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

SHALU SINGH1, VINEET JAIN2, SWATANTRA KUMAR JAIN3, KAILASH CHANDRA1*

1Departments of Biochemistry, Hamdard Institute of Medical Sciences and Research, Jamia Hamdard, New Delhi, India. 2Department of Medicine, Hamdard Institute of Medical Sciences and Research, Jamia Hamdard, New Delhi, India. Email: chandradr795@gmail.com

Received: 25 August 2021, Revised and Accepted: 26 October 2021

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 in 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 chronically high blood sugar levels 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. Polyphenoloids, flavonoids, coumarins, indoles, isoflavones, lignans, organosulfurs, catechins, phenolic acids, stilbenes, isothesiocyanates, saponins, procyadins, 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.
| Plant species (common Name) | Part Used | Pharmacological activity | Active agent (s) | References |
|----------------------------|-----------|--------------------------|------------------|-----------|
| Allium sativum (Garlic)    | Bulbs     | Hypoglycemic, hypolipidemic; cardioprotective, anti-inflammatory | Allicin, Terpenoids, flavonoids, and phenols | [3] |
| Aloe vera (Gheekumari)     | Leaves    | 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, Allcin, peptides, steroids, Terpenoids, flavonoids, and phenols | [4,5] |
| Neem                       | Bulbs     | Anti-inflammatory Inhibitor of carcinoma, chemo preventive, inhibit colon cancer, antiallergic, Blood purifier, Anti malaria, insecticide | Aristolochic Acids, aristolachine, aris tannic acids, aristidinic acids | [6,7] |
| Berberis vulgaris (Barberry)| Fruits    | Anti-diabetic, hepatoprotective, antimicrobial. | Aloin and emodin, campesterol, β-sisosterol, Allicin, peptides, steroids, Terpenoids, flavonoids, and phenols | [8,9] |
| Cannabis sativa L. (Marijuana) | Leaves | Prevention of heart attack and stroke | Capsaicin, Capsaicinoids | [10] |
| Cichorium intybus (chicory) | Leaves | Anti-hyperglycemic, antilipidemic, anti-oxidative, and anti-inflammatory activities | Alkaloids, flavonoids, tannin, s Cichoric acid | [11,12] |
| Coix lacryma-jobi L. (Adlay)| Seeds | Downregulation of adipogenesis, anti-obesity | Alkaloids, flavonoids, tannin, s Cichoric acid | [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 (eg. Citral), Limonine, Camphene, citronella, Geraniol, Alkaloids | [16,17] |
| Digitalis lanata (Tilapushpi) | Leaves | Used in heart diseases. Reduces oxidative stress, decrease fat and sugar absorption | Digoxin, Phytoestrogens, Dipentene | [18,19] |
| Foeniculum vulgare (Mill Fennel) | Seeds | Inhibits glucose absorption and Fatty acid accumulation | Gynemic acids | [20] |
| Hoodia gordoni (Masson) (Kalahari cactus) | Stem | Appetite suppression and weight loss | Oxypregnane steroidal Glycoside | [21] |
| Kedrostis (African) L. (Baboons Cucumber) | Rhizome | Anti-inflammatory, hepatoprotective, and antioxidant effects | 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) | Fruits | Antidiabetic, antioxi dant | Momordicin, charantin | [25] |
| Nigella sativa (Black cumin) | Seeds | Antidiabetic, hepatorenal 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 Hepatoprotective, antioxidant, and anti-diabetic | Apigenin, taxol, and ursolic acid | [28] |
| Phyllanthus emblica (Amla) | Fruit | Hepatoprotective, antioxidant, and anti-diabetic | Emblicamin A, emblicamin B, Punigluconin and pedunculagin | [29] |

(Contd...)
Pharmacological activity

Seed, bark
Fruits, bark
Anti-inflammatory, liver tonic for hepatic disorders
Antidiabetic effect, antiviral, Hepato-renal protective
Antioxidant, Antihyperlipidemic

Whole plant
References

[36] Anthocyanins, polyphenols
[33] Antioxidant, Hepatoprotective, Antidiabetic, Antioxidant etc
[34] Hepatoprotective, antioxidant, Hypoglycemic
[35] Flavonol silymarin (Silibinin)
[36] Anthocyanins, polyphenols
[37] Tannins, shikimic acid
[38] Ellagic acid, tannic acid, tannins, saponins, gallic acid and phytoestrogens
[39] Diterpenoid furanolactones (tinosporin), isoquinoline alkaloids
[40] Penrogroene, nicotinic acid, phytic acid, scopoletin and trigoctline
[41] Mono and sesquiterpenoids, Zingerone and gingerols

