



## Review Article

## Pharmacotherapy in Obesity

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## ABSTRACT

Obesity is one of the most common medical problems in India and a risk factor for illnesses such as hypertension, diabetes, degenerative arthritis, kidney disease and myocardial infarction. In India, more than 135 million individuals were affected by obesity. According to ICMR INDIAB study 2015, prevalence rate of obesity and central obesity are varies from 12% to 31% and 17%–36% respectively. Medications are formulated to reduce energy intake, increase energy output or decrease the absorption of nutrients. Drugs cannot replace diet, exercise and lifestyle modification, which remain the cornerstones of obesity, In 2014 the global economic impact of obesity was estimated to be US \$2.0 trillion or 2.8% of the global gross domestic product (GDP) treatment. Obesity also imposes costs in the form of lost productivity and foregone economic growth as a result of lost work days, lower productivity at work, mortality and permanent disability.

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## 1. Introduction

## 1.1. Definition

Obesity can be defined as a disease in which excess body fat has accumulated to an extent that health is adversely affected. Obesity is characterised by weight exceeding 120% of median weight for height.

Obesity is now recognized as a chronic or non-communicable disease.

Obesity is a multifactorial disease, and caused in the majority of cases simply by an imbalance of energy intake and energy expenditure.<sup>1</sup>

## 2. Classification of obesity according to WHO

The body mass index (BMI) is the most commonly used measure of obesity. The BMI is calculated from a person's height and weight ( $BMI = \text{kg/m}^2$ ). BMI is not a good measure of obesity since the body composition of different people with the same BMI can be highly variable. In

addition, it does not reflect intra-abdominal (visceral) fat that is related to the metabolic syndrome and cardiovascular risks.

CLASSIFICATION OF OVERWEIGHT AND OBESITY BY BMI, WAIST CIRCUMFERENCE AND ASSOCIATED DISEASE RISKS

	BMI (kg/m <sup>2</sup> )	Obesity Class	Disease Risk* Relative to Normal Weight and Waist Circumference	
			Men ≤ 102 cm (≤ 40 in) Women ≤ 88 cm (≤ 35 in)	> 102 cm (> 40 in) > 88 cm (> 35 in)
Underweight	<18.5		—	—
Normal	18.5 – 24.9		—	—
Overweight	25.0 – 29.9		Increased	High
Obesity	30.0 – 34.9	I	High	Very High
	35.0 – 39.9	II	Very High	Very High
Extreme Obesity	≥40	III	Extremely High	Extremely High

## 3. Incidence of Obesity

A recent study demonstrated that India has raced to third place, after the United States of America and China in the highest number of obese people worldwide; the United States of America accounting for 13% of obese people globally and India together with China accounting for 15%

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of the world's obese. The age-standardized prevalence of generalized obesity in South India was 46%. In New Delhi Birth Cohort, the prevalence of obesity was 20% in men and 35% in women using BMI greater than or equal to 30 as the cut off point. The worldwide prevalence of childhood overweight and obesity increased from 4.2% in 1990 to 6.7% in 2010. This trend is expected to reach 9.1% in 2020. The problem is global and is steadily affecting many low- and middle income countries, particularly in urban settings.<sup>2,3</sup>

#### 4. Causes of Obesity

##### 4.1. Food

1. Foods served at fast food restaurants tend to contain a high number of calories with low nutritional values.
2. Sugary drinks are another factor that has been examined as a potential contributing factor to obesity.
3. Snack foods include foods such as chips, baked goods, and candy. Many studies have been conducted to examine whether these foods have contributed to the increase in childhood obesity.
4. Portion sizes have increased drastically in the past decade.

