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PHYTOTHERAPEUTIC APPROACHES TO MANAGE/TREAT OBESITY

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ABSTRACT

Obesity is labeled as the disorder of this century as it forms the first step of other serious diseases. Therefore, World Health Organization (WHO) suggests that management of obesity is the most important for healthy living. Obesity can be controlled either through a healthy lifestyle or regulated eating habits. Alternatively, chemically synthesized medicines are also marketed for weight loss programs. However, the application of drugs is mostly disadvantageous as there are many adverse effects associated with their usage. Therefore, the solution lies in finding healthier alternatives developed from plant origins. To assess the alternates, a thorough screening of medicinal plants for anti-obesity properties is mandated. The prime goal of our review was to understand the efficiency of the selected plants, namely, *Amaranthus spinosus*, *Capsicum annuum*, *Caralluma fimbriata*, *Cinnamomum verum*, *Garcinia cambogia*, *Hoodia gordonii*, *Moringa oleifera*, *Phaseolus vulgaris*, *Lagenaria siceraria*, and *Ziziphus jujuba* against obesity through secondary research methods. Based on the available literature, our study showed that even though most of the plants are traditionally known for their anti-obesity characteristics, not much published information is available at the clinical level. Moreover, our review highlights the requirement of *in vitro*, experimental, preclinical and clinical methods to develop alternate plant-based formulations. In addition, there is a huge gap in research for most of the plants in terms of phytochemistry and their mechanism of action. It was also observed that majority of the studies did not test any associated complications. Therefore, there is a lot of scope of research in this field.

KEYWORDS: Anti-obesity, Clinical trials, Experimental studies, Traditional medicinal plants.

INTRODUCTION

Obesity can be considered to be the foundation stone for potentially serious multiple human health issues of urban populations such as diabetes, hypertension, cardiovascular disorders, dyslipidemia, kidney and liver disorders, cancers, etc.[1] Obesity is labelled as the 'most significant crisis' affecting both adults and children, whereas it is also described as the global 'metabolic disorder' of the modern times.[2,3] The World Health Organization (WHO) define overweight and obesity as anomalous or disproportionate adipose buildup that could pose a health hazard.[4] To classify overweight from obesity, a simple measuring parameter known as body mass index (BMI) is typically employed. This is calculated using the formulae where an individual's body weight (kilograms) is divided by the square of their height (meters) and expressed in kg/m^2 to get their BMI. Adults with a BMI more than or equivalent to 25 are said to be overweight, whereas individuals with a BMI higher or equal to 30 are said to be obese.[4]

Obesity and overweight are becoming more prevalent worldwide, while obesity has tripled by now since 1975.[5] It is estimated that about 135 million Indians are afflicted with obesity.[6] In obesity, there is lack of balance in the rate of energy consumption and energy outflow in an individual due to various factors such as biological, inherited, sociocultural, and epigenetic factors, hormones, microbes and behavior as well as the environment, leading to the accumulation of triglycerides in the adipose tissues.[1] Obesity is linked to be the dominant reason of mortality worldwide with people suffering with cardiac ailments, cerebrovascular and Type 2 diabetes (T2D). It is also associated with dyslipidemia, polycystic ovary (PCOS), hypertension, male hypogonadism, metabolic syndrome, osteoarthritis, non-alcoholic fatty liver disease (NAFLD), depression some kinds of cancers, obstructive sleep apnea (OSA), and Alzheimers disease.[7] The easily accessible excessive calorific food and an inactive lifestyle are the major causes of obesity.[8] Therefore, management of obesity has become the prime criteria for healthy living, irrespective of the country of living. In order to address

this issue, World Health Organization has mandated certain interventions in the diet as well as the lifestyle.[9,2] Several strategies are employed to overcome obesity apart from making lifestyle changes and following diets for loss of body mass, which include excercises, pharmacotherapy, and bariatric surgery to treat obesity.[10] Along with this, anti-hyperlipidaemic drugs like sibutramine, orlistat, metformin, quercetin, etc. are used to control obesity (Saxena et al., 2019). These synthetic chemical drugs have been found to be an expensive proposition and also with adverse side effects.[1] Orlistat was reported to cause diarrhoea, flatulence, oily spotty feces, and vitamin/mineral deficit, while, Phentermine induces dehydrated mouth, blood pressure, sleeplessness, constipation, nervousness, and cantankerousness.[11,12,13] Lorcaserin can cause headache, faintness, fatigue, dry mouth and constipation.[14] Similar symptoms were also observed for Naltrexone/Bupropion sustained release (SR) also.[14] Due to high expenses and potentially dangerous side-effects of the pharmaceutical medicines, the possibility of natural substances for treating weight gain need to be probed by the researchers as this may be an alternative approach for evolving powerful and harmless weight loss medications. Some common mechanisms of weight reduction by herbal drugs were proposed.[15] These include, appetite suppression, reduction in energy consumption, activation of thermogenesis and metabolic promoters, inhibition of pancreatic lipases, decreased absorption of lipids, enhanced lipolysis, and abated lipogenesis. Several studies have used natural plant products and their crude extracts which are acknowledged to induce potentially promising therapeutic characteristics like reduction in body mass and stop diet induced obesity.[16] These medicinal plant extracts contain phytochemical constituents known to prevent diseases.[17,18] These dietary supplements and natural components can be used as alternatives to pharmaceutical drugs.[19] Thus, a thorough filtration of the therapeutic flora for their anti-obesity affinities is the need of the day. This is especially advantageous for the Indian sub-continent as this area has a huge plant diversity. Our current study aims to review some of the commonly available Indian plants for consideration of suitability of candidature for development of herbal medicines in terms of their traditional uses, phytochemical constituents present in them and pharmacological activity. Along with this, wherever possible *in vitro* experiments as well as clinical trials of those plants were also considered as scientific evidence for evaluation of their efficiency. The plants that have been chosen for our study include, *Amaranthus spinosus*, *Capsicum annuum*, *Caralluma fimbriata*, *Cinnamomum verum*, *Garcinia cambogia*, *Hoodia gordonii*, *Moringa oleifera*, *Phaseolus vulgaris*, *Lagenaria siceraria*, and *Ziziphus jujuba*, have been described in detail below. Based on this, the objectives of our study can be defined as follows:

1. To understand the efficiency and efficacy of the chosen plants for the presence of anti-obesity properties.
2. To support these properties of the plants with any reports of clinical trials, experimental studies and case studies.

