

Review Article: Herbal Approach for Obesity Management

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ABSTRACT

Obesity, a complex interplay between environmental and genetic factors and is associated with significant morbidity and mortality. Usage of herbs for the management of obesity in the recent times is attracting attention. A web and manual based literature survey was conducted to assess the amount of information available on the herbal products for weight management. Traditional literature, PubMed, Scopus, Google scholar databases were screened up to February 2012. The search words were “obesity”, “herbal medicine/products/extracts”, “medicinal plants”, “traditional medicine”, “Ayurvedic medicine” without narrowing/limiting searching words or elements. Publications only with abstracts/full articles and books were reviewed in the search. Based on the available literature, for many of the herbal and weight loss products, there is little published information and there have been no clinical trials or the level of evidence is limited. Our literature survey also indicated that these herbal products fall under an acceptable level of evidence or with no scientific background at all, or they have a scientific rational but not to an acceptance level. Attempts were made in the review to define the features of possible herbal weight loss product. An ideal herbal anti obesity product should reduce the weight by 10% over placebo of treatment by showing an evidence of improvement of bio markers like blood pressure, lipids and glycemia without any side effects.

Keywords: Morbidity; *Ayurveda*; Obesity; Literature Survey; Medicinal Plants; Herbal Products; Weight Management

1. Introduction

Accumulation of fat over the limit led to ill/adverse effect in the body known as obesity. Body mass index (BMI) is an index of weight-for-height that is commonly used to classify overweight and obesity in adults. The World Health Organization (WHO) definition is: 1) A BMI greater than or equal to 25 is overweight and, 2) A BMI greater than or equal to 30 is obesity. BMI provides useful population-level measure of overweight and obesity as it is the same for both sexes and for all ages of adults. However, it should be considered as rough guidance because it may not correspond to the same degree of fatness in different individuals.

Obesity and overweight occurs due to imbalance between calories consumed and calories utilized. Globally, there have been two reasons for overweight and obesity: 1) an increased intake of energy-dense foods that are high in fat, salt and sugars but low in vitamins, minerals and other micronutrients; and, 2) a decrease in physical activity due to the increasingly sedentary nature of many forms of work, changing modes of transportation, and

increasing urbanization [1,2]. Changes in dietary and physical activity patterns are often results from sedentary lifestyle, not sleeping enough, endocrine disruptors, such as some foods that interfere with lipid metabolism, medications that make patients put on weight, medical and psychiatric illness and infectious agents.

Overweight and obesity are the fifth leading risk for global deaths. At least, 2.8 million adults die each year as a result of being overweight or obese. In addition, 44% of the diabetes burden, 23% of the ischaemic heart disease burden and between 7% and 41% of certain cancer burdens are attributable to overweight and obesity. WHO global estimates for the year 2008, reported 1.5 billion people were overweight, of these, over 200 million men and nearly 300 million women were obese. Overall, more than one in ten of the world's adult population was obese [1,3].

In 2010, around 43 million children under five were overweight. Overweight and obesity are now on the rise in low and middle income countries, particularly in urban settings. Close to 35 million overweight children are living in developing countries and 8 million in developed countries. Childhood obesity is associated with a higher

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chance of obesity, premature death and disability in adulthood. But in addition to increased future risks, obese children experience breathing difficulties, increased risk of fractures, hypertension, cardiovascular diseases and psychological effects [4].

Overweight and obesity are linked to more deaths worldwide than underweight. For an example, 65% of the world's population live in countries where overweight and obesity kill more people than underweight (this includes all high-income and most middle-income countries). Obesity is a major health threat. The extra weight puts added stress on every part of individual's body. People with obesity are at risk for these health problems: Bone and joint problems due to extra weight puts strain on the bones and joints. This can lead to osteoarthritis, a disease that causes joint pain and stiffness, gallstones and liver problems, heart attack from coronary heart disease, congestive heart failure, and stroke, high blood cholesterol and triglycerides (dyslipidemia or high blood fats), high blood pressure (hypertension), high blood sugar (glucose) or diabetes, stopping breathing during sleep (sleep apnea). This can cause daytime fatigue or sleepiness, poor attention, and problems at work.

