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Review Article

MEDICINAL PLANTS AND PHYTOCHEMICALS IN PREVENTION AND MANAGEMENT OF LIFE STYLE DISORDERS: PHARMACOLOGICAL STUDIES AND CHALLENGES

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ABSTRACT

The prevalence of lifestyle disorders such as hypertension, diabetes mellitus (DM), dyslipidemia, and overweight/obesity is rising rapidly. Recently the popularity of herbal supplements among patients with lifestyle disorders has been increasing. Consumption of a plant-based diet consisted of appropriate phytochemicals has been accepted as a reliable means for the prevention and management of several disorders. Phytochemicals play a crucial role in disease prevention, especially when lifestyle changes alone are not found effective. Various human and animal trials have established the pharmacological action of phytonutrients present in herbal plants. Several bioactive compounds such as polyphenols, flavonoids, alkaloids, and stilbenes. are present in plants such as garlic, *Aloe vera*, turmeric, tulsi, and drumstick. that have shown a significant beneficial effect on DM, metabolic syndrome, lipid disorders, etc. This review focuses on the therapeutic effect of some of the high potential herbal plants and their phytochemicals in the management of lifestyle disorders and the challenges with the use of herbal medicines.

Keywords: Type 2 diabetes mellitus, Lifestyle disorders, Pharmacological studies, Phytochemicals, Herbal drug targets, Adenosine monophosphate-activated protein kinase.

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INTRODUCTION

India has a long history and strong base for the traditional system of medicine. Herbal plants play an important role in the prevention and treatment of human diseases for decades. It is well established that herbal plants are a rich source of phytochemical moieties (primary and secondary metabolites), which serve as the principle element for the medicinal value of these herbs. In recent years, there has been a resurgence of interest to rediscover medicinal plants as potential drug candidates. There have emerged new insights in the field of herbal medicine and these drugs are gaining increasing acceptance in both developing as well as developed countries due to their natural origin and relatively fewer side effects. Nature has been a source of therapeutic agents for thousands of years, and a large number of modern important medications have originally been obtained from natural sources (for example, vincristine from *Vinca rosea*, morphine from *Papaver somniferum*, Taxol from *Taxus brevifolia*, Atropine from *Atropa belladonna*, etc.) [1]. Currently, the revival of interest in natural products as a potential hotspot for new solutions has gained the attention of the academicians and pharmaceutical industry. A large number of plants with the traditional claim of antidiabetic, antioxidative, and anti-inflammatory activities have been studied worldwide and their efficacy has been validated.

HERBAL PLANTS IN LIFESTYLE DISORDERS

In the Indian traditional system of medicine around 20,000 herbal (medicinal) plants have been documented; though only around 7000–7500 plants are being used to cure different diseases. Moreover, the proportion of these plants in Ayurveda, Siddha, and Unani systems is around 2000, 1300, and 1000 respectively. Besides, around 25,000 plant-based formulations are currently in use in Indian traditional systems. Lifestyle disorders are non-communicable diseases and are associated with a sedentary lifestyle, unhealthy food habits, substance abuse like alcohol, smoking habits, etc. Obesity is one of the global epidemics and over the years it has come up as a social issue as it leads to several health risks. Obesity is one of the leading causes of the development of metabolic disorders such as diabetes, hypertension, and cardiovascular diseases. As per the estimate of the International Diabetes Federation, 25% of the global adult population has metabolic syndrome and its prevalence is predicted to increase in the next few decades [2]. Diabetes mellitus (DM) is a lifestyle disorder characterized by chronic hyperglycemia which is accompanied by increased production of free radicals or oxidative stress which leads to inflammation and several microvascular and macrovascular complications. Herbal plants are rich sources of flavonoids and polyphenolic compounds that show antioxidant activities. In the present review, we summarize the role of herbal plants and their phytochemicals in the prevention and management of lifestyle disorders. The therapeutic efficacy of herbal plants in lifestyle disorders has been summarized in Table 1. The traditional systems of medicine have gained acceptance by the vast population due to relatively fewer side effects and these play a crucial role in the overall health care system especially in developing countries. The demand for herbal-based medicine, health products, pharmaceuticals, food supplements, nutraceuticals, cosmetics is continuously increasing worldwide.

