ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 13, Issue 9, 2020

Online - 2455-3891
Print - 0974-2441

Review Article

VITAL POTENTIAL OF MULTIPLE HERBS IN PROPHYLAXIS OF OBESITY

PRANAY WAL, ANKITA WAL, MADHVI CHAUBEY

Department of Pharmacology, Institute of Pharmacy, Pranveer Singh Institute of Technology, Kanpur, Uttar Pradesh, India.
Email: pranaywal@gmail.com

Received: 18 May 2020, Revised and Accepted: 26 June 2020

ABSTRACT

Objective: Allopathic medications are associated with several inconveniences such as drug dependency. More than 2000 herbal medicines have been proved to have a therapeutic effect in multiple disorders. The prominent aim of this review paper is to compute the therapeutic effect of herbal drug against obesity along with their different mechanisms.

Methods: Data have been selected by evaluating merger of specific review and research papers through filtering through data bases such as PubMed, and Google Scholar of last 10 years 2009–2019.

Results: On the basis of our interpretations, we have concluded that the herbal drugs constituting active constituents' as tannins, alkaloids, resins, saponins, and flavonoids are effective in lowering the blood triglycerides level, lipid accumulation in liver, fat accumulation, adipocyte differentiation, and ultimately decrease body weight with almost negligible toxicity.

Conclusion: Obesity is highly related to elevated morbidity rate as well as has become cause of various disorders. Herbal drugs have potential to treat obesity through different mechanisms including lipid peroxidation, free-radical scavenging activity, and inhibition of fat accumulation.

Keywords: Obesity, Leptin, Herbal drugs, Triglycerides.

 DOI: http://dx.doi.org/10.22159/ajpcr.2020.v13i9.38365

INTRODUCTION

Obesity is characterized at an extensive level in the world population in today's scenario. It is an outcome of certain atrocious behavior, hereditary factors, nutrition deficiency, and inadequacy of the physical exercise [1]. The main cause of central and visceral obesity is the storage of diet, having glut energy density. According to the World health organization, obesity, as well as overweight, is defined as "odd and exaggerated aggregation of fat which influences health." A person is said to be obese if assessing BMI rate 30 or above it. The excessive energy accumulation specifically in adipocytes accounts increment in the progression of lipolysis phenomenon, as per its consequence, leukocytes infiltration proceeds cytokines secretion, macrophages produces adipocytes inflammation, leading to a state of pro-inflammation, dysfunction of endothelium, and insulin resistance. Therefore, chances of augmentation of several chronic disorders take place including renal dysfunctions and type 2 diabetes [2]. The frequency of disease prevalence has been doubled in the world population since up to 13% among whom 15% of women and 11% of men comprise the total blood population. The enormous expansion in body fat has serious constrains of serious metabolic syndromes and disorders [3]. Risk factors associated with obesity are predominantly, individual's behaviors, physical activity, and diet play a considerable role in alleviating obesity risk. More than 135 million people in India were influenced by obesity. The rate of prevalence depends on age, geographical environment, gender, socioeconomic status, and other factors. As per ICMR – INDIA epidemiological report of the year 2015, there is variation in the prevalence rate of obesity that is 16.9–36.3%, and prevalence rate of central obesity is 11.8–31.3% [4]. In addition, socioeconomic, environmental, and sociocultural also contribute to the risk factor of the disease. The environment of family and lifestyle patterns can be also influencing risk factors of obesity, especially during a young age [5]. The first and foremost treatment for obese patients is the alteration in lifestyle along with a restricted diet [6]. Those patients who cannot follow a restricted diet and lifestyle are kept on pharmacotherapy [7]. Obedience to a strict diet is quite poor and the synthetic medications have many side effects. Hence, there is an urge to introduce herbal medications in treatment therapy because of their safer therapeutic property and better patient adherence [8,9]. Herbal products have benefits over conventional drugs like these can be included in the diet. Extracts of various plants are effective as antioxidants, anti-inflammatory, antihyperglycemic, and effective against obesity [10-15]. As per jillions of studies, it is reported that plenty of natural herbs encompassing alkaloids, tannins, steroidal saponins, flavonoids, and glycosides as their active chemical constituents, have therapeutic potential to treat obesity. Several phenolic compounds have been found as a stimulating agent at the molecular level against obesity and metabolic disorders related to it [16,17]. Glycoside derived from the specific herb has a fruitful role in lowering down obesity in high fat-induced rats [18]. Furthermore, herbal drugs specifying saponin as active chemical constituents have shown a potent effect in weight loss [19]. In present, natural products and their therapeutic effects are being spotlighted by researchers to minimize the obesity effect along with slight or negligible toxicity [20]. This review accentuates on current research activities performed on herbal drugs in context to obesity. The study comprises the mechanism of obesity, factors responsible for obesity, and summaries of different researcher's activities done using various herbs against obesity along with their mechanisms.

MECHANISM OF OBESITY

Obesity is identified by the disproportionate white adipose tissue (WAT) enlargement [21], due to the multiplication of adipocyte number which is called hyperplasia or because of increment of adipocyte size, called as hypertrophy [22]. Adipocyte is characterized for extra storage of surplus energy which is stored in the form of triglycerides (TGs) and is released in the form of free-fatty acids (FFA) during lack of energy [23]. Hypertrophy of adipocyte is liked with oxidative stress, endoplasmic reticulum stress, fibrosis, hypoxia, adipocyte dysfunction, and insulin resistance [24]. In addition, hypertrophy in the case of adipose tissue causes cell death which results in infiltration mechanisms in which