Obesity is recognized as the most crucial risk factor for type 2 diabetes. Obesity, in particular intraabdominal adiposity, is associated with increased free fatty acid (FFA) concentrations in blood plasma which exercise a major negative effect on insulin sensitivity in both muscle and liver. Besides insulin resistance, defective insulin secretion is a prerequisite for the development of type 2 diabetes. Both lipotoxicity and glucotoxicity may initiate and enable a vicious circle dependable for the metabolic impairment. Diabetes occurs as a late phenomenon in obesity and is preceded by years of impaired glucose tolerance. The progression to diabetes is indicated by an inability of the B cells of pancreatic langerhans to maintain its high rate of insulin secretion in response to glucose in face of insulin resistance [5]. The partial reversibility of the evolution of obesity towards diabetes is well demonstrated today by lifestyle changes and multidisciplinary weight loss programs [6]. Nature is enriched with plant wealth for all living creatures, which possess medicinal virtues [7]. Anti diabetic activity has been reported in many plants during the last couple of years. Moreover, their mechanism of action differs from that of insulin in that they appear to act as anti-metabolites, capable of blocking the pathway of oxidation of fatty acids. Approximately 343 plants of the world have been tested for the blood glucose which found lowering effect in the laboratory experiments. Of them, 158 species are claimed to be used in traditional system on Indian medicine [8].

The chief goal of obesity treatment is to maintain healthy weight. The treatment method to be undertaken often depends on the preferred choice of an individual

undergoing treatment as well as the level of obesity. Common treatment measures include the following methods, dietary changes, exercise and activity, behavior change, prescription weight-loss medications and weight-loss surgery [2].

The preferred treatment modality for weight loss is dieting and physical exercise. But due to busy schedules and sedentary lifestyle follow-up the first two methods never seems to be practiced in a regular manner. On the other hand weight loss surgery runs out of the option considering the cost involved. There is a gradual shift towards an increase use of drugs. Drugs are pharmacological agents that reduce or control weight. These drugs alter one of the fundamental processes of the human body, weight regulation, by altering appetite, metabolism, or absorption of calories. Only one anti-obesity medications orlistat is currently approved by the FDA for long term use. It reduces intestinal fat absorption by inhibiting pancreatic lipase [3]. Rimonabant, a second drug often referred to as "the munchies", had been approved in Europe for the treatment of obesity but has not received approval in the United States and Canada due to safety concerns [9]. Sibutramine, which acts on the brain to inhibit deactivation of the neurotransmitters, thereby decreasing appetite was withdrawn from the United States and Canadian markets in October 2010 due to cardiovascular side effects [6]. Because of potential side effects, it is recommended that anti-obesity drugs only be prescribed for obesity where it is hoped that the benefits of the treatment outweigh its risk [10].

The use of allopathic and pharmacological drugs has become a popular means to overcome excess weight gain [11]. While these drugs generally are effective, severe adverse toxicities may limit their overall usefulness [12, 13]. A nutritional based intervention is being hailed as an inexpensive alternative to aid weight loss, and weight management [14]. Medicinal herbal supplements are being extensively utilized due to their effectiveness in managing many chronic disorders. They are cost-effective, and exert less to no toxic side-effects in comparison with many chemically synthesized drugs [15]. Accordingly, recent preliminary reports suggested that herbs with a long history of use and other natural substances less likely to produce severe toxicity might be effective in reducing appetite and promoting significant weight loss are encouraging [16].

2. Obesity and Psychiatric Co-Morbidity

The evidence for the interplay between certain mental illnesses (binge-eating, anxiety, mood disorders) and obesity is bidirectional [17]. Various demographical groups suggest that social or cultural factors may moderate or mediate the association between obesity and mood dis-

orders. Population with a psychiatric disorder is at higher risk for overweight and obesity than healthy ones [18-20]. At present there is no clear link concluded between obesity and psychopathology, and whether the possible psychological disorders are a cause or a consequence of obesity has not yet been clarified either [21]. Studies do portrays that certain psychological disorders seem to be more common in obese people, such as depression, anxiety, substance abuse, etc., although the direction of the explanatory relation is not clear; moreover, the opposite result has also been found [22]. Furthermore, there are studies which determine high prevalence rates of mental disorders in obese patients seeking treatment, suggesting the psychiatric evaluation of obese patients as a routine practice [23].

