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## A REVIEW ON OBESITY COMPLICATIONS AND ITS MANAGEMENT

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# **Keywords:**

Obesity, BMI, Anti-obesity medication, Natural anti-obesity medication

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**ABSTRACT:** The article focuses on the prevalence of obesity in India, increasing levels of childhood obesity, and the potential health hazards that result from obesity, thereby suggesting the necessary preventive measures and the prevailing natural and synthetic therapy that can help to cure the disease, thus spreading awareness about its severity and necessity for treatment. Obesity in India has reached epidemic proportions in the 21<sup>st</sup> century, with morbid obesity affecting 5% of the country's population. About 3.4 million people die each year due to overweight and obesity. The numbers are only worsening with each passing year. Anti-obesity medication or weight loss 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 either appetite or absorption of calories. Thus proper preventive measures and medication can help in reducing the extent of the disease worldwide.

**INTRODUCTION:** Obesity is a medical condition in which excess body fat has accumulated to the extent that it may have a negative effect on health <sup>1</sup>. Obesity is a leading preventable cause of death worldwide, with increasing rates in adults and children. It is one of the most serious public health problems of the 21<sup>st</sup> century where more than 1.9 billion adults were overweight. Of these over 600 million, or 13 percent of the global population, were obese. About 3.4 million people die each year due to overweight and obesity. The numbers are only worsening with each passing year. Obesity in India has reached epidemic proportions in the 21<sup>st</sup> century, with morbid obesity affecting 5% of the country's population <sup>2</sup>.



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India is following a trend of other developing countries that are steadily becoming more obese. Unhealthy, processed food has become much more accessible following India's continued integration in global food markets. This, combined with rising middle-class incomes, is increasing the average caloric intake per individual among the middle class and above income households. Obesity is emerging as a silent pandemic in India. According to a National Family Health Survey (NFHS), 20.7% of Indian women and 18.6% of Indian men in the age group of 15 to 49 are overweight.

**1.1 Reasons for obesity in India:** The reasons for obesity differ among different communities and their habitats. The most common reasons behind obesity among urban populations and small cities and towns are changing in food habits, sedentary lifestyle, lack of sleep, misconception in parenting and stress. India is facing a double burden of disease. Children in low and middle-income countries are more vulnerable to inadequate

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prenatal, infant, and young child nutrition. At the same time, these children are exposed to high-fat, high-sugar, high-salt, energy-dense, and micronutrient-poor foods, which tend to be lower in cost but also, lower in nutrient quality. These dietary patterns, in conjunction with lower levels of physical activity, result in sharp increases in childhood obesity while undernutrition issues remain unsolved.

**1.2 Urban-Rural Divide:** The urban population is more prone to obesity as compared to their rural counterparts. In Andhra Pradesh, 44.4 percent of urban men suffered from obesity, while the percentage in rural parts was 28 percent. Similarly, 45.6 percent of the urban women in the state were obese against 27.6 percent of women in rural Andhra Pradesh. In Bihar, around 20 percent urban and 11 percent rural men were obese. Additionally, three in ten women are overweight in Andaman and Nicobar Islands, Andhra Pradesh, Goa, Pondicherry and Tamil Nadu.

**1.3 Childhood Obesity:** The healthy BMI range varies with the age and sex of the child. Childhood obesity has reached epidemic proportions in the 21<sup>st</sup> century, with rising rates in both the developed and the developing world. Rates of obesity in Canadian boys have increased from 11% to over 30%, while during this same time period rates increased from 4 to 14% in Brazilian children <sup>3</sup>.

As with obesity in adults, many factors contribute to the rising rates of childhood obesity. Changing diet and decreasing physical activity are believed to be the two most important causes for the recent increase in the incidence of child obesity. Because childhood obesity often persists into adulthood and is associated with numerous chronic illnesses, children who are obese are often tested for hypertension, diabetes, hyperlipidemia, and fatty liver disease.

**1.4 Determination of Obesity Using Body Mass Index (BMI):** The most widely used method to determine obesity is Body Mass Index (BMI). In general, BMI is an inexpensive and easy-to-perform method of screening for weight category, like underweight, normal or healthy weight, overweight, and obesity. The body mass index (BMI) or Quetelet index is a value derived from the mass (weight) and height of an individual. The BMI is defined as the body mass divided by the square of the body height and is universally expressed in units of kg/m², resulting from mass in kilograms and height in meters.