Table 1 summarizes the common names of the selected anti-obesity plants, their traditional uses, the economically important part of the plant, phytochemicals present and their pharmacological activities.

Table 1: List of anti-obesity plants, their common names, traditional uses, economically important part of the plant, phytochemicals present and their pharmacological activities.

Botanical name	Vernacular names	Native country	Traditional use	Economically Important Plant part	Phytochemicals
Amaranthus spinosus L. Family: Amaranthaceae	Hatikhotora, Accho aadar arxa, Kanta bhaji	Tropical America	Consumed by tribes to prevent stomach swelling, jaundice, infections	Young plant, leaves	Amaranthine, isoamaranthine, hydroxycinnamates, rutin, quercetin, and kaempferol glycosides.[20,21,22,23]
Capsicum annum L. Family: Solanaceae	Peppers, Shimla mirch	South America	Anti-arthritis, anti-microbial, toothaches, cough, sore throat treatment, healing of wounds, appetite suppressant and immunomodulator	Fruits and seeds	Capsaicin and Capsiate in fruits, capsicoside-G in seeds.[24,25,26]
Caralluma fimbriata Wall. Family: Apocynaceae	Maakada singi, Mangana kodu, Makad Shing, Kullee Mooliyan,	East Africa	Therapeutic effects such as weight loss, anti-diabetes, digestive	Whole, fruit	Pregnane glycosides, flavone glycosides, megastigmane

	Kallimudayan: kaarallamu, kundelu kommulu		aid and appetite control		glycosides, bitter principles, saponins and various flavonoids.[27,18]
Cinnamomum verum J. Presl Family:Lauraceae	Ceylon cinnamon	Sri Lanka, East and Middle Asia	As antitussive, antiarthritis, antimicrobial, antifungal, anti-oxidant, anti-inflammatory agent	Bark	Cinnamaldehyde, cinnamate and cinnamic acid.[28]
Garcinia cambogia (Gaertn.) Desr. Family: Clusiaceae	Malabar tamarind brindle berry, and kudam puli (pot tamarind)	India and Southeast Asia	Weight loss, anti-obesity	Fruit rind, bark	Hydroxycitric acid.[29,30]
Hoodia gordonii (Masson) Sweet ex Decne. Family: Apocynaceae	Kalahari cactus, bitterghaap	Kalahari, Africa	Natives chew it to satiate hunger	Stems, root, and latex	Pregnane , oxypregnane and steroidal gylcosides such as P57.[31]
Lagenaria siceraria (Molina) Standl. Family: Cucurbitaceae	Bottle gourd, Lauki	India	Antioxidant, analgesic, anti-inflammatory, antimicrobial, hepatoprotection	Fruits, root, leaves, seed oil	Rich source of vitamins B1, B2, B3, B6, C, amino acids, triterpenoids, sterols.[32,33]
Moringa oleifera Lam. Family: Moringaceae	Sigru, Marango	Himalayan region	Cardiac, skin and circulatory disorders, anti-hypertension, anti-diabetic	Root bark, seed, leaves, flowers and pods	Isothiocyanates, fitotesrol[22,,34]
Phaseolus vulgaris L. Family: Fabaceae	Common bean	America	Weight loss, anti-obesity, diuretic, kidney and heart problems, diarrhea	Leaves, bark, fruit and seed	Alpha amylase.[35]
Ziziphus jujuba Mill. Family: Rhamnaceae	Chinese date, ber, Chinee apple, jujube, Indian plum, Regi pandu, Indian jujube, dunks	Southeastern Europe to China	Weight loss, anti-obesity, blood nourishment, sleep improvement, control of digestive system	Bark, leaf	Sterols, alkaloids, serotonin, saponins, flavonoids, polyphenols, triterpenoids, and glycosides[36,37,38]

Plants With Anti-Obesity Properties

Amaranthus spinosus

A. spinosus L. is commonly called the prickly amaranthus, water leaf or spiny pigweed in English.[20,21,39] It belongs to Amaranthaceae Family and is primarily an erect perennial or annual herbaceous plant growing mostly as a weed in tropical regions of Asia (India, Bangladesh and Sri Lanka), Africa and USA among others.[20] In India, it is mostly available during the winter and rainy seasons in Jharkhand.[22] The young plant and the leaves are cooked as a vegetable and consumed by the people. The medicinal properties of leaves and roots include malaria, hyperlipidemia, eczema or abscesses, piles, dysuria, burns, peptic ulcers, stomach disorders, anemia, injuries, gonorrhea and can act as an anti-inflammatory /diabetic/ laxative/ emollient/ spasmolytic /diuretic/ or even as an anti-snake venom.[21,22]

Among phytochemicals, *A. spinosus* has been reported to have spinoside, hydroxycinnamates, amaranthine, gomphrenin, beta-D-ribofuranosyl adenine, betanin, b-sitosteol, linoleic acid, beta-carotene, quercetin, betaxanthin, betacyanin, isoamaranthine, xylofuransyl uracil, rutin, and kaempferol as well asbetasitosterol glycosides.[40,20,41] A high amount of alkaloid content (3.23%) was also observed, followed by 1.15% of total flavonoids, 0.50% of total flavanol and 0.32% of total phenol.[23] The oil obtained from *Amaranthus* causes a decrease in cholesterol levels.[42]

Most of the studies have evaluated the efficiency of *Amaranthus* against the reduction of cholesterol.[40,21] Even though *Amaranthus* is known for its anti-obesity properties, there are hardly some recent studies directly showing the effects of *Amaranthus* on obesity.[20,43,44,42] Within these studies, there was a clear contradiction in the results of loss of body weight due to *Amaranthus*.

