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Review Article

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A Brief Review on Phytoconstituents and Ethnopharmacology of *Scoparia Dulcis* Linn. (Scrophulariaceae)

M.R. Mishra[1*], R.K. Behera[2], S. Jha[3], A.K. Panda[2], A. Mishra[1], D.K. Pradhan[1] P.R. Choudary[4]

***Corresponding author:**

Manas Ranjan Mishra,

Associate Professor,
[1]Gayatri College of Pharmacy,Jamadarpali, Sason, Sambalpur, Odisha-768200.
[2]School of Chemistry, Sambalpur University, Odisha.
[3]Birla Institute of Technology, Mesra, Ranchi, Jharkhand.
[4]The Pharmaceutical College, Barpali, Bargarh, Odisha.

A B S T R A C T

Scoparia dulcis Linn.(S. dulcis)or sweet broom weed commonly known as Mithipatti and Bana Dhania in Western Orissa, it is also known as 'GhodaTulsi'in Hindi. The present review attempts to narrate the chemical constituents of S.dulcis and their uses. S.dulcis is rich in flavones, terpenes and steroids. Main chemical constituents such as scoparic acid A-C, scopadulcic acid A and B, scopadulciol, scopadulin and ammelin have been shown to contribute to the observed medicinal effect of the plant. In this review we have composed the structure and functions of those active ingredients with their melting point and other physical properties individually.Some aspects of the several speculated pharmacological properties of S. dulcis have been validated by scientific research, which includes the presence of hypoglycaemic and anti-tumour promoting compound. It also has antimicrobial and antifungal effects as well as antihyperlipidemic action.

Keywords: Scoparia dulcis, scoparic acid, ammelin, medicinal effect.

Introduction

Scoparia dulcis Linn.is an erect annual herb with serrated leaves, producing white flowers and measuring up to a half meter in height when fully grown, it is an herb widely distributed in tropical and subtropical regions. Its ethno-medicinal uses amongst various indigenous tribes in the rain-forest zone are well-documented [1]. In fresh or dried form S. dulcis plants have been traditionally used as remedies for Diabetes mellitus in India and hypertension in Taiwan [3]. It is used in curing ailments such as fever, diarrhoea, ulcer, cancer, wounds, skin rash, cough and tuberculosis. The fresh or dried plant has been used for treating stomach aches, inflammation, bronchitis, hemorrhoids and hepatosis. In the western part of Orissa its root is traditionally is used as an effective remedy for Jaundice and diarrhoea. It is also used as an analgesic and antipyretic, in stomach troubles,[2] bronchitis, as well as inhibition of herpes simplex virus replication, gastric H+,K+-ATPase activation and antitumor activity. It is deemed to be a panacea for all ills. In Gambia, a lotion prepared from the plant is used in curing fever. A hot water infusion or decoction of the leaves or whole plant is used medicinally by indigenous tribes of Nicaragua to treat malaria, stomach disorders, menstrual disorders, insect bites, fevers, heart problems, liver disorders and venereal diseases. It has been used for blood cleansing, in childbirth and as a general tonic. [3] Phytochemical screening has revealed that the plant contains diterpenoids, flavonoids, tannins, alkaloids, triterpenes, hexacosonol, β-sitosterol, ketone-dulcitone and ammelin, an antidiabetic compound [2-4]. The diterpenoid, scoparic acid A, isolated from the plant has been reported to be a potent β-glucuronidase inhibitor [5]. The constituents, scopadulciol, scopadulcic acid-B and diacetylscopadiol, have been shown to be responsible for the inhibitory activity of the plant on gastric H+-K+ ATPase enzyme [6]. The

diterpenoid, scopadulcic acid-B and flavone, hemenoxin, have been shown to exhibit cytotoxic and antitumor activity [7].

Objective for studying medicinal plants is the discovery of new bioactive components, in the search for promising drugs. This review emphasizes the traditional uses and clinical potential of S.dulcis. Through this review, authors hope to attract the attention of natural productresearchers throughout the world to focus on the unexplored potential of weed like S.dulcis (mithipatti).

The available information on S.dulcis has been divided into four sections, i.e., Plant profile ethnopharmacology, phytoconstituents, pharmacological reports. The reports in which S.dulcis species have been used as a domestic remedy by common men without any prescription for the treatment of various ailments have been discussed under ethnopharmacology.

Plant ProfileofScopariadulcis Linn.-

Fig.1: Plant S.dulcis.

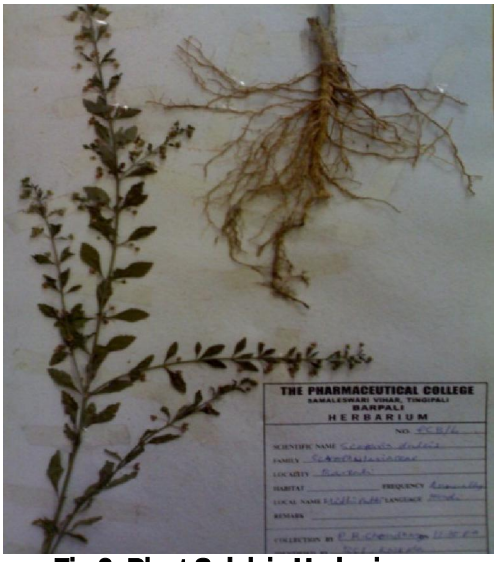


Fig.2: Plant S.dulcis Herbarium.

Vernacular Name

Sanskrit: Asmaghni
Hindi: Mithi Patti, GhodaTulsi, Ban Dhania
English: Sweet broom, Broom weed, Vassourinha

Taxonomy:

Kingdom: Plante
Subkingdom: Trachcobionta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Asteridae
Family: Scrophulariaceae
Genus: Scoparia
Species: dulcis
Botanical name: Scoparia dulcis Linn.

Morphology

It is a small, much branched, glabrous, leafy annual herb or under shrub with erect or ascending branches; Leaves opposite and 3-notely whorled, rhomboid, elliptic or elliptic lanceolate, obtuse at apex, base tapering, margins serrate; Flowers many, in terminal panicles, pedicelate, pedicels slender, rigid, Calyx lobes 4, oblong, Corolla white, tube very short, Capsule globose; seeds minute, many. [8-9]

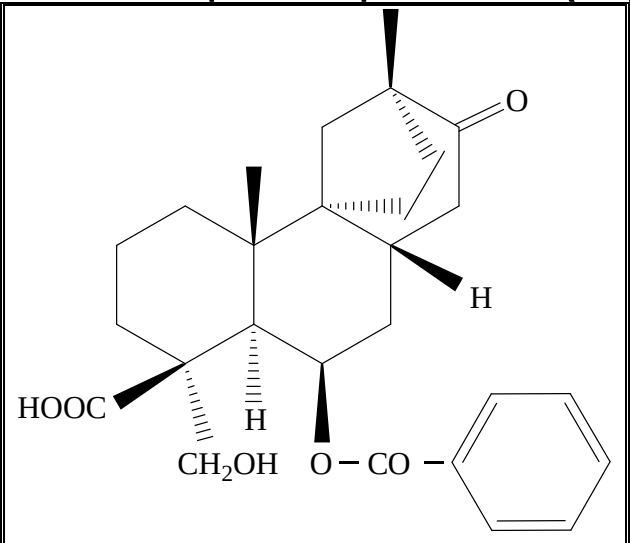
Traditional Uses of Scoparia dulcis Linn. [8-11]