M1 which is known as pro-inflammatory macrophages undergoes infiltration and ultimately leads to inflammation [25-27]. Adipocyte inflammation and dysfunction are accepted as main mechanisms relating to obesity [28-30]. Nonfunctional adipocyte tends to produce a greater quantity of cytokines into the blood circulation, persuading inflammation into peripheral tissues which include the brain, heart, liver, muscle, and pancreas. Analogs to this elevated level of pro-inflammatory cytokines and FFAs transduce signal and assign immune cells within these tissues and which results in inflammation, chronic [31]. The rapid and high concentration of FFAs leads to ectopic accumulation of lipid which generates highly toxic metabolites of lipids, for an instance, ceramides, which ultimately induce oxidative stress and metabolism nonfunctioning [32]. The link between copper balance and metabolism has been evidenced to show an effect on obesity. Copper is crucial for the respiration of adipocyte cells through mitochondrial respiration and functional against free radicals. Lack of copper is interrelated with an elevation of deposition of fat, hypertrophy of adipose tissues due to the changed metabolism process through adipocytes [33]. As per epidemiological reports, more frequent intake of carbohydrates and highly saturated fats leads to deposition of the intra-abdominal mass of fat, followed by variation in adipocytokine release pattern as well as altered lipid metabolism homeostasis [34,35]. Adipose tissue is mainly classified into two types: WAT is found in subcutaneous and visceral adipose tissues are commonly known fatty cells. These WATs are involved in the development of fat bulk, eventually, and cause obesity. The other type of adipose tissue is known as brown adipose tissue (BAT), is tiny and their prominent role is thermogenesis. BAT's deposits mainly occur on perirenal and interscapular and also along the regions of great vessels [36]. Specifically, in the case of some type of obesity BAT functions such as esterification, uptake, and further circulation of fatty acids into the blood circulation and accumulation of TG is responsible for white adipocyte metabolism function for adaptation of energy as per animal requirements. BAT also avoids unwanted lipid accumulation and lipid toxicity in liver and skeletal muscle. Intake of rich caloric diet cause synthesis of TGs and lipogenesis, further released fatty acids are consolidated with TGs, all these processes eventually result in very-low-density lipoproteins (VLDL) secretion. Adipocyte lipoprotein lipase (LPL) activity tends to diminish once WAT fails to store TG because of its bulk quantity, through the hydrolysis process of TG which is carried by chylomicrons through the intestine. After a certain period, cause an increment in TGs levels into blood circulation. Likewise, adipocytes hypertrophy progression indicates inflammation, hypoxia, and macrophages infiltration promotes the generation of different mediators which are pro-inflammatory such as interleukin 6, tumor necrosis factor-alpha, plasminogen inhibitor 1, monocyte chemoattractant protein 1, and C- reactive protein [37]. Transcription factor, peroxisome proliferator-activated receptor gamma, has a major role in proliferation and differentiation of adipocytes, resulting in enlargement and multiplication of tiny adipocytes in response to balance energy along with better insulin sensitivity [38,39]. Insulin resistance in WAT and abdominal obesity facilitates FFAs generation in blood circulation as well as lipolysis. In addition, because of which remnant chylomicrons concentration in the blood increases as a result of diminished LPL in WAT and liver. The secretion of VLDLs from the liver elevates TGs. Increase the flow of FFAs in the portal system, apolipoprotein –B-100 generation increase, reduction of high-density lipoprotein (HDL), and production of low-density lipoprotein particles enhances [40,41]. All these processes are interlinked and associate with obesity. These metabolic disorders are directly or indirectly linked with abdominal obesity (Fig.1).

The antiobesity activity of flavonoids

Flavonoids are defined as familiar polyphenolic compounds, isolated from various plant sources. Flavonoids are characterized as photosynthesis active agents or pigments [42,43]. These compounds are present in a rich amount in human food as polyphenols [44,45]. The polyphenols have high therapeutic value as well as a range of medicinal characteristics [46]. Structurally, the compound consists of two benzene ring linearly joined by carbon chain and with carbon skeleton of 15 carbons (C6-C3-C6). Based on substitution at the carbon ring, flavonoids are classified into different classes [47,48]. Further flavonoids are characterized into various subgroups, majorly into six subgroups which include flavonols along with myricetin, quercetin, and kaempferol, isoflavonoids along with glycitein, daidzein, genistein, and flavanones along with luteolin and apigenin and anthocyanins including delphinidin, petunidin, peonidin, malvidin, pelargonidin, and

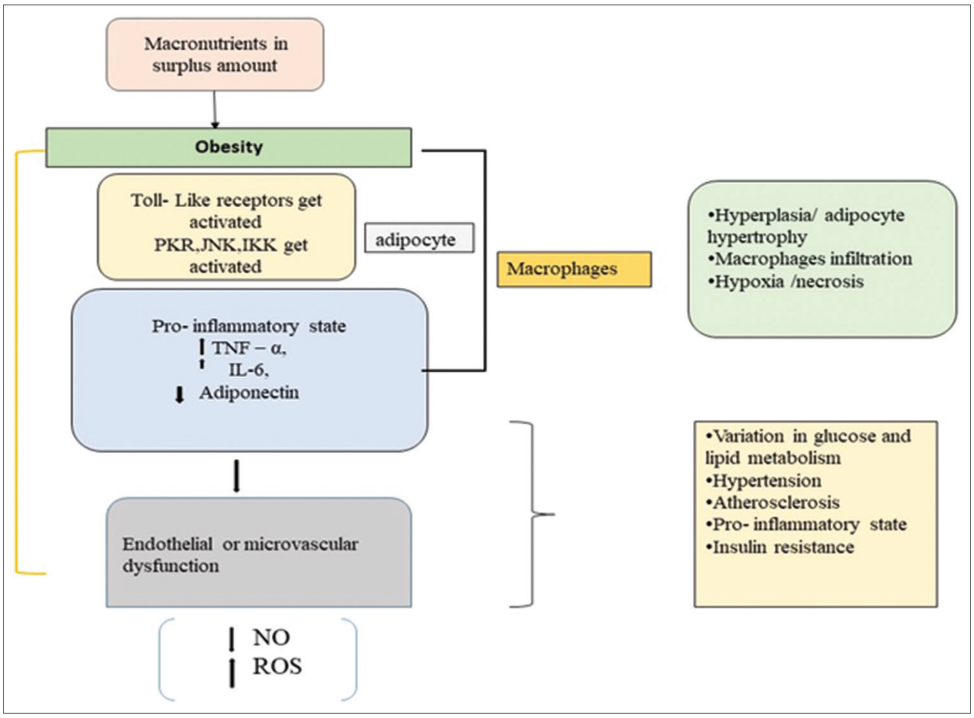

Fig. 1: Representing the mechanism through which multiple metabolic syndromes are interlinked with obesity of abdomen [109-115]. PKR: Protein kinase R, TNF-α: Tumor necrosis factor α, ROS: Reactive oxygen species, IL6: Interleukin 6, NO: Nitric oxide, IKK: Inhibitor of K kinase, JNK: c-jun N – terminal kinase

flavans 3-ol along with quercetin. According to numerous studies, it has been indicated that flavonoids exhibit better therapeutic potential in various diseases [49,50]. Flavonoids tend to improve obesity and are quite helpful in the management of weight [51-53]. The numbers of researches have been done which proves the antiobesity activity of flavonoids [56]. Some of which are summarized in Table 1.

The antiobesity activity of saponins

Saponins are naturally occurring compounds formed through conjugation of isoprenoid aglycone and sugar moieties. The term saponin describes its characteristics to acquire foam like soap because of its high spreadability when dissolved in aqueous solutions. Due to the amphiphilic property of saponins foam formation takes place, as there is a linkage between side chains of hydrophilic saccharides and lipophilic sapogenins [60]. Saponins are separated most widely from plants belonging to the *Magnoliophyta* division, including monocotyledons and dicotyledons, although, dicotyledons cover a wide range of plants that produce saponins in comparison to monocotyledons [61]. Saponin containing herbs is being frequently utilized by the cosmetics and food industry because of its foam-forming property and its chemical characteristics [62,63]. Many medicinal plants such as *Glycyrrhiza glabra* have major chemical constituents as saponins when extracted out [64]. Similarly, the extract of Panax ginseng contains saponins in major amount and is pharmacologically beneficial [65]. Saponins exhibits anti-inflammatory property [66], antiviral property [67], anticancer property [68], antifungal property [69], and antioxidant activity [70]. Few of them are summarized in Table 2.

