Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 6 suppl 2, 2014

Review Article

HERBAL MEDICINES USED IN THE TRADITIONAL INDIAN MEDICINAL SYSTEM AS A THERAPEUTIC TREATMENT OPTION FOR OVERWEIGHT AND OBESITY MANAGEMENT: A REVIEW

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Received: 23 Dec 2013 Revised and Accepted: 01 Jan 2014

ABSTRACT

In recent years, obesity has become a major health problem worldwide, affecting people across all ages, sex, ethnicities, and races, and its prevalence has been increasing at an alarming rate. Currently, pharmacologic agents available to treat obesity carry high costs and serious side effects. In contrast, natural products used in the conventional Indian medicinal system have been applied effectively in clinical practice and may be potential targets in the development of future cost effective anti-obesity drugs with less side effects. A comprehensive chemical and pharmacological review of numerous bioactive constituents established in Indian medicinal plants used to treat obesity was performed. Data on 30 medicinal plants were reviewed, taking into consideration their biological sources, anti-obesity active principles, and pharmacological test results, which are typically applied in the indigenous Indian system of medicine. In the modern era, various medicines have been developed for overweight and obese people, but nearly all are chemical or biochemical agents. There is a need to create awareness regarding the evidence for and use of herbal medicines in the management and treatment of obesity.

Keywords: Obesity; Overweight management; Traditional Indian medicine; Natural medicine; Randomised clinical trial; Clinician-Pharmacist expectations; Appropriate herbal formulation; Potential risks

INTRODUCTION

Characterized as abnormal or excessive fat deposition in adipose tissue and other internal organs such as liver, heart, and skeletal muscle, obesity is a chronic disorder of carbohydrate and fat metabolism and poses a risk to the health and well-being of humans. It is measured by the body mass index (BMI), a ratio of height (in meters) to weight (in kilograms). BMI is a criterion used to classify a person as underweight, normal, overweight, or obese. A BMI ≥ 25 kg/m^2 is considered overweight, while a BMI ≥ 30 kg/m^2 are considered obese.

Overweight or obesity is a major risk factor for many chronic diseases, including diabetes mellitus, cardiovascular diseases, and cancer. Obesity was previously considered a health issue in developed countries, but is now common worldwide, particularly in urban areas. There are many etiologic factors for this, including genetic, metabolic, behavioural, and environmental variables. The rapid increase in the prevalence of overweight and obesity suggests that behavioural and environmental influences are predominant, rather than biological changes.

There are 2 parts to the obesity equation: (1) an increased intake of foods with excessive amounts of fat, salt, and sugars, but less vitamins, minerals, and other nutrients; and (2) a decrease in physical activity due to increasingly sedentary lifestyles, changing modes of transportation, irregular daily routines, and increasing urbanization. Thus, the fundamental cause of obesity and overweight is an energy imbalance between calories consumed and those expended. The body needs a certain amount of energy, or calories, from food to sustain basic life functions. Body weight is maintained when calories eaten equals those used. When more calories are consumed than those burned, the overall energy balance is tilted toward weight gain, predisposing one towards being overweight and possibly obese [1].

Due to the high morbidity and mortality, the management and treatment of obesity requires numerous resources including pharmacologic agents, balanced diets, and physical training costs. There are 5 distinct mechanisms or strategies for weight loss:

1) **Reducing food intake** either by augmenting the inhibitory effects of anorexigenic signals or factors that suppress food intake or by blocking orexigenic signals or factors that stimulate food intake.

2) **Blocking nutrient absorption** in the alimentary canal, in particular, fat.

3) **Increasing thermogenesis** by uncoupling fuel metabolism from the generation of ATP, thereby dissipating food energy as heat.

4) **Modulating fat or protein metabolism or storage** by regulating fat synthesis/lipolysis or adipose differentiation /apoptosis. Enhanced fat or protein turnover might reduce body weight by affecting either food intake or energy expenditure.

5) **Modulating the central controller regulating body weight** by (1) altering the internal reference value sought by the controller or (2) modulating the primary afferent signals regarding fat stores analysed by the controller. This approach would have the potential advantage of forcing the endogenous controller to regulate multiple pathways of energy balance and minimize restitution [2].