##### 4.2. Activity Level

1. Each additional hour of television per day increased the prevalence of obesity by 2%.

##### 4.3. Depression and anxiety

1. Depression may be both a cause and a consequence of obesity. Additionally, in a clinical sample of obese adolescents, a higher life-time prevalence of anxiety disorders was reported compared to non-obese controls.
2. A role for heredity is implied by studies in twins and in genetic epidemiology is well documented.<sup>4</sup>

##### 4.4. Hormones

The main obesity-related hormones are ghrelin, agouti, obestatin, leptin, adiponectin, nesfatin, visfatin, tumor necrosis factor, interleukin-6, and resistin.

1. **Ghrelin** as human natural hormones is involved in fundamental regulatory process of eating and energy balance. Its properties includes increasing appetite.
2. **The Agouti Related Protein (AGRP)** is upregulated in obese and diabetic mice and stimulates hyperphagia and the development of obesity when overexpressed in transgenic mice.
3. **Obestatin** appears to function as part of a complex gut-brain network whereby hormones and substances from the stomach and intestines signal the brain about

satiety or hunger. In contrast to ghrelin, which causes hyperphagia and obesity, obestatin appears to act as an anorectic hormone, decreasing food intake and reducing body weight gain.

4. **Obesity and the Metabolic Syndrome** are distinguished by an increase in circulating leptin concentrations, in parallel to a drop in the levels of adiponectin.
5. **Nesfatin-1** suppresses appetite to make people and animals feel full after a meal. It also stimulates insulin release so that glucose moves from the blood into the cells, thus helping to maintain energy balance.
6. **Increased serum visfatin levels** in obesity and provide evidence that central obesity combined with physical inactivity.
7. **Interleukin -6:** Interleukin -6 (IL-6) is produce in many cells and some tissues such as adipose tissue and its production is increased in obesity
8. **Resistin** is a cysteine-rich peptide hormone which has 108 amino acids. The level of this hormone is high in diabetic and obese people.
9. **TNF- $\alpha$**  causes deterrence of lipoprotein lipase and stimulates lipolysis in adipocytes and leads to increase of unsaturated fatty acids in the blood which causes increased insulin resistance and diabetes.<sup>5</sup>

#### 5. Pathophysiological links of obesity [Figure 1]

The correlation between obesity and its associated links leading to diabetes and raised BP are shown below.

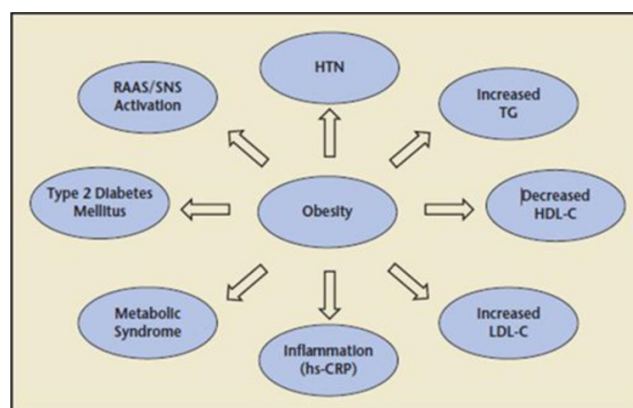


Fig. 1:

#### 6. Complications of Obesity

Obesity is a growing worldwide epidemic

##### 6.1. Renal Disease

Obesity is one of the strongest risk factors for new-onset chronic kidney disease, and also for nephrolithiasis

and for kidney cancer. The putative mechanisms behind the increased risk of kidney cancers observed in obese individuals include insulin resistance, chronic hyperinsulinemia, and increased production of insulin-like growth factor 1.<sup>6</sup>

### 6.2. Cardiovascular disease

It is clear that obesity indirectly contributes to premature coronary heart disease through associated hypertension, diabetes mellitus, depressed plasma HDL concentrations or hypercholesterolemia. Obesity and hypertension are causally linked and together impart considerable risk for stroke, heart attack and congestive heart failure in both men and women. Obesity puts stress on the cardiovascular system by increasing blood volume, stroke volume, cardiac output, total body oxygen consumption. Abnormal plasma lipid and lipoprotein concentrations are commonly associated with obesity. An elevated plasma triglyceride concentration is the commonest abnormality, and is usually due to increased rates of production of very-low-density lipoproteins (VLDL; pre-p-lipoproteins).