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, saponins, 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 inflammation 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, chlorogenic 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) flavonoids, 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, flavonols and condensed tannin depends on the free -OH group, especially hydroxyl group which provides free radical scavenging ability. 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, flavonols and condensed tannin depends on the free -OH group, especially the free -OH group which provides free radical scavenging ability. 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 β-catenin and MAPK/ERK/PI3K/AKT pathways [73]. The sesquiterpene (terpenoid) has shown beneficial effects in the management of diabetes and obesity-related inflammation [74]. Diosgenin, campesterol, brassicasterol, stigmasterol, stigmastanol, and guggulsterone phytochemicals are grouped under the phytosterols and phytosteryl esters. The sesquiterpene (terpenoid) has shown beneficial effects in the management of diabetes and obesity-related inflammation [74]. Diosgenin, campesterol, brassicasterol, stigmasterol, stigmastanol, and guggulsterone phytochemicals are grouped under the phytosterols and phytosteryl esters. Diosgenin, campesterol, brassicasterol, stigmasterol, stigmastanol, and guggulsterone phytochemicals are grouped under the phytosterols and phytosteryl esters.

CHALLENGES IN THE USE OF HERBAL MEDICINES

In recent years, a belief of the general public towards herbal medicines had 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
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

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

| Class of phytocchemicals/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 tetramerpenoids | Powerful antioxidant agents                                                               | [44]       |
| Catechins                           | Derivatives of flavans, possess a 2-phenyl-3,4-dihydropyran-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                       | Pheny propanoid                  | Amelioration of diabetes                                                                  | [47]       |
| Chlorogenic acid and Caffeic acid   |                                 | Ameliorate glucose metabolism                                                             | [48]       |
| Curcuminoids                        | Two linked molecules of ferulic acid | Anti-oxidant, 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]       |
| Flavanols                           | 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-l-atherogenic                                                         | [52]       |
| Flavonoids                          | 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]       |
| Monoterpenes                        | Derivative auraptene             | PPARs\(\alpha\)/\(\gamma\) dual agonist, regulates the transcription of PPAR target genes, induces the expression of adiponectin, and inhibits those of MCP-1 | [58]       |
| Naringenin                          | Flavone                          | Inhibits inflammation                                                                     | [59]       |
| Allicin, allysin, and allyl sulphides| Organsulfur                      | Decrease the synthesis of cholesterol by hepatocytes, lower blood pressure, powerful anti-thrombic, hypoglycemic | [60]       |
| Campesterol, sitosterol, and stigmastanol | Phytosteryl                    | 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, exerts anti-inflammatory, analgesic, and cytotoxic | [63]       |
| Sesquiterpenes                      | Terpenes                         | Activate PPAR\(\gamma\), control energy homeostasis                                        | [64]       |
| Terpenoids (isoprenoids)            | Terpenes                         |                                                                               | [65]       |

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

FUNDING SOURCE
N/A.