	Plant Part			
	Aerial Part	**Leaf**	**Root**	**Whole Plant**
USES	Coughs, diarrhoea, expectorant, fever and stomach pains	Diabetes, diarrhoea, eye problems, fever, headaches, hemorrhoids, infections, insect bites, intestinal worms, kidney disease, liver disorders, malaria, menstrual disorders, migraines, snake bites, stomach disorders, tonic, ulcers, urinary tract disorders, vomiting, wounds, anemia, burns, and cough	Bronchitis, diarrhoea, fever, jaundice, liver disorders, malaria, menstrual disorders, skin infections, stomach pains	Anemia, bronchitis, burns, coughs, diabetes, diarrhoea, dysentery, expectorant, fever, gastric disorders, headache, hemorrhoids, hepatitis, hypertension, infections, insect bites, intestinal worms, jaundice, liver disease, malaria, menstrual disorders, pain, rash, snake bites, swelling and toothache

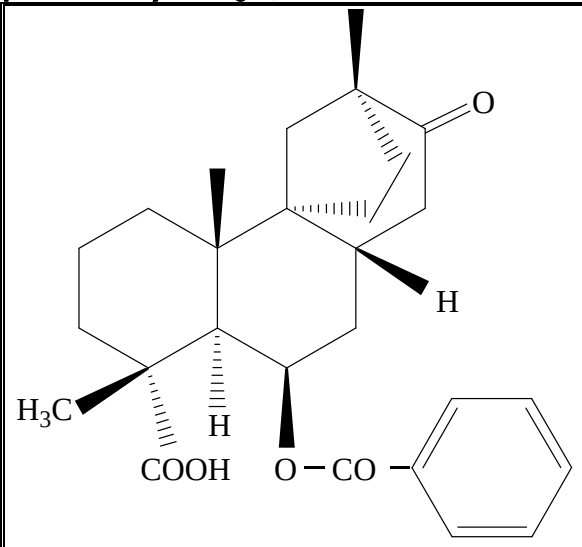
Phytoconstituents

The available literature on phytochemical reports of the S.dulcis reveals that it comprises mainly terpenes and flavones. Fig. 3 to 38 summarizes phytoconstituents reported from various plant parts of S. dulcis.

Plant resources: Whole plants of Scoparia dulcis Linn. (Scrophulariaceae) **Fig-3, 4**

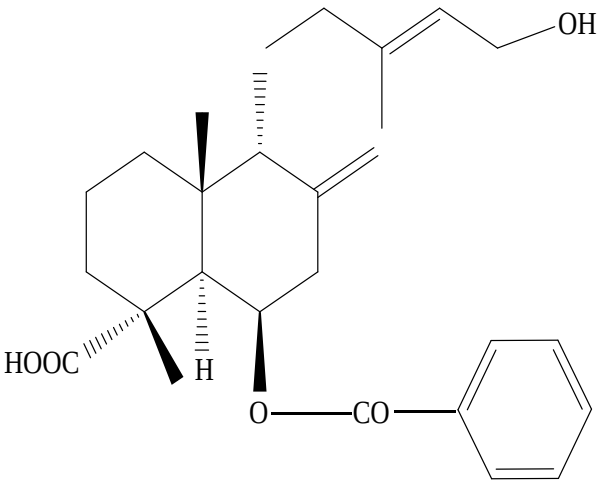


[12]
Compound: Scopadulcic Acid A(Diterpene)
Molecula Formula (M.F.)- $C_{27}H_{34}O_6$
Melting point (m.p.) 172–174°C
colorless prisms (from MeOH)
$[\alpha]D^{27}$–5.7° (MeOH)
Biological activity: Falciparum malaria,

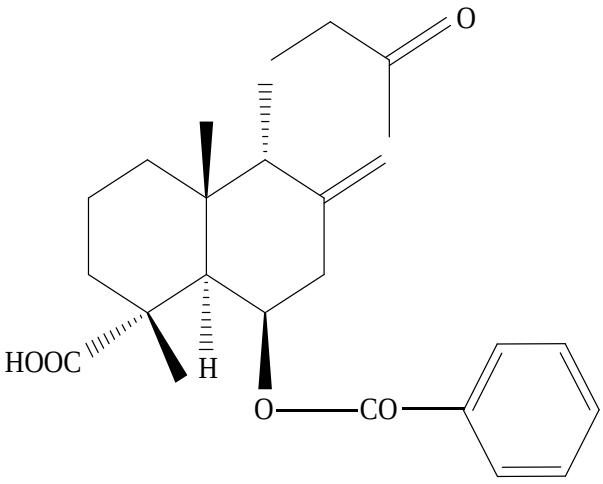


[13]
Compound: Scopadulcic Acid B(Diterpene)
M.F.- $C_{27}H_{34}O_5$
m.p. 228–232°C,
colorless prisms (from MeOH)
$[\alpha]D^{27}$–49.6° (c = 1.02, MeOH)
Biological activity: Antiviral, antitumor activity in various human cell lines.

Fig-5, 6

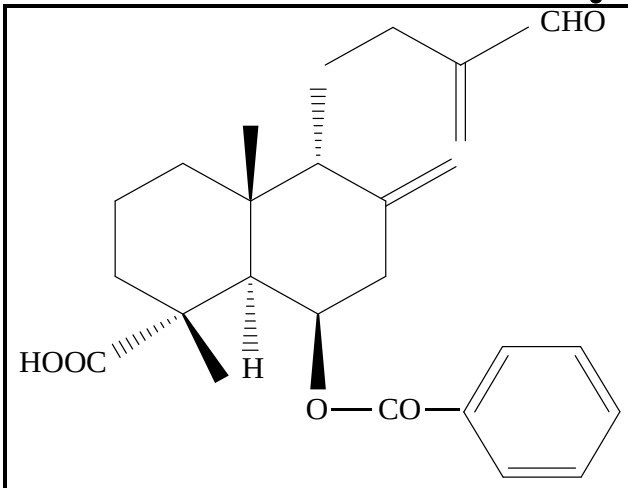


[14,15]
Compound: Scoparic Acid A (Diterpene)
M.F.- $C_{27}H_{36}O_5$
m.p. colorless amorphous powder
$[\alpha]D^{26}$–38.3° (c = 1.00, $CHCl_3$)
Biological activity: β-glucuronidase inhibition