The mere evidences of likely co morbid psychopathology means that the practitioner must consider its assessment in obesity cases, and include a plan for a psychiatric and/or psychological therapeutic intervention. Over the past decade, there has been a great increase in the use of complementary treatment such as herbal remedies for relieving the psychiatric symptoms of obesity and the related morbidities [21,22]. Lee *et al.* has suggested the use of Ob-X, a mixture of three herbs *Melissa officinalis* L. (Labiatae), *Morus alba* L. (Moraceae), and *Artemisia capillaris* Thunb. (Compositae) for regulating hyperlipidemia [23].

3. Herbs Recommended for Obesity

Evidences are emerging to support that an increasing consumption of herbs are effective strategy for obesity control and weight management. Usage of plants and plant products has potential to keep the increasing prevalence of metabolic syndrome in control. There are few drugs in the market to prevent/manage obesity but there are the costs, efficacy and side effects to consider. For centuries people across the countries have been using natural products as plant based dietary supplements for weight control [24].

4. Traditional Medicine and Obesity

Ayurveda (Ayur = life, Veda = knowledge), which is “Science of Life”, originated from the Vedic times and is a part of holistic health care system. The chief source of ancient Indian Aryan culture and medicine are the four *Vedas* that are traditionally believed to be revealed to the sages by Brahma (the creator) some 6000 years before Christian era. *Ayurveda*’s primary emphasis is on preservation and promotion of health, it also provides treatment for disease. Many undesirable constitutions (about eight) in the body are mentioned in “Charaka Samhita”, an authentic source of *ayurveda*. Obesity or “Medoroga” is one among them. It is said that it is comparatively easy

to help an underweight person, rather than an overweight person. The overweight problem can be due to an actual increase in the fat component (Meda Dhatu), or it can be due to malfunctioning. These, accordingly, will need different approaches. In very few cases it can be an offshoot of other metabolic disorders. We have reviewed the available ayurvedic/traditional texts books [25-28] for searching plants which are indicated for obesity. The detailed list of plants has been depicted in **Table 1**.

5. Modern Literature and Obesity

A huge number of herbal supplements are currently present in the market for the management of obesity, although not all of them have the same effect, reason being, supplements targeting different molecules thereby following unique mechanism of action varying completely from the other. The basic principle underlying the mode of action of anti-obesity supplements is regulating the energy balance in the body, which is the balance between energy intake and expenditure. For the convenience of explaining/understanding different studies follow different approaches of categorizing the mechanism, either on the basis of the effect of the drug on nervous system or the effect of a supplement on physiological functions/behavior.

Ample of review on anti-obesity supplements have categorized their mechanism of action primarily on the basis of the activity they regulate. For an example, Yun *et al.* [29] classified the mechanism of anti-obesity action of natural supplements on the basis of the effect they produce 1) decreased lipid absorption, 2) decreased energy intake, 3) increased energy expenditure, 4) decreased pre-adipocyte differentiation and proliferation, or 5) decreased lipogenesis and increased lipolysis. For covering the broader range as well as for the convenience of understanding, Saper *et al.* [30] classified the mechanism of action of anti-obesity product on the basis of: 1) Increase energy expenditure, 2) Modulation of carbohydrate metabolism, 3) Increase satiety, 4) Increase fat oxidation or reduced fat synthesis, 5) Block dietary fat absorption, 6) Increased water elimination, 7) Enhance mood, 8) Miscellaneous and unspecified. We observed that there is plethora of literature on the mechanism of action of synthetic compounds along with convincing number of clinical studies to stand its safety, but continuous withdrawal of the major drugs (USFDA approved) due to the ill effects [31], paved a way for the growth of dietary supplements as a safe option to cure obesity. At the same time the available literature on mechanism of action of drugs will definitely decrypt the likely molecules and the molecular mechanism by which the active phyto-compounds act on. Like a drug, supplements also can act peripherally, centrally or in combination (peripherally &

Table 1. List of herbs indicated for obesity in ayurveda text books.