REFERENCES
1. Cragg GM, Newman DJ. Natural products drug discovery and development at the United States national cancer institute. Drug Discov Tradit Chinese Med 2001;19-32.
2. O’Neill S, O’Driscoll L. Metabolic syndrome: A closer look at the growing epidemic and its associated pathologies. Obes Rev 2015;16:1-12.
3. Thomson M, Al-Amin ZM, Al-Qattan MK, Shaban LH, Ali M. Anti-diabetic and hypolipidaemic properties of garlic (Allium sativum) in streptozotocin-induced diabetic rats. Int J Diabetes Metabolism. 2007;15:108-15.
4. Misawa E, Tanaka T, Yahagi T, Usui S, Nakamura M, Hori K, Itagaki S, Yamada M. The effect of garlic on blood glucose and insulin levels in streptozotocin-induced diabetic rats. Jpn J Pharmacol 2008;106:377-82.
5. Ikekubolo JO, Ifeanyi SO. The antioxidant activities of the bioactive flavonoid (kaempferol-3-0-D-glucoside) isolated from Allium cepa. Recent Pat Antioxid. Drug Discov 2016;11:44-52.
6. Sowonora A, Ogumhodede E, Onayade A. The role and place of medicinal plants in the strategies for disease prevention. Afr J Tradit Complement Altern Med 2013;10:210-29.
7. Chattopadhyay R. Possible mechanism of hepatoprotective activity of Azadirachta indica leaf extract: Part II. J Ethnopharmacol 2003;89:217-9.
8. Rahimi-Madiseh M, Lorigozi Z, Zamani-Gharaghashi H, Rafieian-Kopaei M. Berberis vulgaris: Specifications and traditional uses. Iran J Basic Med Sci 2017;20:569-87.
9. Andre CM, Hausman JF, Guerriero G. Kedlaya R, Vasudevan DM. Inhibition of lipid peroxidation by botanical extracts of Ocimum sanctum: In vivo and in vitro studies. Life Sci 2004;76:21-8.
10. Khan K. Roles of Emblica officinalis in medicine-a review. Bot Res Int 2009;2:218-28.
11. Ekanem AP, Wang M, Simon JE, Obiezieke AI, Morah F. In vivo and in vitro activities of the seed extract of Piper guineense Schum. and Thonn. Against skin and Gill monogenean parasites of goldfish (Carassius auratus auratus). Phyther Res 2004;18:793-7.
12. Shaba P, Pandey NN, Sharma OP, Rao JR, Singh RK. Anti-trypanosomal Activity of Piper Nigrum L (Black pepper) against Trypanosoma evansi. J Vet Adv 2012;2:304-401.
13. Patel MB, Poisson J, Pousset JL, Rowson JM. Alkaloids of the leaves of Rauwolfia vomitoria Afe. J Pharm Pharmacol 1964;16:1635-7.
14. Nicolson G, Blaustein J. The interaction of Ricinus communis agglutinin with normal and tumor cell surfaces. Biochim Biophys Acta 1972;266:543-7.
15. Shaker E, Mahmoud H, Muaa S, Silimyram, the antioxidant component and Silybum marianum extracts prevent liver damage. Food Chem Toxicol 2010;48:803-6.
16. Ma K, Ba B. Chemical composition and pharmacology of a medicinal herb. Swertia chirata. Res Artic Int J Pharm Sci 2020;11:308.
17. Kumar A, Ilavarasan R, Rajachandran T, Deecaraman M, Aravindan P, Padmanabhan N, et al. Anti-diabetic activity of Syzygium cumini and its isolated compound against streptozotocin-induced diabetic rats. J Med Plants Res 2008;2:246-9.
18. Cheng HY, Lin TC, Yu KH, Yang CM, Lin CC. Antioxidant and free radical scavenging activities of Cymbopogon citratus and Ocimum gratissimum in streptozotocin-induced diabetic rats. J Ethnopharmacol 2009;124:263-70.
19. Kedrostis africana (L.) Cogn. Heliyon 2018;4:e00810.
20. Singh et al. Asian J Pharm Clin Res, Vol 14, Issue 12, 2021, 1-6
human health. J Sci Food Agric 2000;80:1744-56.
43. De Lourdes Reyes-Escogido M, Gonzalez-Mondragon EG, Vazquez-Tzompantzi E. Chemical and pharmacological aspects of capsaicin. Molecules 2011;16:1253-70.
44. Fraser PD, Bramley PM. The biosynthesis and nutritional uses of carotenoids. Prog Lipid Res 2004;43:228-65.
45. Boschmann M, Thielecke F. The effects of epigallocatechin-3-gallate on thermogenesis and fat oxidation in obese men: A pilot study. J Am Coll Nutr 2007;26:3898-95.
46. Nowakowska Z. A review of anti-infective and anti-inflammatory chalcones. Eur J Med Chem 2007;42:125-37.
47. Chandra K, Khan W, Jetley S. Antidiabetic, toxicological, and metabolomic profiling of aqueous extract of Cichorium intybus seeds. Pharmacogn Mag 2018;14:377.
48. Chandra K, Jain SK. Therapeutic potential of Cichorium intybus in lifestyle disorders: A review. Asian J Pharm Clin Res 2016;9:20-5.
49. Chandra K, Jain V, Jabin A, Dwivedi S, Joshi S, Ahmad S, et al. Effect of Cichorium intybus seeds supplementation on the markers of glycemic control, oxidative stress, inflammation, and lipid profile in Type 2 diabetes mellitus: A randomized, double-blind placebo study. Phyther Res 2020;34:1609-18.