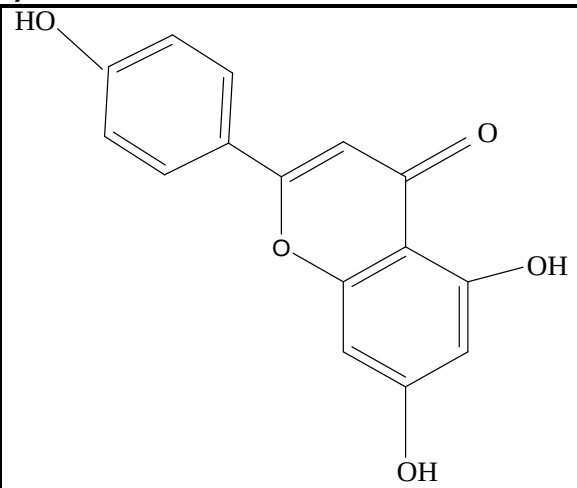


[15]
Compound: Scoparic Acid B (Diterpene)
M.F.- $C_{25}H_{32}O_5$
m.p. colorless amorphous powder
$[\alpha]D^{23}$–9.8° (c = 0.63, $CHCl_3$)
Biological activity: Antiviral

Fig - 7, 8



[15]
Compound: Scoparic Acid C (Diterpene)
M.F.- $C_{26}H_{32}O_5$
m.p. colorless amorphous powder
$[\alpha]D^{22}$–13.9° (c = 0.69, $CHCl_3$)
Biological activity: β-glucuronidase inhibition



[16]
Compound : Apigenin (Flavone)
M.F-$C_{15}H_{10}O_5$
m.p.315°C
yellow crystalline powder
Biological activity: Antioxidant, radical scavenger, anti-inflammatory, carbohydrate metabolism promoter, immunity system modulater.

Fig-9, 10

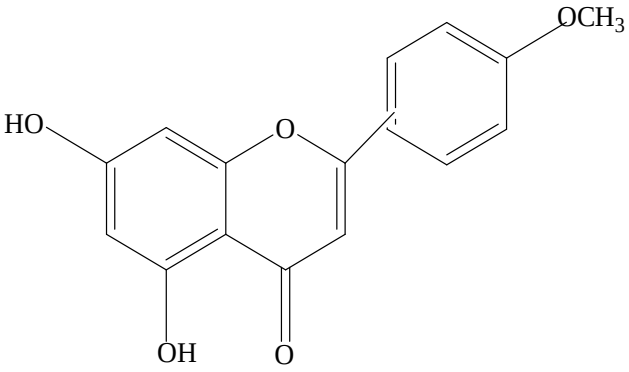
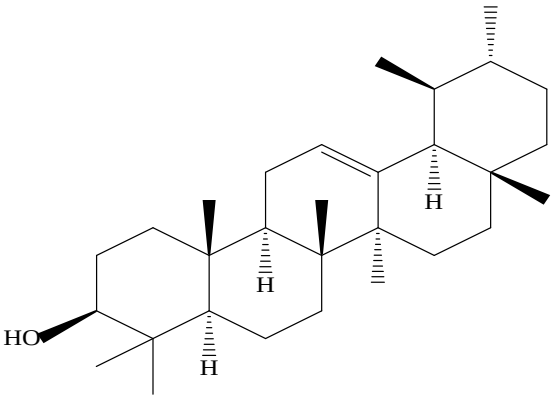
 **[18-20]** **Compound: Acacetin (Flavone)** **M.F.-$C_{16}H_{12}O_5$** **m.p. 268-272°CPale-yellow needles** **[α]D22–13.9° (c = 0.69, CHCl3)** **Biological activity: Inhibits Human Atrial Repolarization Potassium Currents, Antioxidant, radical scavenger, anti-inflammatory, carbohydrate metabolism promoter, immunomodulater.**	 **[17]** **Compound: Amyrin, alpha (Triterpine)** **M.F.-$C_{30}H_{50}O$** **m.p- 188°C** **White crystalline powder** **Biological activity: Anti-elastase activity, and modulates the membrane fluidity PGE2 release inhibition, strong anti-inflammatory activity, PKA inhibitor as well as a selective protease inhibitor.**

Fig-11, 12

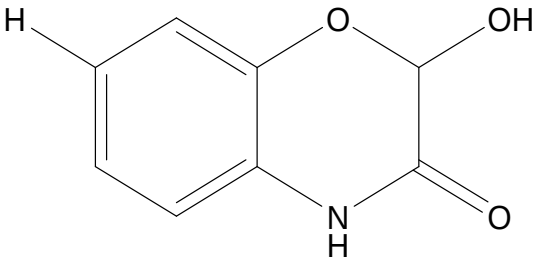
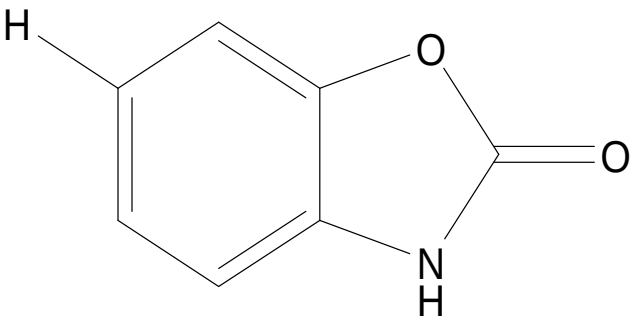
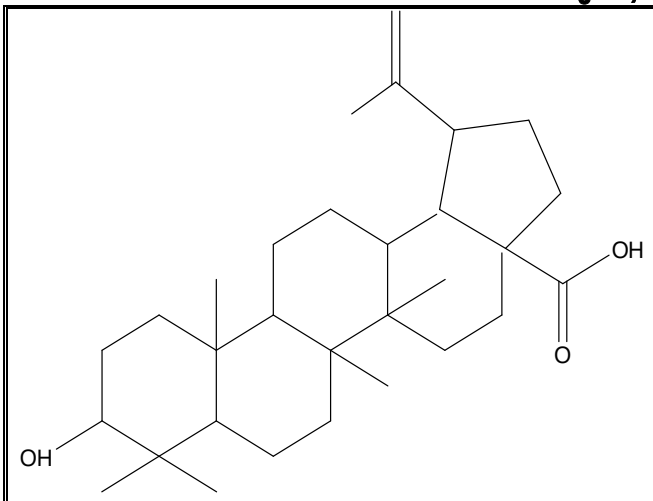
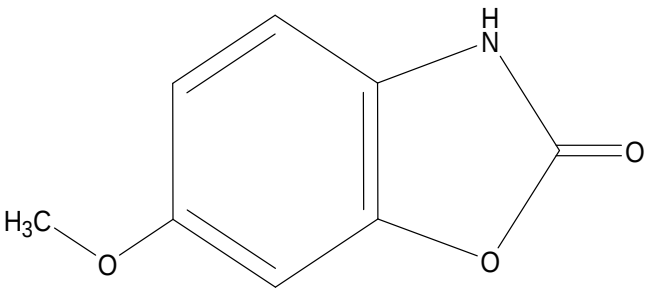
 **[16, 18]** **Compound: Benzoxazin-3-one, 1-4: 2(h): 2-hydroxy (Nitrogen heterocy)** **M.F.-$C_8H_7NO_2$** **m.p.- 172-176 ºC** **Biological activity: Antimicrobial, anticancer and anti-inflammatory.**	 **[16, 18]** **Compound: Benzoxazolinone (Nitrogen heterocy)** **M.F.-$C_7H_5NO_2$** **m.p.- 82-86°C** **Light brown-pink Crystalline powder** **Biological activity: Adrenergic and antihypertensive properties.**