The antiobesity activity of tannins

According to the definition, tannins are defined as the collection of secondary metabolites derived from plants that can convert the skin of animals into the leather. These compounds are phenolic which are water-soluble having molar mass in the range of 300–3000. These compounds are capable to precipitate proteins, gelatins, and alkaloids. However, currently, more compounds have been recognized that of 2000 Da, whose structures are similar [76]. Tannins are classified into two major categories based on hydrolysis into hydrolyzable tannins and nonhydrolyzable or condensed tannins. The hydrolyzable tannins contain different kinds of polyesters. Polyesters of hexahydroxydiphenic acids and gallic acid, the nonhydrolyzable tannins are whereas contain polymers and oligomers. Oligomers are polymers consist of nuclei of favan -3-ol. Further tannins are classified based on structures into gallotannins and ellagitannins [77]. There are different sources of tannins. Tannins are found in different plants and their parts in high

Table 1: The antiobesity activity of specific flavonoids with respective mechanisms

Scientist name	Flavonoids name	Sources of flavonoids	Study models animal/cell culture	Observation for antiobesity activity	Molecular mechanism of action
Isabelle Demonty *et al.*(2002) [54]	Genistein	Soy containing food	Animal model (Sprague Dawley rats)	Reduction in TGs; Reduction in body weight	Increased GLUT4, Decreased NF-κB; Decreased TNF – α
Jin-Taek Hwang *et al.* (2005) [55]	Genistein	Soy containing food	Cell culture(3T3-L1 preadipocyte)	Reduction in adipocyte multiplication	Decreased TGFβ1; Increased AMPK; Increased ACC
Myung Sunny Kim *et al.* (2012) [57]	Tangeretin	Mandarin orange	Cell culture (C2C12) and (3 week old Male C57BL/6J Mice)	Decreased total cholesterol, increased Glycogen and insulin secretion	Decreased IL- 1β; decreased TNF- α; decreased IL-6
Nobutomo Ikarashi *et al.* (2009) [58]	Flavan3-ols, (fisetinidol and robinetinidol)	Bark of black wattle tree (*Acacia mearnsii)*	Animal model (KKAy mice)	Reduction in body weight	Increased mRNA expression for UCP3, CPT1, ACO and PPARγ genes
Ali Imran *et al.* (2018)[59]	Thea flavins; Thearubigins	Black tea leaves (*Salicornia europaea)*	Animal model (Male Wistar Rats)	Decreased adipocyte multiplication; decreased pancreatic lipase activity	PPAR-γ downregulation

GLUT 4: Glucose transporter type 4, NF-κB: Nuclear factor kappa-light- chain- enhancer of activated B cells, TNF – α: Tumor necrosis factor, TGFβ1: Transforming growth factor beta 1, AMPK:5 adenosine monophosphate activated protein kinase, ACC: Acetyl – CoA carboxylase, UPC3: Uncoupling protein 3, mRNA: Messenger ribonucleic acid, PPARγ: Peroxisome proliferator activated receptor gamma. TG: Triglyceride

Table 2: The antiobesity activity of saponins derived from herbal sources

Scientist name	Saponins name	Sources of saponins	Study models animal/cell culture	Observation for antiobesity activity	Molecular mechanism of action
Chia hui Apphia Eu *et al.* (2010) [71]	Glycyrrhizin	*Glycyrrhiza glabra*	Animal model (Sprague Dawley Rats)	Elevated insulin sensitivity; Improved HDL; Upregulation of LPL; decreased lipid deposition	apo- CIII down regulation; decreased TNF- α; activation of PPARα
P. Thiyagarajan *et al.* (2011) [72]	Glabradin, Isoliquiritigenin, Glycyrrhizin	*Glycyrrhiza glabra*	Cell culture (J774A.1Murine macrophages cell line [TTB- 67])	Blocking of lipopolysaccharide-de pro-inflammatory factors	Inhibition of NO; IL-6; IL-1
Jin Kyung Kim *et al.* (2006) [73]	Glycyrrhizin	*Glycyrrhiza inflata*	Cell culture (LPS induced Mouse cell cultureRAW264.7)	Anti-inflammatory activity	Decreased TNF – α; Decreased IL-6; Increased IL- 10
Lin Kun Han *et al.* (2002) [74]	Crude saponin	*Platycodi radix*	Animal model (Male Wistar Rats)	Reduction in body weight	Decreased TGs level
Lu Guo *et al.* (2015) [75]	Saponin extract	*Phonognatha graeffei*	Animal model (C57/BL6 Mice)	Inhibition of pancreatic lipase activity; reduction in bodyweight; reduction in triglycerides; reduction in total cholesterol	ABCA1 upregulation; stimulation of PPARs; upregulation of LXR- β

apo- C III: Apolipoprotein C III, LXR- β: Liver X receptor beta, NO: Nitric oxide, TNF – α: tumor necrosis factor, PPARγ: Peroxisome proliferator activated receptor gamma, PPARα: Peroxisome proliferator activated receptor alpha, IL-6: Interleukins 6, ABCA1: ATP-binding cassette transporter ABCA1, IL-10: Interleukins 10, LXR-β – Liver X receptor beta. TGs: Triglyceride, TNF: Tumor necrosis factor, HDL: High-density lipoprotein concentrations. It can be obtained from seed, bark, wood, leaves, fruit, and plant galls [78]. Tannins can also be isolated from the stem area, from growth areas of plants such as xylem and secondary phloem and between the layer of epidermis and cortex. Some plants tend to be known for very frequently produce tannins and are considered as its sickness. Tannins released from plants protect them from harm from insects and infections from microbes and animals. The condensed form of tannins reserved in tannosomes that are surrounded within the tonoplast, a kind of chlorophyllous organelle which only on cell breakdown or cell death takes its action, it does not take any action in plant metabolism activity [79]. Tannins contain different kind of chemical constituents which includes castalagin, chebulinic acid, pedunculagin [80], Tellimargradin II, Potentillin, Agrimoniin, Gemin A, Oenothein B, epigallocatechin gallate, Acutissimin A, Camellitannin A, Guajavin B, Proanthocyanidin A1, Proanthocyanidin A2, and Proanthocyanidin C1 [81]. Tannins are highly biologically active. According to epidemiological records, tannins show many therapeutic effects in skin diseases, injuries, and inflammation and its administration can help in blocking the growth of long-term diseases. Tannins can act as an antioxidant, antimicrobial, antinutrient, antimutagenic, antiviral, antimicrobial, and radical scavenging. Tannins are also known as highly absorbable as they acquire structures of low molecular weight and show pharmacological effects in various diseases [82]. Tannins are known for its number of *in vitro* activities such as antimicrobial and antioxidant activity. Tannins tend to inhibit the peroxidation of lipids are well known for their free-radical scavenging activity which is majorly dependent on the degree of polymerization and its structure [83-85]. The free-radical scavenging activity is highly beneficial for weight loss. Therefore, tannins can be used for antiobesity activity. It is summarized in Table 3.