### 6.3. Gall Bladder Disease

It is estimated that 30% of individuals with morbid obesity referred for surgical intervention have gallstones

### 6.4. Diabetes

At all ages, the risk of type 2 diabetes rises with increasing body weight. The prevalence of type 2 diabetes is three to seven times higher in those who are obese than in normal weight adults, and is 20 times more likely in those with a body mass index (BMI) greater than 35 kg/m<sup>2</sup>. Syndrome X as a conglomerate of coronary risk factors. It is characterized by the clustering of abdominal obesity, impaired glucose tolerance, elevated triglyceride levels, reduced high-density lipoprotein (HDL) cholesterol levels, and hypertension, often accompanied by a proinflammatory status that predisposes to CVD. Persons with Metabolic syndrome are at increased risk of type 2 DM and CVD. Diabetic retinopathy is a vascular disease of the retina which affects patients with diabetes mellitus. It is the number one cause of blindness in people between the ages of 20-64.

### 6.5. Cancer

Obesity has been associated with an increased risk of esophageal cancer, pancreatic cancer, colorectal cancer, breast cancer, endometrial cancer, kidney cancer, thyroid cancer, liver cancer and gallbladder cancer<sup>7</sup>

## 7. Pharmacological intervention of Obesity

Treatment for obesity includes lifestyle management, consisting of diet therapy, physical activity, and behavioral

modification, and may include pharmacotherapy or surgery based on level of risk. Use of obesity drugs is approved for patients having a BM>30Kg/m<sup>2</sup> or BMI>27kg/m<sup>2</sup> along with one or more comorbidities like high BP or type 2DM. On combination with lifestyle modifications drug therapy can improve weight loss by 3–5kg over placebo. The choice of agent should be individualised and governed by patient comorbidities, relative contraindications, available clinical trial evidence and clinical expertise.

## 8. Evolved medicines

Centrally acting sympathomimetics, such as the amphetamine derivatives desoxyephedrine, phentermine and diethylpropion, were among the earliest pharmacological agents used for weight loss. The serotonin releasing agent fenfluramine and dexfenfluramine were more potent obesity drugs which had to be withdrawn from the market due to reports of increased cardiac valvular disease after the use of these drugs. Sibutramine which also affects the 5HT system and raised BP and heart rate had to be withdrawn because of association with high incidence of CVS events and stroke, Similarly rimonabant which showed great promise as a cannabinoids receptor antagonist in weight loss had to be removed because of severe psychiatric defects including suicidal tendencies.

**Beloranib** is a former drug candidate for the treatment of obesity. It was discovered by CKD Pharmaceuticals and its clinical development was led by Zafgen. Drug development was halted in 2016 after deaths during clinical trials.

**Mirabegron** is a  $\beta_3$ -adrenergic receptor (AR) agonist used in the treatment for overactive bladders. Mirabegron class of medications was initially studied in 1970 for obesity management and metabolic disease. This therapy, however, was not successful enough

**Tesofensine's** mechanism of action prevents the reuptake of serotonin, noradrenaline and dopamine, Tesofensine suppresses appetite and ameliorates thermogenesis. Not appreciated, because it caused tachycardia.

**Velneperit** which acts as a potent and selective antagonist for the Neuropeptide Y receptor Y<sub>5</sub>. It has anorectic effects and was developed as a possible treatment for obesity, but was discontinued from further development after disappointing results.<sup>8</sup>

The drug therapy is needed lifelong and maybe useful in weight maintenance. Tolerance can get developed and weight gain occurs even with the continued drug regimen.

**Orlistat**: is a selective inhibitor of gastric and pancreatic lipase indicated for the treatment of obesity. It is also known to significantly reduce risk of associated co-morbidities such as heart attack, type-2 diabetes mellitus, hypertension and stroke.