Fig-13, 14



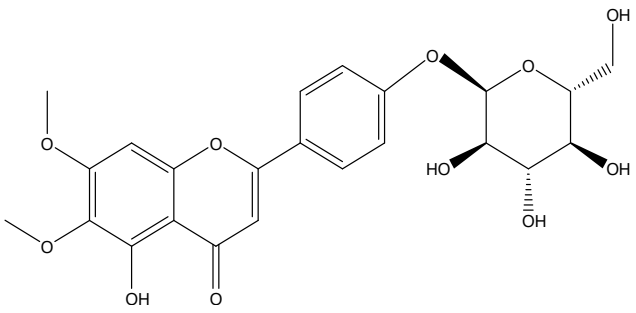
[21-23]
Compound: Betulinic Acid (Triterpene)

M.F.- $C_{30}H_{48}O_3$
m.p.- 295 - 298 °C (decomposes)
White crystalline powder
Optical Rotation: +7° - +9° (c=0.9 in pyridine)
Biological activity: Potential anti-melanoma agent, Effective as a non-steroidal anti-inflammatory agent, anti-malarial, anti-HIV, prostaglandin antagonist.



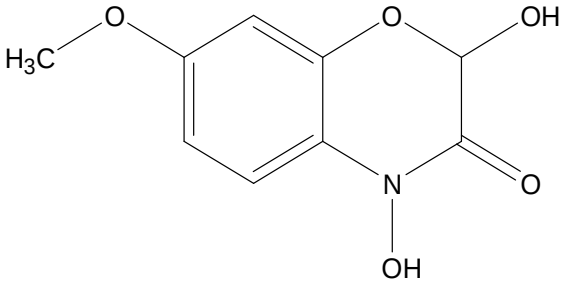
[21-22]
Compound:Benzoxazolin-2-one, 6-methoxy (Nitrogen heterocy):
M.F.-$C_8H_7NO_3$
m.p.-151-156 °C(lit.)
light tancolour
Biological activity: Antimicrobial and anti-inflammatory.

Fig-15, 16



[26-28]
Compound: Cirsimarin (Flavone)

M.F.-$C_{23}H_{24}O_{11}$
m.p. - 244-246 °C
Biological activity: Stimulate lipolysis, anti-inflammatory, anti-diabetic and hypotensive.



[25]
Compound: Benzoxazolone, 2(3H) 6-methoxy (Nitrogen heterocy):
M.F.-$C_8H_7NO_3$
m.p.- 152-156 °C
Biological activity: Antimicrobial, analgesicand anti-inflammatory.

Fig-17, 18

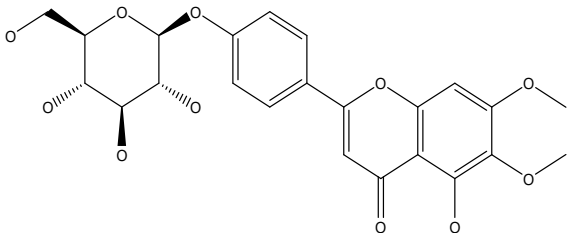
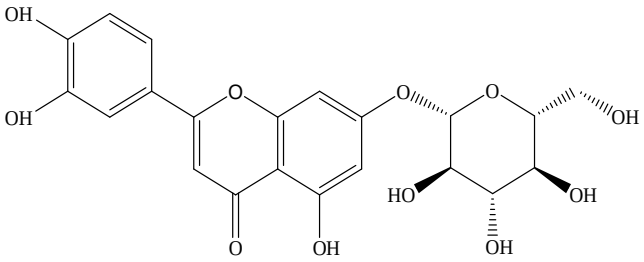
 **[28]** **Compound: Cirsitakaoside (Flavone)** **M.F.-$C_{23}H_{24}O_{11}$** **m.p. - 246-247°C** **Biological activity: Respiratory disease, gastric, hepaticdisturbances,anti-inflammatory, anti-diabeticandhypotension.**	 **[29, 30]** **Compound: Cynaroside Flavone)** **M.F.-$C_{21}H_{20}O_{11}$** **m.p. - 266–268 °C** **Yellow amorphous powder** **Biological activity: Antioxidant, anti-diabetic.**

Fig-19, 20

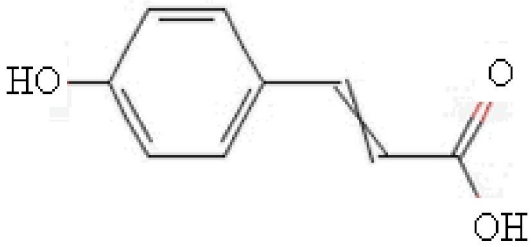
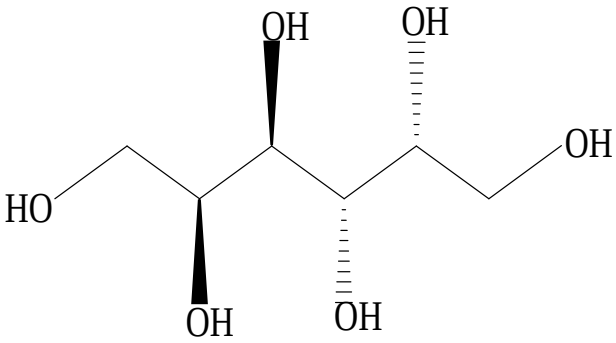
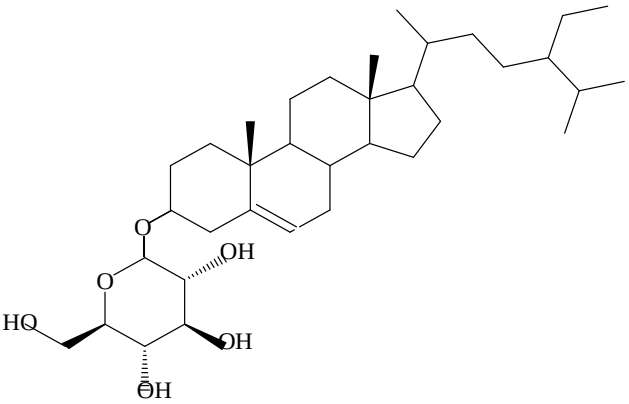
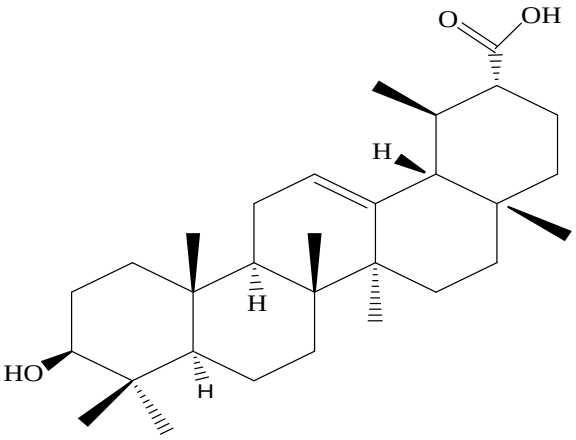
 **[31]** **Compound: Coumaric Acid, para (Phenylpropanoid)** **M.F.-$C_9H_8O_3$** **m.p.-210–213 °C** **Biological activity: Inhibits the development of stomach cancer.**	 **[32]** **Compound: Dulcitol (Diterpene)** **MF:$C_6H_{14}O_6$** **m.p.-188-189 °C** **Biological activity: Antiviral and cytotoxic activity.**