The antiobesity activity of alkaloids

Alkaloids are found through plant tissues in the form of water-soluble salt these organic acids such as tartaric, citric, malic, acetic, and oxalic acids, some esters such as atropine, aconitine, cocaine, and scopolamine. These are combined with sugars or tannins instead bases which are in the free form [90-92]. Alkaloids are isolated in the form of amorphous, non-odorous, nonvolatile, and crystalline compounds from matrices of plants. Those alkaloids which have low molecular weight are found in liquid form, for instance, pilocarpine and arecoline [93]. Alkaloids are pharmacologically very active and are used as antispasmodic, anesthetics, narcotics, hallucinogenic, used in ophthalmic preparations, anti-inflammatory, antiviral, expectorant, cardiotonic, diuretic, analgesic, antiglucosidase, antihypertensive, and hyperglycemia [94]. Alkaloids are also helpful in weight reduction which has been proved by different studies, summarized in Table 4.

The antiobesity activity of resins

Resins are by-products that are metabolically derived from the tissues of plants. Resins consist of combinations of various chemical entities such as terpenoids fatty acids and secondary phenolic constituents. Resins can be obtained from the plants through an incision or can be

Table 3: Representing the antiobesity effect of tannins

Scientist name	Tannins name	Source of tannins	Study model	Observation	Molecular mechanism of action
Jinning Liu *et al.* (2018) [86]	Epigallocatechin gallate	Green tea	Cell culture (C. elegans)	Reduction in fat accumulation; Inhibition of adipogenesis; reduction in fat content	Decreased atgl- 1 expression
L-K Han *et al.* (1998) [87]	(7)-epicatechin, (7)-epigallocatechin, (7)-epigallocatechin gallate	*Thea sinensis* L.	Animal model (ICR female Rats)	Reduction in body weight; Reduction in fat accumulation; Reduction in TGs	Activation of adenylyl cyclase cyclic AMP (cAMP) phosphodiesterase cycle
Zhen-Hui Cao *et al.* (2011) [88]	Catechins	Pu-erh tea	Animal model (Male Sprague Dawley rats)	Increased LPL; Decreased Hepatic lipase; Decreased fat accumulation; Decreased body weight	Increased HSL mRNA expression
T Murase *et al.* (2002) [89]	Catechins Caffeine	Coffee beans	Animal model C57BL/6J mice	Reduction in fat accumulation of liver; reduction of body weight; Reduction in hepatic triglycerides	SREBP-1 regulation lowered down; Acetyl CoA Carboxylase regulation lowered down

atgl- 1: Adipose triglyceride lipase, HSL: Hormone sensitive lipase, SREBP-1 – Sterol regulatory element – binding- protein. TGs: Triglyceride, LPL: Lipoprotein lipase

Table 4: Representing the antiobesity effect of alkaloids

Scientist name	Alkaloid name	Source of alkaloids	Study model animal/cell culture	Observation	Mechanism of action
Kyung Jin Kim *et al.* (2011) [95]	Piperine Pipernonaline dehydropipernonaline	*Piper retrofractum Vahl*	Animal model (C57BL/6J mice); Cell culture (3T3-L1 adipocytes and L6 myocytes)	Animal model (C57BL/6J mice); Cell culture (3T3-L1 adipocytes and L6 myocytes)	Activation of AMP signaling; Altered lipid metabolism; Activation of PPARδ
Hyounjeong Choi *et al.* (2009) [96]	Citric acid Pectin esterase	*Cucurbita moschata*	Animal model (Male C57BL/6 J Mice)	Reduction in TG accumulation; loss in body weight; Loss in fat accumulation	Inhibit adipocyte differentiation; control PPARα, and increase FA-oxidation
Gyo-Nam Kim *et al.* (2016)[97]	Citric acid	*Diospyros kaki*	Animal model (Male ICR mice)	Body weight reduction; reduction in triglyceride level; reduction in fat accumulation	Inhibition of pancreatic lipase by free radical scavenging
S. Haaz *et al.* (2005) [98]	Caffeine	*Camellia sinensis*	Animal model (Sprague-Dawley (SD) male rats)	Decreased adipocyte differentiation; decreased fat accumulation; decreased Triglycerides level	Diminished expression levels of the IL-6 and TNF-α gene

AMP: Adenosine monophosphate, PPARδ: Peroxisome proliferator activated receptor delta, PPARα: Peroxisome proliferator activated receptor alpha, FA: Fatty acid, IL-6: Interleukins 6, TNF – α: Tumor necrosis factor. TGs: Triglycerides

Table 5: The antiobesity activity of resins

Scientist name	Resin name	Source of resin	Model studied animal model/cell culture	Observation	Mechanism of action
Karine Maria Martins Bezerra Carvalho *et al*. (2015) [104]	α-amyrin; Brein; α-amyrenone;	*Protium heptaphyllum*	Animal model (Male Swiss Mice)	Reduction in body weight; Reduction in fat accumulation; Reduction in amylase; reduction in total cholesterol level	Decreased Pro-inflammatory mediators: MCP-1, IL-6, and TNF α
Hossain Azizian *et al*. (2012) [105]	Asafoetida A and B	*Ferula asafoetida*	Animal model (Male Wistar rats)	Decreased body weights abdominal fat; Reduction in size of epididymal adipocyte	Gene responsible for serum leptin secretion inhibited
Adel A. Gomaa *et al*. (2018) [106]	Acetyl-11-keto-β-boswellic acid	*Boswellia serrata*	Animal model (Swiss albino mice)	Reduction in body weight; Reduction in adipocyte differentiation; reduction in body TG	Decreased TNF-α, IL-1β increased adiponectin; decreased frequency of food intake
Srinivas Nammi *et al*. (2009) [107]	Gingerols; Shogaols; Zingerone	*Zingiber officinale*	Animal model (Male Wistar rats)	Reduction in LDL; reduction in glucose level	Restricted mRNA expressions of fatty acid synthase
Ji Hye Kim *et al*. (2016) [108]	Curcumin; desmethoxycurcumin; bisdemethoxycurcumin	*Curcuma longa L.*	Animal model (Sprague Dawley) (SD)	Reduction in body weight; reduction in WAT mass; reduction in triglycerides level; reduction in adipocyte differentiation	Restricted mRNA expressions of fatty acid synthase, acetyl-CoA carboxylase, adipocyte protein 2, and LPL