PHYTOCHEMICALS AND THEIR THERAPEUTIC EFFICACY IN LIFESTYLE DISORDERS

Herbal plants contain several bioactive metabolites whose additive and synergistic therapeutic efficacy is beneficial in the prevention and management of lifestyle disorders [42]. Phytochemicals are the primary and secondary metabolites of herbal plants and are essential for the protection and survival of plants. It is well established that the phytochemicals extracted from plants have therapeutic efficacy for the prevention and management of many disorders. Polypotenoids, flavonoids, coumarins, indoles, isoflavones, lignans, organosulfurs, catechinsthe, phenolic acids, stilbenoids, isothiocyanates, saponins, procyanidins, phenylpropanoids, anthraquinones, ginsenosides are the major classes of phytochemicals present in various herbal plants. The phytochemicals and their pharmacological activities in lifestyle disorders have been summarized in Table 2.

Table 1: Therapeutic efficacy of herbals plants in lifestyle disorders

Plant species (common Name)	Part Used	Pharmacological activity	Active agent (s)	References
Allium sativu (Garlic)	Bulbs	Hypoglycemic, hypolipidemic; cardioprotective, anti-inflammatory	Allicin, Terpenoids, flavonoids, and phenols	[3]
Aloe vera (Gheekumari) *Allium cepa* Linn Onions	Leaves Bulbs	Antidiabetic, Hepatoprotective, and reduces obesity-induced Glucose intolerance, Hypoglycemic, hypolipidemic; Reduces proteinuria, Cardioprotective, anti-inflammatory, Anti-bacteria and also prevents high blood pressure	Aloin and emodin, campesterol, β sisosterol, Allicin, peptides, steroids, Terpenoids, flavonoids, and phenols	[4,5]
Aristolochia albida	Root	Anti-inflammatory	Aristolochic	[6,7]
Duchartre (Dutchman Pipe), *Azadirachta indica* Neem	Leaves, fruits	Inhibitor of carcinoma, chemopreventive, inhibit colon cancer, antiallergic, Blood purifier, Anti malaria, insecticide	Acids, aristolachine, aris tannic acids, aristidinic acids Limonoids (nimbidinin), Di- and tri terpenoids, Quinine	
Berberis vulgaris (Barberry)	Fruitbark, root, and	Antidiabetic, hepatoprotective, antimicrobial.	Berberine	[8,9]
Cannabis sativa L. (Marijuana)	stem Leaves	Psychoactive rapid and long-lasting downregulation of CB1R causes reduction of energy storage and increases metabolic rates	Cannabinoids	
Capsicum annum (Bell pepper)	Fruits, and Leaves	Prevention of heart attack and stroke	Capsaicin, Capsaicinoids	[10]
Carpobrotus edulis (L.) (ice plant)	Leaves	Antioxidant effects	Proanthocyanidins and alkaloids	[11]
Catharanthus roseus (Sadabahar)	Whole, Plants (leaf, root, and stem)	Hypoglycemic; hypolipidemic; Increases the activity of glycolytic, Pathway enzymes	Alkaloid	[12]
Cichorium intybus (chicory)	Leaves, roots	Anti-hyperglycemic, antilipidemic, anti-oxidative, and anti-inflammatory activities	Alkaloids, flavonoids, tannin, s and Cichoric acid	[11,12]
Coix lacryma-jobi L. (Adlay)	Seeds	Downregulation of adipogenesis, anti-obesity	Flavonoid, steroids, and Carotenoïds	[13]
Cucumis africanus L. (Scarlet gourd)	Whole plant	Weight loss	Flavonoids	[14]
Curcuma longa (Haldi)	Rhizome	Anti-inflammatory, hepatoprotective, and antioxidant effects	Flavonoid (Curcumin)	[15]
Curtisia dentata (Assegai tree)	Bark	Weight loss	Not reported	[16,17]
Cymbopogon citratus Lemon grass	Leaves	Anti-malaria	Essential oils (e.g. Citral), Limonine, Camphene, citronella, Geraniol, Alkaloids	
Digitalis lanata (Tilapushpi)	Leaves	Used in heart diseases.	Digoxin	[18]
Foeniculum vulgare (Mill Fennel)	Seeds	Reduces oxidative stress, decrease fat and sugar absorption	Phytoestrogens, Dipentene	[19]
Gymnema sylvestre (*Gurmar*)	Leaves	Inhibits glucose absorption and Fatty acid accumulation	Gymnemic acids	[20]
Hoodia gordonii (Masson) (Kalahari cactus)	Stem	Appetite suppAppetite-suppressanorie intake	Oxypregnane steroidal Glycoside	[21]
Kedrostis Africana (L.) (Baboonts Cucumber)	Tuber	A-amylase, α-glucosidase, and Lipase inhibitory activities	Luteolin and Kaempferol	[22]
Mangifera indica (Mango)	Stem bark, Leaves, fruit	Mangiferin	Mangiferin	[23]
Moringa oleifera (Drum stick)	Leaves, Seeds	Antioxidants, lowers body weight, total Cholesterol, triglycerides, and blood glucose level	Quercetin-3-O-β-D glucoside, Saponins, Sterols	[24]
Momordica charantia (Karela)	Fruit	Antidiabetic, antioxidant	Momordicin, charantin	[25]
Nigella sativa (Black cumin)	Seeds	Antidiabetic, hepato renal protective	Thymoquinone	[26]
Ocimum gratissimum L (Clove basil, Sweet basil)	Leaves, essential oils	Antioxidant activity, cardioprotective	Curcumin, flavonoids, isoflavone, flavones	[27]
Ocimum sanctum (Tulsi)	Whole plant	Antidiabetic, hepatoprotective	Apigenin, taxol, and ursolic acid	[28]
Phyllanthus emblica (Amla)	Fruit	Hepatoprotective, antioxidative, and anti-diabetic	Emblicanin A, emblicanin B, Punigluconin and pedunculagin	[29]