Fig-21, 22

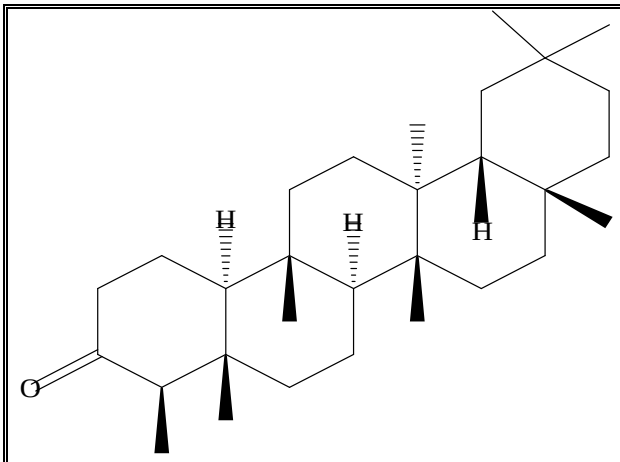


[33]
Compound: Daucosterol(Steroid)
MF: $C_{35}H_{60}O_6$
m.p.- 295 °C
Biological activity: Immunomodulator

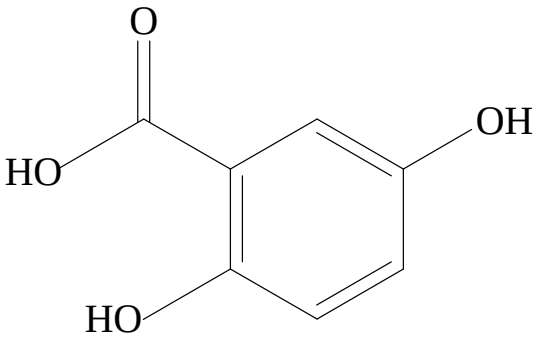


[26]
Compound: Dulcioic Acid (Triterpene)
MF: $C_{30}H_{48}O_3$
m.p.-300 °C
Biological activity: Significant inhibitory effect on cytokine production,antispasmodic.

Fig-23, 24

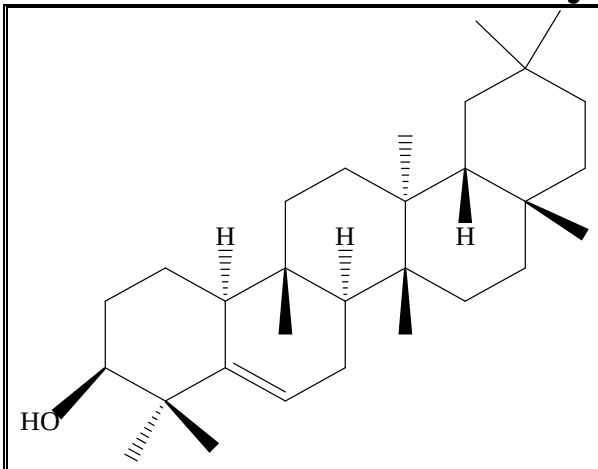


[35]
Compound: Friedelin (Triterpene)
M.F.-$C_{30}H_{50}O$
m.p.-262-265 °C
Biological activity:Estrogenic, Anti-inflammatory, analgesic and antipyretic.

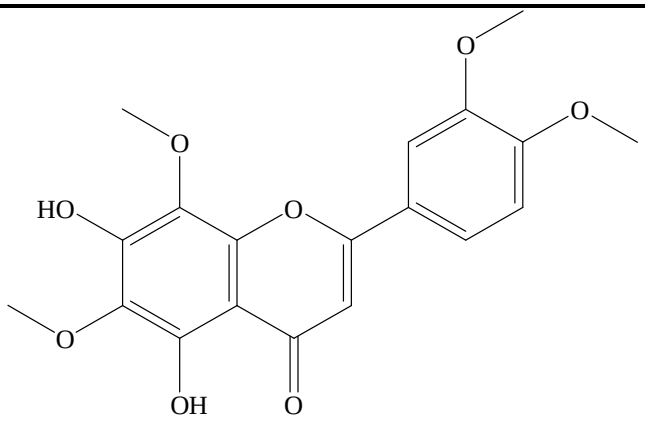


[34]
Compound: Gentisic acid (Benzenoid)
M.F.-$C_7H_6O_4$
m.p.-200 - 205 °C
white to yellow powder
Biological activity: Antispasmodic, local anesthetic, antioxidant and anticonvulsant.

Fig-25, 26

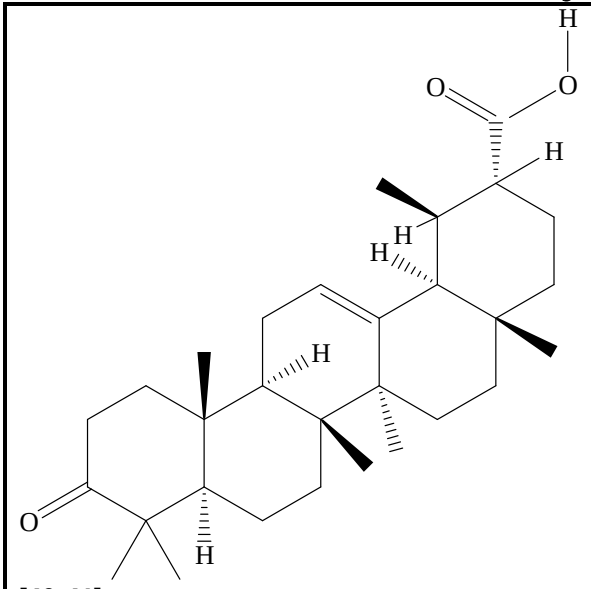


[36, 37]
Compound: Glutinol (Triterpene)
M.F.-$C_{30}H_{50}O$
m.p.- 206-208°C
Biological activity: Anti-inflammatory, analgesic.

