



Management of Obesity and its Related Disease by herbal drugs

Abinaya.K.R and Pavitra.R

Department Biotechnology,
Srimad Andavan Arts and Science college,
Thiruvananthapuram, Trichy-620 005.
Assistant professor in Microbiology
Dhanalakshmi srinivasan college of arts and science for women,
Thuraiyur Road, Perambalur- 621 212.

Email ID: abinaya_biotech12@ymail.com

Abstract

Obesity and its related complication is one of the global wide problems leading to cause more than 53 diseases and in India around 30 million people are suffering with obesity. Modern methods of treatment, such as synthetic drugs and surgery, still have to be improved to show safety and efficacy. Its main concerns with such treatments are the high costs and adverse effects create obesity and its related diseases. As a result, there is great interest in the use of plant-based medicinal agents as an alternative therapy. This review aimed to provide the survey of literature on accessible medicinal plants sources for the treatment of obesity and this study attempts to explain how these medicinal plants act in humans to reduce weight loss, with safer and more efficient treatment.

Key words: Obesity, herbal drugs

Introduction

The global prevalence of overweight and obesity is increasing due to excessive calorie intake and sedentary lifestyle^[12]. Body mass index (BMI) are used to measure healthy weight (BMI between 20 and 25), overweight (BMI greater than 25) and obese (BMI greater than 27)^[18]. Globally, 1.6 billion people are overweight (Body Mass Index, between 25 and 30) 400 million are obese (BMI above 30)^[29]. According to WHO, obesity is related to cardiovascular diseases, hypertension, diabetes mellitus, gallbladder disease, cancer, endocrine and metabolic disturbances, osteoarthritis, gout, pulmonary diseases, as well as psychological issues, including social bias, prejudice, discrimination, and overeating^[30] and also additional features associated with Metabolic Syndrome (dyslipidemia, vascular dysregulation and polycystic ovarian disease (PCOS)). Factor responsible changes in life style (urbanization), sedentary pursuits, reduced physical activity, other factors, genetic/ constitutional predisposition^[2].

Weight is rapidly regained in many cases. Many anti-obesity drugs have adverse effects, so many trials have been recently conducted to find and develop new anti obesity drugs through herbal medicines that would minimize the side effects^[21]. 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. 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^[4]. Sibutramine, which acts on the brain to inhibit deactivation of the neurotransmitters, thereby de-creasing appetite was withdrawn from the United States and Canadian markets in October 2010 due to cardio-vascular side effects^[9].

Because of potential side effects, it is recommended that anti-obesity drugs only be pre-scribed for obesity where it is hoped that the benefits of the treatment outweigh its risk ^[7].

Synthetic drug treatment and its side effect (Anti-hyperlipidemia Drugs) ^{[1],[19],[23],[29]}

(Table no.1)

S. No	Drug Class	Mechanism of Action	Example	Side Effects
1	HMG CoA reductase enzyme inhibitor	Lowering total LDL inhibiting cholesterol biosynthesis	Atrovastatins, Fluvastatin, Lovastatin, Simvastatin	Congestive cardiac failure
2	Fibrates	Enhancing activity of enzyme lipoprotein lipase	Gemfibrozil, Fenofibrate	Upper gastrointestinal disturbance, headache, myalgia
3	Nicotinic acid derivative	Inhibit lipolysis within adipocytes	Niacin	Hyperglycemia, increase uric acid
4	Bile acid sequestrants(Resin)	Bind with bile acid & promote bile acid excretion	Cholestipole, Cholestyramine	Abdominal fullness, constipation
5	Misc.	Inhibit free radicals	Omega 3 fatty acid, Probucol	-

Causes of obesity

At an individual level, a combination of excessive food energy intake and a lack of physical activity are thought to explain most cases of obesity. A limited number of cases are primarily due to genetics, medical reasons, or psychiatric illness. In contrast, increasing rates of obesity at a societal level are felt to be due to an easily accessible and palatable diet. A 2006 review identified ten other possible contributors to the recent increase of obesity: (1) insufficient sleep, (2) endocrine disruptors (environmental pollutants that interfere with lipid metabolism), (3) decreased variability in ambient temperature, (4) decreased rates of smoking, because smoking suppresses appetite, (5) increased use of medications that can cause weight gain (e.g., atypical antipsychotics), (6) proportional increase in ethnic and age groups that tend to be heavier, (7) pregnancy at a later age (which may cause susceptibility to obesity in children), (8) epigenetic risk factors passed on generationally, (9) natural selection for higher BMI, and (10) assortative mating leading to increased concentration of obesity risk factor.