Any form of intolerance such as eructation, nausea, heartburn, bitter taste, abdominal pains and allergy was evaluated in individuals due to the consumption of *Amaranth* oil and no such adverse effects was found among the study samples.[42]

Capsicum annuum

Capsicum annuum, an annual shrub belonging to the family Solanaceae, covers various forms of peppers such as bell pepper, sweet pepper, paprika, chillies, etc.[45] It is usually eaten as a vegetable all over India. In North India, it is locally called as Shimla Mirch.[46] *Capsicums* have been an integral part of pain and obesity management.[47] Other traditional uses include rheumatism, wound healing, antimicrobial, cough treatment, atonic dyspepsia, gastric issues, appetite loss and many others.[25,26]

The two primary phytochemicals present in *Capsicums* are Capsaicin (trans-8-ethyl-N-vanillyl-6-nonenamide) and dihydrocapsaicin (8-methyl-N-vanillylnonanamide).[48] Apart from the above-mentioned constituents, nordihydrocapsaicin, homocapsaicin and homodihydrocapsaicin were also observed in the samples.[3] The mechanism of action of Capsaicin that causes weight loss occurs through the regulation of appetite by suppressing the hunger hormone, 'ghrelin', or by modulating hypothalmic satiety, increasing the metabolism of lipids or by up regulating anti-adipogenic genes and mitochondrial uncoupling proteins (UCP2 and UCP3) for prevention of any gain in body mass.[49,50,51] Furthermore, it is also known to alter microbial fauna of the gut, enhance thermogenesis and mitochondrial biogenesis expression, boosts consumption of oxygen as well as energy and impedes the expression of adipogenic transcription factors.[52,53,54] The seeds are known to reduce the body weight by decreasing the epididymal adipose tissues and enhanced expression of adipocyte differentiation controllers.[55]

There has been multiple *in vitro*, animal as well as human studies where the effect of capsaicin has been successfully tested against obesity apart from glucose metabolism and insulin resistance during the past few years.[56,47,26] Most of the studies support that pepper extract had a major impact on the reduction of obesity by alteration of fat metabolism.[55,54,3] Apart from body weight, histological assays and plasma biochemical aspects were conducted to study the effect of capsicoside on food consumption, food efficiency, organ weight, and adipose tissue weight.[55] It was also reported that the pepper extracts inhibited adipogenic transcription factors as well as adipose genetic markers.[54] Along with the comparison of body weight decrease, the serum lipids were also evaluated and it was suggested that these can form critical biomarkers for understanding cardiovascular diseases. The food intake, liver weight, BMI, fat index and energy absorption along with energy consumption between the freshly extracted and fermented extract were compared and observed that the fermented part was more effective in reducing any induced obesity.[3] Therefore, further studies are essential to corroborate the results obtained above.

Caralluma fimbriata

Caralluma fimbriata, also known as *Caralluma ascendens*, has multiple vernacular names like Kaarallamu, Kallimudayan, Kullee Mooliyan, Kundelu kommulu, Maakada singi, Makad Shing, and Mangana kodu. It is distributed in Asia, starting with India, Sri Lanka over the Arabian peninsula to North Africa and extending to semi-arid region of north-central Africa the Sahel.[57,58] This plant is a succulent cactus belonging to Apocynaceae Family. This is also eaten frequently as a vegetable in the times of famine. Indian tribes bite lumps of *C. fimbriata* to curb their hunger cravings and enhance stamina while hunting [59,57,60]

Several varieties of *Caralluma* are found in India with similar phytochemical compounds. The key chemical constituents present in *Caralluma* include flavone glycosides, pregnane glycosides, megastigmane glycosides, saponins, bitter principles, and numerous flavonoids.[57,18] The mode of working starts when the pregnane glycosides of *Caralluma* act on sites of the hypothalamus.[60] These are hypothesized to have a role in appetite suppression due its capacity to cause interference in the signalling of the brain causing the stomach to feel full.[61] Pregnane glycoside inhibits adipocyte proliferation and differentiation, which results in the prevention of weight gain.[60] Another hypothesis could be the down regulation of *Caralluma fimbriata* extracts (CFE) in ghrelin synthesis –a peptide released from the stomach and also from neuropeptide-Y neurons, which stimulates food intake in the abdomen and the hypothalamus.[62,18,63]