MCP-1: Monocyte chemoattractant protein, IL-6: Interleukins 6, TNF – α: Tumor necrosis factor, IL-1β: Interleukins 1- beta. WAT: White adipose tissue. TG: Triglyceride, LPL: Lipoprotein lipase, LDL: Low-density lipoprotein

naturally exuded out by the plants surface, sometimes infections also cause resins to exude out of the plant surface and hence are also termed as internal resins [99,100]. Resins are also obtained from insects, for an instance Laccifer lacca, an insect species produces resins which are known as lac resin [101]. There are classified into different types such as lacquer resins, oleoresins, varnish, balsams, and miscellaneous resins. The mono and sesquiterpenes are volatile whereas resins belonging to angiosperms are nonvolatile [102]. Resins are potentially beneficial for therapeutic effects as they act as anti-inflammatory, analgesic, antispasmodic, antihyperlipidemic, and antimicrobial and are used in wound healing. Resins are beneficial in respiratory disorders [103]. However, resins are also beneficial in weight reduction and management. Some of the studies evidencing the antiobesity activity of resins are summarized in Table 5.

RESULTS

Jillions of studies have confirmed the therapeutic effect of herbal drugs in the management of various illness and disorders. More than 2000 herbs are known and verified for its pharmacological activities. Herbal drugs have the potential to treat obesity through different mechanisms including lipid peroxidation, free-radical scavenging activity, and inhibition of fat accumulation. Based on our interpretations, we have concluded that the herbal drugs constituting active constituents such as tannins, alkaloids, resins, saponins, and flavonoids are effective in lowering the blood TGs level, lipid accumulation in the liver, fat accumulation, adipocyte differentiation, and ultimately decrease body weight with almost negligible toxicity.

CONCLUSION

In this review, we have discussed the different mechanisms of action of multiple herbs in obesity treatment. Herbal drugs have potential to treat obesity through different mechanisms including lipid peroxidation, free-radical scavenging activity, and inhibition of fat accumulation. On the basis of our interpretations, we have concluded that the herbal drugs constituting active constituents as tannins, alkaloids, resins, saponins, and flavonoids are effective in lowering the blood TGs level, lipid accumulation in liver, fat accumulation, adipocyte differentiation, and ultimately decrease body weight with almost negligible toxicity.

AUTHOR'S CONTRIBUTIONS

Literature search, manuscript framing, and preparation have been done by Madhvi Chaubey. Reviewed and editing have been done by Dr. Ankita Wal. The concept has been presented by Dr. Pranay Wal.

CONFLICTS OF INTEREST

The authors have declared no conflicts of interest.

FUNDING SOURCE

Nil.

REFERENCES

1. Meneses MM, Flores ME. Flavonoids: A Promising Therapy for Obesity Due to the High-fat Diet. London, United Kingdom: IntechOpen; 2019.
2. Bollapragada MK, Shantaram M, Kumar R. Obesity: Development, epidemiology, factors affecting, quantity, health hazards, management and natural treatment-a review. Int J Pharm Pharm Sci 2017;9:12-26.
3. Yoon YS, Kwon AR, Lee YK, Oh SW. Circulating adipokines and risk of obesity related cancers: A systematic review and meta-analysis. Obes Res Clin Pract 2019;13:329-39.
4. Ahirwar R, Mondal PR. Prevalence of obesity in India: A systematic review. Diabetes Metab Syndr 2019;13:318-21.
5. Bjelanovic J, Velicki R, Popovic M, Bjelica A, Jevtic M. Prevalence and some risk factors of childhood obesity. Nutrition 2017;19:138-45.
6. Lagerros YT, Rossner S. Obesity management: What brings success? Ther Adv Gastroenterol 2013;6:77-88.
7. Patel DK, Stanford FC. Safety and tolerability of new-generation anti-obesity medications: A narrative review. Postgrad Med 2018;130:173-82.
8. Wharton S. Current perspectives on long-term obesity pharmacotherapy. Can J Diabetes 2016;40:184-91.
9. Oo SS, Rao M, Zin T. Prevalence and factors associated with obesity among adult at the Kampung Kolam, East coast Malaysian peninsula-a cross sectional study. Int J Pharm Pharm Sci 2017;9:273-28.
10. Chellan N, Joubert E, Strijdom H, Roux C, Louw J, Muller CJ. Aqueous extract of unfermented honeybush (*Cyclopia maculata*) attenuates STZ-induced diabetes and β-cell cytotoxicity. Planta Med 2014;80:622-9.
11. Schulze AE, Beer D, Mazibuko SE, Muller CJ, Roux C, Willenburg EL, *et al*. Assessing similarity analysis of chromatographic fingerprints of *Cyclopia subternata* extracts as potential screening tool for *in vitro*

