



Impacts of Extracts of Select Easily Available Plants on Obesity: Initial Quest for an Anti - Obesity Oral Supplement – A Review

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ABSTRACT

Obesity, defined as a Body Mass Index (BMI) of greater than equal to 30 kg.m⁻² has become one of the most common, neglected and ever-rising public health problem where socio-economic development, sedentary job patterns, preference for high-calorie junk foods and reluctant nature of people to engage in physical activities act as the contributing factors. The prevalence of non-communicable disease like cardiovascular diseases, diabetes, osteoarthritis (especially in obese women) and hypertension which are considered co-morbid conditions associated with obesity is increasing in epidemic proportions. There has been an eventual increase in the mean BMI since 1980 by 0.4-0.5 kg.m⁻² per decade in adults, aged ≥ 20 years. Nearly 2.8 million individuals die each year due to being overweight or obese. India is the 3rd most obese country in the world having more than 30 million obese people with a higher prevalence in women (more than 23 %) than men (20 %). Diet and exercise together is considered the most effective means to curb the rising trend in obesity. In situations where diet and exercise alone cannot serve the purpose use of pharmaceutical anti-obesity drugs and sometimes surgical assistance are required to control obesity. Since, these anti-obesity drugs and surgical methods are at times associated with future complications and have high toxic effects and are costly they are not opted often. This led to the use of medicinal plant and plant-products in obesity management which are usually cost-effective and produces relatively less toxic. The available related documents are reviewed to find that use of plants like *Camellia sinensis*, *Coffea canephora*, *Capsicum annum*, *Allium sativum*, *Zingiber officinale*, *Curcuma longa*, *Citrus limon*, *Hypericum perforatum*, *Aloe vera*, *Garcinia cambosa* etc. either in the form of extracts or as pure compounds consumed orally as natural supplements, may prove to be effective in combating steep rise in obesity; there could be attempts to make them available in a rational combination.

Keywords: Obesity, Plant Extracts, Oral Supplementation, BMI, traditional knowledge, public health.

INTRODUCTION

Obesity, a multisystem disorder, is defined as abnormal or excessive accumulation of fat, particularly in the abdominal region, that may be associated with alterations in metabolic factors that can affect immune function and at the same time it leads to several non-communicable life threatening diseases including Type 2 Diabetes mellitus, cardiovascular disorders, osteoarthritis, insulin resistance and so on. There are many ways of assessing obesity in different age groups but one of the most commonly used option is finding out the Body Mass Index (BMI), the ratio of body weight (in kg) to square of body height (in metre) (kg.m⁻²). According to WHO, an individual with BMI of ≥ 30 kg.m⁻² is considered as obese. On the other hand, it has been found that increased levels of circulating of leptin, coupled with reduced concentrations of ghrelin and adiponectin is a biochemical indicator of obesity. Excess high-fat diet increases circulating leptin levels and leptin resistance develops which alters the normal physiological functions of leptin¹. Altered circulating levels of leptin,

ghrelin and adiponectin stimulate inflammatory responses followed by release of pro-inflammatory cytokines from immune cells and activation of important stress pathways that disturbs critical metabolic processes². Globally one in six adults are obese and nearly 2.8 million individuals die each year due to being overweight or obese³. India is the 3rd most obese country in the world having more than 30 million obese people⁴ out of a total population of 1.21 billion. Diet and exercise perhaps are the safest means to combat obesity but due to sedentary lifestyle, change in job-patterns and busy schedules people nowadays avoid consuming traditional healthy foods and are reluctant to indulge into daily physical activities. As a result, various anti-obesity drugs are demanded in order to check rising obesity. Since the toxic effects of these anti-obesity drugs at times exceeds that of its beneficial effects use of complementary and alternative herbal supplements either in the form of extracts or as pure compounds are being encouraged for management of obesity⁵.



Modes of Obesity Management: Obesity can be managed by means of diet, exercise, use of homoeopathic nanomedicine, and surgical methods.

