d	Tripathi and Kohli (2014)
		In vivo	BA	Methanol	GLD	5 mg/20 mg bw	30 min	Rafiullah et al. (2006)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	BA	Methanol	GID	5 mg/20 g	30 min	Villaseñor and Lamadrid (2006)
		In vivo	LE	Chloroform	AAI	25 mg/ml	NA	Bhat et al. (2011)
		In vivo	LE	Ethanol	AID	125 mg/kg	1 h	Schoenfelder et al. (2010)
		In vivo	LE	Ethanol	NOR	200 mg/kg twice a d	7 d	Oliveira et al. (2005)
		In vivo	MS	Mycaminose	SID	50 mg/kg	15 d	Kumar A. et al. (2013)
		In vivo	MS	Ethyl acetate, Methanol	SID	200 mg/kg	15 d	Kumar A. et al. (2013)
		In vivo	SE	Aqueous	AID	200 mg/g	NS	Peixoto and Freitas (2013)
		In vivo	SE	80% Ethanol	SID	1.25 g/kg	21 d	Bhuyan et al. (2010)
		In vivo	SE	Chloroform	SID	2 g/ml	21 d	Bopp et al. (2009)
		In vivo	SE	Cuminoside	SID	50 mg/kg	21 d	Farswan et al. (2009)
		In vivo	SE	Petroleum ether, Chloroform, Acetone, Methanol, Aqueous	SID	100 mg/kg	21 d	Farswan et al. (2009)
		In vivo	SE	Ethanol	SID	NS	NS	Mandal et al. (2008)
		In vivo	SE	Aqueous	SID	200 mg/kg	4 h	Randriamampionona et al. (2008)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	SE	Ethanol	AID	75 mg/100 g bw	30 d	Singh N. and Gupta (2007)
		In vivo	SE	15% Unextracted (intact) diet	AID, NOR	3 g	21 d	Pandey and Khan (2002)
		In vivo	SE	15% defatted seed diet	AID, NOR	3 g	21 d	Pandey and Khan (2002)
		In vivo	SE	6% Gummy fibre diet	AID, NOR	3 g	21 d	Pandey and Khan (2002)
		In vitro	LE	Aqueous	ADI	60 µg/ml	NA	Teixeira et al. (2004)
		In vitro	SE	Belulinic acid, 3,5,7,4'-tetrahydroxy flavanone	AAI	NS	NA	Karthic et al. (2008)
		In vitro	SE	Aqueous	AAI	NS	NA	Singh N. et al. (1990)
		In vitro	SK	70% Ethanol	AGI (SUC), AGI (MAL)	299.2 µg/ml	NA	Shinde et al. (2008)
		In vitro	SK	Acetone	AGI (SUC), AGI (MAL)	120.9 µg/ml	NA	Shinde et al. (2008)
Tamarindus indica L.	Fabaceae	*In vivo*	SB	90% Methanol	AID	250 mg/kg	16 h	Yerima et al. (2014)
		In vivo	SB	90% Methanol	AID	1000 mg/kg	4 h	Yerima et al. (2014)
		In vivo	SB	90% Methanol	GID	250 mg/kg	5 h	Yerima et al. (2014)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vivo	SB	90% Methanol	GID	500 mg/kg	1 h	Yerima et al. (2014)
		In vivo	SB	90% Methanol	GID	1000 mg/kg	3 h	Yerima et al. (2014)
		In vivo	SB	90% Methanol	DIA	100 mg/kg	24 h	Yerima et al. (2014)
		In vivo	SE	Methanol	AID	200 mg/kg	2 week	Nahar et al. (2014)
		In vivo	SE	Aqueous	SID	120 mg/kg	4 week	Sole and Srinivasan (2012)
		In vivo	SE	Aqueous	FRF	20 mg/0.5 ml water/100 g bw	8 week	Shahraki et al., (2011)
		In vivo	SE	Aqueous	SID	50 mg/kg	1 week	Hamidreza et al. (2010)
		In vivo	SE	Aqueous	SID	80 mg/0.5 ml water/ 100 g bw	14 d	Maiti et al. (2005)
		In vivo	SE	Aqueous	SID	80 mg/0.5 ml water/ 100 g bw	7 d	Maiti et al. (2004)
		In vivo	TL	Petroleum ether	Fluoride exposed	NS	4 week	Vasant and Narasimhacharya (2012)
		In vitro	SE	Phenol	AAI	1 mg/ml	NA	Gautam et al. (2012)
		In vitro	SE	L-Dopa	AAI	1 mg/ml	NA	Gautam et al. (2012)
		In vitro	SE	Phytic acid	AAI	1 mg/ml	NA	Gautam et al. (2012)