Botanical name	Sanskrit/official name	Part(s) used
<i>Acacia arabica</i>	Babbula	Gum, bark, leaf, fruit-pods
<i>Acacia catechu</i>	Khadira	bark, heartwood, flower
<i>Achyranthus aspera</i>	Apamarga	Root, seed, leaf, whole plant
<i>Aconitum heterophyllum</i>	Ativisha	Root, rhizome
<i>Acorus calamus</i>	Vacha	Rhizome
<i>Adathoda vasica</i>	Vasa	Leaf, root, flower
<i>Aloe vera</i>	Kumari	Leaf, root
<i>Alstonia scholaris</i>	Saptaparna	Bark, latex, flower
<i>Ananas comosus</i>	Ananas	Fruit
<i>Anthocephalus chinensis</i>	Kadamba	Bark, leaf, fruit, root
<i>Azadirachta indica</i>	Nimba	All parts
<i>Berberis aristata</i>	Daruharidra	Root, stem, fruit
<i>Betula utilis</i>	Burja	Bark, nodes
<i>Calatropis gigantea</i>	Arka	Root, bark, flower, leaf, latex, seed
<i>Callicarpa macrophylla</i>	Priyangu	Flower, leaf
<i>Capsicum annuum</i>	Kutavira	Fruit
<i>Cassia tora</i>	Chakramardha	Seed, leaf, root
<i>Cedrus deodara</i>	Devadaru	Heartwood oil
<i>Cinnamomum zeylanicum</i>	Twak	Bark, leaf, oil
<i>Cissampelos pareira</i>	Patha	Root, stem
<i>Clerodendrum phlomidis</i>	Agnimantha	Root, bark, leaf
<i>Cocos nucifera</i>	Narikela	Fruit, flower, oil, root
<i>Commiphora Mukul</i>	Guggulu	Gum-resin
<i>Coriandrum sativum</i>	Dhanyaka	Whole plant, leaf, fruit
<i>Costus speciosus</i>	Kebuka	Rhizome
<i>Cuminum cyminium</i>	Jeeraka	Seed
<i>Curcuma longa</i>	Haridra	Rhizome
<i>Desmostachya bipinnata</i>	Kusa	Root
<i>Dolichos biflorus</i>	Kulatta	Seed
<i>Embelia ribes</i>	Vidanga	Fruit
<i>Emblica officinalis</i>	Amalaki	Fruit
<i>Euphobia nerifolia</i>	Snuhi	Latex, stem, leaf, root
<i>Ferula nortex</i>	Hingu	Oleo-gum resin
<i>Ficus Glomerata</i>	Udumbara	Bark, fruit, latex

Continued

<i>Ficus lacor</i>	Plaksha	Bark
<i>Ficus religiosa</i>	Ashwattha	Bark, fruit, leaf
<i>Ficus rumphii</i>	Asmanthaka	Stem, bark, latex, fruit
<i>Garcinia indica</i>	Vrikshamla	Fruit, root, bark, oil
<i>Gymnema sylvestre</i>	Meshashringi	Leaf, root, seed
<i>Holarrhena antidysentrica</i>	Kutaja	Seed, bark
<i>Innula racemosa</i>	Pushkaramula	Root
<i>Marsdenia tenacissima</i>	Murva	Root
<i>Momordica charantia</i>	Karavellaka	Fruit, whole plant, leaf, root
<i>Moringa oleifera</i>	Sigru	Root, bark, seed
<i>Ougenia dalbergioides</i>	Tinisa	Heart wood
<i>Picrorhiza kurroa</i>	Katuka	Root
<i>Piper chaba</i>	Chavya	Root, fruit
<i>Piper longum</i>	Pippali	Fruit, root
<i>Piper nigrum</i>	Maricha	Fruit
<i>Plumbago zeylanica</i>	Chitraka	Root, bark
<i>Pongamia pinnata</i>	Karanja	Fruit, seed, oil, root
<i>Pterocarpus marsupeum</i>	Bijaka	Heart wood
<i>Randia dumetorum</i>	Madanaphala	Fruit
<i>Santalum album</i>	Candana	Heartwood
<i>Saussurea lappa</i>	Kushta	Root
<i>Sphaeranthus indicus</i>	Munditaka	Whole plant
<i>Stereosprum sauvealens</i>	Patala	Root, bark, flower, seed, leaf
<i>Symplocos racemosa</i>	Lodhra	Bark
<i>Terminalia arjuna</i>	Arjuna	Bark, root, leaf
<i>Terminalia bellerica</i>	Bibhitaka	fruit
<i>Terminalia chebula</i>	Haritaki	fruit
<i>Terminalia tomentosa</i>	Asana	Bark, heartwood
<i>Thea sinensis</i>	Oolong tea	Leaf
<i>Tinospora cordifolia</i>	Guduchi	Stem, root
<i>Trachyspermum ammi</i>	Yavani	Fruit
<i>Tragia involucrata</i>	Yavasa	Whole plant
<i>Tribulus terrestris</i>	Gokshura	Fruit, root, whole plant
<i>Trigonella foenum graecum</i>	Methika	Seed, leaf, whole plant
<i>Valeriana jatamansi</i>	Tagara	Root
<i>Zingiber officinale</i>	Shunti	Rhizome
<i>Ziziphus mauritiana</i>	Badara	Root, leaf, fruit