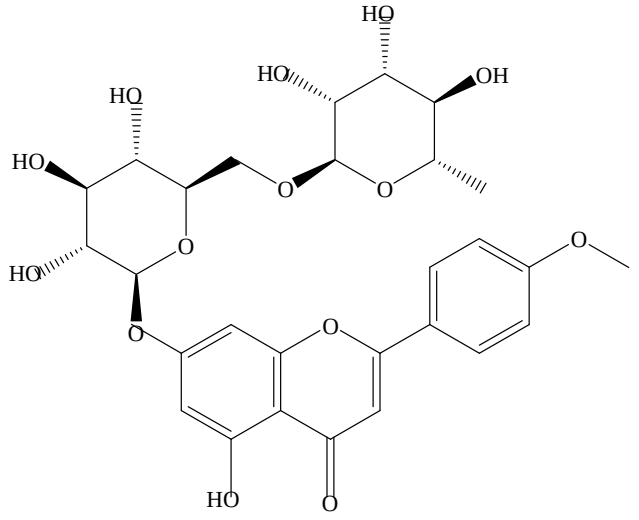


]38, 39]
Compound: Hymenoxin (Flavone)
M.F.-$C_{19}H_{18}O_8$
m.p.-215-. 216°C
Biological activity: Estrogenic, antispasmodic.

Fig-27, 28

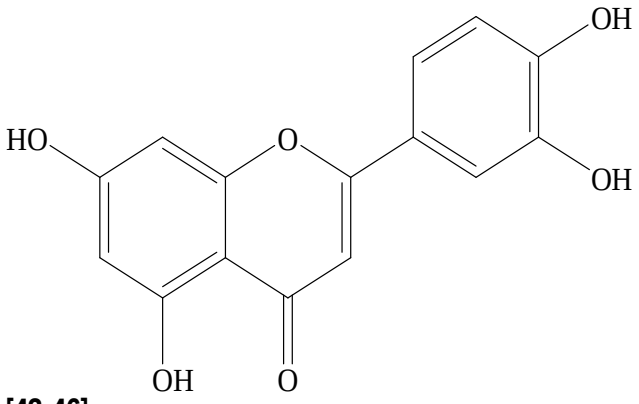


[40-41]
Compound: Ifflaionic Acid (Triterpene)
M.F.-$C_{30}H_{46}O_3$
m.p.-303°C
Biological activity: Hypotensive

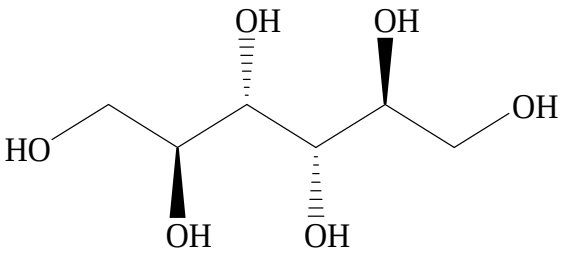


[42]
Compound: Linarin (Flavone)
M.F.-$C_{28}H_{32}O_{14}$
m.p.- 258-260°C
Biological activity: Sedative and sleep-enhancing properties.

Fig-29, 30

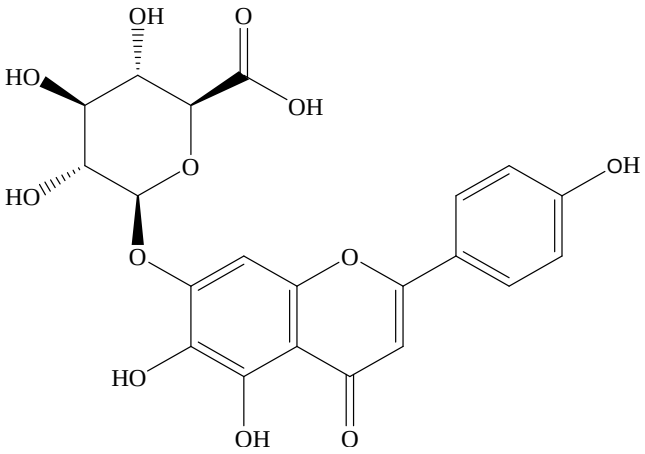


[43-46]
Compound: Luteolin (Flavone)
M.F.-$C_{15}H_{10}O_6$
m.p.->330 °C
yellow crystalline compound
Biological activity: Anti-oxidant, anti-cancer, immunomodulator, anti-inflammatory.

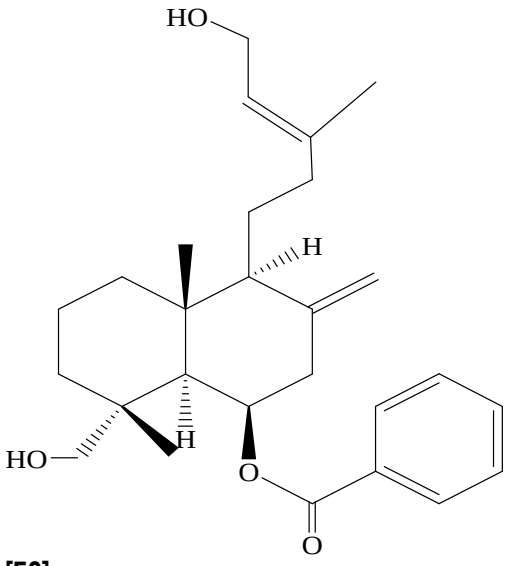


[47, 48]
Compound: Mannitol, d (Carbohydrate)
M.F.- $C_6H_{14}O_6$
m.p.- 164 – 169 °C
white, crystalline
Biological activity: Diuretic, of Alzheimer's disease, chemotherapy for brain tumors.

Fig-31, 32

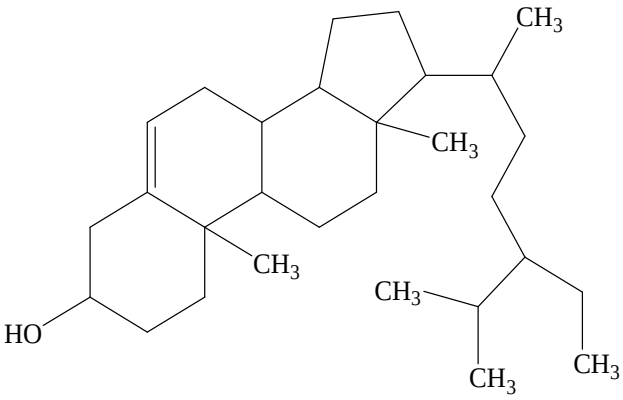


[49, 50]
Compound: Scutellarein (Flavone)
M.F.-$C_{21}H_{18}O_{12}$
m.p.-218-220" C
Biological activity: Induce apoptosis of ovarian and breast tumor cells in vitro.