Drugs commonly used to control obesity are categorized as follows:

Serotonergic agents*:* fluoxetine, dexfenfluramine, fenfluramine

Noradrenergic agents*:* amphetamine, phendimetrazine, phentermine, diethylpropion, pseudoephedrine, phenylpropanolamine, mazindol

Noradrenergic and Serotonergic agents*:* sibutramine

Drugs acting on the gastrointestinal system*:* orlistat (pancreatic lipase inhibitor) [3]

Centrally acting drugs (anorectic or appetite suppressants)*:* sibutramine, rimonabant

Suppressive effect on food intake (Promotes feeling of satiety)*:* liraglutide, a glucagon-like peptide-1 analogue (incretin mimetic), exenatide (analogue of the hormone GLP-1), pramlintide (synthetic analogue of the hormone Amylin).

Herbal medicinal therapy is the unique alternative for overweight or obese people. Thus far, the majority of the various different types of remedies developed are chemical or biochemical agents. The purpose of this review was to examine medicinal plants that may be promising alternative treatments in the management and treatment of obesity.

A comprehensive chemical and pharmacological review of numerous bioactive constituents established in Indian medicinal plants used to treat obesity was performed. A literature search was also conducted to investigate medicinal plants with anti-obesity properties. Web- and manual-based literature surveys were conducted to assess the information available on the herbal medicines for obesity treatment. Pubmed, Scopus, and Google scholar databases were screened, using the terms 'overweight and obesity management', 'herbal medicines', 'traditional Indian medicines', and 'chemical/phytochemical constituents'. Publications with abstract/full articles and books were reviewed. Based on the available literature, there have been very limited randomised clinical trials (RCTs) and high level of evidence studies.

Indian herbal plants used in the Ayurvedic medicine to treat obesity

Natural medicines used to treat obesity in the traditional Indian medical system include herbal plants from Ayurvedic medicine and chemical constituents with anti-obesity potential.

Garcinia cambogia (Vrikshamla)

Extracts from the dried peel from the fruits of *Garcinia cambogia* Linn, family *Clusiaceae*, are ingredients in some herbal appetite suppressants and energy products. The active ingredient in *Garcinia cambogia* is (-)-hydroxycitric acid, which works against obesity by suppressing appetite and inhibiting lipid synthesis. Studies suggest that this natural extract may also slow down the conversion of excess calories to body fat. *Garcinia cambogia* is thus a very effective herbal medicine for controlling obesity and cholesterols level. HCA, or hydroxycitric acid, is a natural substance extracted from the peels of the fruits of *Garcinia cambogia*. In animal studies, HCA successfully inhibits lipogenesis and therefore lowers cholesterol and fats, increases glycogen production in the liver, suppresses appetite, and increases the body's thermogenesis process, thereby promoting weight reduction. Furthermore, by changing metabolic activity, HCA decreases the conversion rate of carbohydrates to fats. Some studies also indicate that HCA suppresses the activity of the enzyme ATP citrate lyase, which is responsible for the conversion of carbohydrates to fats, present in the liver [4, 5].

Commiphora mukul (Guggul/Guggulu)

The resins from the *Commiphora mukul*, family *Burseraceae*, have been indigenously used in Ayurvedic system of medicine to treat obesity. *Commiphora mukul* enhances the body's metabolic activity by improving thyroid function, increasing the body's fat-burning activity, and augmenting thermogenesis or heat production. Extracts containing ketonic steroid active substances such as guggulsterones have been shown to significantly lower serum low-density lipoprotein and very low-density lipoprotein (LDL and VDRL, respectively) and triglycerides [6]. Furthermore, it raises levels of high-density lipoprotein (HDL) cholesterol. Studies demonstrated a decrease in total cholesterol up to 30% in 12 weeks and a reduction of LDL by 35% and increase in HDL by 20% in 3 months [7]. As the active ingredient obtained from *Commiphora mukul*, guggulsterone acts as an antagonist to the farnesoid X receptor, which is involved in reducing cholesterol synthesis in the liver [8].

