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Review Article

**HERBAL APPROACH FOR TREATMENT OF OBESITY
– A REVIEW****Namrata Parikh, Ritav Brahmhatt, Kushal Shah, Shachi Engineer,
Mr. Bhavik Chauhan ***

Faculty of Pharmacy, G.H.Patel Building, Donor's Plaza, The Maharaja Sayajirao University of Baroda, Vadodara-390002, India.

Abstract:

Obesity is termed as “New World Syndrom” and considered as major health problem by WHO. It is associated with excessive fat accumulation in the body and measured by BMI [Body mass index]. It is caused by imbalance between food intake and energy expenditure. Various pharmacological treatments are available to affect different targets but the incidence of side effect of these compounds like rhabdomyolysis and others. Therefore herbal path is most effective and give less or no side effects as compared to pharmacological treatment. Datas on 15 recent medicinal plants are reviewed and taking consideration for exact mechanism of action, related phytoconstituent and pharmacological evaluation etc.

In the modern era there is need for developing awareness regarding more use of herbal preparation thereby promoting weight loss and combating obesity.

Key Words: *Obesity, Body mass index, rhabdomyolysis, Phytoconstituents, herbal preparation.*

Corresponding author:**Namrata Parikh,**

Faculty of Pharmacy,

G.H.Patel Building, Donor's Plaza,

The Maharaja Sayajirao University of Baroda,

Vadodara-390002, India.

Email: namrataparikh@yahoo.com

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1. INTRODUCTION:

Obesity is disorder which involves excessive body fat. This fat accumulates into the adipose tissues and other organs like liver, skeletal muscles. It is measured by Body mass index[BMI] which is used to differentiate person as underweight, overweight, normal or obese. BMI is ratio of person's weight in kilogram to the square of heights in meters. A BMI ≥ 25 kg/m² is defined the person is overweight and ≥ 30 kg/m² is obese. Obesity is a one of the major risk factor for increasing health problems. It leads to hypercholesteremia, hyperlipidemia, atherosclerosis, hypertension, diabetes mellitus etc.[1]

The obesity can be categorised into two way .1] excessive intake of foods with high salt, fats and sugars but loss of minerals, vitamins and other nutrients. 2] decreased or no exercises and other physical activity because of more sedentary life style and more use of transportation. Therefore the main etiology behind obesity is an imbalance between energy uptake and expended. Our body needs some energy or calories from foods for basic functions. When calorie consumed and expended are equal then body weight is maintained.

If more calorie taken then burned, the resulting condition moves towards weight gain, over weight and finally obese. Because of highest mortality and morbidity, an obesity requires proper management and treatment[2]. This includes pharmacotherapy, diet plan and exercises. Certain foods that inverts metabolism of fats and lipids should be avoided. Statins like drugs, for example Atorvastatin inhibits HMG Co A reductase enzyme and widely used as allopathic treatment for obesity. Others are bile acid sequestrants, Fibrates, Niacin and Orlistat are the pharmacological treatment for obesity. But the major side effects associated with these drugs are rhabdomyolysis and others are allergic reactions such as wheezing, shortness of breathing, cough, swelling of face, tongue etc[3]. To overcome all these side effects herbal products are safe, having no or less side effects as compared to chemically synthesized compounds. Although herbal drugs are easily available without any prescription and advancement in technology, herbal preparations are still in contact with pharma market due to their wider acceptance, cost effective and faith of people in using herbs that it is 100% natural origin means safe, thereby nowadays herbal products and their demand is going to be increased[4]. Present review focuses on mechanism, Pathophysiology behind the obesity and various herbs used in treatment of obesity.

2. Epidemiology:

Obesity and overweight are the major leading cause of death. Obesity is found in almost all countries in the world. Around 2.8 millions die due to obesity. WHO found that in the year 2016, around 1.9 billions adults, 18 years and above were overweight and of these 650 millions were obese. 41 million children under the age of 5 were overweight or obese in 2016. Over 340 million children and adolescents aged 5-19 were overweight or obese in 2016. Overall one in tenth populations in the world are obese. WHO have noticed that the new number of cases of obesity around the World within next two decades will exceed hundred of millions. Childhood obesity is major risk of obesity, premature death and disabled during adulthood. In addition to the future risk, childhood obesity children have suffering from breathing problem, hypertension and cardiovascular disease[5].