(Table No.2) ^{[28],[30],[37],[38],[40]}

Drug	Mechanism action	Adverse effects
Orlistat	Reduces fat absorption from the intestine by inhibiting pancreatic lipase and reduces triglyceride hydrolysis. Low fat diet is generally advised.	Steatorrhoea (oily stools).

Sibutramine	Centrally acting sympathomimetic amine that enhances satiety by inhibiting non-selective uptake of nor adrenaline, serotonin and dopamine	Hypertension, serotonin syndrome
Metformin	It activates cAMP-activated protein kinase and suppresses hepatic gluconeogenesis activity.	Lactic acidosis, Gastro-intestinal upset.
Rimonabant	It is an approved but infrequently used drug. It is a cannabinoid CB1 receptor antagonist. It selectively acts on CB1 receptor in brain and peripheral organs. reduces lipogenesis in liver. They not only cause weight loss but in addition reverse metabolic effects of obesity.	Severe depression and predisposes to neurodegenerative diseases E.g. Alzheimer's disease, amyotrophic sclerosis.

Synthetic Anti obesity drugs

Drugs alter the fundamental metabolic process of the human body and thereby regulate weight. The benefits are out weighted by their adverse effects. Anti-obesity drugs are long term solution for obesity [23], [24]. Combination of drugs may be effective by regulating multiple pathways and possibly inhibiting feedback pathways.

Global scenario of obesity

The World Health Organization (2000:14) estimated for the first time in human history that the number of overweight people is higher than the number of starving or undernourished people of the world. WHO's latest projections indicate that globally in 2005: approximately 1.6 billion adults (age 15+) were overweight; at least 400 million adults were obese. WHO further projects that by 2015, approximately 2.3 billion adults will be overweight and more than 700 million will be obese. At least 20 million children under the age of 5 years are overweight globally in 2005.

Indian scenario of obesity

Statistics point to an increase in overweight or obese citizens by 20% between 1998 and 2005. Presently, one in 6 women and one in 5 men are overweight in India. Obesity figures are bulging dangerously at a staggering 70 million in India. Another study published in the Lancet, has revealed that "by 2030, non communicable disease will account for nearly 70% of all global deaths and 80% of these deaths will occur in developing countries like India" [2] The latest obesity statistics shows that 75 percent of Indian women and 58 percent of Indian men are obese. Estimated prevalence (%) of Overweight & Obesity (BMI \geq 25 kg/m²) females and males (Aged 15+) is 18 and 20.1 respectively [15].

Natural medication

Studies show that natural food ingredients and medicinal plant preparations are able to enhance satiety, boost metabolism, and speed up weight loss [16],[17]. On the other hand, despite the global market for satiety, fat burning, dietary supplements and other weight management remedies, the awareness of the usefulness of these products is neither sufficient nor clearly perceived by patient [9]. This study aims to provide a review of previous reports about the availability of natural medicinal agents and their potential for assisting in losing weight. This information could aid patients in their selection of the appropriate botanical product to develop

a lean and healthy body. Here brief review of the anti-obesity agents from natural products is presented which have promising field to approach the solution to a global health problem such as obesity.

Reason for using herbal drug:

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 and (5) 100% natural origin and perception that natural means safe [5]. Herbal plants for weight reduction may be effective in the treatment 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 plants showed potential effects on weight control. However, for the majority of products, more data are needed to assess the suitability as an anti obesity plants.

Methods of data collection

Data were acquired from various databases, including Science Direct, Pub-Med, Scopus, Web of Science, and from books and theses for the period from 1995 until 2014. Key search words included: traditional medicine, medicinal herbs, plant extracts, anti-obesity, weight loss, overweight, efficacy, safety, appetite, satiety. Papers on human and animal studies, clinical trials, and related to plant-based obesity medication are discussed.

The herbs reported to have effect on obesity by either Animal studies or Clinical trials or Treatments are mentioned below:

Aloe Barbadensis

Description:

Aloe vera or "*Aloe Barbadensis*" is a plant which originated in North Africa and spread to the fertile lands with mild climate. Its physical aspect is similar to that of the cactus; the thick rind hides a succulent core formed mostly of water. Because it is not a pretentious herb, aloe vera can be easily tended for. This herb requires a great amount of light (even if it is artificial - 16 hours a day) and a little bit of water (especially in the cold season).