central) on the receptors of the nervous system, thereby managing appetite, metabolism (lipid and carbohydrate) or caloric absorption.

In the present review, we surveyed the natural products with anti-obesity potential and reviewed the scientific data, including experimental methodologies, active components, and mechanisms of action against obesity. We classified the mechanism of action of herbs viz., 1) Peripherally acting and 2) Centrally acting.

5.1. Peripherally Acting Mechanism

Substances acting peripherally, mediate their effects by reducing the calorie absorption in the gastrointestinal system or by affecting metabolic and/or control systems outside the central nervous system (CNS). One of the way to reduce energy intake is through gastrointestinal mechanisms such as nutrients digestion and absorption [32].

5.1.1. Lipase Inhibition

Dietary fat is not directly absorbed by the intestine unless the fat has been subjected to the action of pancreatic lipase. Therefore, pancreatic lipase is one of the most widely studied mechanisms for determining natural products' potential efficacy as anti-obesity agents [32]. Supplement acts in the gut lumen by forming a covalent bond with the active serine site of gastric and pancreatic lipases. By forming the covalent bond, it inhibits these lipases from hydrolyzing the ingested fat into absorbable free fatty acids and monoglycerides. The decreased absorption of ingested fat leads to an overall decreased caloric absorption, in turn leading to weight loss [33].

A wide variety of plants possess pancreatic lipase inhibitory effects, including *Panax japonicus* [34], *Platycodi radix* [35], *Salacia reticulata* [36], *Nelumbo nucifera* [37]. These pancreatic lipase inhibitory phytochemicals include mainly saponins, polyphenols, flavonoids, and caffeine [38-40]. The most studied natural sources of pancreatic lipase inhibitors are derived from different types of tea (e.g. green, oolong, and black tea). A significantly different type of polyphenols isolated from tea leaves, showed strong inhibitory activity towards pancreatic lipase [41-43]. These polyphenols require galloyl moieties within their chemical structures and/or polymerization of their flavan-3-ols for enhanced pancreatic lipase inhibition [42].

5.1.2. Adipogenesis down Regulation

Energy balance and lipid homeostasis is maintained in the body by specialized cells called as adipocytes. Adipocytes primarily store triglycerides and release them in the form of free fatty acid with the change of energy demand in the body [44].

Adipogenesis is a complex process regulated by the expression of several hundred genes. The primary adipogenic transcription factors involved in adipocyte differentiation belongs to the peroxisome proliferator activator receptor (PPAR), C/EBP, and sterol regulatory element binding protein (SREBP) families. PPAR- γ expression during differentiation is an important event in adipogenesis process in fat cells [45]. Polyunsaturated fatty acids (PUFAs), a vital components of the phospholipids of cell membranes and acts as a signal transducer regulating adipocyte-specific gene expression involved in lipid metabolism and adipogenesis [46]. Various phytochemicals like quercetin, kaempferol and catechin and dietary flavonoids found in vegetables, fruits, green tea and herbs are reported to down-regulate the adipogenesis-related transcriptional factors PPAR- γ , C/EBP- α and SREBP-1 and to inhibit adipocyte differentiation during the early stage. Tea catechins and epigallocatechin gallate (EGCG) decreased the weight of subject adipose tissue [47-50].

In addition to showing inhibitory activity against adipocyte differentiation, several naturally-occurring compounds have displayed apoptotic effects on maturing pre-adipocytes, e.g. phytochemicals, such as esculetin, resveratrol, quercetin, genistein, capsaicin, and conjugated linoleic acids induced apoptosis of maturing 3T3-L1 pre-adipocytes through suppression of ERK1/2 phosphorylation, activation of the mitochondrial pathway, AMPK activation, or anti-oxidant activity [51-55]. Sirtuin 1 is another target molecule for anti-obesity treatment. Decreased adipogenesis due to resveratrol correlated with increased expression of Sirtuin1, which promotes fat mobilization by repressing PPARc [56,57].