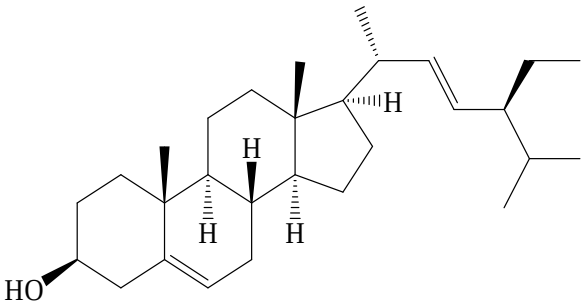


[50]
Compound: Scoparinol (Diterpene)
M.F.- $C_{27}H_{38}O_4$
m.p.-
Biological activity: Anti-inflammatory, analgesic

Fig-33, 34

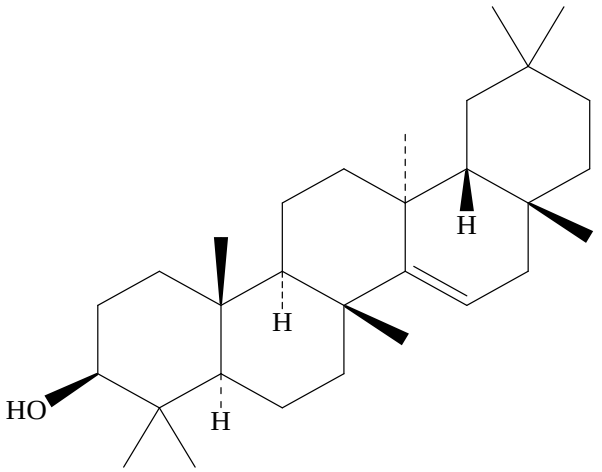


[51]
Compound: Sitosterol, beta (Steroid)
M.F.-$C_{29}H_5O$
m.p.- 136-140 °C
Biological activity: Antioxidant, anti-cancer, anti-tumor, reduce blood cholesterol levels.

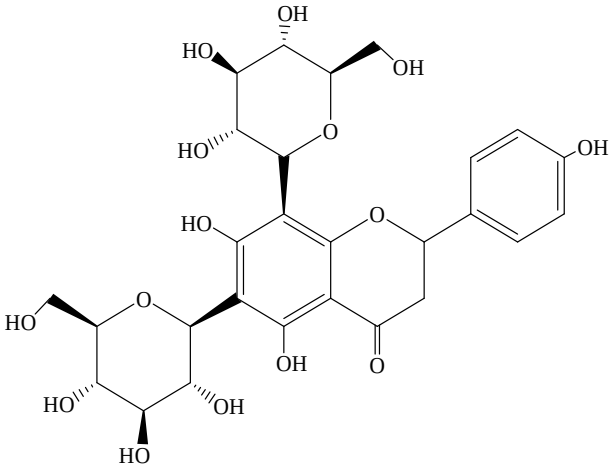


[52, 53]
Compound: Stigmasterol (Steroid)
M.F.- $C_{29}H_{48}O$
m.p.- 161-170 °C
Biological activity: Anti-cancer, lower serum cholesterol, antioxidant, hypoglycemic.

Fig-35, 36

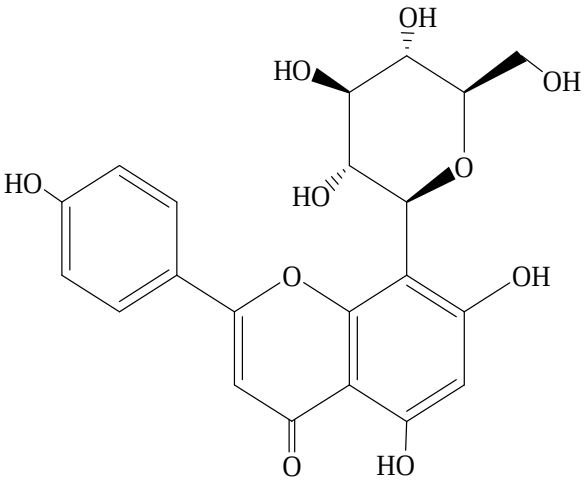


[54]
Compound: Taraxerol (Steroid)
M.F.-$C_{30}H_{50}O$
m.p.- 282-285° C
Biological activity: Anti-cancer, anti-tumor

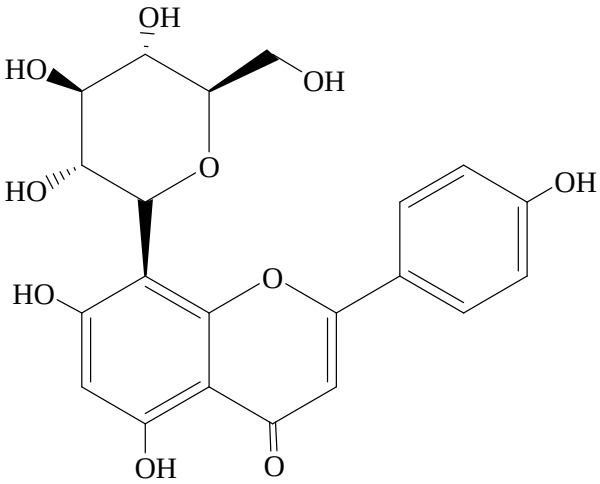


[55- 57]
Compound: Vicenin 2 (Flavone)
M.F.- $C_{27}H_{30}O_{15}$
m.p.-271-272 .
Biological activity: Anti-cancer, anti-inflammatory

Fig-37, 38



[58, 59]
Compound: Vitexin (Flavone)
M.F.-$C_{21}H_{20}O_{10}$
m.p.- 256-257°C
Biological activity: Antioxidant, hypotensive



[58, 59]
Compound: Vitexin, iso (Flavone)
M.F.- $C_{21}H_{20}O_{10}$
m.p.- 203–204 °C
Biological activity: Antioxidant, hypotensive

Pharmacological Activity

The use of whole herb of S. dulcis in painful conditions acting both centrally and peripherally is well documented. It was found that the observed analgesia in S. dulcis was demonstrated by the active constituents, Glutionl, a triterpene [60-61] and Scoparinol, a diterpene [62] isolated from the plant extract through a peripherally acting mechanism similar to thenon-steroidal anti-inflammatory agents, such as indomethacin and diclofenac sodium.

The possible antioxidant property of aqueous extract of S. dulcis was tested in rats exposed to cadmium. Different group of animals were treated with CdCl2 alone or in combination with graded levels of S. dulcis (i.e. 250, 500 and 1000 mg/kg body wt, respectively). The results show that relative to controls, cadmium significantly reduced superoxide dismutase activity while significantly increasing catalase activity and malondialdehyde levels in the liver and kidney.