Cyperus rotundus (Mustak)

The rhizomes or tubers of *Cyperus rotundus* L., family *Cyperaceae*, are commonly known as 'Nut Grass'. In the conventional medical system, it was used in both its fresh and dry forms. Cyperine is the active ingredient, working as a hypotensive agent (low blood pressure), anti-inflammatory, and diuretic (increases urine secretion), as well as reducing fat in the body. According to Ayurveda medicine, it improves digestive functions. It is believed that altered regulation of the digestive system results in indigestion and obstruction of the channels through which energy is controlled in the body, thus leading to obesity. *Cyperus rotundus* helps clear the blocked channels and is hence very effective against obesity. In rat studies, *Cyperus rotundus* stopped weight gain, and *in vitro*, stimulated lipolysis in 3T3-F442 adipocytes, suggesting that purple nutsedge can activate beta-adrenoreceptors [9].

Picrorhiza kurroa (Kutki)

The root or rhizome of *Picrorhiza kurroa*, family *Scrophulariaceae*, is the source of the active ingredient. *Picrorhiza kurroa* improves gallbladder secretions, thus aiding in the digestion and metabolism of fats. It is very effective in regulating fat metabolism in the liver. In a study of hyperlipaemic mice on a high-fat diet, daily doses of water extract of *Picrorhiza kurroa* significantly reduced total cholesterols, triglycerides, and LDL levels after 12 weeks [10].

Areca catechu (Khadir)

The seed of *Areca catechu,* family *Arecaceae,* maintains healthy fat metabolism and reduces the conversion of carbohydrates to fats. It also decreases false hunger and augments exercise results to enhance weight loss and decrease excess body fat. In studies of rats fed on a diet containing cholesteryl oleate, betel nut extracts significantly lowered cholesterol and triglycerides [11, 12].

Boerhavia diffusa (Punarnava)

The entire herb of *Boerhaavia diffusa*, family *Nyctaginaceae*, Punarnava has been used in the traditional medicine since ancient times. It is present in almost all anti-obesity herbal medicine in one form or another and plays an important role in the treatment of obesity [13].

Embelia ribes (Vidanga)

The root of *Embelia ribes* Burm. f., family *Myrsinaceae*, Vidanga is another herb used in traditional medicine since ancient times. In India, it is the most commonly used Ayurvedic herb for weight reduction or lipid-lowering activity [14]. Studies report that the lipid-lowering activity of ethanolic extracts of *Embelia ribes* can potentially help regulate diabetic dyslipidaemia [15].

Boswellia serrata (Shallaki; Salai Guggul)

The resin extract of *Boswellia serrata*, family *Burseraceae*, is very useful. Boswellic acids have been found to reduce serum cholesterol and triglyceride levels in rat studies [16]. However, the exact mechanism is not well understood.

Plumbago zeylanica (Chitrak)

The root bark of *Plumbago zeylanica*, family *Plumbaginaceae*, is used to treat obesity [17, 18].

Achyranthes aspera (Apamarga)

The seeds of *Achyranthes aspera* L., family *Amaranthaceae*, have been shown to reduce blood glucose levels and stimulate the production of thyroid hormones in animal models. Both these actions would help combat obesity and promote weight loss. Moreover, the seeds also have an appetite-suppressant effect. A study of the anti-obesity effects of 4 herbs traditionally used in Ayurveda, including Apamarga, was conducted in 60 patients and found encouraging results [19].

Clerodendrum multiflorum (Agnimantha)

The shrub *Clerodendrum multiflorum* Burm f., family *Verbenaceae*, is beneficial in weight loss [19].

Glycyrrhiza glabra (licorice)

The roots from *Glycyrrhiza glabra*, family *Leguminosae*, had hypocholesterolemic effects in animal studies [20]. In human studies, a daily dose of licorice (3.5 g) potentially reduced body fat by inhibiting 11-β-hydroxysteroid dehydrogenase type-1, an NADPH-dependent enzyme in the adipose tissue [21]. In some

studies, *Glycyrrhiza glabra* roots have antihyperlipilaemic and anti-hypertriglyceridaemic properties [22, 23]. The anti-obesity activity of *Glycyrrhiza glabra* appears to be partly mediated by decreasing dietary fat absorption from the intestines [24]. Licorice flavonoid oil (LFO) is a new dietary ingredient in functional foods with potential benefits for overweight subjects [25].