5.1.3. Thermogenesis

Excessive adiposity results from an imbalance in energy homeostasis as a result of excessive food intake are not balanced by increased energy expenditure [58,59]. To regulate body weight and energy expenditure, mammalian BAT (brown adipose tissues) establishes non-shivering thermogenesis through dissipation of excess energy as heat [60]. BAT plays an important role in obesity control by controlling energy balance.

The key player in this process is UCP (Mitochondrial uncoupling protein), which discharges the proton gradient generated in oxidative phosphorylation, thereby dissipating energy as heat. Thus, searching for substances that upregulate UCP1 gene expression may be a worthy strategy for achieving obesity control through increased energy expenditure [61]. Yoon *et al.* has shown that ethanolic extract of *Solanum tuberosum*, can activate the expression of UCP3 in BAT and the liver and significantly reduced fat weight in HFD-fed rats [62]. Numerous naturally-occurring compounds have been proposed

as treatments for weight loss via enhanced energy expenditure, including caffeine [63,64] and capsaicin [57,65].

5.1.4. Lipid Metabolism

The pharmacological targeting of lipolysis can be envisaged in two different ways. The first strategy entails stimulating triglyceride hydrolysis in order to diminish fat stores, thereby combating obesity. This option requires the associated oxidation of the newly released fatty acids and led to the development of the β 3-adrenergic agonists [66]. Some examples of the natural compounds involved in β 3-adrenergic receptor activation are the various flavonoids in the leaf of *Nelumbo nucifera* (NN). Through this pathway, NN extract dietary supplementation resulted in significant suppression of body weight gain in A/J mice fed a HFD [67]. Caffeine, one of the major bioactive components in oolong tea (*Thea sinensis*) possesses both a positive charge and a hydrophobic area like that of adrenaline. Caffeine's mechanism of lipolytic action might be due to its binding to the phospholipid phosphate groups and the subsequent interactions between the lipase and triglyceride portions of lipid droplets, eliciting lipolysis [41].

5.2. Centrally Acting Mechanisms

Body mass can also be maintained by restricting the intake of food. Many products act in a way through their effect on the receptor within the central nervous system thereby developing a sense of satiety within the body.

5.2.1. Neuropeptide Signaling Modulators

The dietary intake of humans varies routinely; still weight remains remarkably stable in most humans because overall energy intake and expenditure are exquisitely matched over long periods of time through the process of energy homeostasis [68,69]. The status of body energy stores is communicated to the central nervous system by the adiposity-associated hormones leptin, insulin, and possibly selected gastrointestinal (GI) peptides, such as ghrelin [69]. The arcuate nucleus of the hypothalamus, the primary neuronal signaling site for appetite regulating hormones, is mainly composed of two types of neurons:

- 1) Anorexigenic (appetite suppressing) neuropeptides, pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART).

- 2) Orexigenic (appetite stimulating) neuropeptide, agouti-related peptide (AgRP) and neuropeptide Y (NPY).

Leptin and insulin stimulate the activity of neurons that express the neuropeptide precursor proopiomelanocortin (POMC), while inhibiting neurons that produce the anabolic mediator's neuropeptide Y (NPY) and agouti-related protein Ghrelin exerts the opposite effects on this

circuitry, directly activating NPY/AgRP cells and thereby indirectly silencing POMC cells. Leptin, insulin, and ghrelin communicate with neurons in the hypothalamus and thereby modulate appetite and energy expenditure to regulate body weight. Leptin, Ghrelin and Neuropeptide Y therefore pops up as a hot targets as well as marker for obesity. Green tea extract has been reported to regulate the plasma leptin concentration [70]. Treatments of adlay seed crude extract (ACE) modulated expressions of leptin and TNF- α and reduced body weights, food intake, fat size, adipose tissue mass and serum hyperlipidemia in obesity rat fed HFD [71].