Scientific name	Family	Level of scientific evidence	Part used	Active compound / extract	Bioassay / model	Dosage / concentration	Duration	Reference
		In vitro	SE	Methanol	AAI	NS	NA	Vadivel et al. (2011b)
		In vitro	SE	Methanol	AGI	1 mg/ml	NA	Vadivel et al. (2011b)
		In vitro	LE	NA	AAI	23.2 µM	NA	Funke and Melzig (2006)
Thespesia populnea (L.) Sol. ex Corrêa	Malvaceae	*In vivo*	FP	Aqueous, 5% Chloroform	AID	200 mg/kg	28 d	Belhekar et al. (2013)
		In vivo	FP	Ethanol	AID	200 mg/kg	28 d	Belhekar et al. (2013)
		In vitro	LE	Methanol	AAI	20 µg/ml	NA	Sangeetha and Vedasree (2012)
		In vitro	LE	Ethyl acetate	AAI	50 µg/ml	NA	Sangeetha and Vedasree (2012)
Vitex negundo L.	Lamiaceae	*In vivo*	LE	Iridoid glucoside	SID	50 mg/kg	30 d	Sundaram et al. (2012)
		In vivo	LE	Methanol	GID	5 mg/20 g bw	60 min	Villaseñor and Lamadrid (2006)
Ziziphus jujuba Mill.	Rhamnaceae	*In vivo*	NS	Aqueous	SID	25 mg/kg	21 d	Hemmati et al., (2015)
		In vivo	NS	Hydroalcoholic	SID	25 mg/kg	21 d	Hemmati et al., (2015)

Abbreviation

NA: not applicable, NS: not stated

Part used

AE: aerial, BA: bark, EP: edible part, FB: flower bud, FE: fruit peel, FL: flower, FP: fruit pulp, FR: fruit, HE: heartwood, HR: herb, HW: hard wood, IN: inflorescence, IS: infructescence stalk, LA: latex, LE: leaf, MA: mace / aril, ML: mature leaf, MS: mature seed, PO: pod, RA: radix, RH: rhizome, RO: root, RT: root tuber, SB: stem bark, SE: seed, SK: seed kernel, ST: stem, SU: sucker, TL: tender leaf, TW: twig, UF: unripe fruit, WO: wood, WP: whole plant

Model

ADI: Adenosine deaminase inhibition, AID: Alloxan induced diabetic, AMY: Amylum loaded, AGL: Antiglycation assay, BSA: Bovine serum albumin glycosylation inhibition assay, CID: Chlorpromazine induced diabetic, DIO: diet induced obese, FDI: fat diet induced, FRF: Fructose fed, GD: Glucose diffusion, GID: Glucose induced diabetic, GLD: Glucose loaded, GLU: Glucose, MAL: Maltase, NGL: normoglycemic, NOR: normal, PLI: Pancreatic lipase inhibition assay, RHE: rat hemidiaphragm, SID: Streptozotocin induced diabetic , SNI:, Streptozotocin Nicotinamide induced diabetic, SUC: Sucrase, T1D: Type 1 diabetic, T2D: Type 2 diabetic, AAI: α-amylase inhibition assay, AGI: α-glucosidase inhibition assay, BGI: β-glucosidase inhibition assay.