Diet - Since obesity is characterized as a state of chronic calorie excess reducing energy intake through meals can be effective in managing obesity. Diet should include whole grains, fruits, vegetables and dietary fibres. Daily fibre intake of 38 g (men) and 25 g (women) for persons over 50 years of age and 30 g (men) and 21 g (women) for those less than or equal to 50 years is recommended⁶. Exercise - Exercise combined with diet results in a greater weight reduction than diet alone. Regular dancing for an hour, for at least 6 days in a week, performance of 30 minutes of moderate-intensity physical activity like brisk walking, skipping, climbing of stairs etc. for ≥ 5 days a week can prove to be effective in losing weight⁶. It has been found that individuals receiving football training have better physical fitness and obesity indices than sedentary individuals who are deprived of such training.⁷ Various dance forms like Kathak⁸, Bharatnatyam⁹ also help to effectively reduce weight and manage obesity. Use of Homoeopathic nanomedicine - Recent advances in the field of homoeopathy has shown that active components of drug in the form of low-dose nanoparticles may amplify the effects of homoeopathic remedies. *Phytolacca* (poke-root) has a powerful effect on fibrous and osseous tissues of the human body. Tincture of *Phytolacca berry* is used in homoeopathic remedy for weight loss¹¹.

Surgical methods - Treatment of severe obesity requires assistance of surgical intervention along with diet and exercise. A surgical method known as bariatric surgery has been shown to be effective in treating morbid obesity. In bariatric surgery weight loss is achieved either by reducing the size of stomach with a gastric band or through removal of a portion of stomach (sleeve gastrectomy) or by resetting the small intestine to a stomach pouch (gastric bypass surgery).

Importance of use of anti-obesity compounds of plant origin in management of obesity

Diet and exercises are perhaps the safest and most effective means to combat the rising trend in obesity. But sedentary lifestyle, change in job-patterns and busy schedules of people (especially those who are obese) who avoid consuming traditional healthy foods and are reluctant to indulge in daily physical activities led to development of various anti-obesity drugs. However, for probable toxic effects of these molecules they are prescribed only when the benefits are more than the risks.⁵ Orlistat is one such anti-obesity drug currently approved by the Food and Drug Administration (FDA), US for long-term use¹⁰. Treating morbid obesity sometimes requires surgical assistance (bariatric surgery) along with diet and exercise. Since such surgical intervention is exorbitantly costly and is also associated with potential future complications, it not preferred and accepted globally as first choice. Simultaneously there are reports

that many substances present in plant extracts are effective, albeit to a different degree, in combating the ever-increasing menacing challenge posed obesity and associated problems, and also the chance of unintended effects is relatively less¹². Some of them are also consumed as per habit or custom in foods and /or beverages. In this backdrop an attempt has been made to document following a systematic review, the findings of studies to investigate the effect of administration - oral or otherwise – of different plants in order to get a possible cue for development of an oral supplement consisting of active ingredients of plant origin effective against obesity and associated maladies.

METHODOLOGY

Information was searched in Google, PubMed through Google, Google scholar. The keywords for search inter alia included obesity, anti-obesity drugs, plant extracts, oral supplementation. The search was restricted for a period of 12 years, 2004 to 2016.

FINDINGS

There are many plants which have potential anti-obesity actions. On the basis of mode of action anti-obesity extracts, plants are categorized as centrally acting and peripherally acting where centrally acting substances exert their effect on receptors located within the CNS by developing a sense of satiety which in turn reduces food intake⁵ and peripherally acting substances mediate their effect by either reducing gastrointestinal calorie absorption or on metabolic and/or control systems outside the CNS¹³. The effects including the mechanisms of action, names of active ingredients of select plants with potential anti-obesity effects are presented below:

Camellia sinensis

It is a peripherally acting anti-obesity substance, and is one of the most studied and widely used plant having potent antioxidant and anti-obesity properties¹⁴. *C. sinensis* extract exhibits high pancreatic lipase inhibitory activity and increases fecal excretion of lipids¹⁵. The other modes of action include appetite repression, adipogenesis down-regulation, thermogenesis and lipid metabolism¹⁴. Inhibition of pancreatic lipase activity is mediated by formation of a covalent bond within the active site of serine residues of gastric and pancreatic lipases⁵. White tea (unfermented tea obtained from young shoots of *C. sinensis*) supplementation can reduce blood triacylglycerol levels in obese mice¹⁶. The active chemical compounds having anti-obesity effects are the catechin type polyphenols. White tea contains the highest concentration of catechins as they are made from young leaves of the plant with minimal processing. Catechin like flavonoids present in *C. sinensis* reduces gain in body weight by increasing whole body fat utilization, oxidation and lipolysis. Green tea prepared from leaves of *C. sinensis* without withering and oxidation is another rich source of flavonoids and catechins that functions by down-regulating the expression of adipogenesis-related



transcriptional factors Peroxisome proliferator activated receptor gamma (PPAR γ), CCAAT enhancer binding protein (C/EBP α) and Sterol regulatory element binding protein (SREBP1)¹⁴. Epigallocatechin gallate (EGCG) the most active component of green tea acts by this mechanism and has been found to increase fat oxidation and thermogenesis and reduce adipocyte differentiation and proliferation in animal models of obesity^{5,17}. Not only the leaf, but also the fruit peel can exert anti-obesity effects. Administration of ethanolic extract of green tea fruit peel may reduce the weight of white adipose tissue with a subsequent decrease in body weight¹⁴. Flavonoids present in green tea leaves can act as potent anti-inflammatory substance by suppressing the activation of nuclear factor kappa-light-chain-enhancer (NF κ B) of activated β cells and by dampening inflammatory responses in animal models of obesity¹⁸.