(Contd...)

Table 1: ***(Continued)***

Plant species (common Name)	Part Used	Pharmacological activity	Active agent (s)	References
Piper guineense (African black pepper)	Fruits, Leaves, Seeds	Antipyretic, Antiemetic, Antiparasitic, Antimicrobial and antifungal activities	Alkaloidal amides (Piperanine, Dihydrowasanine, Isobutyl-(E, E)-2, 4-Decadienamide)	[30]
Piper nigrum (Kali mirch)	Mirchs	Anti-hyperlipidaemic	Piperidine, dehydropipernonaline, eugenol, kaempferol, myrcene, piperine	[31]
Rauvolfia vomitoria afz (Serpent wood)	Leaves, Seeds	Antihypertensive	Reserpine, Deserpidine, Rescinamine, Yohimbine	[32]
Ricinus communis (Castor bean)	Leaf, root, and seed	Hepatoprotective, anti-oxidant, Hypoglycemic	Alkaloid (ricinine), lectin (ricin)	[33]
Silybum marianum (Milk thistle)	Fruits, seeds, and leaves	Anti-inflammatory, liver tonic for hepatic disorders	Flavonoid silymarin (Silibinin)	[34]
Swertia chirata (Chirayita)	Whole plant	Antidiabetic effect, antiviral, Hepato-renal protective	Ophelic acid, sawertiamarine, Mangeferin and amarogenitine	[35]
Syzygium cumini (Jamun)	Seed, bark	Antidiabetic	Anthocynins, polyphenols	[36]
Terminalia chebula (Harra)	Fruits, Bark	Anti-oxidant, anti-diabetic, Renoprotective, hepatoprotective	Tannins, shikimic acid compounds, triterpenoids, Ellagic acid	[37]
Terminalia arjuna (Arjuna)	Stem-bark	Cardioprotective, hepatoprotective	Arjunic acid, tannic acid, tannins, saponins, gallic acid and phytosterols	[38]
Tinospora cordifolia (Geloy)	Arial plant part	Antidiabetic, Antioxidant etc	Diterpenoid furanolactones (tinosporin), isoquinoline alkaloids	[39]
Trigonella foenum-graecum (Methi)	Seeds, leaves	Antidiabetic	Fenugreekine, nicotinic acid, phytic acid, scopoletin and trigonelline	[40]
Zingiber officinalis (Ginger)	Rhizome	Antioxidant, Hepatoprotective, hypercholesterolaemic	Mono and sesquiterpenoids, Zingerone and gingerols	[41]