Many pre-clinical and clinical reports have been published for studying the impact of *Caralluma* on obesity. The study of men and women in a randomized control trial treated with CFE at a dosage of 1g/day for 60 days showed appetite suppression and reduced weight in comparison to the placebo subjects.[57] A dose dependent anorexic, anti-obesogenic and anti-atherosclerotic effect on diet was reported to cause weight gain in mice that have been administered with a cafeteria diet plus (CFE) at different dosages of 25 to 100 mg/kg body weight everyday for 90 days.[60] Similar research conducted on Wistar rats displayed that a dosage of cafeteria plus CFE 100 mg/day that was given for 50 days, prevented the weight gain and maintained the lipid profiles.[64] A double blind placebo regulated randomized clinical experiment was conducted on 43 adults where individuals were given CFE at a dose of 500 mg/day for 3 months with controlled dietary intake and exercise. It was found that there was a noteworthy deterioration in palatability and body mass, BMI, systolic BP, hip circumference, triglyceride levels, and total lipids.[18] This implies that *Caralluma* has a huge potential role in curbing corpulance. The kids and adults

with Prader-Willi syndrome was studied, where the patients show a hyperphagic condition which causes an individual to ingest food excessively using a placebo-regulated, double-blind, random, crossover experimental research design for a 10-week time frame to examine the impact of *Caralluma* extracts at a dosage of 1000 mg/day on hunger control.[65] It was confirmed that these plant extracts could ease the hyperphagic behavior without causing any adverse effects. The above preclinical and clinical studies imply that the pregnane glycosides present in these extracts perform a key part in the decline of food ingestion, which reflects appetite suppression by neurons in the hypothalamus, where they are known to act.

Cinnamomum verum

Cinnamon is obtained from the outermost layer (bark) of a small tropical tree, *Cinnamomum verum*, which was previously known as *Cinnamomi zeylanicum* belonging to Family Lauraceae.[28] This is commonly found in India, Sri Lanka and the other Mediterranean countries.[66] It is typically used as a spice while cooking and traditionally used as an herbal remedy for multiple disorders like anti-tussive, anti-tumor, anti-hypertensive, anti-arthritis, anti-microbial, anti-fungal, anti-lipemic, antioxidant as well as anti-inflammatory agent. It also finds its application in toothpastes, perfumes and incenses. The therapeutic advantages include treatment for diabetes, flatulence, eye inflammation, cough, rheumatism, colon cancer, infections, multiple sclerosis, Alzeihmer disorders, amenorrhea, diarrhea, erectile dysfunction, etc..[28,67] Moreover, it is also known to act on hypertension, obesity, dyslipidemia and hyperglycemia.

The important phytochemicals include cinnamaldehyde, cinnamate and cinnamic acid, mostly obtained from the bark, whereas the leaves have 70-95% Eugenol.[28] The mode of action to reduce obesity includes the reduction of the hunger hormone (Ghrelin), insulin resistance, lipolysis, lipogensis and intestinal lipid absorption, however, there is an increase in the peroxisome proliferator-activated receptors (PPAR-α and γ).

Cinnamon as a drug formulation has been widely used for studies involving anti-obesity studies. Recent studies include systematic reviews that have been published detailing the understanding the impact of supplementation of *cinnamon* as there are conflicting reports among the tested ones.[67,68,66] Twelve random clinical trials showed that there were differences between the trails with respect to *cinnamon* dosage and duration, gender of the groups in the evaluation of body and fat mass, BMI, and waist circumference.[66] Any side effects occurring due to *cinnamon* consumption were evaluated in the selected 38 reports that includes clinical trials, case reports and case series and found stomachache, nausea, headache or rash as adverse effects in a few of the studies.[67] Most of them did not show any side effects and concluded that *cinnamon* was safe for routine consumption as well as for use in clinical trials. Similarly, a systematic review summarizing 21 studies was also reported which supported that *cinnamon* supplementation was useful for overweight and obese individuals in terms of body weight reduction and not help in decrease of waist circumference. In this case, only study described any adverse effects faced by the study samples.[68] Studies were done on hamsters, Wistar rats, zebra fish, and human beings and all of these emphasized the positive effects of *cinnamon* in reducing obesity.[69,70,71,72] An indigenous *cinnamon* (*Cinnamomum osmophloeum*) leaf powder was used for the study on hamsters.[69] In the case of Wistar rats, although loss in body mass was reported for the mother rats, nevertheless, the results showed that the offspring had a high amount of visceral fat.[70] In the study on human beings, the same dosage of orlistat, a weight management drug was compared with *cinnamon* and advocated that *cinnamon* was more capable of improving the BMI and the glycemic targets, which is helpful for patients in a holistic manner.[72]

Garcinia cambogia

Garcinia cambogia (Family Clusiaceae) is commonly called as Malabar tamarind. It is being eaten for centuries as a condiment and flavoring agent to make meals more filling.[73] It is geographically distributed in Southeast Asia, coastal Karnataka, Kerala in India, and west and central Africa.[29] It is attributed to have various effects on health such as anti-obesity, anti-ulcerogenic, anti-oxidative, anti-diabetes, anti-microbial, treatment of constipation, hemorrhoids and cancer.[74,75,76]

The plant contains hydroxycitric acid (HCA) as a major ingredient, which is found as over the counter supplements in the market. This plant is popular for its role in weight loss and appetite suppression through the creation of hepatic glycogens and activating the glucoreceptors, which produce perception of eating saturation.[29]

Many scientists have reported the use of *Garcinia* as an anti-obesity agent. The impact of hydroxy citric acid (HCA)-SX, a novel derivative of HCA obtained from *Garcinia* was studied on Sprague Dawley rats. The oral application of this compound at a lower dosage combined with water (10 mg/day for 8 weeks, 5 days/week, respectively) restricted the body weight of adult rats by affecting certain set of genes sensitive to HCA-SX.[75] In another study, the impact of HCA-SX on oxidative stress, inflammation, and resistance to insulin was observed in the growing obese Zucker rats, which can be considered as an animal prototype of T2D related with inflammation and oxidative stress.[77] HCA-SX at the level of 500 mg/kg of body mass/day for 2 weeks was administered, which was later on enhanced to 1,500 mg/kg of body mass per day. The experimental animals were given the dosage for another 5 weeks. The HCA-SX effect on obese Zucker rats showed that there was a decrease in their food-ingestion, body mass increase,