Orlistat could effectively manage obesity related co-morbidities, especially insulin resistance and atherosclerosis

**Table 1:** Drugs withdrawn due to their side effects

Drug	Introduced	Mechanism	FDA status
Fenfluramine	1973-U.S	Sympathomimetic amine (appetite suppression)	Withdrawn 1997: valvular heart disease, pulmonary hypertension
Dexfenfluramine	1996-U.S	As above	Withdrawn 1997: valvular heart disease, pulmonary hypertension
Rimonabant	2006-Europe	Selective CBI receptor blocker	Not approved in U.S.: concern over psychiatric side effects Withdrawn 2009: potential of serious psychiatric disorder Temporarily withdrawn 2000
Sibutramine	1997-U.S. 2001-Europe	Selective combined serotonin and noradrenaline Reuptake inhibitor (appetite suppression)	Withdrawn 2010: increased risk of heart attack and stroke in high-risk cardiac patients

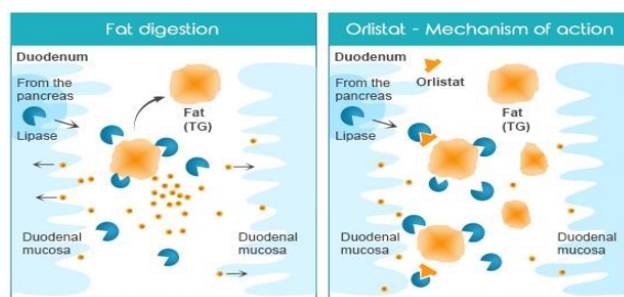
**Table 2:** Modern drug therapy for weight reduction

Drug	Mechanism of action	Effect	Daily Dosageb
Orlistat (Xenical)	Inhibits pancreatic and gastric lipase	Decrease fat absorption	120 mg 3 times a day with each main meal containing fat
Phentermine (Adipex-P, Lomaira)	Augments central norepinephrine release	Decrease appetite	8 mg to 37.5 mg once daily
Phentermine and topiramate extended release (Qsymia)	Augments central norepinephrine and gamma-amino butyric acid release	Decrease appetite	Phentermine 3.75 mg/topiramate 23mg once daily (initial); Phentermine 7.5 mg/topiramate 46mg once daily (maintenance)
Bupropion and naltrexone sustained- release (Contrave)	Inhibits dopamine and norepinephrine reuptake; blocks opioid receptor	Decrease appetite	1 tablet (bupropion 90mg/naltrexone 8mg) once daily in morning (initial); 2 tablets (bupropion 180mg/naltrexone 16mg) twice daily (usual); maximum daily dose: bupropion 360 mg/ naltrexone 32mg
Diethylpropion (Tenuate, Tenuate Dospan)	Augments central norepinephrine release	Decrease appetite	25 mg 3 times a day (immediate release); 75 mg once daily, midmorning (controlled release)
Lorcaserin (Belviq)	Activates serotonin 5-HT receptor	Decrease appetite	10 mg twice a day (immediate release)
Liraglutide (Saxenda)	Activates glucagon like peptide 1 receptor	Decrease appetite	3 mg subcutaneously once a day

risk. It decreases leptin and increases adiponectin independent of body fat percent and waist circumference. Therefore, orlistat appears to have anti-diabetic and anti-atherogenic properties and may help prevent metabolic syndrome in the overweight people.

Orlistat is a **reversible inhibitor of lipases**. It exerts its therapeutic activity in the lumen of the stomach and small intestine by forming a covalent bond with the active serine residue site of gastric and pancreatic lipases. Orlistat works by inhibiting pancreatic lipase, an enzyme that breaks down triglycerides in the intestine.[Figure 2] The weight-independent improvement in glycemic control to orlistat therapy may be attributed to a decrease in post-prandial NEFA (nonesterified fatty acid) concentration. Orlistat is used 120 mg orally 3 times a day with each main meal

containing fat.