3. Etiology:

Factors responsible for obesity are: 1. Environmental factors: This include increase the amount of food intake especially junk food and reducing physical activity like exercises. All these because of busy schedule and sedentary life style, which ultimately leads to accumulation of fats in the body. 2. Genetic factors: Some genes are responsible for predisposing obesity and if parent gene is obese then chances of getting their child become obese or overweight. 3. Physiological factors: There are some internal mechanism in the body including neurotransmitters that stimulate the appetite and reduces energy expenditure. 4. Diseased condition: Diseases like diabetes, hypothyroidism and heart problems are closely related to obesity. 5: Drug induced obesity: For treatment, some pharmacological active ingredients like antipsychotic drugs for example diazepam, clomiphene causes obesity[6].

4. Pathophysiology:

Fat cells consist of 21-38% of total body weight of normal individual, in case of obese people consumption of more calorie than the expended and appetite can not reduce to compensate the more storage of the fats. Adipose tissue is regulated by signals transmitted to brain. The imbalance between transferring a signal from adipose tissue to brain and response of brain to signals results in obesity. This system of energy stores will determine the food intake and energy expenditure[7]. The another mechanism include **Leptin** hormone secreted by adipose tissue, can give signals to brain about the amount of fat stores. Leptin is secreted in favour of food deprivation, exercises and cold exposure and is inhibited in obesity stage. Now this leptin goes to the

brain and inhibit the release of NPY [NeuroPeptide Y], which stimulate the appetite, synthesis and storage of fats and reduces the energy expenditure. Adipocyte secretes **Interleukin-6[IL-6]** and its concentration in blood is increased in obese subjects and association with fat mass and BMI.

Adinopectine is also adipocytes derived insulin sensitizing hormone which is decreased in obesity and increased in weight reduction. Adipose tissue of the obese person also expresses the other proteins like TNF α and β 1,IL-1,IL-6,inducible nitric oxide synthase [iNOS] and increased in obesity[8].

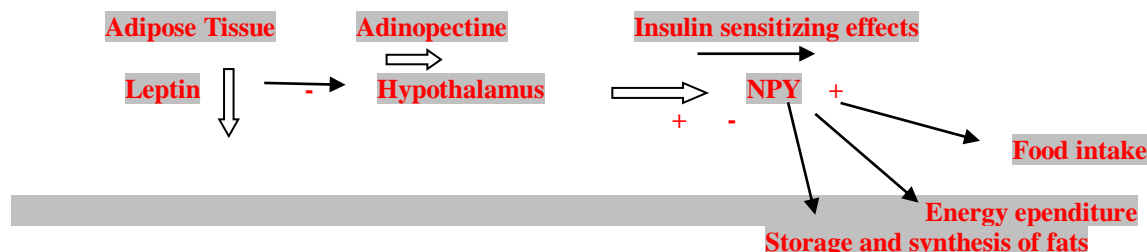
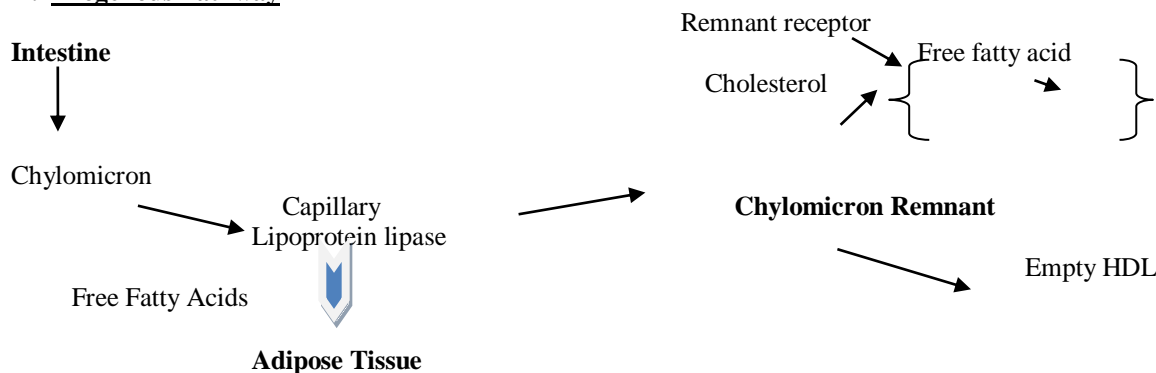


Fig 1: pathways by which fats stores in the adipose tissue.