along with the increase in inflammation, oxidative stress, and insulin resistance detected in the control subjects The decrease in body mass of the obese rats was probably due to its action as an inhibitor to ATP-citrate cyclase, an enzyme required for the creation of fatty acids.[76,78] It can be suggested that HCA-SX may have a role in the upregulation of genes encoding serotonin as serotonin is known to reduce appetite, then the possible role of HCA-SX may have stimulated the receptors of serotonin in the brain, thus, reducing appetite. Serotonin toxicity was reported in a patient who was on medication for depression such as Escitalopram.[29] The observed toxicity symptoms when *Garcinia cambogia* supplements were added showed ataxia, diaphoresis, hallucinations, hypertension, muscle rigidity, ocular clonus, spontaneous lower extremity clonus, tachycardia, and tremors. However, no association between *Garcinia cambogia* and serotonin harmfulness was established. Combined administration of *Garcinia cambogia* with Glucomannan, a weight loss drug on 214 overweight or obese subjects at a dosage of 500 mg twice everyday for half a year was assessed for Basal Metabolic Rate (BMR), fat and body weight, visceral fat along with lipid, glucose and blood charts. The weight loss was accompanied by the decrease in visceral fat, fat mass and blood glucose levels, and augmented BMR.[79] A clinical trial on 100 obese individuals by administering *Garcinia* caplet for three months analyzed the anthropometric and plasma lipid profile levels.[30] A significant body weight reduction along with improved anthropometric measurements and metabolic state were reported in the samples.

Hoodia gordonii

Hoodia gordonii (Mason) Sweet ex Decne can be described as a leafless, succulent cactus belonging to the Family Apocynaceae, indigenous to the Kalahari Desert and found only in South Africa and Namibia.[31,80] It is used to satisfy hunger pangs at the time of long hunting by natives from Africa. This plant is known to have weight loss abilities, enhanced the consumption of water and can suppress appetites.[80] In addition, anti-HIV properties have also been observed by the compounds isolated from them.[81]

The active agents found in *Hoodia gordonii* has been identified as pregnane, oxypregnane and steroidal gylcosides.[82] One of the glycosides is named 'P57'.[31] These enhance ATPs in the hypothalamus so that the intake of food can be controlled. It is commercially successfully sold in the markets.[83] Antioxidants, fatty acids and steroidal glycosides were listed as the phytochemicals present in this plant.[84] The mechanism of action in reducing obesity by *Hoodia* involves the use of a combination of liver glycogen, mitochondrial protein and thyroid hormones for sending messages of increased glucose levels, thereby leading to less eating by the individuals. The anorectic reaction can be arbitrated by suppressing adrenal steroidogenesis through the suppression of the steroidogenic cytochrome P450 enzymatic breakdown in human adrenocortical cells.[85] Along with this, it caused anti-inflammation by reducing IL-6 and enhanced leptin amounts.

Both animal studies as well as human trials dealing with the action of *Hoodia* were reported to be limited, even though some studies showed positive results towards reduction of obesity.[86,85,82,31] The BMI was found to be significantly reduced in the case of overweight females.[87] However, no vicissitudes in the body mass or energy consumption was noted. Moreover, adverse effects such as nausea and vomiting were also stated. In the case report indicating positive result towards reduction of obesity, there were no reports of any side effects on the consumption.[85] It was emphasized that the safety of the drug with respect to *Hoodia* has hardly been studied.[88] No proper dosage has been established and therefore, needs further analysis in this regard. This may be due to the interaction of the drugs with anti-diabetic medications.[89]

Lagenaria siceraria

Lagenaria siceraria belongs to the family of Cucurbitaceae, is a climber that produces the bottle gourd as a fruit, which is used as a vegetable crop.[33] It is commonly grown in Asian and African nations, for example, Japan, Egypt, India, and Thailand. This plant is traditionally known to have a number of medicinal properties starting with reducing fevers, pains, asthma, ulcers, headaches, hair loss, dropsy, rheumatism, tetanus, cancer and protection from cardiovascular and liver issues. It also acts as an antioxidant, anti-inflammatory, antimicrobial, anti-tetanus, analgesic, anti- diuretic and aphrodisiac agent.[32]

Apart from vitamins, minerals flavonoids, tritepenes, some of the identified phytochemicals in bottle gourd include, triterpenoids such as triterpenoid cucurbitacins, deoxy-cucurbitacin, sterols such as Fucosterol, Campesterol, retinoids, saponins and enzymes β-glycosidedase-elastase.[90,33] There are hardly any studies describing the mechanism of action of the phytochemicals of bottle gourd on reducing obesity. It was bottle gourd has lipase inhibitory activities, thereby suppressing digestion of fats and reducing the entry of fats into the body.[91]

Many studies have reported the reduction in body mass due to the use of bottle gourd extracts.[90,92,32,33] In addition, the regulation of the lipid profile such as triglycerides, cholesterol, LDL and HDL has been reported from both fruit, the juice of the fruit and leafy extracts. The phytochemical scanning for the existence of phytosterols, saponins, tannins, and alkaloids tested positive.[92] A huge difference in body weight of rats was observed that had consumed bottle gourd juice. It was also suggested that this reduction in lipid levels will also help in controlling diabetes, renal disorders and other complications associated with obesity. This regulation was being conducted by the inhibition of catabolizing

enzymes like lecithin cholesterol acetyl transferase (LCAT) as well as lipoprotein lipase (LPL). It was reported that along with the body weight, there was a loss in the liver weight in the higher dosage sample.[32] In addition, the extraction methods from the plants, aqueous and alcoholic were compared in terms of efficiency and it was found that the alcoholic extract had better anti-obesity abilities compared to the aqueous one. In a separate toxicity study of extracts from *Lagenaria* fruits on rats reported no hematological or biochemical imbalances even after a high dosage of 2000 mg/ kg of body weight, thereby evidently supporting the use of *Lagenaria*.[93]