Neuropeptide Y and its many receptors, in addition to stimulating melanocortins and other catabolic pathways, the adiposity hormones leptin and insulin inhibit anabolic neuropeptides, such as hypothalamic NPY, and chronic NPY administration powerfully increases food intake and body weight. Thus, pharmacological blockade of NPY signaling is a potential antiobesity strategy. Many natural appetite suppressants mediate the reduced expression of hypothalamic neuropeptide Y (NPY) or serum leptin levels [72]. For instance, Kim *et al.* [71] proved that, in HFD-induced obesity in rats, a crude saponin of Korean ginseng effectively regulated serum leptin and NPY expression in the rat hypothalamus. Limited number of reports were published with regard to interaction of natural substances with appetite suppressing and appetite stimulating molecules.

5.2.2. Monoamine Neurotransmitters

Body weight regulation through appetite control is a multifactorial event resulting from neurological and hormonal interrelationships. A line of evidence indicates that serotonin, histamine, dopamine, and their associated receptor activities are closely associated with satiety regulation. Serotonin is a monoaminergic neurotransmitter that modulates numerous sensory, motor, and behavioral processes, acting through a family of at least fourteen 5-HT receptor subtypes. These receptors may enable researchers to better target their searches for drugs that treat obesity through energy intake reduction [73]. Agents that act via peripheral satiety peptide systems, alter the various hypothalamic neuropeptides' CNS levels, or alter the key CNS appetite monoamine neurotransmitters' levels may be suitable candidates for drugs that will suppress appetite [74,75]. Green tea and its constituents (catechins, such as epigallo catechin (EGC) and epigallo catechin gallate (EGCG), have received tremendous attention [76,77], as several lines of evidence suggest EGCG to stimulate thermogenesis through inhibition of the *catechol-O-methyltransferase* enzyme involved in degradation of norepinephrine [43,57,73,78,79].

Natural hydroxycitric acid (HCA), prepared from *Garcinia cambosia*, is a potential natural appetite sup-

pressant. HCA is a competitive inhibitor of adenosine 5-triphosphate-citrate lyase, leading to a decreased acetyl coenzyme A production and decreased fatty acid synthesis. HCA is also thought to suppress feed intake via loss of appetite by stimulation of liver gluconeogenesis. HCA

is also reported to act by increasing the availability of 5-hydroxytryptamine or serotonin, serotonin is a neurotransmitter implicated in regulating eating behavior and appetite control [24]. Central metabolism of glucose also suppresses food intake, mediated by the hypothalamic

Table 2. Herbal products for weight management with human studies.

Author	Name of the herbal product	Formulation information	Study/Method	Subjects	Dose/Duration	Result
Singh <i>et al.</i> , [82]	Ayurslim	<i>Garcinia cambogia</i> , <i>Balsamodendron mukul</i> , <i>Gymnema sylvestre</i> , <i>Terminalia chebula</i> , <i>Trigonella foenum-graecum</i>	Phase IV clinical trial	42 obese patients of either sex	2 capsules, twice daily for 6 months	Significant effect in reducing body weight and lipid levels
Godard <i>et al.</i> , [83]		Forslean from <i>Coleus forskohlii</i> root	Randomized, double-blind, placebo-controlled study	30 men who were overweight/obese	250 mg of extract twice a day for a 12-week period	Causes positive changes in body composition in overweight and obese adult men
Lieberman, [84]	Forslean	250-mg capsule of a standardized extract of <i>Coleus forskohlii</i> [forskolin (25 mg)]	Open blind study	6 overweight, but otherwise healthy, women	1 capsule in the morning and 1 in the evening, 30 minutes before a meal. For 4 - 8 weeks	Mean values for body weight and fat content were significantly decreased
Henderson <i>et al.</i> , [85]		250 mg of ForsLean, supplying 25 mg of forskolin	Double blinded placebo controlled randomized study	60 obese male and female volunteers	1 capsule twice daily for 12 weeks	Total body weight significantly decreased
Brown, [86]	Lipotrim	Chromium 100 mcg, <i>Garcinia cambogia</i> fruit extract 50 mg.	NA	72 patients of which 58 (80.5%) completed the diet and 39 attended follow-up.	NA	Sixteen of the 39 patients had a similar weight from when they started, three had gained more than 6 kg, seven had lost 6 to 12 kg, and 13 had lost more than 12 kg.
Udani <i>et al.</i> , [87]	Phase 2	Water-extract of a common white bean (<i>Phaseolus vulgaris</i>)	Randomized, double-blind, placebo-controlled study	Adults of 35 females, 4 males	1500 mg Phase 2 twice daily with meals for 8 weeks	Treated group lost an average of 3.79 lbs (average of 0.47 lb per week) compared with the placebo group, which lost an average of 1.65 lbs (average of 0.21 lb per week). Triglyceride levels in the Phase 2 group were reduced an average of 26.3 mg/dL, more than three times greater a reduction in the placebo group
Ignjatovic, [88]	Slimax	Aqueous extract of <i>Hordeum vulgare</i> , <i>Polygonatum multiflorum</i> , <i>Dimocarpus longan</i> , <i>Ligusticum sinense</i> , <i>Lilium brownii</i> and <i>Zingiber officinale</i>	Double-blind experimental method	Human Subjects	Six week period	Significant decrease in parameters such as body weight, waist and hip circumference, and Body Mass Index (BMI), in all subjects tested
Toromanyan <i>et al.</i> , [89]	Slim339	Proprietary blend of <i>Garcinia cambogia</i> extract with calcium pantothenate (standardized for the content of hydroxycitric acid and pantothenic acid) and extracts of <i>Matricaria chamomilla</i> , <i>Rosa damascena</i> , <i>Lavandula officinalis</i> and <i>Cananga odorata</i>	Double-blind, randomized, parallel-group, placebo-controlled study	30 subjects	1 tablet of Slim339 three times per day (60 - 90 min before a meal), for 60 days	Daily oral self-administration of Slim339 in the community reduced body weight in overweight and obese healthy human subjects