Properties:

The most oftenly used substance from this herb is the aloe gel, a thick viscid liquid found in the interior of the leaves. The leaves are used in the treatment of burns and the aloine - a bitter milky yellowish liquid is used as a laxative. The herb contains: 20 minerals (*Calcium, Magnesium, Zinc, Chromium, and Selenium*), 12 vitamins (*A, B, C, E, and folic acid*), 20 aminoacids from the 22 which are necessary to the human body, over 200 active components including enzymes and polysaccharides. All the active substances enumerated before contribute to the therapeutical value of the herb and it toughens up the immune system owing to the 23 peptides contained by the aloe vera, it accelerates and regulates the metabolism, purifies the human body from toxins, bringing about a feeling of calm. Moreover, aloe vera has an antiseptic effect (by destroying the bacteria's, viruses and fungi), disinfectant capabilities and can also stimulate the cell-renewing process. Aloe vera nourishes and supports the digesting of aliments. Cutting across the human organism, aloe vera manages to bring the human body to a general balanced state.

Treatments:

Aloe vera has proved its efficiency from the simplest allergies to the treatment of wounds and skin infections and even to its usage in alleviating more serious afflictions. With the help of this herb a wide variety of internal and external afflictions are controlled, like: asthma, virosis, arthritis, arthrosis, gingivitis, bronchitis, pharyngitis, intestinal inflammations, constipations, obesity, sprains, muscle strains, cutaneous inflammations. The efficiency of the herb was also proven in the cases of anemia, deficiency illnesses, insomnia and depressions and the B-sisterole from the Aloe vera brings about the lowering of the cholesterol level.

Foeniculum vulgare

Family: Apiaceae (=Umbelliferae)

Common Name(s): Fennel

Description:

Fennel (*Foeniculum vulgare*) is an edible, perennial herb which resembles dill. It was discovered in the Mediterranean region and south-east Asia (from east of Morocco and Portugal all the way to Pakistan). The biggest growers of fennel today are: the United States, France, India and Russia. Fennel was brought to North America by the Spanish missionaries to be grown in their own medicinal gardens.

Properties:

It was believed that this herb has a rejuvenating effect on man and helps the eye sight. Moreover, fennel stimulates lactation and loss of weight. **Fennel contains many minerals and vitamins: vitamin C, fibers, manganese, potassium, magnesium, calcium, iron, vitamin B3 etc.** The vitamin C from the bulb of the plant is antibacterial and very useful to the immune system. Furthermore the fennel bulb is an important source of fibers which help reduce the cholesterol level. Also, the fibers from this herb can prevent intestinal cancer owing to the fact that they can eliminate toxins and cancerous substances from intestines. The herb is rich in potassium - an essential mineral which helps decrease the high blood pressure that can cause a heart attack. Fennel seeds, leaves and roots are edible, but the fat extracted from the fennel seeds was proved to be toxic even in small quantities - leading to skin rashes, breathing problems and nausea.

Treatments:

Owing to the invigorating and purifying effects that fennel has over the human body, it can be used in treating bruises, cellulitis, obesity, retaining water, eliminating the toxins from the body, halitosis, inflammations of the mouth. Fennel helps eliminate the common cold and reduce the bouts of cough due to its expectorant nature (contains big quantity of alpha-pinen). The steam resulting from the boiling of the fennel leaves in water alleviates asthma and bronchitis. The tea from fennel leaves and seeds is beneficial for removing intestinal worms and bacteria. The syrup made from fennel juice alleviates the violent bouts of cough.

Animal studies:

White male albino rats weighing 80-90 gm, 60 days old. 10 rats were fed a normal basal diet, 30 rats fed a high fat diet (HFD) for 14 weeks during the entire study. Rats of the HFD group were equally divided into 3 subgroups each one include 10 rats. The 1st group received HFD with no supplement (HFD), the 2nd group HFD+L-carnitine and the third group received HFD+HMF (Herbal Mixture Formulation). Carnitine and HMF were administered at 10th week (start time for treatments) for 4 weeks. Body weight, lipid profile were analyzed. Data showed that feeding HFD diet significantly increased final body weight, triglycerides

(TG), total cholesterol & LDL concentration compared with controls, while significantly decreasing HDL; meanwhile treatment with L-carnitine, or HMF significantly normalized the lipid profile.

Myristica fragrans

Family: *Myristicaceae*

Common Name: Nutmeg

Description:

It is an aromatic tree. The plant is a native of Moluccas, now cultivated in many tropical countries of both hemispheres. In India, it is grown in Tamil Nadu.