Aloe vera

Although bitter in taste, the leaves of *Aloe vera*, family *Xanthorrhoeaceae*, are one of the Ayurvedic remedies for obesity. Studies of hyperlipidaemic patients have shown that it has serum lipid-lowering activity [26].

Operculina turpethum (Nisonth)

The roots of *Operculina turpethum*, family *Convolvulaceae*, are beneficial in treating fatty liver and improving fat metabolism in the liver. It works effectively against obesity by decreasing excessive body fat [27].

A clinical trial study showed that the *Operculina turpethum* containing preparation called Nishottar, which is used to treat obesity, significantly decreases serum cholesterol and triglycerides levels [28].

Acorus calamus (Vacha)

The roots and rhizomes of *Acorus calamus*, family *Araceae*, are useful for weight loss and reducing LDL cholesterol and triglycerides. Based on animal studies, alcoholic or aqueous extracts of calamus roots and rhizomes decreased cholesterol and triglyceride levels and increased the concentration of HDL during the period of an atherogenic diet [29].

Although these studies support a possible antihyperlipidaemic action of calamus, its clinical relevance remains unknown.

Gymnema sylvestre

The anti-obesity effects of the leaves of *Gymnema sylvestre,* family *Asclepiadaceae*, were investigated in Wistar rats fed with high-fat diets. The saponins-rich aqueous extract administered to Wistar rats suppressed increases in body weight, organs weight, and plasma lipids [30]. *Gymnema sylvestre* can be used to treat obesity as well as alter lipid and glucose metabolism [31].

Camellia sinensis (green tea)

Although the leaves of *Camellia sinensis*, family *Theaceae,* will not lead to rapid body weight reduction, it induces thermogenesis and stimulates fat oxidation, thus enhancing the metabolic rate by 4% without increasing the heart rate.

A human study of green tea extract concluded that men taking the extract containing epigallocatechin-3-gallate (EGCG) burned more calories per day in comparison to the placebo group and that the thermogenic effects of green tea extract may play an important role in controlling obesity [32].

Withania somnifera (Ashwagandha)

The roots of *Withania somnifera*, family *Solanaceae*, promote natural weight loss without any negative side effects and are very efficient in the development of good health. In human case studies, treatment with Ashwagandha caused significant reductions in serum total cholesterol, triglycerides, LDL, and VDRL levels [33].

Clerodendron glandulosum

The leaves of *Clerodendron glandulosum* Coleb, family *Lamiaceae*, are used in aqueous extracts by the natives of North-East India to treat obesity.

Its method of action involves the prevention of the differentiation of adipocytes and visceral adiposity through the down regulation of peroxisome proliferator-activated receptor γ-2 (PPARγ-2)-related genes and Lep expression [34].

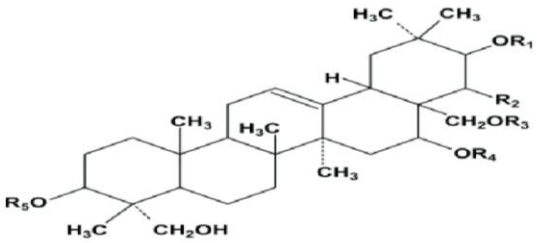
Chemical constituents with anti-obesity potential obtained from Indian medicinal plants

Numerous chemical constituents have been found in Indian medicinal plants to treat obesity. There are various compounds, with anti-obesity potential, obtained from medicinal plants.

Terpenoids

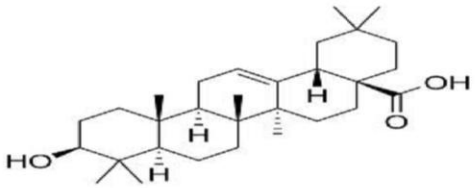
Triterpenoids

Gymnemic acid (from *Gymnema sylvestre*), oleanolic acid (from *Panax ginseng*), and corosolic acid (from *Lagerstroemia speciosa L.*) have potential action on obesity (Figure 1).