Moringa oleifera

Moringa oleifera is an annual tree that belongs to family Moringaceae and is geographically distributed throughout 20 tropical and subtropical countries, including India.[94] This plant is commonly identified as drumstick and eaten as a source of vegetables.[95,22] *Moringa*, considered as the 'miracle tree' is highly known to be medicinally and nutritionally valuable as it has all the essential nutrients for human growth and development.[34] Some of the medicinal properties include, anti-inflammation, anthelminthia, hypoglycaemia, treatment for skin disorders, anti-hypertension, anti-diabetic, diuretic, antipyretic, ear and tooth infections, cancer as well as cardiac and circulatory activator.[96,97]

The active component called fitosterol is obtained from *Moringa oleifera* and works by reducing the atherogenic index and reversing the fat diet.[95] *Moringa* leaves have elevated levels of phenolic acids like gallic acid and cholorogenic acids, quercetin, myricetin and kaempferol.[98] 13 compounds in the fresh extracts were identified.[99] Apart from the acids mentioned above, Luteolin, Apigenin, Feruloylquinic acid and Kaempferide were also detected using HPLC-MS analysis. The mechanism of action that *Moringa* is involved in for reduction of obesity is by increasing the lipid metabolism followed by the inversion of the generation of hepatic steatosis and henceforth, reduces liver disorders.[100] It was reported that the isothiocyanates present in *Moringa* restrict liver gluconeogenesis, thereby increasing insulin sensitivity, whereas, the extract stops adinopectin formation.[101,102] However, none of the mechanisms have been justified. Recently, the anti-obesity and apoptosis aspects of *Moringa* extracts were elaborated, where it was schematically shown that the extract acts on preadipocytes and up regulated the adipogenesis genes.[34]

Most of the studies that have proven the anti-obesity properties of *Moringa* have concentrated on the anti-adipogenic character of *Moringa* extracts.[34] This anti-adipogenic properties were tested on using various methods such as TUNEL assay, Hoesch staining, PI staining and Caspase assay for the presence of the matured adipocytes and promotion of apoptosis. The results showed that there was a molecular interaction between quercetin and various molecules such as BXL-Xl, FABP4 and PPAR-.Y. The induction of apoptosis due to overexpression of BAX and decrease of BCL-2 and increase of caspase 3 activity proved that the oral administration of *Moringa* can be helpful in reducing obesity. Even in fructose fed diets, *Moringa* was able to restrict lipid accumulation, which was tested using several parameters such as weight gain, lipid volume and blood glucose levels. The expression of mRNA of the foremost enzymes like fatty acid synthase (FAS) and HMG-CoA reductase got suppressed, however, there was an increase in Melanocortin-4 receptor (MC4R) and Peroxisome Proliferator-Activated Receptor alpha (PPARα), leading to reduction in fat accumulation.[99] The main outcome exhibited a distinct decline in body weight, BMI, lipid levels and adiposity index with samples treated with *Moringa* extracts.

Phaseolus vulgaris

Phaseolus vulgaris (Family Fabaceae) is a highly consumed vegetable, which is known for its effects on weight reduction in overweight individuals.[103] In recent times it is used as a bioceutical owing to the presence of bioactive substances like resistant starch, polyphenols, bioactive peptides, oligosaccharides, and nutrients.[104,105]

Phaseolus vulagaris extract (PVE) has promising influence on the well being of humans and possesses antioxidant, anti-obesity, anticarcinogenic, anti-diabetes, anti-inflammation, and cardioprotective properties.[106,107,108,109]

The consumption of beans has shown preventive impact on the hunger cravings and advantageous aspects on carbohydrate breakdown.[110,111] A potent inhibitor present in *Phaseolus vulgaris* was purified, which restricted the action of human salivary alpha amylase and affected carbohydrate metabolism. Thus, it was implied that beans causes weight reduction in human beings and other animals.[103] Cooked beans are nutritious food ingredient for dogs, a study was conducted to evaluate the alterations in metabolic parameters in dogs consuming controlled diet of cooked bean powders and dogs not consuming beans. The dogs consuming control diet lost an average weight of 4.20% (± 0.88), while 5.22% (± 0.91) for dogs consuming black bean diet and 6.52% (± 0.95) for dogs consuming navy bean diet. The study further proved that the bean powder regulated serum lipids and biochemical analytes. Triglycerides, high-density lipoprotein, and lowdensity lipoprotein were also differently modulated in bean groups compared to control kidney bean.[112] Another experiment was conducted on *P. vulgaris* dry kidney bean extracts, which were administered on Zucker fa/fa rats at 5 and 500 mg/kg dosage for 5 days and left for a recovery period of 20 days.[113] A dose dependent decrease in body mass and food intake was observed. This was due to the bean extracts even after repeated

cycles of treatment. *Phaseolus vulgaris* may have exerted two additive effects:[114,115,113]

a) restriction of pancreatic alpha amylase leads to the slowing of the carbohydrate metabolic process and absorption, the reduction of glycemia and the creation of feeling of engorgement and b) decrease in feelings of hunger induced by lectin and interruption in gastrointestinal pathway was possibly due to the modifications in the discharge of cholecystokinin and glucagon-like peptides. These growth regulators are well-known for their functioning in the digestive systems and the primary regulation of hunger craving.[116,117,113] A random, double blinded placebo regulated experimental study was conducted with a dietary supplementation of 445 mg of *Phaseolus vulgaris* extracts on 60 slightly overweight individuals for thirty days.[118] A significant decrement in the body and fat mass was observed. The mechanism behind weight loss of *Phaseolus vulgaris* extracts involve the inhibition of the action of alpha amylase and encourage weight reduction by meddling with the absorption of sugars, thereby, theoretically decreasing sugar derived calories.[119,120] Another mechanism contributing to weight loss was due to some carbohydrates that contain a form which is unreachable to alpha amylase and thus, resilient to absorption in the human GI tract.