A wide range of chemical compounds is synthesized by plants, which are classified based on their chemical nature, biosynthetic origin, and functional groups into primary and secondary metabolites. Secondary metabolites have a wide range of medicinal properties and are the basic source for several current allopathic drugs also [66]. Alkaloids, tannins, flavonoids, saponin, and glycosides are the important secondary metabolites present in plants. Polyphenols and flavonoids are the families of phytochemicals known for their health benefits due to their antioxidative and anti-inflammatory effects [67]. Lifestyle disorders are characterized by inflammati on and an increased level of oxidative stress [68]. Hence, intake of antioxidants in the diet could have positive effects on lifestyle disorders such as obesity, Type 2 DM, etc. Polyphenols are grouped into different classes as per their structure: (i) Simple phenolic acid, for example., ferulic, gallic, ellagic, cholorogenic acid, etc., (ii) curcuminoids, for example., curcumin, (iii) stilbenes e.g. Resveratrol, (iv) lignans, for example., matairesinol, (v) chalcones, for example. phlorizin, chalcone and (vi) flavonoids. The flavonoids are further classified in different subclasses: (a) Flavonols e.g. quercetin, proanthocynidins, (b) anthocyanins, (c) flavanonols, for example. taxifolin, (d) flavanones, for example. naringenin, and (e) isoflavones, e.g. genistein. As discussed earlier, DM is significantly associated with several macro and microvascular complications. These complications are due to chronically elevated hyperglycemia and subsequent oxidative stress. Moreover, a mechanism that contributes to the elevation of oxidative stress in diabetic patients includes nonenzymatic glycosylation, auto-oxidation of glucose, and metabolic stress and may partially be reduced by antioxidants [69]. The phenolic content of plants could be used as the basis for rapid screening of antioxidant activity due to the presence of hydroxyl group which provides free radical scavenging ability. The antioxidant activity of flavonoids which include flavones, flavanols and condensed tannin depends on the free -OH group, especially 3-OH. Resveratrol is present in various plants and has a plethora of therapeutic efficacy including anti-inflammatory and antioxidant [70]. It regulates cellular energy metabolism and mitochondrial homeostasis by targeting sirtuin 1 and (AMPK) [71]. Luteolin (flavones) imparts its anti-inflammatory activity by the inhibition of nuclear factor kappa B gene expression [72]. The phytochemicals present in herbal plants have anti-obesity activities; these suppress the growth of adipocytes, inhibit preadipocyte differentiation and stimulate lipolysis. Genistein suppresses preadipocyte proliferation and adipogenic differentiation of adipose tissue by the instigation of Wnt signaling via ERs-dependent pathways such as Erk/JNK signaling and lymphoid enhancer factor/T cell factor (LEF/TCF4) co-activators [72]. Organosulfurs are widely distributed in several herbal plants and the phytochemicals under this group exert antilipidemic activities through inhibition of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase. These also lower blood pressure and have antithrombotic and hypoglycemic efficacy [73]. The sesquiterpene (terpenoid) has shown beneficial effects in the management of diabetes and obesity-related inflammation [74]. Diosgenin, campesterol, brassicasterol, sitosterol, stigmasterol, and guggulsterone phytochemicals are grouped under the phytosterols and have efficacy in the management of obesity and decrease serum total and low-density lipoprotein-cholesterol levels [75].

CHALLENGES IN THE USE OF HERBAL MEDICINES

In recent years, a belief of the general public towards herbal medicines had is significantly increased due to several factors as follows: (a) Promotion of the traditional systems and herbal medicines by the government and other agencies, (b) several claims on the efficacy of herbal medicines and their wide advertisement in mass media, (c) preference of consumers for herbal therapies as it is generally believed that these are less toxic as compared to synthetic drugs, (d) discontent with the results from pharmaceutical molecules and synthetic drugs and increasing acceptance in the efficacy of herbal medicines in the treatment, (e) pharmaceutical drugs have a relatively higher cost and more side effects, (f) inferential approach based on subjective information, that is, "it worked for my family") treatment based on the faith rather than scientific information. Although the use of herbal medicines has both benefits and risks, it provides an alternative and

Table 2: Summary of potential phytochemicals present in several herbal plants and their pharmacological activities