BMI is calculated the same way for both adults and children based on the following formulas mentioned in **Table 1**. The standard weight status categories associated with BMI ranges for adults are shown in the following **Table 2**.

TABLE 1: FORMULAS AND CALCULATION OF BMI

Measurement Units	Formula and Calculation	
Kilograms and meters	Formula: weight (kg) / [height (m)] <sup>2</sup>	
(or centimeters)	With the metric system, the formula for BMI is weight in Kilograms divided by	
	height in meters squared.	
	Example: Weight = $68 \text{ kg}$ , Height = $165 \text{cm} (1.65 \text{m})$	
	Calculation: $68 \div (1.65)^2 = 24.98$	
Pounds and inches	Formula: weight (lb) / [height (in)] $^2 \times 703$	
	Calculate BMI by dividing weight in pounds (lbs) by height in inches (in) squared	
	and multiplying by a conversion factor of 703.	
	Example: Weight = $150 \text{ lbs}$ , Height = $5'5''$ (65")	
	Calculation: $[150 \div (65)^2] \times 703 = 24.96$	

TABLE 2: CLASSIFICATION OF OBESITY BASED ON BMI

BMI (kg/m²) from	BMI (kg/m²) up to	Classification
	18.5	Underweight
18.5	25.0	normal weight
25.0	30.0	Overweight
30.0	35.0	Class I obesity
35.5	40.0	Class II obesity
40.0		Class III obesity

BMI is interpreted differently for children and teens, even though it is calculated using the same

formula as adult BMI. Children and teen's BMI need to be age and sex-specific because the amount of body fat changes with age and the amount of body fat differs between girls and boys. Athletes may have a high BMI because of increased muscularity rather than increased body fatness. In general, a person who has a high BMI is likely to have body fatness and would be considered to be overweight or obese, but this may not apply to

athletes. A trained healthcare provider should perform appropriate health assessments in order to evaluate an individual's health status and risks.

**1.5 Risk Factors:** Obesity results in a number of potentially serious health problems, including High triglycerides and low high-density lipoprotein (HDL) cholesterol, Type 2 diabetes, High blood pressure, heart disease, stroke, cancer, including cancer of the uterus, cervix, endometrium, ovaries, breast, colon, rectum, esophagus, liver, gallbladder, pancreas, kidney and prostate, breathing disorders, including sleep apnea a potentially serious sleep disorder in which breathing repeatedly stops and starts, gallbladder disease, gynecological problems such as infertility and irregular periods, erectile dysfunction and sexual health issues, nonalcoholic fatty liver disease, a condition in which fat builds up in the liver and can cause inflammation or scarring, osteoarthritis and metabolic syndrome, a combination of high blood sugar, high blood pressure, high triglycerides and low HDL cholesterol.

**1.6 Current Interventions:** At present, lifestyle modifications, adjunct pharmacotherapy and endoscopic and surgical interventions are the mainstays of management of obesity <sup>4, 5</sup>.

1.6.1 Genetics of Obesity: Obesity results from interactions between environmental and genetic factors. Despite a relatively high heritability of common, non-syndromic obesity (40-70%), the search for genetic variants contributing to susceptibility has been a challenging task. Genomewide association (GWA) studies have dramatically changed the pace of detection of common genetic susceptibility variants. To date, more than 40 genetic variants have been associated with obesity and fat distribution. However, since these variants do not fully explain the heritability of obesity, other forms of variation, such as epigenetics marks, must be considered. Epigenetic marks, or "imprinting", affect gene expression without actually changing the DNA sequence. Failures in imprinting are known to cause extreme forms of obesity (e.g. Prader-Willi syndrome), but have also been convincingly associated with susceptibility to obesity. The first gene unequivocally associated to common, non-syndromic obesity, FTO (fat mass and obesity-associated), was initially identified as a result of a GWA.

Fat mass and obesity-associated protein also known as alpha-ketoglutarate dependent dioxygenase an enzyme that in humans is encoded by the FTO gene located on chromosome <sup>16</sup>. Certain variants of the FTO gene appear to be correlated with obesity in humans <sup>17</sup>. In 2007, an association of single nucleotide polymorphisms (SNPs) in the fat mass and obesity-associated (FTO) gene region with body mass index (BMI) and risk of obesity was identified in multiple populations, making FTO the first locus unequivocally associated with adiposity.