Animal Studies:

The ethanolic extract of this plant extract demonstrated significant hypolipidaemic effects in experimentally induced hyperlipidaemia in rabbits. It lowered the lipoprotein lipid levels, total cholesterol, LDL cholesterol and triglycerides. HDL cholesterol was not significantly affected. Total cholesterol, HDL and LDL: HDL ratios were also significantly lowered. It lowered the level of total cholesterol in the heart and liver and demonstrated platelet antiaggregatory activity. Seed extract administration reduced both total and LDL cholesterol, lowered the cholesterol/ phospholipid ratio and elevated the decreased HDL ratio significantly in hypercholesterolemic rabbits. This extract also prevented the accumulation of cholesterol, phospholipids and triglycerides in liver, heart and aorta and dissolved atheromatous plaques of aorta. Fecal excretion of cholesterol and phospholipid were significantly increased in these rabbits ^[44].

Holoptelea integrifolia

Family: *Ulmaceae*

Syn: Indian Elm

Description:

H.integrifolia is a large deciduous tree that grows up to 15 to 25 meters in height. Its bark: is whitish yellowish grey, and exfoliates with regular intervals and offensive smell when cut. Leaves: are simple alternates, elliptic, usually distichously, acuminate and the base is rounded or cordate. Leaf: margin is entire glabrous and leaf blade is pinnately veined with 3 to 7 veins on each sides ^[31].

Properties:

The bark and leaves are used as bitter, astringents, anthelmintic and used in treatment of diabetes, skin disease, intestinal disorder, leprosy, rheumatism and wound healing in the form of paste.it is an important pollen allergent plant of India. Plant is useful in treatment of obesity, edema and bronchitis ^[33].

Clinical Trials:

The petroleum ether extract and methanolic extract of *H.integrifolia* leaves showed antidiabetic effect induced by alloxan and standard drug used for camparison is gilencamide. In which petroleum ether extract given at concentration of 100 and 200 mg/kg whereas methanolic extract given at concentration of 200 mg/kg showed positive Antidiabetic potentials ^[32]

Emblica officinalis

(Family: *Phyllanthaceae*),

Syn.Amla

Clinical Trial:

Zanjabeel & amla were given at 10g/ day and 3g/ day respectively to all the 40 cases of test groups irrespective of age, sex & lipid levels. Both the drugs were given in powdered form in to two divided dosage, before meal orally. Duration of study was 60 days and follow up for all the cases was done at regular interval of 20 days. It may be concluded that the effect of test combination of drugs in lowering the level of serum total cholesterol, serum triglycerides, serum LDL cholesterol, and serum VLDL cholesterol and in increasing the level of serum HDL cholesterol is significant in patient of primary hyperlipidemia ^[17]

Cocos nucifera

(Family: Palmae),

Clinical Trial:

The randomized, double-blind, clinical trial involved 40 women aged 20-40 years. Groups received daily dietary supplements comprising 30 ml of either soy bean oil (group S; $n = 20$) or coconut oil (group C; $n = 20$) over a 12-week period, during which all subjects were instructed to follow a balanced hypo caloric diet and to walk for 50 min per day. Data were collected 1 week Before (T^1) and 1 week after (T^2) dietary intervention. Energy intake and amount of carbohydrate ingested by both groups diminished over the trial, whereas the consumption of protein and fiber increased and lipid ingestion remained unchanged. At T^1 there were no differences in biochemical or anthropometric characteristics between the groups, whereas at T^2 group C presented a higher level of HDL and a lower LDL: HDL ratio. Reductions in BMI were observed in both groups at T^2 , but only group C exhibited a reduction in Waist Circumference. Group S presented an increase in total cholesterol, LDL and LDL: HDL ratio, whilst HDL diminished. Such alterations were not observed in group C. It appears that dietetic supplementation with coconut oil does not cause dyslipidemia and seems to promote a reduction in abdominal obesity ^[20].

Conclusion

Ayurveda classics give sufficient focus on obesity (sthulya or medoroga) and serves as a guideline to advise diet etc. and to prevent or to control the disease. Obesity is not limited to developed countries but it is spreading globally. Traditionally obesity was believed to be associated with life style; several studies have shown that changes in dietary pattern, physical activity levels, and life styles are related to increasing frequencies of obesity and risk of associated diseases. With this study, we have made an attempt to present collective information about the various herbs showing effects on obesity.

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