Hyperlipidemia and Obesity:

Hyperlipidemia and obesity both are interrelating condition. Hyperlipidemia is a condition in which there are elevation of plasma lipids in the blood, commomnly LDL. It is also termed as hypercholesterolemia or hypelipoproteinemia[9]. Increasing in lipids like LDL, triglyceride and cholesterol are mainly responsible. Hyperlipidemia can occur either due to over production or impaired removal of lipoproteins and defects in lipoprotein or its receptor. There are three types of lipoproteins – LDL, VLDL and HDL. Almost all the dietary fats are absorbed from the intestinal lumen into the intestinal lymph and packed into chylomicrons. These

1. Exogenous Pathway



2. Endogeneous Pathway

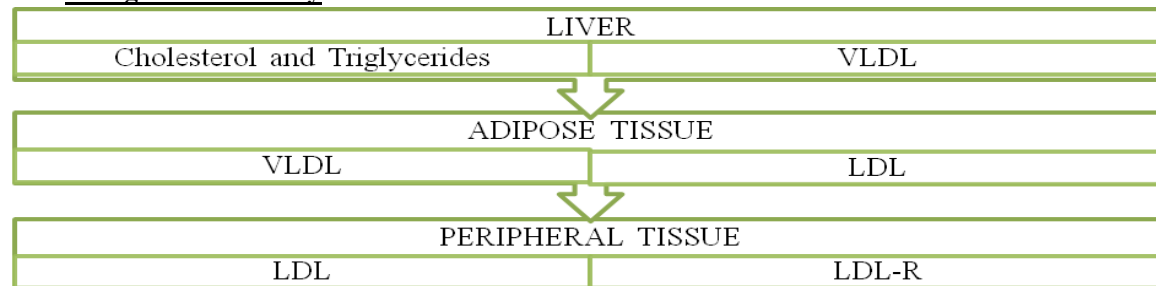


Fig: 2 Two pathways by which fats accumulates in the adipose tissue.

5. List of Herbal plants utilized for treatment of Obesity:

Botanical name	English name/Common name	Parts used	Reference
<i>Acacia arabica</i>	Babbula	Gum, bark, leaf, fruit-pods	[11]
<i>Achyranthus aspera</i>	Apamarga	Root, seed, leaf, whole plant	[12]
<i>Aconitum heterophyllum</i>	Ativisha	Root, rhizome	[13]
<i>Acorus calamus</i>	Vacha	Rhizome	[14]
<i>Adathoda vasica</i>	Vasa	Leaf, root, flower	[15]
<i>Allium sativum</i>	Garlic	Stem, Fruit	[16]
<i>Aloe vera</i>	Kumari	Leaf, root	[17]
<i>Betula utilis</i>	Burja	Bark, nodes	[18]
<i>Camelia sinensis</i>	Green Tea	Leaves	[19]
<i>Catharuths roseus</i>	Barmasi	Whole plant	[20]
<i>Coriander sativum</i>	Coriander	Fruits	[21]
<i>Cassia tora</i>	Chakramardha	Seed, leaf, root	[22]
<i>Cedrus deodara</i>	Devadaru	Hearwood oil	[23]
<i>Embelia ribes</i>	Vidanga	Fruit	[24]
<i>Emblica officinalis</i>	Amalaki	Fruit	[25]
<i>Garcinia indica</i>	Vrikshamla	Fruit, root, bark, oil	[26]
<i>Gymnema sylvestre</i>	Meshashringi	Leaf, root, seed	[27]
<i>Holarrhena antidysentrica</i>	Kutaja	Seed, bark	[28]
<i>Momordica charantia</i>	Karavellaka	Fruit, whole plant, leaf, root	[29]
<i>Moringa oleifera</i>	Sigru	Root, bark, seed	[30]
<i>Picrorhiza kurroa</i>	Katuka	Root	[31]
<i>Piper longum</i>	Pippali	Fruit, root	[32]
<i>Piper nigrum</i>	Maricha	Fruit	[33]
<i>Plumbago zeylanica</i>	Chitraka	Root, bark	[34]
<i>Punica granatum</i>	Pomegranate	Fruit rind ,leaves	[35]
<i>Terminalia arjuna</i>	Arjuna	Bark, root, leaf	[36]
<i>Terminalia bellerica</i>	Bibhitaka	fruit	[37]
<i>Terminalia chebula</i>	Haritaki	fruit	[38]
<i>Terminalia tomentosa</i>	Asana	Bark, heartwood	[39]
<i>Thea sinensis</i>	Oolong tea	Leaf	[40]
<i>Tinospora cordifolia</i>	Guduchi	Stem, root	[41]
<i>Trachyspermum ammi</i>	Yavani	Fruit	[42]
<i>Tribulus terrestris</i>	Gokshura	Fruit, root, whole plant	[43]
<i>Trigonella foenum graecum</i>	Methika	Seed, leaf, whole plant	[44]
<i>Valeriana jatamansi</i>	Tagara	Root	[45]
<i>Zingiber officinale</i>	Shunti	Rhizome	[46]