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At the time, FTO was a gene of unknown function and it was not known whether these SNPs exerted their effect on adiposity by affecting FTO or neighboring genes. Therefore, this breakthrough association inspired a wealth of *in-silico*, *in-vitro*, and *in-vivo* analyses in model organisms and humans to improve knowledge of FTO function. These studies suggested that FTO plays a role in controlling feeding behavior and energy expenditure.

**1.6.2 Obesity Prevention Programs and Activities:** Obesity prevention programs have been found to reduce the cost of treating obesity-related diseases. The Department of Health works with many partners and contractors to develop and implement a range of obesity prevention programs in the community, child care, school and health care settings. Some of the obesity prevention programs include:

**1.6.3** Hunger Prevention and Nutrition Assistance Program (HPNAP): HPNAP provides funding to 47 contractors and their 2,400 emergency food programs to provide nutritious food to supplement meals to that in need throughout New York State. HPNAP policies assure that healthy foods, such as fresh produce, low-fat milk and whole-grain cereals are available through eight regional food banks and 2,400 food pantries, soup kitchens and shelters supported by HPNAP.

**1.6.4 Just Say Yes to Fruits and Vegetables Project (JSY):** The JSY program is a comprehensive nutrition education and obesity prevention program. Using nutrition education workshops, food demonstrations and environmental strategies to improve access to healthier foods and

physical activity, JSY helps to ensure low-income families to eat nutritious foods make the most of their food budgets and prepare foods safely. Workshops provide practical nutrition information using USDA approved lesson plans, recipes and cooking demonstrations focusing on fruits and vegetables and low-fat ingredients.

- 1.6.5 Special Supplemental Nutrition Program for Women, Infants and Children (WIC): The Program provides supplemental food, WIC participant-centered nutrition education and counseling, breastfeeding support and linkages with health and social services for eligible low-income women and children to improve pregnancy promote optimal growth outcomes, development for infants and children, and influence lifetime nutrition and health behaviors. NYS has developed many initiatives that assist WIC participants in achieving healthier lifestyles and contribute to decreasing overweight and obesity.
- **1.6.6 Eat Well Play Hard in Child Care Settings** (EWPHCCS): The Child and Adult Care Food Program (CACFP) provides reimbursement to child care and daycare programs that serve nutritious meals and snacks to children and adults in care.
- **2. Prevention of Obesity:** Whether you're at risk of becoming obese, currently overweight or at a healthy weight, you can take steps to prevent unhealthy weight gain and related health problems. Not surprisingly, the steps to prevent weight gain are the same as the steps to lose weight: daily exercise, a healthy diet and a long-term commitment to watch what you eat and drink. The preventive measures include:
- **2.1 Exercise Regularly:** You need to get 150 to 300 minutes of moderate-intensity activity a week to prevent weight gain. Moderately intense physical activities include fast walking and swimming.
- **2.2 Follow a Healthy Eating Plan:** Focus on low-calorie, nutrient-dense foods, such as fruits, vegetables, and whole grains. Avoid saturated fat and limit sweets and alcohol. Eat three regular meals a day with limited snacking. You can still enjoy small amounts of high-fat, high-calorie foods as an infrequent treat. Just be sure to choose foods that promote a healthy weight and good health most of the time.

2.3 Know and Avoid the Food Traps that Cause You to Eat: Identify situations that trigger out-of-control eating. Try keeping a journal and write down what you eat, how much you eat, when you eat, how you're feeling and how hungry you are. After a while, you should see patterns emerge. You can plan and develop strategies for handling these types of situations and stay in control of your eating behaviors.

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- **2.4 Monitor Your Weight Regularly:** People who weigh themselves at least once a week are more successful in keeping off excess pounds. Monitoring your weight can tell you whether your efforts are working and can help you detect small weight gains before they become big problems.
- **3. Anti-Obesity Medication:** Anti-obesity medication or weight loss 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 either appetite or absorption of calories.