glucose utilization. Anal Bioanalytic Chem 2015;408:639-49.
12. Joubert E, Richards ES, Merwe JD, Beer D, Manley M, Gelderblom WC. Effect of species variation and processing on phenolic composition and *in vitro* antioxidant activity of aqueous extracts of *Cyclopia* spp. J Agric Food Chem 2008;56:954-63.
13. Dudhia Z, Louw J, Muller C, Joubert E, Beer D, Kinnear C, *et al.* *Cyclopia maculata* and *Cyclopia subternata* (honey bush tea) inhibits adipogenesis in 3T3-L1 pre-adipocytes. Phytomedicine 2013;20:401-8.
14. Pheiffer C, Dudhia Z, Louw J, Muller C, Joubert E. *Cyclopia maculata* (honeybush tea) stimulates lipolysis in 3T3-L1 adipocytes. Phytomedicine 2013;20:1168-71.
15. Muller CJ, Joubert E, Gabuza K, Beer D, Fey SJ, Louw J. Assessment of the antidiabetic potential of an aqueous extract of honey bush (*Cyclopia intermedia*) in streptozotocin and obese insulin resistant Wistar rats. Phytochemical 2011;2011:113-332.
16. Meydani M, Hasan ST. Dietary polyphenols and obesity. Nutrients 2010;2:737-51.
17. Wang S, Moustaid N, Moussa L, Chen L, Mo H, Shastri A, *et al.* Novel insights of dietary polyphenols and obesity. J Nutr Biochem 2014;25:1-18.
18. Abdel-Sattar E, Mehanna E, Ghaiesh SH, Mohammad MF, Elgendy HA, Zaitone SA. Pharmacological action of a pregnane glycoside, russelioside B, in dietary obese rats: Impact on weight gain and energy expenditure. Front Pharmacol 2018;9:990.
19. Kim JH, Kang SA, Han S, Shim I. Comparison of the antiobesity effects of the protopanaxadiol and protopanaxatriol type saponins of red ginseng. Phyther Res 2009;23:78-85.
20. Sharma S, Hatware K, Deshpande A, Karri S, Dande P. Antiobesity potential of fresh cow urine and its distillate-a biomedicine for tomorrow. Indian J Pharm Educ Res 2017;51:712-21.
21. Romieu I, Dossus L, Barquera S, Blottiere HM, Franks PW, Gunter M, *et al.* Energy balance and obesity: What are the main drivers? Cancer Causes Control 2017;28:247-58.
22. Jo J, Gavrilova O, Pack S, Jou W, Mullen S, Sumner AE, *et al*. Hypertrophy and/or hyperplasia: Dynamics of adipose tissue growth. PLoS Comput Biol 2009;5:e1000324.
23. Kim SM, Lun M, Wang M, Senyo SE, Guillermier C, Patwari P, *et al.* Loss of white adipose hyperplastic potential is associated with enhanced susceptibility to insulin resistance. Cell Metab 2014;20:1049-58.
24. Sun K, Kusminiski CM, Scherer PE. Adipose tissue remodeling and obesity. J Clin Invest 2011;121:2094-101.
25. Boutens L, Stienstra R. Adipose tissue macrophages: Going off track during obesity. Diabetologia 2016;59:879-94.
26. Morris DL, Singer K, Lumeng CN. Adipose tissue macrophages: Phenotypic plasticity and diversity in lean and obese states. Curr Opin Clin Nutr Metab Care 2011;14:341-6.
27. Cinti S, Mitchell G, Barbatelli G, Murano I, Ceresi E, Faloia E, *et al.* Adipocyte death defines macrophage localization and function in adipose tissue of obese mice and humans. J Lipid Res 2005;46:2347-55.
28. Bahceci M, Gokalp D, Bahceci S, Tuzcu A, Atmaca S, Arikan S. The correlation between adiposity and adiponectin, tumor necrosis factor α, interleukin-6 and high sensitivity C-reactive protein levels. Is adipocyte size associated with inflammation in adults? J Endocrinol Invest 2007;30:210-4.
29. Lumeng CN, Saltiel AR. Inflammatory links between obesity and metabolic disease. J Clin Invest 2011;121:2111-7.
30. Jung UJ, Choi MS. Obesity and its metabolic complications: The role of adipokines and the relationship between obesity, inflammation, insulin resistance, dyslipidemia and nonalcoholic fatty liver disease. Int J Mol Sci 2014;15:6184-223.
31. Choe SS, Huh JY, Hwang IJ, Kim JI, Kim JB. Adipose tissue remodeling: Its role in energy metabolism and metabolic disorders. Front Endocrinol 2016;7:30.
32. Guri AJ, Bassaganya-Riera J. Systemic effects of white adipose tissue dysregulation and obesity-related inflammation. Obesity 2011;19:689-700.
33. Yang H, Ralle M, Wolfgang MJ, Dhawan N, Burkhead JL, Rodriguez S, *et al*. Copper-dependent amino oxidase 3 governs selection of metabolic fuels in adipocytes. PLoS Biol 2018;16:e2006519.
34. Balkau B, Valensi P, Eschwege E, Slama G. A review of the metabolic syndrome. Diabetes Metab 2007;33:405-13.
35. Jean PB, Mustapha M, Claire L, Min JK, Martine C, Hubert V, *et al.* Recent advances in the relationship between obesity, inflammation, and insulin resistance. Eur Cytokine Netw 2006;17:4-12.
36. Rutkowski JM. The cell biology of fat expansion. J Cell Biol 2015;208:501-12.
37. Palou A, Bonet ML, Pico C, Rodriguez AM. Nutrigenomics and obesity. Rev Med Univ Navarra 2004;48:36-48.