50. Srinivasan M, Sudheer AR, Menon VP. Furalic acid: Therapeutic potential through its antioxidant property. J Clin Biochem Nutr 2007;40:92-100.
51. Do GM, Kwon EY, Kim HJ, Jeon SM, Ha TY, Park T, et al. Long-term effects of resveratrol supplementation on suppression of atherogenic lesion formation and cholesterol synthesis in apo E-deficient mice. Biochem Biophys Res Commun 2008;374:55-9.
52. Cotelle N, Bernier JL, Catteau JP, Pommeroy J, Wallet JC, Gaydou EM, et al. Antioxidant properties of hydroxy-flavonoids. Free Radic Biol Med 1996;20:35-43.
53. Sartelet H, Serghat S, Lobstein A, Ingenbleek Y, Anton R, Petitfrère E, et al. Flavonoids extracted from fomio millet (Digitaria exilis) reveal potent antithyroid properties. Nutrition 1996;12:100-6.
54. Kim MH, Park JS, Seo MS, Jung JW, Lee YS, Kang KS, et al. Genistein and daidzein repress adipogenic differentiation of human adipose tissue-derived mesenchymal stem cells via Wnt/beta-catenin signalling or lipidysis. Cell Prolif 2010;43:594-605.
55. Adlerecreutz H. Lignans and human health. Crit Rev Clin Lab Sci 2007;44:483-525.
56. Rezai-Zadeh K, Ehrhart J, Bai Y, Sanberg PR, Bickford P, Tan J, et al. Apigenin and luteolin modulate microglial activation via inhibition of STAT1-induced CD40 expression. J Neuroinflammation 2008;5:41.
57. Stahl W, Sies H. Lycopene: A biologically important carotenoid for humans? Arch Biochem Biophys 1996;336:1-9.
58. Kuroyanagi K, Kang MS, Goto T, Hirai S, Ohyama K, Yasuda T, et al. Citrus aurantiifolia acts as an agonist for PPARs and enhances adiponectin production and MCP-1 reduction in 3T3-L1 adipocytes. Biochem Biophys Res Commun 2008;366:219-25.
59. Galluzzo P, Ascanzi P, Bulzomi P, Marino M. The nutritional flavanone naringenin triggers antiestrogenic effects by regulating estrogen receptor alpha-palmitoylation. Endocrinology 2008;149:2567-75.
60. Williams DJ, Edwards D, Hamernig I. Vegetables containing phytochemicals with potential anti-obesity properties: A review. Food Res Int 2013;52:323-33.
61. Marangoni F, Poli A. Phytosterols and cardiovascular health. Pharmacol Res 2010;61:193-9.
62. Smith C, Lombard KA, Pfeffley EB, Liu W. Genetic analysis of quercetin in onion (Allium cepa L.) Lady raider. Texas J Agric Nat Resour 2003;16:24-8.
63. Pervaiz S, Holme AL. Resveratrol: Its biologic targets and functional activity. Antioxidants Redox Signal 2009;11:2851-97.
64. Rodriguez E, Towers GH, Mitchell JC. Biological activities of sesquiterpene lactones. Phytochem Pergamon 1976;15:1573-80.
65. Kawada T, Goto T, Takahashi N, Hirai S. Various Terpenoids derived from herbal and dietary plants function as PPAR modulators and regulate carbohydrate and lipid metabolism. PPAR Res 2010;2010:483958.
66. Rao ML, Savithramma N, Ankanna S. Phytochemical screening of traditional medicinal plants. J Pharm Res 2011;4:3414-6.
67. Bravo L. Polyphenols: Chemistry, dietary sources, metabolism, and nutritional significance. Nutr Rev 1998;56:317-33.
68. Marseglia L, Manti S, D’Angelo G, Nicotera A, Parisi E, Di Rosa G, et al. Oxidative stress in obesity: A critical component in human diseases. Int J Mol Sci 2015;16:378-400.
69. Schultz A, Johannsen J, Harris AK, Rychly D, Ercal A. Oxidative stress and the use of antioxidants in diabetes: Linking basic science to clinical practice. Cardiovasc Diabetol 2005;4:1-11.
70. Xia N, Daiber A, Förstermann U, Li H. Antioxidant effects of resveratrol in the cardiovascular system. Br J Pharmacol 2017;174:1633-46.
71. Tomé-Carneiro J, Gómez-Moreno M, Larrosa M, Garcia-Almagro FJ, Avilés-Plaza F, Parra S, et al. Consumption of a grape extract supplement containing resveratrol decreases oxidized LDL and ApoB in patients undergoing primary prevention of cardiovascular disease: A triple-blind, 6-month follow-up, placebo-controlled, randomized trial. Mol Nutr Food Res 2012;56:810-21.
72. Middleton E, Kandaswami C, Theoharides TC. The effects of plant flavonoids on mammalian cells: Implications for inflammation, heart disease, and cancer. Pharmacol Rev 2000;52:673-751.
73. Benkabila N, Lanzotti V. Global science books allium thiosulfinates: Chemistry, biological properties and their potential utilization in food preservation. Food 2007;1:193-201.
74. Zhang L, Denua AL. Natural products and drug discovery. Nat Prod Drug Discov Ther Med 2005;3:29.
75. Iazar M, Tegani DM, Soraia HK, Fonseca FA. Flavonoids and phytosterolemia: Gene-diet interactions. Genes Nutr 2011;6:17-26.
76. Ministry of AYUSH. Acts, Rules and Notifications. India: Ministry of AYUSH, GOI; 2021.