Anti-obesity medications in current use can be categorized as:

# 3.1. Centrally Acting Appetite Suppressants:

- **3.1.1 Sibutramine:** Sibutramine is a monoamine reuptake inhibitor (MRI) that, in humans, reduces the reuptake of norepinephrine (by ~73%), serotonin (by ~54%), and dopamine (by ~16%)6, thereby increasing the levels of these substances in synaptic clefts and helping enhance satiety; the serotonergic action, in particular, is thought to influence appetite. Despite having a mechanism of tricyclic similar action to antidepressants, sibutramine failed demonstrate has to antidepressant properties in animal studies. It was approved by the U.S. Food and Drug Administration (FDA) in November 1997 <sup>6</sup> for the treatment of obesity. It has been associated with increased cardiovascular events and strokes and has been withdrawn from the market in several countries. However, the drug remains available in some countries.
- **3.1.2 Lorcaserin:** Lorcaserin is used long term for weight loss in those who are obese along with other co-morbidities. It reduces appetite by activating serotonin 5-HT2C receptor in a region of the brain called the hypothalamus, which is known to control

appetite through the feeling of satiety <sup>7</sup>. 5-HT2C receptors are located in the brain and can be found in the choroid plexus, cortex, hippocampus, cerebellum, amygdala, thalamus, and hypothalamus.

The activation of 5-HT<sub>2C</sub> receptors in the hypothalamus is supposed to activate (POMC) proopiomelanocortin production and consequently promote weight loss through satiety.

The US Drug Enforcement Administration classified lorcaserin as a Schedule IV drug under the Controlled Substances Act. There has been concern that lorcaserin can cause cardiac valvulopathy based upon the reports of subjects taking the drug in phase 2 trials.

**3.1.3 Orlistat:** Orlistat primary function is preventing the absorption of fats from the human diet by acting as a lipase inhibitor, thereby reducing caloric intake. Orlistat works by inhibiting gastric and pancreatic lipases, the enzymes that break down triglycerides in the intestine. When lipase activity is blocked, triglycerides from the diet are not hydrolyzed into absorbable free fatty acids, and instead are excreted unchanged. Only trace amounts of orlistat are absorbed systemically; the primary effect is local lipase inhibition within the GI tract after an oral dose. The primary route of elimination is through the feces.

Pooled data from clinical trials suggest that people given orlistat lose about 2–3 kilograms (4.4–6.6 lb) more than those not taking the drug over the course of a year. At the standard prescription dose of 120 mg three times daily before meals, or listat prevents approximately 30% of dietary fat from being absorbed. Orlistat also modestly reduces blood pressure and appears to prevent the onset of type 2 diabetes. The primary side effects of the drug are gastrointestinal related and include steatorrhea (oily, loose stools with excessive flatus due to unabsorbed fats reaching the large intestine), fecal incontinence and frequent or urgent bowel movements. Long-term effects include a higher of breast colon incidence cancer and carcinogenesis.

3.1.4 Biguanides - Metformin: In people with Diabetes mellitus type 2, the drug metformin (Glucophage) can reduce weight. Metformin limits the amount of glucose that is produced by the liver as well as increases muscle consumption of glucose. It also helps in increasing the body's response to insulin 8.

- 3.1.5 GLP-1 Analogues: Exenatide is a longacting analog of the hormone GLP-1 (glucagon-like peptide-1), in which the intestines secrete in response to the presence of food. GLP-1 delays gastric emptying and promotes a feeling of satiety. It is currently available as a treatment for obesity in Diabetes mellitus type 2. Some, but not all patients find that they lose substantial weight when taking exenatide. Drawbacks include that it must be injected subcutaneously twice daily and that it causes severe nausea in some patients.
  - ✓ Liraglutide (Saxenda) is another GLP-1 analog for daily administration.
  - ✓ Semaglutide (Ozempic) is yet another GLP-1 analog, more effective and approved once weekly.

# 3.1.6 Amylin Analogue:

**Pramlintide:** Pramlintide is a synthetic soluble form of the naturally occurring hormone, amylin, which is co-secreted with insulin from the  $\beta$ -cell. In synergy with endogenous amylin, pramlintide aids in the regulation of blood glucose by slowing promoting gastric emptying, satiety hypothalamic receptors (different receptors than for GLP-1), and inhibiting the inappropriate secretion of glucagon, a catabolic hormone that opposes the effects of insulin and amylin. Both a reduction in glycated hemoglobin and weight loss has been shown in insulin-treated patients with type 2 diabetes taking pramlintide as an adjunctive therapy <sup>9</sup>. Pramlintide induces modest weight loss through the control of appetite centers in the brain. Pramlintide is currently only approved for use in conjunction with insulin in patients with type 1 or type 2 diabetes.