38. Singh B, Arora S, Goswami B, Mallika V. Metabolic syndrome: A review of emerging markets and management. Diabetes Metab Syndr 2009;3:240-54.
39. Sugii S. PPARγ activation in adipocytes is sufficient for systemic insulin sensitization. Proc Natl Acad Sci 2009;106:22504-9.
40. Rodgers JT. Metabolic adaptations through the PGC-1 alpha and SIRT1 pathways. FAEB Letters 2008;582:46-53.
41. Yu YH, Ginsberg HN. Adipocyte signaling and lipid homeostasis: Sequelae of insulin resistant adipose tissue. Circ Res 2005;96:1042-52.
42. Havsteen BH. The biochemistry and medical significance of the flavonoids. Pharmacol Ther 2002;96:67-202.
43. Middleton E, Kandaswami J, Theoharides C. The effects of plant flavonoids on mammalian cells: Implications for inflammation, heart disease, and cancer. Pharmacol Rev 2000;52:673-751.
44. Prasad S, Phromnoi K, Yadav VR, Chaturvedi MM, Aggarwal BB. Targeting inflammatory pathways by flavonoids for prevention and treatment of cancer. Planta Med 2010;76:1044-63.
45. Castellarin SD, Di Gaspero G. Transcriptional control of anthocyanin biosynthetic genes in extreme phenotypes for berry pigmentation of naturally occurring grapevines. BMC Plant Biol 2007;7:46.
46. Barnes S, Prasain J. Current progress in the use of traditional medicines and nutraceuticals. Curr Opin Plant Biol 2005;8:324-8.
47. Prasain J, Carlson S, Wyss J. Flavonoids and age-related disease: Risk, benefits and critical windows. Maturitas 2010;66:163-71.
48. Middleton E. Effect of Plant Flavonoids on Immune and Inflammatory Cell Function. Berlin, Germany: Springer; 1998. p. 175-82.
49. Hossain MK, Choi HY, Hwang JS, Dayem AA, Kim JH, Kim YB, *et al.* Antiviral activity of 3, 4'-dihydroxyflavone on influenza a virus. J Microbiol 2014;52:521-6.
50. Kumar S, Gupta A, Pandey AK. *Calotropis procera* root extract has the capability to combat free radicalmediated damage. ISRN Pharmacol 2013;9:691372.
51. Sen S, De B, Devanna N, Chakraborty R. Total phenolic, total flavonoid content, and antioxidant capacity of the leaves of *Meyna spinosa* Roxb, an Indian medicinal plant. Chin J Nat Med 2013;11:149-57.
52. Cook N, Samman S. Flavonoids chemistry, metabolism, cardioprotective effects, and dietary sources. Nutr Biochem 1996;7:66-76.
53. Rice-Evans CA, Miller NJ, Bolwell PG, Bramley PM, Pridham JB. The relative antioxidant activities of plant-derived polyphenolic flavonoids. Free Radic Res 1995;22:375-83.
54. Demontya I, Lamarchea B, Lamarchea Y, Jacquesa H. Role of soy isoflavones in the hypotriglyceridemic effect of soy proteinin the rat. J Nutr Biochem 2002;13:671-7.
55. Hwang JT, Park IN, Shin JI, Lee YK, Lee SK, Baik HW, *et al*. Genistein, EGCG, and capsaicin inhibit adipocyte differentiation process via activating AMP-activated protein kinase. Biochem Biophys Res Commun 2005;338:694-9.
56. Rauter AP, Martins A, Borges C, Mota-Filipe H, Pinto R, Sepode B, *et al.* Antihyperglycaemic and protective effects of flavonoids on streptozotocin-induced diabetic rats. Phytother Res 2010;24:133-8.
57. Kim MS, Hur HJ, Kwon DY, Hwang JT. Tangeretin stimulates glucose uptake via regulation of AMPK signaling pathways in C2C12 myotubes and improves glucose tolerance in high-fat diet-induced obese mice. Mol Cell Endocrinol 2012;358:127-34.
58. Ikarashi N, Toda T, Okaniwa T, Ito K, Ochiai W, Sugiyama K. Anti-obesity and anti-diabetic effects of acacia polyphenol in obese diabetic KKAy mice fed high-fat diet. Evid Based Complement Alternat Med 2011;2011:952031.
59. Imran A, Butt MS, Arshad MS, Arshad MU, Saeed F, Sohaib M. Exploring the potential of black tea based flavonoids against hyperlipidemia related disorders. Lipids Health Dis 2018;17:57.
60. Hostettmann K, Marston A. Saponins: Chemistry and Pharmacology of Natural Products. Vol. 59. Cambridge, UK: Cambridge University Press; 1996. p. 96.
61. Vincken JP, Heng L, de Groot A, Gruppen H. Saponins, classification and occurrence in the plant kingdom. Phytochemistry 2007;68:275-97.
62. Guclu-Ustundag O, Mazza G. Saponins: Properties, applications and processing. Crit Rev Food Sci Nutr 2007;47:231-58.
63. San Martin R, Briones R. Industrial uses and sustainable supply of *Quillaja saponaria* (*Rosaceae*) saponins. Econ Bot 1999;53:302-11.
64. Asl MN, Hosseinzadeh H. Review of pharmacological effects of *Glycyrrhiza* sp. and its bioactive compounds. Phytother Res 2008;22:709-24.
65. Xiang YZ, Shang HC, Gao XM, Zhang BL. A comparison of the ancient use of ginseng in traditional Chinese medicine with modern pharmacological experiments and clinical trials. Phytother Res 2008;22:851-8.
66. Sun SX, Li YM, Fang WR, Cheng P, Liu L, Li F. Effect and mechanism