6. Recent literature and Current Drug targets of obesity:

A large number of herbal medicines and supplements are available in current market for the management of obesity. They all are having not same effects, reason behind this is the target they focuses are unique so all follow different mechanism of action. The basic principle behind antiobesity drugs are maintaing the energy balance in the body, that is equilibrium between energy intake and expenditure[47]. The main

approaches follows either effect of these drugs on nervous system or effect of supplement on physiological function. All targets by which antiobesity drugs or supplements acting are described as below:

6.1. Pancreatic lipase enzyme inhibition:

Dietary fats are absorbed in the intestine by action through Lipase enzyme that converts fats in to the free fatty acids and monoglycerides. If pancreatic

lipase enzyme is inhibited then ultimately the formation of fatty acid is blocked which in turn leading to weight loss. This inhibitory activity possesses phytoconstituents which includes saponins, phenolic compounds and flavanoids and caffeine. Pharmacological agent Orlistat works on this target[48].

6.2. Thermogenesis:

Increases thermogenesis by metabolism from generation of ATPs thereby conversion of food energy as heat and it ultimately leads to weight loss. There are three types of adipose tissue: White, brown and beige adipose tissue. In thermogenesis, brown adipose tissue plays important role in obesity by dissipating excess energy as heat and thereby controlling energy balance. Various naturally occurring compounds like caffeine, capsaicin are used in treatment for obesity[49].

6.3. Lipid Metabolism:

The pharmacological target for lipolysis can be envisaged by stimulating triglyceride hydrolysis in order to lower down to the fat stores. This will require oxidation of newly released fatty acid, some examples are the flavanoids of leaves of the plant *Nelumbo mucifera*

activate the B-adrenergic receptor and through this pathway it leads to suppress the body weight gain. The another example is caffeine, a major phytoconstituent found in oolong tea acts by binding with the phospholipid phosphate group and interaction between the lipase and triglyceride portion of lipid droplets and thereby enhances lipolysis[50].

6.4. Centrally acting mechanism: Body weight can be maintained by intake of foods. Many drugs act directly on their effect on the receptor within the central nervous system. The status of body stores and adiposity is regulated by three main hormones leptin, insulin and gastrointestinal peptide such as ghrelin and they all communicate to the central nervous system. For example green tea extract has reported to regulate the plasma leptin concentration. A number of natural appetite suppressants herbs reduce the expression of hypothalamic neuropeptide Y or serum leptin levels. The another mechanism is to alter the various hypothalamic neuropeptide's CNS level and key CNS appetite neurotransmitter's level via peripheral satiety peptide system and thereby suppress the appetite[51]. The phytoconstituents found in green tea like catechin- epicatechin, epigallocatechin stimulate thermogenesis by inhibition of catechol- O-methyltransferase enzyme that is responsible for degradation of norepinephrine. The naturally occurring Hydroxy citric acid obtained from

Garcenia cambogia is a potential appetite suppressant. It inhibits adenosine 5- triphosphate-citrate lyase which stops acetyl co enzyme A production and decreases fatty acid synthesis.

7. Screening method for antiobesity agents:

The invitro methods and invivo animal models are available for screening of antiobesity drugs.