AMPK/malonyl-CoA signaling system [80]. Central administration of glucose increases hypothalamic malonyl-CoA, decreases orexigenic neuropeptide expression, and suppresses food intake. Centrally-administered fructose provokes feeding, via the AMPK/malonyl-CoA signaling pathway. Thus, decoctions prepared from natural sources containing excessively high fructose levels may suppress the hypothalamic malonyl-CoA signaling pathway, thereby exerting an orexigenic effect [80,81].

6. The Probable Reasons for Obese Person to Prefer Herbal Products for Weight Management

- 1) Health benefits of weight loss without any side effects.
- 2) Less demanding than accepted lifestyle changes, such as exercise and diet.
- 3) Easily available without a prescription.
- 4) More easily accepted than a professional consultation with a physician or a nutritionist.
- 5) 100% natural origin and perception that natural means safe.

7. Remarks on Available Information about Herbal Treatment for Obesity

For many of the herbal weight loss products, there is little published information and there have been no clinical trials or the level of evidence is limited. Some of the herbal products fall under an acceptable level of evidence viz., clinical trials and with no scientific background or scientific rational.

Table 2 compiles available clinical trial literature on various herbal products which have weight reducing effects. Few of the products, which underwent clinical trial, have significant weight reduction as an overall result. The other products have shown comparatively good results in pre clinical studies but lack clinical studies. There are several products in the market claimed to have remarkable weight reducing effects, however there is no supporting published pre clinical and clinical data evidences.

8. An Ideal Herbal Remedy for Obesity: A Proposal

Herbal products for weight reduction may be effective in the management of obesity and associated disorders. Consistent and safe herbal product for weight reduction is a need of developed and developing countries. In our literature survey, herbal products showed potential effects on weight control. However, for the majority of products, more data are needed to assess the suitability as an anti obesity product. We have attempted to provide

salient futures for an ideal herbal product for the management of obesity.

- 1) Should bring down the body weight by 10% over placebo in a well designed randomized placebo controlled clinical trial.
- 2) Should show evidence of improvement of bio markers like blood pressure, lipids and glycemia.
- 3) Should have known mechanism of action.
- 4) Should be standardized with bioactive phytochemicals which is/are responsible for anti obesity activity.
- 5) Should not have any kind of side effects.

9. Conclusion

There are several plants described in *ayurveda* for weight management. But so far, no systematic and well designed screening is attempted to come up with an effective herbal weight loss product. A better understanding in the existing evidence based science on herbs will further guide a qualitative research in obesity management that will attract the end users by the effective benefits. True randomized, double blinded, placebo-controlled clinical trials using herbal products will demonstrate their potential benefits. Significant weight loss after placebo subtraction along with known mechanism of action are required in order to generate conviction amongst users as effective agent for weight management.

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