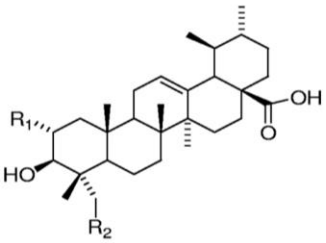
Gymnemic acid

(From *G. sylvestre* [35-37])



Oleanolic acid

(From *P. ginseng* [38-39])



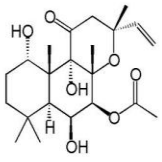
Corosolic acid

(From *L. speciosa* [40])

Fig. 1: Chemical structure of triterpenoids.

Diterpenoid

Forskolin (from *Coleus forskohlii (Willd.) Briq.*) and gingerol, shogaol, and galanolactone (from *Zingiber officinale Roscoe*) with anti-obesity potential (Figure 2).



Forskolin

(From *C. forskohlii* [41])

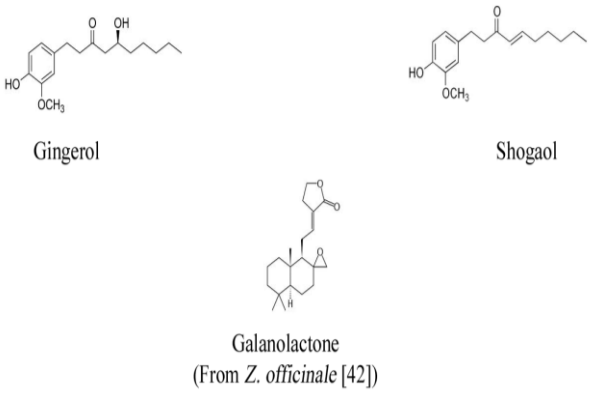


Fig. 2: Chemical structure of diterpenoids.

Flavonoids

Flavonoids such as (+)-1(R)-coclaurine, (-)-1(S)-norcoclaurine, and quercetin: 3-*O*-β-D-glucuronide (from *Nelumbo nucifera Gaertn)* have the potential to reduce body weight (Figure 3).

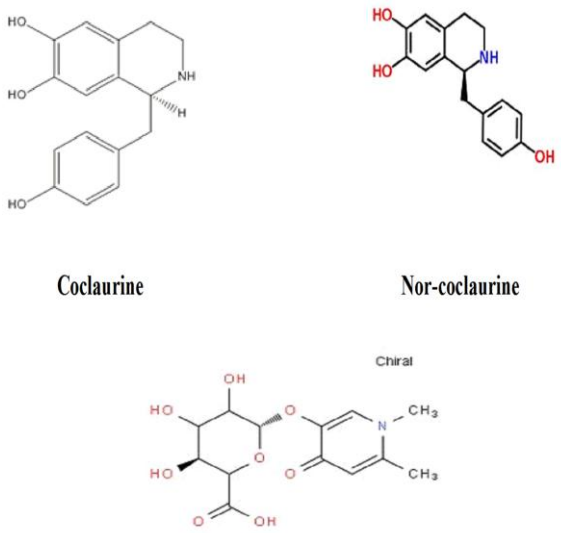
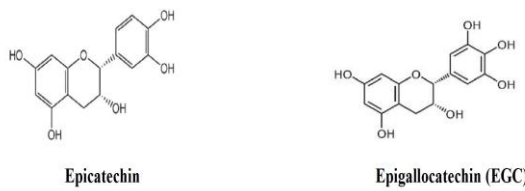


Fig. 3: Chemical structure of flavonoids.

Polyphenols

Catechins include epicatechin, epicatechin-3-gallate, epigallocatechin, and EGCG (from *Camellia sinesis (L.) Kuntze*), luteolin, quercetin and kaempferol (from *Panax ginseng*) and Resveratrol, a phytopolyphenol (from *Vitis vinifera L.*) (Figure 4).