**Fig. 2:**

Reported side effects of orlistat include: bowel urgency, frequent bowel movements, oily evacuation, oily rectal leakage, steatorrhea, and flatulence with discharge. Over a 1-year period, obese patients taking orlistat in combination with a hypocaloric diet show a reduction of 2-5 kg over the weight decrease with placebo.

Orlistat is thought to cause Acute kidney injury (AKI) through enteric hyperoxaluria, which can also be seen in patients with fat-malabsorption syndromes. Supersaturation of oxalate in renal tubules is a risk factor for calcium oxalate precipitation, which can result in AKI

A study conclusively revealed that incidence of acute hepatotoxicity was significantly raised in the period both immediately before and after commencement of orlistat therapy, suggesting its restrained usage.

**Cetilistat** It acts in the same way as the older drug orlistat by inhibiting pancreatic lipase, an enzyme that breaks down triglycerides in the intestine. A published phase 2 trial found cetilistat significantly reduced weight and was better tolerated than orlistat. Studies demonstrated that patients administered with 120mg of Cetilistat three times a day showed 2.776% reduction in average body weight when compared to 1.103% in placebo-administered patients. Cetilistat reduced HbA1c and LDL cholesterol and was also well tolerated in clinical studies.<sup>9,10</sup>

**Liraglutide** : It is a glucagon-like peptide-1 receptor agonist (GLP-1 receptor agonist) also known as incretin mimetics. It works by increasing insulin release from the pancreas and decreases excessive glucagon release. [Figure 3] Liraglutide may also be used together with diet and exercise for chronic weight management in adult patients. The body mass index (BMI) needs to be greater than 30 kg/m<sup>2</sup>, or greater than 27 kg/m<sup>2</sup> together with high blood pressure, type 2 diabetes mellitus, or dyslipidemia. Adding a daily dose of liraglutide to consistent diet and exercise can lead to a 7.1% reduction in body weight after 6 months for adults with obesity, according to findings published in Obesity.

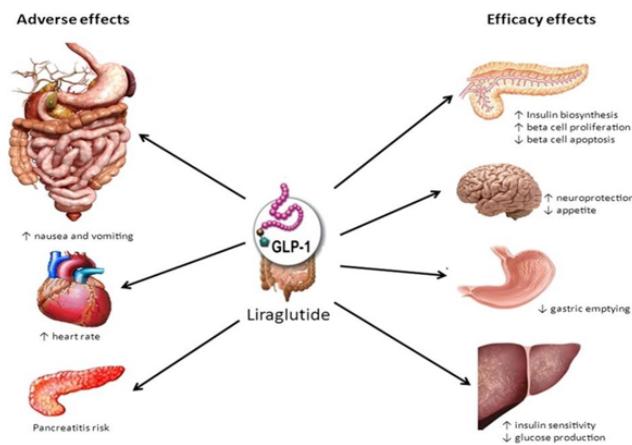


Fig. 3:

Below is a dosing schedule to guide through the starting dosage of 0.6 mg to the dosage of 3 mg.



The most common side effects reported by liraglutide participants related to GI upset, including nausea (40%), diarrhea (21%), and vomiting (16%). More serious events, including cholelithiasis (0.8%), cholecystitis (0.5%), and pancreatitis (0.2%), were also reported<sup>11</sup>

**Lorcaserin** is believed to act as an agonist at central serotonin subtype 2C (5-HT<sub>2C</sub>) receptors located on hypothalamic pro-opiomelanocortin neurons. Agonism of the 5-HT<sub>2C</sub> receptor is believed to reduce food intake and increase satiety, leading to weight loss. [Figure 4]