of AR-6 in experimental rheumatoid arthritis. Clin Exp Med 2010;10:113-21.
67. Cinatl J, Morgenstern B, Bauer G, Chandra P, Rabenau H, Doerr HW. Glycyrrhizin, an active component of liquorice roots, and replication of SARS associated coronavirus. Lancet 2003;361:2045-6.
68. Musende AG, Eberding A, Wood C, Adomat H, Fazli L, Hurtado-Coll A, *et al*. Pre-clinical evaluation of Rh2 in PC-3human xenograft model for prostate cancer *in vivo*: Formulation, pharmacokinetics, biodistributionand efficacy. Cancer Chemother Pharmacol 2009;64:1085-95.
69. Coleman JJ, Okoli I, Tegos GP, Holson EB, Wagner FF, Hamblin MR, *et al.* Characterization of plant-derived saponin natural products against *Candida albicans*. ACS Chem Biol 2010;5:321-32.
70. Chen Y, Miao Y, Huang L, Li J, Haiyan S, Zhao Y, *et al.* Antioxidant activities of saponins extracted from radix trichosanthis: An *in vivo* and *in vitro* evaluation. BMC Complement Alternat Med 2014;14:86.
71. Eu CH, Lim WY, Ton SH, Kadir KA. Glycyrrhizic acid improved lipoprotein lipase expression, insulin sensitivity, serum lipid and lipid deposition in high-fat diet-induced obese rats. Lipids Health Dis 2010;9:81.
72. Thiyagarajan P, Chandrasekaran CV, Deepak HB. Modulation of lipopolysaccharide-induced pro-inflammatory mediators by an extract of *Glycyrrhiza glabra* and its phytoconstituents. Inflammopharmacology 2011;19:235-24.
73. Kim JK, Oh S, Kwon HS, Oh YS, Lim SS, Shin HK. Anti-inflammatory effect of roasted licorice extracts on lipopolysaccharide-induced inflammatory responses in murine macrophages. Biochem Biophys Res Commun 2006;345:1215-23.
74. Han LK, Zheng YN, Xu BJ, Okuda H, Kimura Y. Saponins from platycodi radix ameliorate high fat diet-induced obesity in mice. J Nutr 2002;132:2241-5.
75. Guo L, Ziyang G, Zhang L, Guo F, Chen Y, Li Y, *et al.* Saponin-enriched sea cucumber extracts exhibit an antiobesity effect throughinhibition of pancreatic lipase activity and upregulation of LXR-β signaling. Pharm Biol 2015;54:1312-5.
76. Khanbabaee K, Van Ree T. Tannins: Classification and definition. Natl Prod Rep 2001;18:641.
77. De Bruyne T, Pieters L, Deelstra H, Vlietinck A. Condensed vegetable tannins: Biodiversity in structure and biological activities. Biochem Syst Ecol 1999;44:559.
78. Sieniawska E. Activities of tannins-from *in vitro* studies to clinical trials. Natl Prod Commun 2015;10:1877-84.
79. Brillouet JM, Romieu CH, Schoefs B, Solymosi K, Cheynier V, Fulcrand H, *et al.* The tannosome is an organelle forming condensed tannins in the chlorophyllous organs of tracheophyta. Ann Bot Lond 2013;112:1003-14.
80. Okuda T, Yoshida T, Hatano T, Ito H. Ellagitannins renewed the concept of tannins. In: Quideau S, editor. Chemistry and Biology of Ellagitannins: An Underestimated Class of Bioactive Plant Polyphenols. Singapore: World Scientific; 2009. p. 1-54.
81. Okuda T, Ito H. Tannins of constant structure in medicinal and food plants hydrolyzable tannins and polyphenols related to tannins. Molecules 2011;16:2191-217.
82. Serrano J, Pimi RP, Dauer A, Aura AM, Calixto FS. Tannins: Current knowledge of food sources, intake, bioavailability and biological effects. Mol Nutr Food Res 2009;53:310-29.
83. Okuda T. Systematics and health effects of chemically distinct tannins in medicinal plants. Phytochemistry 2005;66:2012-31.
84. Tian Y, Zou B, Li CM, Yang J, Xu SF, Hagerman AE. High molecular weight persimmon tannin is a potent antioxidant both *ex vivo* and *in vivo*. Food Res Int 2012;45:26-30.
85. Jerez M, Tourio S, Sineiro J, Torres JL, Nuez MJ. Procyanidins from pine bark: Relationships between structure, composition and antiradical activity. Food Chem 2007;104:518-27.
86. Liu J, Peng Y, Yue Y, Shen P. Epigallocatechin-3-gallate reduces fat accumulation in *Caenorhabditis elegans*. Prev Nutr Food Sci 2018;23:214-9.
87. Han LK, Takaku T, Li J, Kimura Y, Okuda H. Anti-obesity action of oolong tea. Int J Obes 1999;23:98-105.
88. Cao ZN, Gu DH, Lin QY, Xu ZQ, Huang QC, Rap H, *et al.* Effect of pu-erh tea on body fat and lipid profiles in rats with diet-induced obesity. Phytother Res 2011;25:234-8.
89. Murase T, Nagasawa A, Suzuki J, Hase T, Tokimitsu I. Beneficial effects of tea catechins on diet-induced obesity: Stimulation of lipid catabolism in the liver. Int J Obes 2002;26:1459-64.
90. Murase T, Misawa K, Minegishi Y, Aoki M, Ominami H, Suzuki Y. Coffee polyphenols suppress diet-induced body fat accumulation by downregulating SREBP-1c and related molecules in C57BL/6J mice. Am J Physiol Endocrinol Metab 2010;13:122-33.
91. Kar A. Pharmacognosy and Pharmacobiotechnology. 2nd ed. New Delhi: New Age International Ltd.; 2003.
92. Svendsen AB, Verpoorte R. Chromatography of Alkaloids. Part A: Thin-layer Chromatography. Vol. 23. Amsterdam, Oxford, New York: Elsevier Scientific Publishing Company; 1983.
93. Aniszewski T. Alkaloids Secrets of Life: Alkaloid Chemistry, Biological Significance, Applications and Ecological Role. 1sted. Netherlands: Elsevier; 2007.
94. International Programme on Chemical Safety, WHO. Pyrrolizidine Alkaloids. Environmental Health Criteria 80. Geneva International Programme on Chemical Safety, WHO. Available from: http://www.inchem.org/documents/ehc/ehc/ehc080.htm.
95. Kim KJ, Lee MS, Jo K, Hwang JK. Piperidine alkaloids from *Piper retrofractum* Vahl. Protect against high-fat diet-induced obesity by regulating lipid metabolism and activating AMP-activated protein kinase. Biochem Biophys Res Commun 2011;411:219-25.
96. Choi H, Eo H, Park K, Jin M, Park EJ, Kim SH, *et al*. A water-soluble extract from Cucurbita moschatashowsantiobesity effects by controlling lipid metabolism in a high fatdiet-induced obesity mouse model. Biochem Biophys Res Commun 2007;359:419-25.
97. Kim GN, Shin MR, Shin SH, Lee AR, Lee JY, Seo BI, *et al*. Study of antiobesity effect through inhibition of pancreatic lipase activity of *Diospyros kaki* fruit and *Citrus unshiu* Peel. Bio Med Res Int 2016;2016:1723042.
98. Haaz S, Fontaine KR, Cutter G, Limdi N, Chaney SP, Allison DB. *Citrus aurantium* and synephrine alkaloids in the treatment of overweight and obesity: An update. Obes Rev 2006;7:79-88.
99. Xu Y, Zhang M, Wu T, Dai S, Xu J, Zhou Z. The anti-obesity effect of green tea polysaccharides polyphenols and caffeine in rats fed with a high-fat diet. Food Funct 2015;6:297-304.
100. Barnett JR, Langenheim JH. Plant resins: Chemistry, evolution, ecology, and ethnobotany. Ann Bot 2004;93:784-5.
101. Perveen A, Jahan N, Abdul W, Tanwir AM. Methods of processing of Lac (*Laccifer lacca* Kerr) described in Unani system of medicine. Res J Pharm Sci 2013;2:5-7.
102. Bohlmann J, Keeling CI. Terpenoid biomaterials. Plant J 2008;54:656-69.
103. Mahendra P, Bisht S. *Ferula asafoetida*: Traditional uses and pharmacological activity. Pharmacogn Rev 2012;6:141-6.
104. Carvalho KM, Filho JD, de Melo TS, Araújo AJ, Quetz S, *et al*. The resin from protium heptaphyllum prevents high-fat diet-induced obesity in mice: Scientific evidence and potential mechanisms. Evid Based Complement Alternat Med 2015;2015:106157.
105. Aziziani H, Rezvani E, Esmaeilidehaj M, Majid S, Sadoughi BS. Anti-obesity, fat lowering and liver steatosis protective effects of ferula asafoetida gum in Type 2 diabetic rats: Possible involvement of leptin. Iran J Diabetes Obes 2012;4:120-5.
106. Yadav KD, Chaudhary AK. New world syndrome (obesity) gone by guggul: A review. J Ayurveda Holist Med 2014;9:2.
107. Nammi S, Sreemantula S, Roufogalis BD. Protective effects of ethanolic extract of *Zingiber officinale* rhizome on the development of metabolic syndrome in high-fat diet-fed rats. Basic Clin Pharmacol Toxicol 2009;104:366-73.
108. Kim JH, Kim OK, Yoon HG, Park J, You Y. Anti-obesity effect of extract from fermented *Curcuma longa* L. through regulation of adipogenesis and lipolysis pathway in high-fat diet-induced obese rats. Food Nutr Res 2016;60:34028.
109. Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: The linking mechanism and the complications. Arch Med Sci 2017;13:851-63.
110. Danesh J, Kaptoge S, Mann AG, Sarwar N, Wood A, Angleman SB, *et al*. Long-term interleukin-6 levels and subsequent risk of coronary heart disease: Two new prospective studies and a systematic review. PLoS Med 2008;5:78.
111. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med 2005;352:1685-95.
112. Sarvottam K, Yadav RK. Adiponectin, interleukin-6, and endothelin-1 correlate with modifiable cardio metabolic risk factors in overweight/obese men. J Alternat Complement Med 2014;20:419-20.
113. Chen SJ, Yen CH, Huang YC, Lee BJ, Hsia S, Lin PT. Relationships between inflammation, adiponectin, and oxidative stress in metabolic syndrome. PLoS One 2012;7:e45693.
114. Arican O, Aral M, Sasmaz S, Ciragil P. Serum levels of TNF-alpha, IFN-gamma, IL-6, IL-8, IL-12, IL-17, and IL-18 in patients with active psoriasis and correlation with disease severity. Mediators Inflamm 2005;5:273-9.
115. Trayhurn P, Wood I. Adipokines: Inflammation and the pleiotropic role of white adipose tissue. Br J Nutr 2004;92:347-55.