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COMPARATIVE STUDY ON NATURAL AND SYNTHETIC WEIGHT LOSING AGENTS

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ABSTRACT

Weight management is a time consuming process. Therefore it is important to find out a safe and effective way to reduce body weight of obese persons. For this purpose studies focusing on the components of the anti-obesity category are very important. Recent researches demonstrated the potential of natural and synthetic products to reduce body weight. Multiple natural products have safe results than synthetic products. In this review, we discussed the both natural and synthetic products with their effects and adverse effects.

1. Introduction:-

In 1997, the world health organization (WHO) described obesity as an epidemic hazard worldwide, based on the data analysis of body mass index (BMI). Since then, obesity incidence and increased at an alarming rate and it's becoming a major public health concern. Indeed, obesity facilitate the development of metabolic disorders (e.g. diabetes, hypertension), and cardiovascular diseases in addition to chronic diseases (e.g. stroke, osteoarthritis, sleep apnea, cancers and inflammation-based pathologies).^{1,15}

Obesity has been increasing rapidly in recent years and now has become a public health problem in the world. It not only affect the body image and self-esteem but also it is associated with increased risk for numerous chronic diseases therefore it is important to find a safe and effective way to manage body weight especially in obese patient.²

The fundamental treatment is calorie restricted diet and exercise. Many other alternative methods for losing weight has been suggested which of them are very popular among consumers. For example , pharmacological agents, medicinal herbal supplements, dietary supplements, botanicals, hypnotherapy, homeopathy, surgery, low laser therapy, high intensity focused ultrasound, radiofrequency, non-invasive body contouring and acupuncture. Among all these people are eager to use methods that are cost-effective and with no side effect. Many people have come to this point and also recent studies have confirmed that preliminary reports suggested that natural products and herbal products are very effective in reducing appetite and helping lose weight. Thus, the objective of this review was to assemble review related to the study of natural and synthetic weight losing agents.

2. Definition:-

The word obesity is derived from Latin word 'obesitas' which means stout or fat or plump. Medically, obesity is a condition in which excess body fat has accumulated to the extent that it may have an adverse effect on health, leading to reduced life expectancy and increased health problems.^{1,16}

3. How to assess obesity:-

3.1. Body mass index:

Body mass index is a measurement which relates to weight and height: $BMI = \text{Mass (kg)} / [\text{Height (m)}^2]$.¹

3.2. Waist circumference (WC) and Waist to Hip Ratio (WHR):

WHR is used as a measurement of obesity, which in turn is possible indicator of other more serious health conditions. $WHR = \text{Waist circumference} / \text{Hip circumference}$.¹

4. Causes of obesity:-

The combination of excessive food intake and lack of physical activity leads to obesity. In limited cases, it is due to genetic factors, medical reasons, or psychiatric illness. On the other hand, it is due to easily accessible and palatable diet, increased reliance on cars, and mechanized manufacturing. Other causes include insufficient sleep, endocrine disruptors, decreased variability in ambient temperature, decreased rates of smoking, as smoking suppresses appetite, increased use of medications that can cause weight gain (e.g., atypical anti-psychotics), proportional increases in ethnic and age groups that tend to be heavier, pregnancy at a later age (which may cause susceptibility to obesity in children), epigenetic risk factors passed on generationally, natural selection for higher BMI, and assortative mating leading to increased concentration of obesity risk factors.¹

5. Treatment of obesity:-

5.1. Natural products:

The potential of natural products for treating obesity is under exploration. This may be an excellent alternative strategy for developing future effective, safe anti-obesity drugs. A variety of natural products, including crude drug extracts and isolated pure natural compounds can induce body weight reduction and prevent diet-induced obesity. Therefore, they have been widely used in treating obesity.¹

5.1.1. Natural products with lipase inhibitory effect:

Dietary fat is absorbed by the intestine when it has been subjected to the action of pancreatic lipases. Few substances directly interact with lipases as orlistat. It is a derivative of the naturally occurring lipase inhibitor from *Streptomyces toxytricini*. Orlistat is clinically approved for obesity treatment, though it has certain unpleasant gastrointestinal side effects. A variety of plant products such as saponins, polyphenols, flavonoids and caffeine possess lipase inhibitory effects. Some carbohydrates also possess pancreatic lipase inhibitory effects, for example chitin/chitosan.^{1,2,11,17}

5.1.2. Natural appetite suppressants:

A line of evidence indicates that serotonin, histamine, dopamine, and their associated receptor activities are closely related to satiety regulation. They alter the key CNS appetite monoamine neurotransmitter levels and may be suitable candidates for appetite suppressants. Appetite suppressants control the hunger centers in brain, resulting in a sense of fullness. An example of natural appetite suppressant is *Hoodia gordonii*. It regulates appetite and significantly reduces calorie intake and boosts weight loss. Natural (-)-hydroxycitric acid (HCA) from *Garcinia cambogia*, is a potential natural appetite suppressant.^{1,2,18}