Another study summarizes the effect of S. dulcis on the population of immune cells during a 28 day experimental T. brucei infection in rabbits. The result obtained showed that infection resulted in an initial rise in both total white blood cells (WBC) and the absolute number of circulating lymphocytes followed by a progressive decrease in total WBC and all WBC subtypes namely; lymphocytes, monocytes and granulocytes, although the % lymphocytes (lymphocytes expressed as % of total WBC) remained consistently higher than normal throughout the study period. Treatment with S. dulcis at a daily oral dose of 25 mg/Kg body weight significantly reduced the severity of the observed lesions ($p < 0.05$) when compared with untreated infected animals. Thus the herb demonstrates significant potency in protecting against the parasite induced decrease in the population of immunologically active cells.

The antioxidant efficacy of S. dulcis in STZ diabetic rats was compared with Glibenclamide. A significant increase in the activities of plasma insulin, superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase and reduced glutathione was observed in brain on treatment with 200 mg/kg body weight of S. dulcis plant aqueous extract and glibenclamide for 6 weeks. Both the treated groups

showed significant decrease in thiobarbituric acid reactive substances (TBARS) and hydroperoxides formation in brain, suggesting its role in protection against lipid peroxidation induced membrane damage [62]. It may be concluded that in diabetes, brain tissue was more vulnerable to oxidative stress and showed increased lipid peroxidation. The above observation shows that the aqueous extract of S. dulcis plant possesses antioxidant activity, which could exert a beneficial action against pathological alterations caused by the presence of free radicals in STZ diabetes.

Scoparia dulcis was investigated for anti-HSV-2 activity by plaque reduction assay. It was found that water extract of S. dulcis was active against HSV-2 with 50% effective dose of 1,190.4μg/ml and ED50 of ethanol extract of S. dulcis was 13.8μg/ml. Ethanol extract of S. dulcis showed highest Therapeutic Index (TI) (2.9) against HSV-2G.

The cytochrome P450 protective activity of the aqueous extract of S. dulcis was evaluated against CCl4 induced prolongation of pentobarbitone sleep time in Sprague-Dawley rats. The results indicate that, the aqueous extract of S. dulcis, at an oral dose of 0.5 g/kg, p.o., shows a significant protective effect against CCl4 induced cytochrome P450 damage and also show a significant intrinsic cytochrome P450 inhibition activity.

Hyperlipidemic effect of oral administration of the herb, S. dulcis, on T. brucei induced changes in plasma lipid profile in rabbits over a period of twenty eight days. Results obtained show that infection with T. brucei resulted in significant increases in plasma total cholesterol, trriacylglycerol, and low density lipoprotein (LDL)-cholesterol, while the level of high density lipoprotein (HDL)-cholesterol was also significantly reduced. Further comparative analysis of data revealed that these lesions were significantly less severe ($p<0.05$), in the infected and treated group relative to their untreated counterparts. The ability of S. dulcis to mitigate against these plasma lipid anomalies is underscored in the present study The level of total cholesterol, LDL cholesterol and triacylglycerol in treated animals were significantly lower ($p<0.05$) relative to the infected but untreated group. Furthermore, the parasite induced decrease in HDL cholesterol was also significantly resisted in the treated group, thus enhancing the HDL: total cholesterol and the HDL: LDL ratios. This phenomenon no doubt favours a reduction in cardiovascular risk.

A group of experiments were performed on normal and experimental male Wistar rats treated with S. dulcis plant extract. The effect of extract was tested on streptozotocin (STZ) treated Rat insulinoma cell lines (RINm5Fcells) and isolated islets in vitro.

The extract markedly reduced the STZ-induced lipid peroxidation in RINm5F cells. Further, extract protected STZ-mediated cytotoxicity and nitric oxide (NO) production in RINm5F cells. Treatment of RINm5F cells with 5mMSTZ and 10g of extract completely abrogated apoptosis induced by STZ, suggesting the involvement of oxidative stress. Flow cytometric assessment on the level of intracellular peroxides using fluorescent probe 2‘7‘-dichlorofluorescein diacetate (DCF-DA) confirmed that STZ (46%) induced an intracellular oxidative stress in RINm5F cells, which was suppressed by extract (21%). In addition, extract also reduced (33%) the STZ-induced apoptosis (72%) in RINm5F cells indicating the mode of protection of extract on RIN m5Fcells, islets, and pan-creatic cell mass (histopathological observations). Present study thus confirms antihyperglycemic effect of extract and also demonstrated the consistently strong antioxidant properties of S. dulcis used in the traditional medicine [63-65]

Much of the recent research on S. dulcis has centered around one powerful phytochemical called scopadulcic acid B (SDB). In a 1993 clinical study, SDB inhibited the growth of tumors in a test tube and in mice. The potency of SDB proved to be stronger than that of other natural antitumor-promoting terpenoids, such as glycyrrhetinic acid. [66].One of the chemical constituent is an aphidicolin-like tetracyclic diterpene named scopadulciol (SDC), which was isolated from S.

dulcis. SDC showed stimulatory effect on antiviral potency of acyclovir (ACV) or ganciclovir (GCV).

The effect of S. dulcis on T. brucei induced anaemia was investigated on rabbits. Changes in Packed cell volume (PCV), Haemoglobin (Hb) concentration, Red blood cell count (RBC), Mean cell haemoglobin (MCH), Mean cell haemoglobin concentration, (MCHC) and Mean cell volume (MCV) were monitored. The results obtained indicate that infection with T. brucei results in a significant decrease in PCV, Hb concentration and RBC. No significant changes were observed in MCH, MCHC and MCV. However the severity of observed anaemia was significantly less pronounced in the infected rabbits that were treated with S. dulcis when compared with their infected but untreated counterparts. It was concluded that S. dulcis therapy may prove useful in the management of T. brucei anaemia, and possibly other forms of anaemia. The herb may possess a measure of trypanocidal activity or immuno-stimulating properties that help to put the parasite in check and thus also control the deleterious effect of uncontrolled parasite proliferation. The plant has also been used in the management of sickle cell anaemia from decades (Hilda Ogbe, personal communication).

Fruit Juice, Seed Extract and leaf extract of S. dulcis was used for the mineralization of calcium oxalate, calcium carbonate and calcium phosphate. Four experimental models namely 'simultaneous flow static model' (S.S.M.), 'simultaneous flow dynamic model' (S.D.M.), 'reservoir static model' (R.S.M.) and 'reservoir dynamic model' (R.D.M.) were used for the study. The study suggests that the increased intake of fruits juice and seed extract of Scoparia dulcis would be helpful in urinary stone prophylaxis.

Conclusion

From this review we can conclude that studies with new active principles obtained from the whole plant of Scopariadulcis can results in novel and effective pattern of treatment. Chemical substances derived from this plant have been used to treat human diseases since the dawn of medicine. This plant may provide leads to find therapeutically useful compounds.Thus more efforts should be made towards isolation and characterization of the active principles and their structure activity relationship. The combination of traditional and modern knowledge can produce better drugs for the treatment of various ailments with fewer side effects.

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