3.1.7 Phentermine and **Topiramate:** The combination of phentermine and topiramate is used for obesity treatment. Phentermine and topiramate is associated with modest weight loss when placebo. Phentermine is a compared with sympathomimetic amine that acts as an appetite suppressant and stimulant. Topiramate is an anticonvulsant that has weight loss side effects. The European Medicines Agency, by contrast, rejected the combination as a treatment for obesity, citing

concerns about long-term effects on the heart and blood vessels, mental health and cognitive side-effects. In clinical trials, people treated with the highest dose of phentermine/topiramate combination with a program of diet and exercise lost 10% to 11% of their body weight compared to 1% to 2% for those who received a placebo. In clinical trials, the most common adverse events which occurred at a rate  $\geq$ 5% and  $\geq$ 1.5 times placebo included paraesthesia (tingling in fingers/toes), dizziness, dysgeusia (altered taste), insomnia, constipation and dry mouth.

3.1.8 Bupropion and Naltrexone: Bupropion/ naltrexone is a combination drug used for weight loss in those that are either obese or overweight with some weight-related illnesses. It combines low doses of bupropion and naltrexone. Both drugs have individually shown some evidence of effectiveness in weight loss, and the combination has been shown to have some synergistic effects on weight. In September 2014, a sustained release formulation of the drug was approved for marketing in the United States under the brand name Contrave. The combination was subsequently approved in the European Union in the spring of 2015, where it will be sold under the name Mysimba. It was approved in Canada under the Contrave brand name in 2018.

Individually, bupropion and naltrexone each target pathways in the central nervous system that influence appetite and energy use. Bupropion is a reuptake inhibitor and it activates proopiomelanocortin (POMC) neurons in the hypothalamus which results in loss of appetite and increased energy output. Naltrexone, by contrast, is a pure opioid antagonist, therefore further augmenting bupropion's activation of the POMC. The FDA has put a boxed warning onto this medicine because it may affect mood and increase the likelihood of suicide.

**3.1.9 Other Drugs:** Tesofensine is a serotonin noradrenaline dopamine reuptake inhibitor from the phenyltropane family of drugs, which is being developed for the treatment of obesity <sup>10</sup>. Tesofensine has been evaluated in Phase 1 and Phase 2 human clinical studies with the aim of investigating treatment potential with regards to obesity.

Pyruvate, which is found in red apples, cheese, and red wine, is sometimes marketed as a weight-loss supplement but has not been thoroughly studied and its weight loss effect has not been demonstrated <sup>11</sup>.

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**Diuretics:** Diuretics cause loss of fluids that may result in gradual weight reduction. Diuretics cause temporary weight loss with no loss in body fat. Their use should be avoided due to the serious side effect of electrolyte imbalance.

Surgical Treatment for Obesity: Bariatric or Weight Loss Surgery (WLS) was previously categorized as malabsorptive, restrictive, or a combination of both. However, with a greater understanding of the extensive neural-hormonal effects of WLS on satiety, hunger and metabolism, the above mentioned broad categories are no longer appropriate. In fact, today Bariatric or WLS is perhaps better referred to as Metabolic Surgery. The most common metabolic surgical procedures include Roux-en-Y gastric bypass, adjustable gastric band, sleeve gastrectomy biliopancreatic diversion.

- **4. Natural Remedies for Obesity:** The potential of natural products for treating obesity is under exploration. This may be an excellent alternative strategy for developing future effective, safe antiobesity drugs <sup>12</sup>. A variety of natural products, including crude extracts and isolated pure natural compounds can induce bodyweight reduction and prevent diet-induced obesity. Therefore, they have been widely used in treating obesity <sup>13</sup>. They include:
- **4.1 Dietary Phytochemicals:** Dietary phytochemicals might be employed as anti-obesity agents because they may suppress the growth of the adipose tissue, inhibit differentiation of preadipocytes, stimulate lipolysis, and induce apoptosis of existing adipocytes, thereby reducing adipose tissue mass.

Examples: Curcumins, Flavonoids (e.g. quercetin).