7.1 Invitro methods:

7.1.1. Pancreatic Lipase Inhibition Assay[52]:

Porcine pancreatic lipase [PPL, type II] activity was measured using p-nitrophenyl butyrate [p-NPB] as a substrate. The method used for measuring the pancreatic lipase activity was modified. PPL stock solutions [1 mg/mL] were prepared in a 0.1 mM potassium phosphate buffer [pH 6.0] and the solutions were stored at -20 °C. To determine the lipase inhibitory activity, the extracts [final concentrations 100, 50, 25, 10, 5, 2.5, 1.25 µg/mL] or Orlistat [at same concentrations] as a positive control were pre-incubated with PPL for 1 h in a potassium phosphate buffer [0.1 mM, pH 7.2, 0.1% Tween 80] at 30 °C before assaying the PPL activity. The reaction was then started by adding 0.1 µL NPB as a substrate, all in a final volume of 100 µL. After incubation at 30 °C for 5 min, the amount of p-nitrophenol released in the reaction was measured at 405 nm using a UV-Visible spectrophotometer. The activity of the negative control was also examined with and without an inhibitor. The inhibitory activity [I] was calculated according to the following formula:

Inhibitory activity [I%]=100-[[B-b]/[A-a]×100]

7.2. Invivo Animal models[53]:

There are various animal models used for screening of antiobesity drugs.

1. Diet-induced [hypercaloric diets] obesity
2. Chemical agents induced obesity
3. Drug induced obesity
4. Genetic models
5. Monogenic
6. Polygenic models
7. surgical model.

In general, Diet induced and genetic models are more useful for screening of antiobesity effect.

8. Recent herbs used in obesity :

8.1 *Achyranthus aspera* [Amaranthaceae]:

This plant is having saponins, examples are triterpenoid saponin – Oleanolic acid and others are Pentatriacontane, 6-pentatriacontanone, Hexatriacontane and Tritriacontane. The ethanolic extract of plant shows significant reduction of body

weight and triglyceride and cholesterol level in mice fed a high fat diet for 6 weeks. The mechanism behind this is inhibition of pancreatic lipase enzyme[54].

8.2 *Nelumbo nucifera* [Nelumbonaceae]:

Several bio active phytoconstituents derived from seed, flowers, leaves and rhizomes are belonging to different chemical groups like alkaloids, flavanoids, glycosides, and terpenoids. *N.nucifera* alkaloids such as roemerine, nuciferin, nelumboside, anonaine shows to inhibit 3T3-L1 preadipocyte differentiation and improve high fat diet induced obesity and body fat accumulation in rats. The flavanoids also inhibit the pancreatic lipase enzyme[55].

8.3 *Salacia reticulata* [Celastraceae]:

S. reticulata leaves and root bark extracts in the management of patients with prediabetes and mild to moderate hyperlipidemia. Active ingredients of *Salacia* include salacinol, kotalanol, kotalagenin-16 acetate, and mangiferin. The active ingredients have a variety of actions, including postprandial glucose decrease by inhibiting α -glucosidases in the intestinal brush border, and thus slowing carbohydrate breakdown into absorbable monosaccharides. It contains kotalanol, an α -glucosidase inhibitor, which has an action similar to that of acarbose[56].

8.4 *Taraxacum officinale* [Astraceae]:

It is known as dandelion, which belongs to *Asteraceae* or *Compositae* family. As a food, dandelion is used as a salad ingredient, in deserts. Leaves are a rich source of a variety of vitamins and minerals. Chemical constituents present in the leaves are bitter sesquiterpene lactones principally also known as bitter principles, several polyphenols and coumarins. Other related compounds include β -amyrin, taraxasterol and taraxerol as well as free sterols [sitosterin, stigmasterin, phytosterin]. The inhibitory activity of dandelion on the pancreatic lipase enzyme has been demonstrated in vitro and in vivo indicating the potential of dandelion as an anti-obesity agent with limited side effects[57].

8.5 *Camelia sinensis* :

The leaf of *camellia sinensis* is source of tea and consumed for thousands of year. It contains polyphenol flavanoids epigallocatechin gallate which has lipid lowering properties. Green tea consumption reduces obesity through lowering leptin levels and its effect on hypothalamus[19].

8.6 *Mellissa officinalis*:

This plant is commonly used as antistress herb. An active fraction denominated ALS-L1023 [ALS] extracted from *Melissa* leaves by organic solvents exhibited antiangiogenic and studies suggested that the effect of ALS on angiogenesis and ALS can regulate adipose tissue growth in high fat diet-induced obese mice. When high fat diet-induced obese mice were treated with ALS for 8 weeks, adipose tissue mass and adipocyte size were significantly reduced in treated mice compared to control mice[58].