Duration

d: day, h: hour, min: minute

Appendix D

Ethnobotanical survey questionnaire

Section A

1. Have any diabetic patients consulted you?

(i) Yes (ii) No

2. How many diabetic patients consult you in a week?

3. How do you diagnose diabetes?

4. Name the preparations you use to treat diabetic patients who consult you?

5. Describe the procedures used to prepare the antidiabetic preparations?

6. What are the plant species and parts that you use in the antidiabetic preparations?

7. What animal parts do you use in the antidiabetic preparations?

8. What are the inorganic substances you use in the antidiabetic preparations (e.g. borax and mercury)?

Section B

To compare the responses, we need some general demographic data about you.

10. Age:

11. Gender: Male / Female

12. Number of years practicing Siddha Medicine:

Glossary

Alloxan-induced diabetic model

Alloxan (2,4,5,6-tetraoxypyrimidine; 5,6-dioxyuracil) is toxic to β-cells in the pancreas and destroy them to produce T1D conditions.

Biomedicine

"A system in which medical doctors and other healthcare professionals (such as nurses, pharmacists, and therapists) treat symptoms and diseases using drugs, radiation, or surgery. It is also called allopathic medicine, conventional medicine, mainstream medicine, and Western medicine".

db/db (diabetic dyslipidaemia) mouse

The db/db mouse is a T2D model with dyslipidemia (harmful levels of one or more types of lipid in the blood) and obesity metabolic conditions.

fa/fa (Zucker fatty) rat

Fa/fa rat is a genetic obesity animal model and shows hyperlipidemia (high level of lipids in the blood), hyperphagia (excessive eating), and hyperinsulinemia (excess levels of insulin in the blood than glucose level).

KKA^{y} (Kyoji Kondo A^{y}/a) mouse

Prof. Kyoji Kondo developed a diabetic mouse strain called KK (Kyoji Kondo) mouse. Then Prof. Kyoji Kondo and Prof. Masahiko Nishimura introduced an obesity gene A^{y} into KK mouse to create a developed T2D model.

OLETF (Otsuka Long-Evans Tokushima Fatty) rat

This is an obesity model originated from an outbred colony of Long Evans rat and distinguished by hyperphagia-induced obesity. It is used as a late onset T2D model.

Streptozotocin-induced diabetic model

Streptozotocin [2-deoxy-2-(3-(methyl-3-nitrosoureido)–D-glucopyranose] is also toxic to β-cells in the pancreas and destroy them to create T1D conditions.

Publications associated with this thesis

1. Saravanan V. Sathasivampillai, Pholtan R.S. Rajamanoharan, Michael Munday, Michael Heinrich, 2017. Plants used to treat diabetes in Sri Lankan Siddha Medicine – an ethnopharmacological review of historical and modern sources. J. Ethnopharmacol., 198, 531 – 599.

2. Saravanan V. Sathasivampillai, Pholtan R.S. Rajamanoharan, Michael Heinrich, 2018. Siddha Medicine in Eastern Sri Lanka today – Continuity and change in the treatment of diabetes. Front. Pharmacol., 9, 1022.

Conference presentations associated with this thesis

1. Saravanan V. Sathasivampillai, Pholtan R.S. Rajamanoharan, Michael Munday, Michael Heinrich. Preparations and plants used to treat diabetes in Sri Lankan Siddha Medicine. 3rd International Conference on Ayurveda, Unani, Siddha and Traditional Medicine, Colombo, Sri Lanka, December 2015.

2. Saravanan V. Sathasivampillai, Pholtan R.S. Rajamanoharan, Michael Munday, Michael Heinrich. Plants currently used to treat diabetes in Sri Lankan Siddha Medicine – an ethnobotanical survey in the Eastern Province
World Congress Integrative Medicine & Health 2017 - 10th European Congress for Integrative Medicine and 12th International Society for Complementary Medicine Research Congress, Berlin, Germany, May 2017.