**4.2 Natural Products with Lipase Inhibitory Effect:** Dietary fat is absorbed by the intestine when it has been subjected to the action of pancreatic lipases. Pancreatic lipase is a key enzyme in dietary triacylglycerol absorption,

hydrolyzing triacylglycerols to monoacylglycerols and fatty acids. Natural products provide a vast pool of pancreatic lipase inhibitors. A wide variety of plant products such as saponins, polyphenols, flavonoids, and caffeine possess lipase inhibitory effects <sup>14</sup>.

Different types of tea (*e.g.*, green, oolong, and black tea) are among the most widely-studied materials for lipase inhibitors. Various polyphenols isolated from tea leaves showed strong inhibitory activity against pancreatic lipase. Several carbohydrates also possess pancreatic lipase inhibitory effects, for example, chitin/chitosan.

**4.3 Natural Appetite Suppressants:** Appetite suppressants control hunger centers in the brain, resulting in a sense of fullness. However, ghrelin secretion in the stomach may increase with decreased food intake, stimulating more food intake. Therefore, ghrelin antagonism may decrease the appetite that potentially occurs with decreased feeding, thus, maybe a potential adjunctive treatment for obesity.

Example: Natural hydroxyl citric acid (HCA) from *Garcinia cambogia* is a potential natural appetite suppressant. It is available under the name CitriMax.

**4.4 Natural Energy Expenditure Stimulants:** To regulate body weight and energy expenditure, mammalian brown adipose tissue (BAT) establishes non-shivering thermogenesis through dissipation of excess energy as heat.

BAT plays an important role in obesity control by controlling energy balance through UCP1 (Uncoupling protein). UCP1 is responsible for oxidative phosphorylation. Thus, searching for substances that up-regulate UCP1 gene expression may be a worthy strategy for achieving obesity control through increased energy expenditure <sup>15</sup>. B. Cannon, J. For example, the ethanolic extract of *Solanum tuberosum* activated the expression of UCP in BAT and the liver, and significantly reduced fat weight.

**4.5 Natural Adipocyte Differentiation Inhibitors** (**Decreased Lipogenesis**): Adipocytes play a central role in the maintenance of lipid homeostasis and energy balance by storing triglycerides and

releasing free fatty acids in response to change in energy demands <sup>16</sup>. Natural products that specifically target adipogenesis inhibition had been considered promising potentials in obesity treatment. Several natural products have apoptotic effects on maturing pre-adipocytes. *e.g.* esculetin, resveratrol, quercetin, capsaicin.

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- 4.6 Natural Lipid Metabolism Regulators (Increased Lipolysis): The pharmacological targeting of lipolysis can be achieved by stimulating triglyceride hydrolysis in order to diminish fat stores, thereby combating obesity. The flavonoids from *Nelumbo nucifera* leaves are examples of the natural products involved in  $\beta$ -adrenergic receptor activation<sup>17</sup>.
- **4.7 Natural Products with Combined Effect:** As mentioned above, many natural products show antiobesity activities with varying mechanisms. Perhaps the recommended approach to search for more efficient obesity treatments and achieving the synergistic effects of natural products should seek treatments using multiple products or products that have multiple activities <sup>18</sup>.
- **4.8 Enzymatic Treatment of Obesity:** Eating a whole fresh pineapple (*Ananas comosus*, *A. sativus*) per day can decrease the body weight by 100 pounds on a pineapple regimen. Its content of bromelain enzyme helps to digest both proteins and fats <sup>19</sup>.
- **4.9 Bulk Producers:** Many herbs and natural products are significant in the treatment of obesity through a bulk-producing activity that produces a sense of fullness, thereby reducing appetite <sup>20</sup>.
- **4.10 Stimulant Laxative (anthraquinones):** Some herbal preparations used in obesity include anthraquinones containing plants such as senna (Cassia species), cascara (Rhamnus species), rhubarb (*Rheum palmatum*) and aloe (*Aloe vera*, *A. ferox*). The laxative effect of anthraquinones leads to rapid excretion of foods and water loss which can aid in weight reduction <sup>21</sup>.
- **4.11 Non-Calorie Sweeteners:** Sucrose substituent (*e.g.* saccharin, aspartame) may allow significant calorie reduction in certain patients. There are a number of additional low-calorie sweeteners waiting for approval for use in foods and beverages as:

- 1. Neohesperidin dihydrochalcone derived from bioflavonoids of citrus fruits. Currently, neohesperidin-DHC synthesized from Seville oranges has been found to have great potential in food applications.
- **2.** Naringin isolated from grapefruit (*Citrus paradisi*) is converted to naringin dihydro chalcone which is 1000 times sweeter than sucrose and is used to reduce body weight <sup>22</sup>.
- 4.12 Marine Natural Products: Astaxanthin, a xanthophyll carotenoid, isolated the marine algae Haematococcus pluvialis, Chlorella zofingiensis, and Chlorococcum sp was found to inhibit the increase in body weight and weight of the adipose whereas reduce liver weight, tissue. triglyceride, plasma triglyceride, and total cholesterol. Krill oil is extracted from Antarctic krill, Euphausia superba, a zooplankton crustacean rich in phospholipids. Additionally, Krill oil also contains various potent antioxidants, including vitamins A and E and astaxanthin. It has been reported that krill oil could reduce the level of glucose, total cholesterol, triglycerides, LDL and HDL with no indication of adverse effects on safety parameters <sup>23</sup>.

## 5. Suggestions and Recommendations:

- **A.** Be active, walk for 30 min a day especially before breakfast to burn off fat. Exercise is the best way to get rid of excess body fat and to maintain good muscle tone.
- **B.** Check with the doctor, underactive thyroid can cause obesity to be a problem.
- **C.** Rotate foods and eat a variety of foods, asks the dietitian to regulate your food intake and drink 6–8 glasses of liquids every day.
- **D.** Cut down on salt, it makes you thirsty and causes retention of water.
- **E.** Make sure bowels are regular. Use extra fibers in the diet every day. Put less food on your plate. Chew slowly.
- **F.** Do not chew gum, because it starts the gastric digestive juices flowing and will make you feel hungry sooner, in addition to overworking your digestive system.

**G.** Never consume animal fats; butter, cream, ice cream, whole milk, rich dressing, mayonnaise and fried foods.

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- **H.** Do not eliminate sources of good fat, containing unsaturated fatty acids, such as avocados, olive oil and nuts.
- I. Avoid white flour products, salt, white rice, or processed foods. Eat complex carbohydrates that offer protein: lentils, plain baked potatoes, sesame seeds, beans, brown rice, and whole grains.
- **J.** Eat fresh fruits and raw vegetables (good fiber sources). At least one meal a day should be only fruits and vegetables.
- **K.** Make lunch the main meal of the day, no later than 3 PM to give the body time to burn some calories before bedtime <sup>24, 25</sup>.

**CONCLUSION:** Obesity is a continuing issue around the world and in many contexts. The growing number of obese people is an increasing concern for those in the medical profession, and obesity can pose specific challenges in relation to fertility and pregnancy. Patients who are obese require specific considerations and knowledge. The current recommendations for the treatment of obese people include increased physical activity and reduced calorie intake. When the behavioral approach is not sufficient, pharmacologic treatment is recommended. Numerous drugs have been withdrawn from the market because of their adverse effects. Orlistat is presently the most widely used medication to treat obesity because of its safety margin for cardiovascular events and positive effects on diabetic control. The potential of natural products for treating obesity is under exploration. This may be an excellent alternative strategy for developing future effective, safe antiobesity drugs. Hopefully, more effective and better tolerated anti-obesity drugs will be developed through an improved understanding of the multiple mechanisms and complex physiological systems targeting appetite.

Obesity is thus a choice. Everyone must be aware of the health consequences of being obese and must follow a healthy diet schedule to prevent the onset of the disease. Thus, proper preventive measures

and medication can help in reducing the extent of the spread of the disease worldwide.