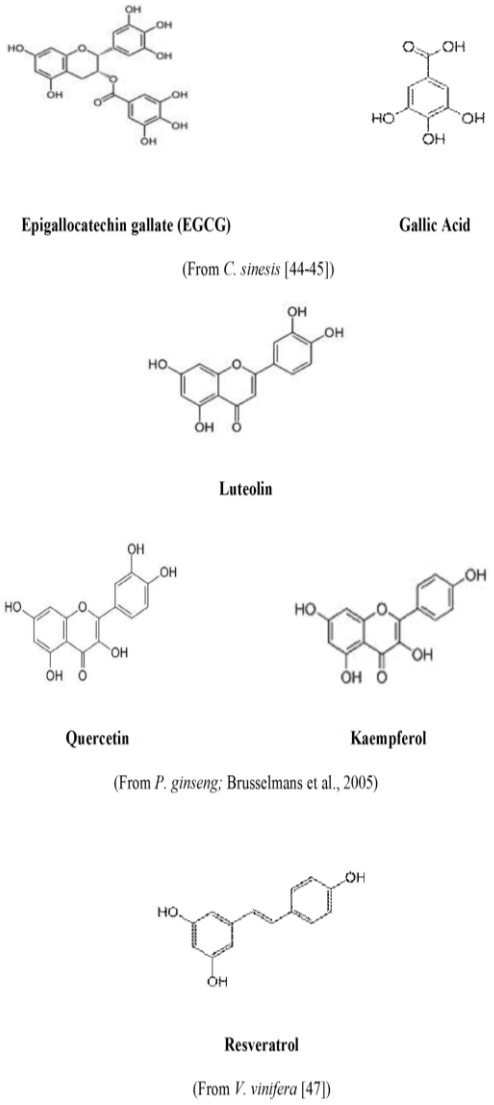
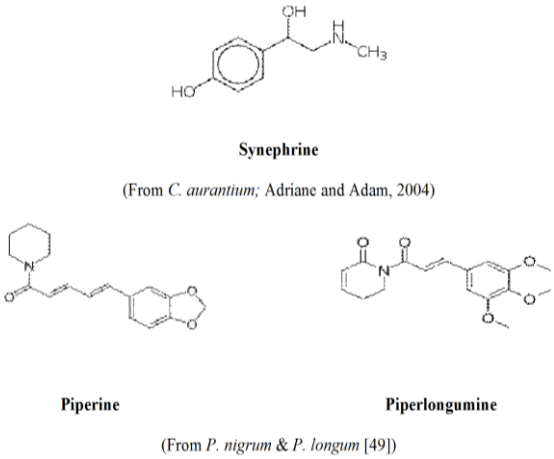
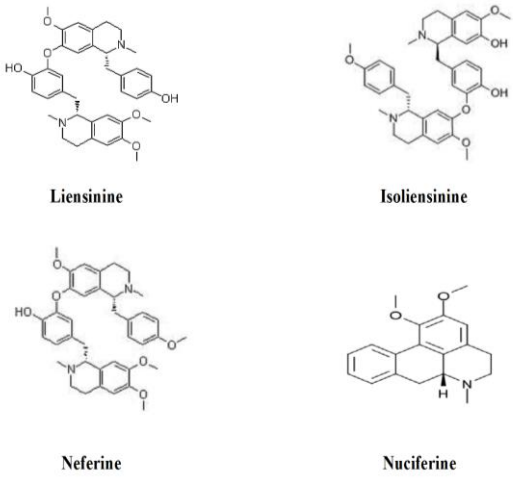


Fig. 4: Chemical structure of polyphenols.

Alkaloids

Alkaloids include synephrine (from *Citrus aurantium L.*), piperine (from *Piper nigrum L.*), piperlongumine (from *Piper longum L.*), and liensinine, isoliensinine, neferine, and nuciferine from *Nelumbo nucifera Gaertn* (Figure 5).



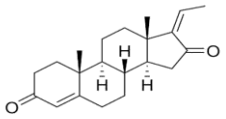


(From *N. mucifera Gaertn* [43])

Fig. 5: Chemical structure of alkaloids.

Steroid

Z-guggulsterone, a plant ketosteroid (from *Commiphora mukul*) plays a significant role in weight loss (Figure 6).



Z- Guggulsterone
(From *C. mukul* [50-51])

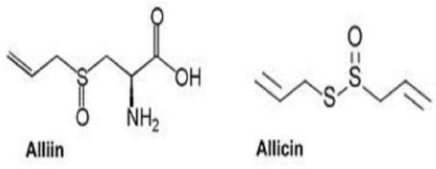
Fig. 6: Chemical structure of steroids.