8.7 *Bambusa textilis* [Bambusoideae]:

Bamboo leaves are potential source of functional foods and are worthy of future development because of their abundance as a natural source with various biological activity. Different phytochemicals, including flavonoids, phenolic acids, phenols and sterols, were found in this bamboo species. Study shows that methanolic extract of *Bambusa textilis* reduces lipid levels in high fat diet induced rats[59].

8.8 *Medicago sativa* [Fabaceae]:

Medicago sativa is commonly known as Alfalfa. Alfalfa is mostly seen as a food for grazing animals. Its related to clove and fenugreek. Study suggested that petroleum ether extract of roots of *Medicago sativa* shows antihyperlipidemic effect. The administration of extract for 4 weeks decreases triglycerides, total cholesterol, LDL, VLDL in comparison to rovastatin[60].

8.9 *Ephedra sinica* [Gnetaceae]:

Ephedra has been used as a supplement for weight loss and its effects have been reported. studies found that the influence of *Ephedra* on the composition of gut microbiota, and its correlation with weight loss. Body weight, body mass index and body fat percentage of subjects were reduced after the consumption of the stem extract of the plant[61].

8.10 *Carum carvii* [Umbelliferae]:

Caraway [*carum carvii*] is wellknown plant that is traditionally utilized to treat obesity. It contains multiple phytoconstituents like fatty acid, polyphenols and volatile oils. Weight and fat lowering effect of caraway extract is due to carvacrol [polyphenol] and unsaturated fatty acids[62].

8.11 *Morus bombycis* [Moraceae]:

Morus bombycis root extract shows strong anti-lipase activity. The extract shows increased lipolytic effect by decreasing intracellular triglyceride and release of glycerol. It also inhibit phosphodiesterase activity that's why study suggested the plant has an antiobesity effect[63].

8.12 *Moringa oleifera* [Moringaceae]:

This plant commonly known as Drumstick tree that possesses medicinal values attributed to its whole plant parts such as leaves, root, bark, fruits, and seeds. It contains alkaloids, tannins, terpenoids, flavanoids and steroids. The high concentration of various vitamins and minerals makes it virtually ideal dietary supplements. The hypolipidemic activities of Moringa leaves are associated with β -sitosterol. Study suggested that the methanolic extract of Moringa leaves decreases triglyceride and total cholesterol level in High Fat Diet induced Obesity in rats[30].

8.13 *Coleus forskohlii* [Lamiaceae]:

Coleus forskohlii is an traditional ayurvedic indian plant used as slimming aids. It belongs to mint family and rich in alkaloids such as forskolin which acts as adenylate cyclase activator. It stimulates the production of cAMP that triggers metabolic processes, thermogenesis, and stimulates the loss of body fat. Clinical studies on overweight/obesity showed that the extract of *Coleus forskohlii* acts as antiobesity agent was well tolerated and having no adverse effects[64].

8.14 *Garcenia indica* [Clusiaceae]:

Garcenia is a plant of Clusiaceae family, commonly used as flavouring agent. A number of phytochemicals including flavanoids and organic acids are found in plant. Among them Hydroxy Citric Acid is a potential supplement for weight management and as antiobesity agent. The antiobesity effect of HCA is due to serotonin regulation and food intake suppression, decreased lipogenesis, increased fat oxidation and downregulation of spectrum of obesity associated genes[65].

8.15 *Syzygium cumini* [Myrtaceae]:

It is known as Jamun fruits. Study investigated that ethanolic crude extract of *Syzygium cumini* was screened for hypoglycemic and hypolipidemic effect. It reduces triglyceride and cholesterol level in alloxan induced diabetic rats. The exact mechanism is not known but it normalizes plasma lipids[66].

CONCLUSION:

Dietary fat is absorbed by action of pancreatic lipase enzyme into the intestine. Therefore the most important target of newer antiobesity agent is pancreatic lipase inhibition and by which the potential of herbs and their effects are to be determined. Various bioactive phytochemicals derived from above mentioned herbs are belonging to different chemical class like alkaloids, glycosides,

phenolics and flavanoids that are safe to treat obesity due to harmful side effects from synthetically derived compounds. Herbal products using weight loss plants are marketed nowadays, but so far no systematic screening is attempted to come up with the effect of them. Clinical trials of herbal products are to be must to potentiate their effects and therefore to generate the attraction of herbal products among the users.

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