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#### **REFERENCES:**

- 1. Rao BB and Junapudi SS: A comparative study of prevalence of overweight and obesity among urban, and rural population of South India. International Journal of Community and Public Health 2019; 6(3).
- 2. Hruby A and Hu FB: The Epidemiology of Obesity: A Big Picture. Pharmacoeconomics 2015; 33(7): 673-89.
- Flynn MA, McNeil DA, Maloff B, Mutasingwa D, Wu M and Ford C: Reducing obesity and related chronic disease risk in children and youth: a synthesis of evidence with 'best practice' recommendations. Obesity Reviews 2006; 7.
- Genco A, Bruni T and Doldi SB: BioEnterics intragastric balloon: the Italian experience with 2,515 patients. Obes Surg 2005; 15: 1161-4.
- Schouten R, Rijs CS and Bouvy ND: A multicenter, randomized efficacy study of the endo barrier gastrointestinal liner for presurgical weight loss prior to bariatric surgery. Ann Surg 2010; 251: 236-43.
- 6. Hillhouse TM and Porter JH: A brief history of the development of antidepressant drugs: From monoamines to glutamate. Exp Clin Psychopharmacol 2015; 23(1): 1-21
- 7. Shukla AP, Kumar RB and Aronne LJ: "Lorcaserin HCl for the treatment of obesity". Expert Opinion on Pharmacotherapy 2015; 16(16): 2531-8.
- 8. Nasri H and Rafieian-Kopaei M: Metformin: Current knowledge. J Res Med Sci 2014; 19(7): 658-64.
- 9. Priscilla H, David GM, James AR, Mark F, Larry S, Orville GK and Christian W: Effect of pramlintide on weight in overweight and obese insulin-treated type 2 diabetes patients. Obesity 2004; 12(4): 661-68.
- Doggrell SA: Tesofensine-a novel potent weight loss medicine. Evaluation of: Effect of tesofensine on bodyweight loss, body composition, and quality of life in obese patients: a randomised, double-blind, placebocontrolled trial. Expert Opin Investig Drugs 2009; 18(7): 1043-6.

11. Bray GA and Greenway FL: Current and potential drugs for treatment of obesity: postabsorptive modifiers of nutrient metabolism. Endocrine Reviews 1999; 20.

E-ISSN: 0975-8232; P-ISSN: 2320-5148

- 12. Mayer MA, Hocht C, Puyo A and Taira CA: Recent advances in obesity pharmacotherapy. Curr Clin Pharmacol 2009; 4.
- 13. Han LK, Kimura Y and Okuda H: Anti-obesity effects of natural products. Stud Nat Prod Chem 2005; 30: 79-110.
- Takao I, Fujii S, Ishii A, Han LK and Kumao T: Effects of manno oligosaccharides from coffee mannan on fat storage in mice fed a high fat diet, J Health Sci 2006; 52: 333-37.
- Cannon B and Nedergaard J: Brown adipose tissue: function and physiological significance. Physiol Rev 2004; 84: 277-59.
- Madsen L, Petersen RK and Kristiansen K: Regulation of adipocyte differentiation and function by polyunsaturated fatty acids. Biochim Biophys Acta 2005; 1740(2): 266-86.
- 17. Ohkoshi E, Miyazaki H, Shindo K, Watanabe H and Yoshida A: Constituents from the leaves of *Nelumbo nucifera* stimulate lipolysis in the white adipose tissue of mice. Planta Med 2007; 73: 1255-59.
- 18. Rayalam S, Della-Fera MA and Baile CA: Phytochemicals and regulation of the adipocyte life cycle. J Nutr Biochem 2008; 19: 717-26.
- 19. Mohamed GA, Ibrahim SRM, Elkhayat ES and El-Dine RS: Natural anti-obesity agents. Bulletin of Faculty of Pharmacy, Cairo University 2014; 52(2): 269-84.
- Rock CL, Flatt SW, Sherwood NE, Karanja N and Pakiz B: Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. JAMA 2010; 304: 1803-10.
- 21. Frati-Munari A, Fernandez J, Becerril M, Chavez A and Banles M: Decrease in serum lipids, glycemia and body weight by *Plantago psyllium* in obese and diabetic patients. Arch Invest 1983; 14: 259-68.
- Panigrahi T, Vishwas S and Dash D: A herbal approach to obesity management: a review. Asian Journal of Pharmaceutical Education and Research 2017; 6(3): 1-15.
- 23. Bunea R, El-Farrah K and Deutsch L: Evaluation of the effects of neptune krill oil on the clinical course of Hyperlipidemia. Altern Med Rev 2004; 9: 420-28.
- 24. Loos RJ and Yeo GS: The bigger picture of FTO: the first GWAS-identified obesity gene. Nature Reviews. Endocrinology 2014; 10(1): 51-61.
- 25. Dedov II, Melnichenko GA, Troshina EA, Mazurina NV and Galieva MO: Body weight reduction associated with the sibutramine treatment: overall results of the PRIMAVERA primary health care trial. Obesity facts 2018; 11(4): 335-43.

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