Tannins

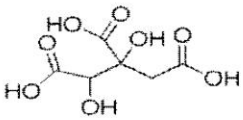
Some ellagitannins such as lagerstroemia, flosin B, and reginin A (from *Lagerstroemia speciosa* L.) have anti-obesity properties [40].

Miscellaneous

An organosulphur compound allicin and alliin (from *Allium sativum*); (-)-hydroxycitric acid (from *Garcinia cambogia*); (+)-hydroxycitric acid, anthocyanins- delphinidin-3-*O*-(2-*O*-β-D-xylopyranosyl)-β-D-glucopyranoside, and cyanidin 3-*O*-(2-*O*-β-D-xilopyranosyl)-β-D-glucopyranoside (from *Hibiscus sabdariffa*), and the polyacetylene compounds panaxynol and panaxydol (from *Panax ginseng C. A. Mayer*) have all been found to have anti-obesity activity (Figure 7).

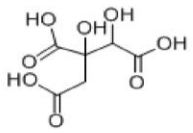


(From *A. sativum* [52])



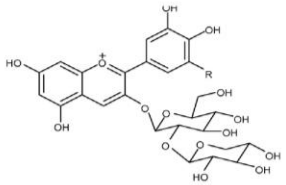
(-)- Hydroxycitric Acid

(From *G. cambogia* [4,5])



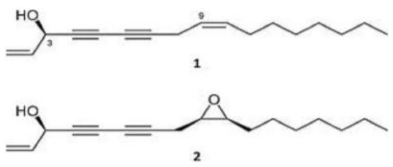
(+)-Hydroxycitric acid

(From *H. sabdariffa* [53])



Anthocyanins: [delphinidin-3-*O*-(2-*O*- β-D-xylopyranosyl)-β-D-glucopyranoside (R = OH), cyanidin 3-*O*-(2-*O*-β-D-xilopyranosyl)-β-D-glucopyranoside (R = H)]

(From *H. sabdariffa* [54-55])

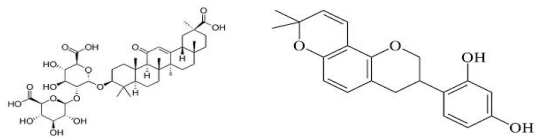


Panaxynol (1) and Panaxydol (2)

(From *P. ginseng* [38])

Fig. 7: Chemical structure of miscellaneous compounds.

The LFO containing Glycyrrhizin or Glycyrrhizic acid (triterpenoid saponin glycoside) and glabridin (from *Glycyrrhiza glabra*) are promising in promoting weight loss. (Figure 8)



Glycyrrhizic acid Glabridin

(From *G. glabra* [56])

Fig. 8: Chemical structure of glycyrrhizic acid and glabridin.

Why does an obese patient prefer herbal medicines for weight management? Possible reasons

The majority of obese patients consider these drugs to be natural and 100% safe. Furthermore, these drugs are readily available and can be taken without any expert supervision. Moreover, patients may hesitate to contact healthcare professionals such as physicians, pharmacists, dieticians, or nutritionists.

Table 1 is self-explanatory about available clinical trials on herbal products/formulations which have implication in weight reduction. Number of formulations/products is available in market assuring weight reducing effects, but as usual like other herbal products, anti-obesity herbal formulations potency is always debatable and demanding more evidences.

Table 1: Randomised clinical trials (RCTs) on herbal products for the treatment of overweight and obesity management [57]