Class of phytochemicals/metabolites	Chemical nature/characteristics	Pharmacological activity	References
Capsaicin	8-methyl-*N*-vanillyl-6-nonenamide	Weight-loss, attenuate obesity-related, metabolic disorders and liver diseases, enhances adiponectin levels	[43]
Carotenoids	Lipophilic pigments tetraterpenoids	Powerful antioxidant agents	[44]
Catechins	Derivatives of flavans, possess a 2-phenyl-3,4-dihydro-2*H*-chromen-3-ol skeleton	Inhibit gastric lipases and increase thermogenesis	[45]
Chalcones	Open-chain flavonoids in which the two aromatic rings are joined by a three-carbon unsaturated carbonyl system	Anti-inflammatory and antioxidant	[46]
Chicoric acid	Phenyl propanoid	Amelioration of diabetes	[47]
Chlorogenic acid and Caffeic acid		Ameliorate glucose metabolism	[48]
Curcuminoids	Two linked molecules of ferulic acid	Antioxidant, and anti-inflammatory activities, Anti-obesity, anti-hyperglycemic, and anti-hyperlipidemia	[15]
Lactucin	Sesquiterpene lactones	Antioxidative, Anti-inflammatory, and anti-hyperglycemic activities	[49]
Ferulic acid	Phenolic compound	In-vitro antioxidant activities, hypolipidemic properties, an in-vitro inhibitor of tumor promotion	[50]
Flavanonols	3-hydroxy-2,3-dihydro-2-phenylchromen-4-one backbone	Anti-inflammatory activities in-vitro, inhibits cholesterol synthesis	[51]
Flavones	Glycosides of luteolin and apigenin	Weight loss, anti-atherogenic	[52]
Flavonols	Flavonoids	Anti-inflammatory, anti-oxidant, and anti-proliferative effects, beneficial effects on endothelial function	[53]
Genistein and daidzein	Isoflavones	Suppress adipogenic differentiation of adipose tissue	[54]
Lignans	Polyphenol	Antioxidant and reduces total and LDL cholesterol	[55]
Luteolin	Flavone	Antioxidant and anti-inflammatory activities	[56]
Lycopene	Red carotenoid	Powerful antioxidant, inhibit of LDL oxidation and lipid peroxidation	[57]
Monoterpene	Derivative auraptene	PPARα/γ dual agonist, regulates the transcription of PPAR target genes, induces the expression of adiponectin, and inhibits those of MCP-1	[58]
Naringenin	Flavanone	Inhibits inflammation	[59]
Allicin, allixin, and allyl sulphides	Organosulfurs	Decrease the synthesis of cholesterol by hepatocytes, lower blood pressure, powerful anti-thrombic, hypoglycemic	[60]
Campesterol, sitosterol, and stigmasterol	Phytosterols	Protect against atherosclerosis, decrease serum total and LDL-cholesterol levels, inhibit cholesterol absorption	[61]
Quercetin	Flavonol	Anti-lipase activity	[62]
Resveratrol	Stilbenoid	Decrease LDL-cholesterol, exert anti-platelet	[63]
Sesquiterpenes	Terpenes	Anti-inflammatory, analgesic, and cytotoxic	[64]
Terpenoids (isoprenoids)	Terpenes	Activate PPARγ, control energy homeostasis	[65]

LDL: Low-density lipoprotein, MCP-1: Monocyte chemoattractant protein-1, PPAR: Peroxisome proliferator-activated receptors

effective treatment for many disorders. However, there is a lack of safety studies on herbal medicines. We strongly advocate the following issues for the use of herbal medicines as follows: (i) Quality certification is strictly required for herbal products that include authentication, standardization, and stability of the product. (ii) Safety of the herbal product: The consumers erroneously recognize that as the herbal medicines are natural so these are safe, which is not always true. (iii) Pharmacokinetic profile: The efficacy of any drug depends on the optimum dose. Hence, the selection of key metabolite(s) and their pharmacokinetic profile is essential. (iv) Efficacy of herbal products: A well-planned, scientifically designed preclinical and clinical study is crucial for the efficacy of herbal products. Hence, a pertinent regulatory system is required to take suitable measures for ensuring the quality of herbal medicines in respect to safety, efficacy, uniformity, and other factors of the herbal products.

CONCLUSION

Similar to conventional synthetic medicines, there needs to be a licensing system for herbal medicine based on safety, quality, and

efficacy. Moreover, all this comprehensive information such as indications, precautions, how to use the product, side effects, how to store the product, and regulatory information should accompany a leaflet that should be inserted into the product package. Recently in India, the Ministry of AYUSH has formulated the guidelines for licensing the herbal product (Ministry of AYUSH) [76]. However, more work is needed to be done for maintaining the quality and safety of herbal products. Many of the unregistered herbal products are sold freely in the market globally especially in developing countries with very little or no restraint. Further, the common belief is that natural products are not toxic and these drugs are routinely taking by the population. This needs to be cautioned. At the last, it has become essential that herbal products/medicines are put under the umbrella of drug regulatory framework in every country to maintain the drug standards of safety, quality, uniformity, and efficacy.

AUTHOR CONTRIBUTIONS

All the authors have made equal contribution.

DECLARATION OF COMPETING INTEREST

No potential conflicts of interest were disclosed.

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