Coffea canephora

It is commonly known as coffee. Its beans are another popularly consumed beverage worldwide. The two active components of coffee beans reported to have anti-obesity properties are caffeine and chlorogenic acid¹⁹. Chlorogenic acid is a polyphenol reported to reduce body weight and regulate lipid metabolism by increasing beta-oxidation of fatty acids and elevated expression of PPAR- α on one hand and on the other hand by inhibiting the activities of cholesterol acyltransferases (CAT)²⁰. Caffeine present in coffee bean extract can reduce weight of adipose tissue in experimental animal models by suppressing accumulation of visceral fat and stimulating catecholamine secretion that accelerates degradation of fat in adipose tissues. Apart from this, caffeine has also been reported to slower the rate of absorption of dietary fat with a consequent reduction in serum triglyceride level and suppression of postprandial hypertriglyceridemia²¹.

Capsicum annuum

It is commonly known as capsicum (hot pepper) and is mostly consumed as food in the form of vegetables. It is another natural anti-obesity substance. Administration of methanolic extracts of seeds of *C. annuum* can inhibit adipogenesis, lower lipid accumulation in adipocytes; reduce expressions of important adipogenic transcription factors like C/EBP β , C/EBP α and PPAR γ and inhibit the activity of glycerol-3-phosphate dehydrogenase (major enzyme of lipid biosynthetic pathway)²². The active chemical compounds of *C. annuum* having anti-obesity properties are capsaicin and capsaicinoids. Capsaicinoids administration can decrease body weight by causing a 21.1 % reduction on abdominal adiposity¹⁴. Dietary capsaicin has been reported to reduce metabolic dysregulation in obese mice by elevating expressions of adiponectin receptors, PPAR- α and transient receptor potential vanilloid-1. Capsaicin can also induce apoptosis and inhibit adipogenesis in preadipocytes and adipocytes. Oral and

gastrointestinal exposure to capsaicin may increase satiety and reduce energy and fat intake²².

Allium sativum

It is (garlic) commonly used as a flavouring ingredient in cooking is investigated to have a strong anti-obesity effect. Extracts of garlic contains various biologically active compounds such as alliin, allicin, ajoene etc. having potent hypocholesterolemic, hypoglycemic, anti-hypertensive, anticancer, anti-obese and anti-oxidant effects¹⁴. Dietary garlic can reduce mass of white adipose tissue and decrease body weight by reducing expressions of adipogenic genes in white adipose tissues (WAT), elevating expression of mRNA for uncoupling proteins and activity of Adenosine monophosphate activated protein kinase (AMPK) in brown adipose tissue (BAT), liver, WAT, and skeletal muscle, influences oxygen consumption, and body temperature. The active sulphide ajoene has been shown to induce apoptosis and decrease lipid accumulation by influencing the process of energy expenditure²³.

Zingiber officinale

It is commonly referred to as ginger and its supplementations have been seen to improve various obesity-associated parameters in both animal models and human subjects¹⁴. Chronic exposure to ginger supplementation can improve body weight, body mass index, waist and hip circumferences, body composition, appetite score, and dietary intake in human subjects²⁴. Apart from regulating PPAR- γ signalling pathways in adipocytes ginger extract may also modulate PPAR- δ signalling where active ginger extract components viz. 6-Shogaol and 6-gingerol by acting as ligands for the receptors up-regulate their expression especially in skeletal muscles with a subsequent increase in energy expenditure, oxygen consumption rate and fatty acid metabolism by the muscles²⁵.

Curcuma longa

It (turmeric) is a plant of ginger family and used worldwide as a spice has potent anti-obesity and anti-inflammatory properties. Newly discovered active component of turmeric known as curcumin, a diarylheptanoid belonging to the group of curcuminoids i.e. natural phenols can directly interact with WAT and suppress chronic inflammation by inhibiting activation of NF- κ B by inflammatory agents. Curcumin on one hand can induce expression of adiponectin which increases their secretion from adipocytes that has anti-inflammatory property while on the other hand reduce expression of pro-inflammatory cytokines like tumor necrosis factor alpha (TNF- α)²⁶.