5.1.3. Natural energy expenditure stimulants:

Excessive adiposity results from energy imbalance, where the consequences of excessive food intake are not balanced by increasing energy expenditure. To regulate body weight and energy expenditure, mammalian brown adipose tissue (BAT) establishes non shivering thermo genesis through UCP1 (Uncoupling protein). Many natural compounds are have been used as treatment for obesity via enhanced energy expenditure including caffeine, capsaicin, and green tea and its extract.^{1,2,3,19}

5.1.4. Natural adipocyte differentiation inhibitors:

Adipocytes play a important 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. Several natural products have apoptotic effects on maturing pre-Adipocytes. Examples of some natural products with adipocyte differentiation inhibitory effect are *Garcinia cambogia*, *Camellia sinensis*, *Panax ginseng*, *Glycine max*, Capsicum, Fish oil, Palm oil, Garlic, Sterol.^{1,2,20}

5.1.5. Natural lipid metabolism:

The pharmacological targeting of lipolysis can be achieved by stimulating triglyceride hydrolysis in order to diminish fast stores, thereby combating obesity. The flavonoids from *Nelumbonucifera* leaves are examples of the natural products involved in beta-adrenergic receptor activation. Examples are Soybean, *Coffeacaneophora*, *Curcuma longa*.^{1,7}

5.2. Synthetic products:**5.2.1 Phentermine:**

Phentermine is one of the centrally acting appetite-suppressant drugs of the beta-phenethylamine family, which was approved for short term use in the treatment of obesity by the U.S. FDA in 1959 and remains available today. Phentermine had been used in combination with fenfluramine. However, fenfluramine was withdrawn from the market by the U.S. FDA in 1997. A preliminary report identified heart valve damage and pulmonary arterial hypertension in association with the use of fenfluramine. Nowadays phentermine is currently under evaluation in combination with topiramate.⁸

5.2.2 Sibutramine:

Sibutramine is a selective noradrenaline/ serotonin reuptake inhibitors was widely used after approval by the U.S. FDA in 1997. Sibutramine led to a 4.5% body weight loss for long term treatment and also showed benefits by improving cardio metabolic factors including plasma glucose, insulin and lipid. It was relatively well tolerated because common side effects included only constipation, headache, dry mouth and insomnia. The U.S. FDA requested healthcare

professionals be notified Sibutramine should not be used in patients with known cardiovascular disease. Long term sibutramine treatment was shown to increase the risk of nonfatal myocardial infarction and nonfatal stroke.⁸

5.2.3. Metformin:

Metformin is widely recognized by endocrinologist and diabetologist as a weight reducing agent in clinical practice. Even in recently published reviews on anti-obesity drugs metformin is not mentioned. Metformin is administered to obese patients in high enough doses it is a beneficial and cost effective drug to reduce weight. The effectiveness of metformin as a weight reducing agent is not restricted to insulin resistant patients although a greater weight loss can be expected if patients exhibit biochemical signs of insulin resistance prior to metformin treatment.⁹

5 2.4. L-Carnitine:

Positive influence of carnitine on weight loss was found in chronic conditions such as diabetes and obesity. Evidence about pharmacotherapy of obesity have addressed the long term use of orlistat, sibutramine and phentermine on weight loss in people. Although carnitine has a lower magnitude of weight loss than these drugs, unlike them, it does not suffer from some side effects such as gastrointestinal issues, rising blood pressure, and pulse rate and increased risk if psychological disorder. It might be an effective drug for weight loss in adults.¹⁰

6. Salient features for an ideal product for the management of obesity:-

- 1) Should bring down the body weight by 10% over placebo in a well designed randomized placebo controlled clinical trial.⁴
- 2) Should show evidence of improvement of bio markers like blood pressure, lipids, glycemia.⁴
- 3) Should have known mechanism of action.⁴
- 4) Should be standardized with bioactive phytochemicals which are responsible for anti obesity activity.⁴
- 5) Should not have any kind of side effects.⁴

7. Suggestions and recommendations:-

- a) Be active, walk for 30 min a day especially before breakfast to burn off fat.¹
- b) Check with the doctor, underactive thyroid can cause obesity to a problem.¹
- c) Rotate foods and eat a variety of foods, ask dietitian to regulate your food intake and drink 6-8 glasses of liquids every day.¹
- d) Cut down on salt, it makes you thirsty and causes retention of water.¹
- e) Make sure bowels are regular. Use extra fiber in the diet every day. Put less food in you plate. Chew slowly.¹

8. Conclusion:-

The use of allopathic and pharmacological drugs has become a popular means to overcome excess weight gain. While these drugs generally are effective, severe adverse toxicities may limit their overall usefulness. Natural products are being extensively utilized due to their effectiveness in managing obesity. They are cost-effective, exert less to no toxic side-effects in comparison with synthetic products.

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