Ziziphus jujuba

Zizyphus jujuba belongs to the family Rhamnaceae is a deciduous large plant and found commonly in India, Middle East, South Africa, and China. The uses of various parts of the plant include anti-cancer, anti-inflammatory, anti-obesity, anti-helminthic, antioxidant, hepatoprotective and reduces gastrointestinal issues. The phyotchemicals present in the leaves, bark, fruit and seed have sterols, alkaloids, serotonin, saponins, flavonoids, polyphenols, triterpenoids, and glycosides.[36,37,38]

The impact of albino rats fed on cafeteria diet/atherogeneic diet that were given a dose of *Ziziphus jujuba* leaf extracts at 500 mg/day for 40 days was reported.[121] A substantial level of decline in the body weight, lipid levels, food consumption, serum glucose, internal organs and fat pads had anti-obesogenic, hypolipidemic and hypoglycemic effects. The study on high fat induced obese rats treated with barks of *Ziziphus jujuba* was administered dosage of 250 mg, 500 mg, and 900 mg for 90 days.[122] It was found that there is a decrease in total fat mass. A clinical study on the activity of *Ziziphus jujuba* extracts on 83 persons and found a significant decrease in weight at a dosage of 30 g/day, suggesting that these plants are hypolipidemic and anti-obesogenic.[123]

Table 2 elaborates on some of the reported studies using medicinal plants for the treatment of obesity.

Table 2: Studies using herbal plants for the treatment of obesity.

Name of the plant	Type of study	Study location	Objectives	Dose/Duration	Intervention	Main outcome
Amaranthus spinosus	Experimental study on rats	Korea	Effect of oil and grain on diabetics	500g/kg for grain, 100g/kg for oil	Amaranth oil and grain	Reduction in body weight.[43]
	Randomized placebo-controlled clinical trial	Not mentioned	Effect of *Amaranthus* on coronary heart disease, hypertension and obesity	100 to 600 mg/ day for 3 weeks	Amaranth oil	No major difference between the Amaranth group and control.[42]
	Experimental study on rats	Bangalore, India	Anti-diabetic and anti-cholesterolemic activity	200 and 400 mg/kg for 3 weeks	Amaranth powder made from fresh leaves	Reduction in body weight.[44]
Caralluma fimbriata	Experimental study on rats	India	The Diet-Induced Obesity (DIO) rat model was used to investigate CFE's anorexigenic effects	25,50,100mg/kg BW per day for 90 days	Oral gavage	Dose dependent inhibition of food intake, prevented weight gain, liver weight, fat pad mass.[60]
	Experimental study on rats	Bijapur, India	Effect on appetite and lipid profile	100 mg/kg/day for 50 days	Pellet chow and cafeteria diet	Prevented weight gain and alterations in lipid profile.[64]
	Randomized double blind	Australia	Central obesity	12 weeks	Oral administratio	Decline in waist circumference,

Name of the plant	Type of study	Study location	Objectives	Dose/Duration	Intervention	Main outcome
	placebo controlled clinical trial				n of the extract	palatability, body weight reduction, total fat reduction.[18]
	Placebo-controlled, double-blind, randomized crossover trial	Australia	Attenuation of *Caralluma* supplement on hyperphagia or associated appetite behaviors in people with PWS syndrome	10 weeks, 1000 mg/day for 10 weeks	Supplement oral ingestion	Eases hyperphagic appetite behavior.[65]
Capsicum annuum	Experimental study on humans	Japan	Adipose tissue density	1,5 mg for to 8 weeks daily	Capsule	Increase in human brown adipose tissue, decrease in body weight.[124]
	Experimental study on rats	Korea	Anti-obesity effects	10 or 100 mg/ kg for 7 weeks	Oral administration of extract obtained from seeds	Reduction in body weight even after having high fat diets.[55]
		China	Anti-obesity effects	0.05% for 7 weeks	Fermented and fresh capsicum extract	Reduced food intake and BMI.[3]
		Korea	Suppression of high-fat diet-induced obesity	100 mg/ kg for 13 weeks	Red pepper powder	Reduction in body weight.[54]
Cinnamomum verum	Experimental study on hamsters	Taiwan	Reduction of hypercholesterolemia	2% and 5% for 10 weeks	Ground leaf powder	Slow body weight gain.[69]
	Experimental study on Wistar rats	Brazil	Visceral obesity	400 mg/kg for 20 days	Aqueous extract	Reduction in visceral adipose tissue.[70]
	Experimental with human subjects	Egypt	Cinnamon compared with Orlistat, a weight loss drug	1200 mg for 60 days	Capsule form	Both reduced BMI and lipid profile.[72]
	Experimental with zebra fish	India	Anti-obesity effects of Cinnamon	2 mg/ fish/day	Powder	Reduced level of BMI, lipids and blood glucose.[71]
Garcinia cambogia	Experimental study on Sprague Dawley rats	USA	HCA-SX effects on bodyweight and abdominal fat gene expression	10 mg / kg for 8 weeks (5 days/week)	Standard chow	Restricted body weight gain; upregulation of genes encoding serotonin.[75]
	Case study	USA	Serotonin toxicity in presence of therapeutic SSRIs	Daily for 3 months (dosage not given)	Oral	Lose weight.[29]
	Clinical trial	Spain	Effects of *G. cambogia* and Glucomannan on weight loss in overweight or obese people	500 mg twice/day	Oral	Reduced weight and improved lipid, glucose blood profiles.[79]