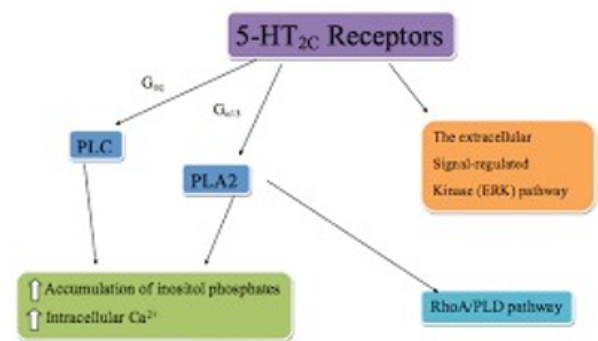


Fig. 4:

Lorcaserin approval was based on data by three main studies; behavioral modification and lorcaserin for overweight and obesity management (BLOOM) study, behavioral modification and lorcaserin for overweight and obesity management in patients of diabetes mellitus type 2 (BLOOM DM) study; and one year nonrandomized trial of lorcaserin for weight loss in obese and overweight adults the BLOSSOM study.

The common adverse drug reactions are nausea, dizziness, headache, vomiting, and cardiovascularopathy.

It is available as 10 mg film-coated tablets, taken twice daily, with or without food for 12 weeks. If weight is not decreased by 5% or more, treatment should be discontinued.<sup>12</sup>

**9. SGL2 Inhibitors and weight loss**

Patients treated with SGLT2 inhibitors have reported weight loss of around 1 to 3 kg. The dramatic and rapid metabolic improvement preceding any significant weight loss is explained by mobilization of liver fat (reducing hepatic glucose output with enhanced hepatic insulin resistance,



The mechanisms by which SGLT2 inhibitors affect weight loss may include the following. First, these mechanisms are likely driven by the loss of calories associated with increased urine glucose excretion (UGE). The SGLT2 inhibitors inhibit renal glucose reabsorption and induce UGE. The weight loss observed with SGLT2 inhibitor treatment might be associated with fat loss. The SGLT2 inhibitors should be taken after fasting [Figure 5]

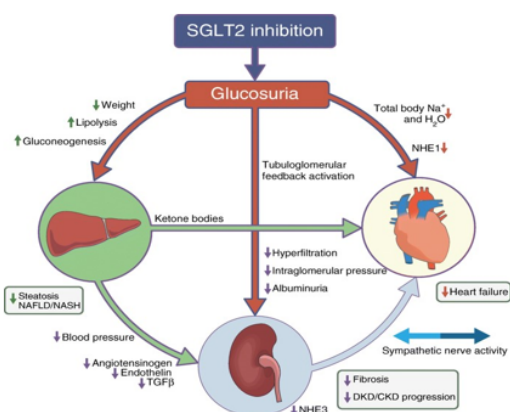


Fig. 5:

Phase II trials have considered SGLT2i in subjects who are overweight or with obesity without diabetes (SGLT2i are not currently licensed for this indication). Weight loss observed over 12 weeks in one randomized controlled trial (RCT) was relatively modest but significant (placebosubtracted changes for all canagliflozin doses, percent body weight change less than 2%). Canagliflozin 50, 100, and 300 mg produced approximately 2 to 3 kg of weight loss compared with baseline, and approximately 1 to 1.5 kg of weight loss compared with placebo.<sup>13</sup>

## 10. Centrally acting drugs for Obesity

### 10.1. Topiramate

Topiramate is believed that the same properties that enable it to control migraines and seizures also work to inhibit the brain networks that cause food cravings. Treatment of obese diabetic patients with 150 mg/day topiramate can be suitable for near 5% weight loss. Topiramate may be effective in improving metabolic parameters associated with obesity and glycemic control in diabetes type two patients.<sup>14</sup>

### 10.2. Bupropion SR

in conjunction with a lifestyle intervention program was associated with a dose-related reduction in body weight at 24 weeks. Subjects who completed 24 weeks of treatment with bupropion SR 400 mg/d lost 10.1% of their initial body weight.