Citrus limon

It (Lemon plant) belongs to the Rutaceae family, and is the third most important Citrus species after orange and mandarin. Anti-bacterial and anti-cancer properties of different parts of lemon are well established but several



experiments carried out on diet-induced obese mice reveal anti-obesity actions of the plant possibly by up-regulation of mRNA levels of PPAR- α and increased peroxisomal β -oxidation. Supplementation with lemon plant extract can improve conditions in cases of insulin-resistance and hyperlipidemia in experimental animals¹⁴.

Hypericum perforatum

It is a perennial plant used for its sedative effects in treating depression, anxiety, and neuralgia etc¹⁴. Active biological components with anti-obesity activity found in *H. perforatum* includes hyperforin, flavonoids (quercetin, isoquercitrin), and proanthocyanidins¹³. Quercetin inhibit adipocyte differentiation by downregulating adipogenesis related transcriptional factors PPAR- γ , C/EBP α and SREBP1²⁷. Experimental trials have revealed that infusion of *H. perforatum* can reduce hyperglycemia, leptin levels, and TNF- α and may increase adiponectin concentration in diet-induced obese rats¹⁴.

Aloe vera

It is primarily used in the production of foods and drink, cosmetics and pharmaceuticals. Research studies have reported anti-obesity effects of *A. vera* along with anti-inflammatory, laxative and anti-oxidant properties. In a study administration of *A. vera* gel powder for 90 days resulted in reduced subcutaneous and visceral fat weight in diet-induced obese rat¹⁴. *A. vera* chemically consists of phytosterols like lophenol, cycloartanol, 24-methylenecycloartanol, 24-methyllophenol, 24ethyllophenol etc. Lophenol, cycloartanol have been found to significantly reduce visceral fat weights in diabetic rats. Some of the proposed anti-obesity mechanisms of action are by stimulation of energy expenditure, regulation of expressions of hepatic genes encoding lipogenic enzymes, increased activities of hepatic- β -oxidation enzymes²⁸.

Plant extracts exerting anti-obesity effects by reducing food intake and controlling appetite: Green tea extract has been reported to regulate the plasma leptin concentrations. Treatments of adlay seed crude extract can reduce body weight, food intake, adipose tissue mass and serum lipid concentrations by modulating expressions of leptin and TNF- α ⁵. *Garcinia cambosia* is a potent natural appetite suppressor. It has been reported that *G. cambosia* mediates this effect probably by three mechanisms - by stimulating liver gluconeogenesis, by decreasing fatty acid synthesis and by increasing the availability of the neurotransmitter serotonin which is actively involved in eating behaviour and appetite control. *Hypericum perforatum* is also known to increase the serotonin quantity present within synaptosomes by inhibiting synaptosomal uptake of serotonin, which suppresses the appetite and reduces food intake¹³.

DISCUSSION

Obesity is considered as a global epidemic which is affecting not only the developed countries of the world but also the so called less developed countries like India where sudden socio-economic development and change in lifestyle is contributing to its prevalence. Though diet and exercise are the safest and probably the most effective ways to check obesity, they are sometimes not well accepted by common people. It demands discipline, self – restraint and habit modification, if not practised from early age. Often some individuals who are unable to follow the discipline of diet and exercise management demand some oral therapeutic agents. And there is growing tendency to go for plant origin compounds. Another positive fact is that many of them have been knowingly or unknowingly consumed for generations as food, beverage even spices. And hence does not demand much life style modification. Another important fact that deserves a mention is that the extracts of commonly available plants with anti - obesity effects, as detailed above, should preferably be tried, in form of supplement – oral or other - from childhood and adolescence, preferably together with proper diet and enjoyable exercise regimen²⁹⁻³⁶; this will reduce the chances of onset obesity in later life.³⁷

CONCLUSION

In the wake of ever increasing challenge of obesity and associated problems even in not so affluent countries like India, which is also undergoing a lifestyle transition, there is urgent need for management of emerging public health challenge of obesity. It is also no denying that dietary management and physical exercise, in spite of being effective, have their own inherent limitations. And hence grows the demand and quest for therapeutic agents that can be administered orally. In view of the above discussion on the impacts including the mechanisms of action of plant extracts, it may be mentioned that an anti-obesity supplement may be developed, through repeated trials, using a judicious ad mixture of safe and compatible active ingredients of plant origin.

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