Name of the plant	Type of study	Study location	Objectives	Dose/Duration	Intervention	Main outcome
	Clinical trial	Mumbai, Bangalore	HCA effects on human anthropometric and plasma lipid profile levels	600 mg for 3 months	Oral administration capsules	Antiobesity effects reduced body weight, fat accumulations.[30]
Hoodia gordonii	Clinical trial	USA	Effect of *Hoodia* on reduction of obesity	500 mg in 4 weeks	Commercial grade	Reduction in body weight.[86]
	Case study	Canada	Efficiency of weight loss	Twice daily for 15 days	Capsules	Daily intake and body fat content reduced.[85]
	Randomized controlled trial	USA	Effect of *Hoodia* on reduction of obesity	1.1 mg (duration not given)	Plant extract	BMI was significantly reduced.[87]
	Experimental on rats	Delhi, India	Effect on *Hoodia* supplementation along with carnintine on metabolic markers	100 mg/kg for 5 days	Crude extract	Significant decrease in ghrelin, leptin and thyroid levels.[82]
Lagenaria siceraria	Experimental study with albino rats	India	Anti hyperlipidemic activity	10, 20, 40 mg/ kg	Fruit extract	Reduction in lipid profile.[90]
	Experimental study with Wistar rats	UK	Anti hyperlipidemic activity	200 g/ kg for 4 weeks	Fruit extract	Reduction in body weight, lipid profile.[92]
	Experimental study with Wistar rats	India	Anti-obesity potential	200 mg/kg per day and 400 mg/kg per day after week 10 and 12	Alcoholic and aqueous extracts	Reduction in total body weight, waist girth, lipid levels.[32]
Moringa oleifera	Experimental study on Wistar rats	India	Anti-obesity activity	200 mg/kg and 400 mg/kg for 49 days	Methanolic extract	Change in body weight, lipid profile and blood glucose.[100]
	In vitro studies	-	Anti-obesity properties	0-2000 µg/ ml for 72 h	*Moringa* leaf extract	Anti-adipogenic activities observed.[34]
	Experimental study on rats		Protective effects of *Moringa* in frustose fed diets	400 mg/kg daily for 10 weeks	Methanolic extract	Reduction in hepatic lipids[125]
	Experimental study on albino rats	Egypt	Anti-obesity activities	200 mg/kg and 400 mg/kg for 2 months	*Moringa* leaf extract	Body weight reduction.[99]
Phaseolus vulgaris	Experimental study on rat	UK	Effect of raw kidney bean on growth and metabolism of obese Zucker fafa rats	Varying doses(90, 130,180, 260g/kg)	Oral	Stimulate gut function and ameliorate obesity.[112]
	Preclinical study	Italy	Effect on body weight and food intake of obese zucker fafa rats	Multiple dose cycles (50 and 500 mg/day)	Oral administration of dry extracts	Dose dependent suppression of glycaemia, anorectic.[113]
	Experimental study on rat	Pune, India	Antiobesity activity of	ZMBP powder 250,500mg/kg for 90 days	Pellets	Decrease in weight gain and fat mass in obese rats.[122]

Name of the plant	Type of study	Study location	Objectives	Dose/Duration	Intervention	Main outcome
Ziziphus jujuba	Clinical	Syria	Anti-obesity and hypolipidemic activity	5, 15, and 30g/day	Oral administration of leaf extract	Antiobesity, reduced body weight, food intake.[121]
	Clinical	Syria	Anti-obesity and hypolipidemic activity	5, 15, and 30g/day	Oral in powder form	High doses had impact on weight loss.[123]
	Triple-blind randomized placebo-controlled clinical trial	Iran	Control of dyslipidemia in obese adolescent	5 g 3 times/day for 3 months	Oral	Effects on serum lipid profile.[126]

CONCLUSION

Our review recognizes obesity as a global disorder affecting adults and children that needs immediate attention. As identification for phytotherapeutic purposes, thorough screening of the selected plants was conducted. It can be concluded from our review that all the studied plants, namely, *Amaranthus spinosus*, *Capsicum annuum*, *Caralluma fimbriata*, *Cinnamomum verum*, *Garcinia cambogia*, *Hoodia gordonii*, *Moringa oleifera*, *Phaseolus vulgaris*, *Lagenaria siceraria*, and *Ziziphus jujuba* have a good potential for demonstrating the anti-obesity characteristics. Some of the plants like *Capsicum*, *Moringa* and *Lageneria* are commonly consumed as vegetables, while *Phaseolus* is consumed as legume and *Cinnamomum* as a spice and therefore, can be a part of our daily consumption. On the basis of Table 1, it can be inferred that the phytochemicals present in the selected plants has been identified and their mode of action for almost all the plants except *Zizyphus* had been extensively studied. In terms of *in vitro*, experimental and clinical studies, the anti-obesity properties of *Amaranthus* and *Zizhyphus* needs to be worked upon as there are very few studies in total. However, even for other plants, the studies are mostly at the experimental level. There is a clear dearth of clinical reports supporting the anti-obesity studies. Our studies met the objectives of finding the gap in research that exists in phytotherapeutic research. Moreover, the toxicity studies on most of the plant extract is also lacking. Therefore, this review can function as a 'ready reference' for the latest studies involving the anti-obesity features of these plants. This review should motivate more researchers to conduct further investigations involving these plants.

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