**Bupropion/naltrexone** is a combination drug used for weight loss in those that are either obese or overweight with some weight-related illnesses.

Bupropion is a reuptake inhibitor and releasing agent of both norepinephrine and dopamine, and a nicotinic acetylcholine receptor antagonist, and it activates proopiomelanocortin (POMC) neurons in the hypothalamus which give an effect downstream, resulting in loss of appetite and increased energy output. The POMC is regulated by endogenous opioids via opioid-mediated negative feedback.

Naltrexone by contrast is a pure opioid antagonist, therefore further augmenting bupropion's activation of the POMC

The combination of 32 mg of naltrexone and 360 mg of bupropion in a sustained-release combination pill form has been recently approved for obesity treatment<sup>15</sup>

The combination of zonisamide 400 mg/day and bupropion SR 300 mg/day has been shown to be more effective for weight loss than either monotherapy or placebo in subjects with uncomplicated obesity. **The combination is better than monotherapy.**<sup>16</sup>

**Phentermine:** Phentermine alone is designed for **short-term use** only, as there are no long-term studies on its safety. Phentermine and Topiramate ER have been developed as combination therapy and approved by the FDA for weight reduction in 2012. Phentermine comes under category of narcotic drug (under NDPS act) and hence not easily available in India,<sup>17</sup>

### 10.3. Metformin

Reduces hepatic glucose production, which is a major source of circulating glucose. Metformin also reduces intestinal absorption of glucose, which is a second source of circulating glucose. Metformin has been associated with significant weight loss when compared with sulfonylureas or placebo. Compared metformin and glipizide in a randomized double-blind study of Type 2 diabetic individuals who had failed on diet. The FDA have not approved metformin for weight loss purposes. Extended-release metformin and tablets, doses are between 500 and 1000 milligrams (mg) and should not exceed 2,500 mg in a day for adults.<sup>18</sup>

Acarbose administration with the low calorie diet seems to be an effective treatment for lowering weight in the overweight and obese patients with the high carbohydrate utilization. 100mg before major meal was dose evaluated. Acarbose causes flatulence.<sup>19</sup>

### 10.4. Herbal Drugs for Obesity

There are several plants described in ayurveda for weight management. But so far, no systematic and well designed screening is attempted to come up with an effective herbal

**Table 3:** Drugs under evaluation<sup>20</sup>

Drug	Features	Remarks
Obinipitide Synthetic analog of two naturally occurring human hormones: PYY3-36 and pancreatic polypeptide	well tolerated and inhibited food consumption for up to 9 h after dosing	Under development
Agouti-related protein (AgRP) Peptide	Shown to reduce food intake and body weight gain, reduce fat composition, and reduce insulin levels in a dose-dependent fashion.	Assessed in obese subjects in clinical trials.
methionine aminopeptidase 2 inhibitor	Reduction in median body weight of 1 kg per week	Under Trial
D3 antagonist	Blocking dopamine may reduce the intake of foods high in fat and sugar, and may be a potential treatment option for compulsive overeaters.	Under Trial
Ezlopitant is a neurokinin receptor-1 antagonist	Decreasing the consumption of sweetened foods and drinks	Under Trial

weight loss product. Anti-obesity mechanisms for herbal plants included reduced energy intake, increased energy expenditure. Lipid absorption was mainly influenced by decreased pre-adipocyte differentiation and proliferation, or decreased lipogenesis and increased lipolysis.

### 10.5. *Withania Somnifera*

Ameliorates diet-induced obesity by enhancing energy expenditure via promoting mitochondrial function in adipose tissue and skeletal muscle.

**Zingiber officinale** Most of the experimental studies supported the weight lowering effect of ginger extract. Ginger could modulate obesity through various potential mechanisms including increasing thermogenesis, increasing lipolysis, suppression of lipogenesis, inhibition of intestinal fat absorption, and controlling appetite.