Author/RCT Publication Year	Name of the herbal product and formulation information	Trial design	Subjects	Dose/Duration	Result
Brown 1999	**Lipotrim** *Chromium 100 mcg, Garcinia cambogia fruit extract 50 mg.*	NA	72 patients	NA	• 16 of the 39 patients had a similar weight compared to the baseline. Three gained more than 6 kg, 7 lost 6–12 kg, and 13 lost more than 12 kg.
Ignjatovic 2000	**Slimax** *Aqueous extract of Hordeum vulgare, Polygonatum multiflorum, Dimocarpus longan, Ligusticumsinense, Lilium brownie and Zingiber officinale*	Double-blind	Human subjects	6 weeks	• There was a significant reduction in BMI, body weight, and hip circumference.
Lieberman 2004	**Forslean** *250 mg capsule of a standardized extract of Coleus forskohlii forskolin (25 mg)]*	Open-blind	6 overweight, but otherwise healthy, women	Dose: 1 capsule 2 times a day Direction: 30 minutes before a meal. Duration: For 4-8 weeks	• Mean values for body weight and fat content were significantly decreased.
Singh et al. 2005	**AyurSlim** *Garcinia cambogia, Balsamodendron mukul, Gymnema sylvestre, Terminalia chebula, Trigonella foenum-graecum*	Phase IV open clinical trial	32 obese patients (4 men and 28 women)	Dose: 2 AyurSlim capsules Frequency: twice daily Duration: 6 months	• AyurSlim was associated with a significant reduction in body weight. • Weight loss was directly proportional to the initial weight. • Appreciable changes were observed in the BMI, skin-fold thickness, and serum lipid parameters.
Toromanyan et al. 2007	**Slim 339** *Garcinia cambogia* extract with calcium pantothenate (standardized for the content of hydroxycitric acid and pantothenic acid) and extracts of *Matricaria chamomilla*, *Rosa damascena, Lavandula officinalis* and *Cananga odorata*	Double-blind, randomized, parallel-group, placebo-controlled trial	30 subjects	Dose: 1 tablet Frequency: 3 times/day Duration: 60 days Direction: (60–90 minutes before a meal)	• There was a significant reduction in body weight in healthy overweight and obese human subjects. • The average reduction in body weight in those receiving Slim 339 (n = 30) was 4.67% compared to 0.63% in those taking a placebo (n = 28) • Weight losses of ≥3 kg were recorded for 23 subjects in the treatment group and only 1 subject in the placebo group. • The authors concluded that Slim 339 is a potential therapy for obesity.

Herbal anti-obesity products and potential risks

The general public wants an easy method to control obesity. Anti-obesity herbal products attract users with their health claims, assumed safety, easy availability, and extensive marketing. These products can be very heterogeneous in nature and have unpredictable levels of active ingredients, with unpredictable and potentially harmful effects. Thus, anti-obesity herbal products can cause direct toxicity or adverse interactions with concurrent medications. Physicians and other healthcare professionals need to be aware of these potential complications.

They should advise and warn their patients about the heterogeneous nature of these agents and the potential risks associated with their use. They should report suspected adverse reactions to their national spontaneous reporting system [58].

Clinicians' and patients' expectation from an appropriate anti-obesity herbal medicine:

A high quality anti-obesity herbal remedy should be standardized by laboratory investigations and according to quality control protocols. Its mechanism of action should be well established, and the herbal medicine should have less side effects and be cost effective in order to improve patient adherence. The medication's effectiveness should be proven by RCTs to decrease body weight by 5–10% compared to baseline for better clinical outcomes**.**

CONCLUSIONS

The obesity epidemic in the India has led to a high-priority search for Indian herbal therapies that work effectively. Many Indian and other herbs have been aggressively marketed and used for weight reduction, but only a few products have been evaluated in rigorous trials. Although there is no magic bullet available among Indian herbs that can melt the kilogrammes of fat in a short period, there is a need to create awareness regarding the evidence for and use of natural products in the form of raw materials, crude extracts, or isolated compounds to promote weight loss and thus control obesity. Traditional Indian medicine is based on good clinical practice and holds much promise in the treatment of obesity. These herbal products from Indian medicinal plants have been widely used to treat obesity, and it is important to understand how these natural medicines from traditional medicinal plants act. Nearly all the medicines currently available to treat overweight and obese patients are chemical or biochemical and greater attention should be directed towards the use and research of herbal medicines of natural origin with minimal side effects in the management and treatment of obesity.

ACKNOWLEDGEMENT

The authors wish to thank Universiti Kebangsaan Malaysia for financial support for this work through a grant UKM-GUP-2011-021.

Authors' Contributions

RKV drafted the manuscript and PTT supervised the manuscript writing. All authors have read and approved the final manuscript.

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