**Momordica charantia (M. charantia)**, commonly known as bitter melon, bitter melon, kugua, balsam pear, or karela, is a tropical and sub-tropical vine belonging to the Cucurbitaceae family. The major bioactive components that showed anti-obesity activities included proteins, triterpenoids, saponins, phenolics, and conjugated linolenic acids. Their mechanisms included inhibition of fat synthesis, promotion of glucose utilization, and stimulation

of auxiliary lipid-lowering activity.

**Camellia sinensis** L Studies with cells suggest that green tea can reduce glucose absorption and fat by inhibiting digestive enzymes. Green tea extract inhibited marked digestive lipases in vitro and might reduce fat digestion in humans.

**Safflower oil**, through the linoleic acid, reduces body fat by inhibiting the lipoprotein lipase (LPL), an enzyme responsible for transferring the lipids present in the blood current into the adipose cells. These cells are responsible for storing body fat and make up the adipose tissue of the human body

**Apple** whole apple consumption is associated with a lower prevalence of obesity and a lower likelihood of obesity.

**Nelumbonucifera** leave extract prevent the increase in body weight, parametrial adipose tissues weight and liver triacylglycerol level.

### 10.6. *Garcinia cambogia*

Garcinia contains citrine, an extract that is 50-60% HCA (garcinic acid) which inhibits an enzyme that helps the body synthesize fat for storage in adipose tissue.

### 10.7. *Arachishypogaea*

This plant is free from Transfats. So, it decreases body weight gain, liver triglyceride content and liver size in association with increased fecal lipid excretion, suggesting an inhibitory mechanism on lipid absorption.

**Cassia nomame** prevents the stomach and intestines from absorbing dietary fat. This causes dietary fat to be excreted in feces, which might promote weight loss in some people.

**Panax ginseng** suppress lipid accumulation and reactive oxygen species (ROS) production, and improve insulin resistance

**Clerodendrum phlomidis** anti-obesity activity produced by is because of inhibition of pancreatic lipase activity which delays the intestinal absorption of dietary fat.[22.23]

### 10.8. *Surgical Management of Obesity*

The indications to undergo bariatric surgery, are based on body mass index (BMI) as well as the presence of comorbidity. Patients with a BMI of 40 kg/m<sup>2</sup> or greater without coexisting medical problems, and for whom bariatric surgery would not carry an excessive risk, should be candidates. Laparoscopic sleeve gastrectomy (LSG) and laparoscopic Roux-en-Y gastric bypass (LRYGB) are the 2 main types of surgeries that are current standards of care in weight loss surgery. Complications in severely obese include thromboembolism, pulmonary or respiratory insufficiency, haemorrhage, peritonitis, and wound infection.<sup>21</sup>

## 11. Conclusion

Obesity has been defined as an ‘abnormal and excessive fat accumulation that may impair health’. In practice, obesity is diagnosed by body mass index (BMI), which is taken as a surrogate of percentage fat mass. Obesity is a serious global health issue and a leading risk factor for type 2 DM. The main treatment for obesity consists of weight loss via dieting and physical exercise. Diet programs can produce weight loss over the short term and long-term, although combining with exercise and counseling provide greater results. Drug therapy has palliative role, weight reduction can be nullified once treatment is stopped. Drugs for obesity have to be monitored for safety as in past many drugs have been discontinued. Pharmacologic approaches may be helpful for some severely obese people, but will not be applicable for prevention of moderate obesity for the whole population. New studies combining antiobesity and antidiabetes medications in the context of lifestyle interventions should help define the optimal therapeutic approach for patients with type 2 DM and obesity. The prescribing practices of trained obesity medicine physicians are based upon the scientific literature, expert opinion and the clinical needs of the individual patient. Patients should be made aware of their weight problems and should be instructed for regular exercise and dietary control, since drugs need to be used with optimal caution.

## 12. Source of Funding

None.

## 13. Conflict of Interest

None.

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