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ABSTRACT

The main target of this study was investigate the effect of feeding obese rats with different portions of (protein and fat) in enhancing the effect of some (drugs and herbs) used in weight loss. Male albino rats (96 rats) weighing (200 ± 5 g) fed on basal diet for one week for adaptation. Then, the rats were divided into two main groups : *The first main group (6 rats)* fed on basal diet (as a control negative group). While, *The second main group (90 rat)* was fed 6 week on high fat diet HFD to induce obesity. *The second main group* divided into fifteen subgroups (n = 6 each). ***Subgroup 1:*** fed on high fat and low protein diet (20% fat and 10% protein) as a positive control . ***Subgroups: 2, 3, 4and*** 5 fed on the same diet and treated daily with 5 mg Orlistat, 5 mg chitosan, 5 mg neopuntia and 5 ml jamu tea/ rat, respectively. ***Subgroup 6:*** fed on low fat and high protein diet (10% fat and 20% protein) as a positive control. ***Subgroups: 7, 8, 9 and 10*** fed on the same diet and treated daily with 5 mg Orlistat, 5 mg chitosan, 5 mg neopuntia and 5 ml jamu tea/ rat, respectively. ***Subgroup 11:*** fed on high fat and high protein diet (20% fat and 20% protein) as a positive control. ***Subgroups: 12, 13, 14 and 15*** fed on the same diet and treated daily with 5 mg Orlistat, 5 mg chitosan, 5 mg neopuntia and 5 ml jamu tea/ rat, respectively.

Feeding obese rats on a diet containing different portions of protein and fat induced significant increase in the % of (liver, kidney, heart and spleen) weights/body weights , also increased lipid fractions, kidney functions, liver enzymes, thyroid

hormones, as compared to the negative control group. The highest increase in these organs and parameters recorded for the obese groups fed on diet containing (10% protein & 20% fat). On the other hand, feeding obese groups on a diets containing the different portions of (protein & fat) and treated with (5 mg orlistat/ rat), (5 mg chitosan / rat), (5 mg neopuntia / rat) or (5 ml jamu tea / rat) decreased the percent of (liver, kidney, heart and spleen) weights/body weights and improved the above parameters, as compared to the positive control groups, especially, treated obese rats (5 mg orlistat/ rat), (5 mg chitosan / rat).

Key words: obese rats, weight loss, protein, fat, Orlistat, chitosan, neopuntia, jamu tea, lipid fractions, kidney functions, liver enzymes, thyroid hormones.

Introduction

Obesity is becoming increasingly common and is recognized as a major public health problem worldwide **(Toplak et al., 2005).**

Obesity is an important public health problem associated with multiple chronic health conditions including heart disease, hypertension, hyperlipidemia, diabetes, hyperinsulinemia, and cancer. Recommendations for treatment of adults who are overweight or obese focus on energy balance with lifestyle modifications designed to reduce daily energy intake and increase physical activity **(National Heart, Lung and Blood Institute, 1998).**

Dietary fat is considered to be one of the important environmental factors contributing to the obesity **(Peters, 2003)**.

Fat content is one of the main factors influencing the energy density of diets and an increase in energy density was shown to result in excess intake of calories; passive over consumption in humans in turn promotes the development of obesity **(Westerterp-Plantenga, 2004).**

Obesity is a major health concern because it is implicated in the development of many chronic diseases. Strategies

recommended for weight control are the adoption of low-fat dietary patterns, which facilitate energy restriction and cardiovascular disease risk reduction. However, studies of the role of a high dietary ratio of protein to carbohydrate in enhancing weight loss and disease risk management have emerged along with an increasing public interest in weight control. From an epidemiologic perspective, a positive health benefit from a high protein intake was observed in the Nurses' Health Study, which found a 26% lower rate of cardiovascular disease in those women in the highest protein intake group than in those in the lowest protein intake group **(Hu et al., 1999).**

Clinical intervention studies have provided sound evidence that an ad libitum high-protein diet from mixed sources in free-living overweight people increases the amount of weight lost in a 6-month weight-loss program (by 3.8 kg), compared with a high-carbohydrate diet by enhancing satiety **(Skov et al., 1999).**

Furthermore, weight-loss studies in overweight women have shown that diets with a high ratio of protein to carbohydrate have positive effects on markers of disease risk, including body composition, blood lipids, and glucose homeostasis, and that these benefits may be mediated partly by the effect of protein on satiety and by a lower glycemic load because of a lower carbohydrate intake **(Layman et al., 2003 [a,b]).**

A higher protein intake during weight loss may also prevent some of the inevitable loss of lean body mass and, thus, may enhance insulin sensitivity (**Baba et al., 1999)**.

Manny et al., (2005) reported that, energy-restricted, high-protein, low-fat diet in obese women provides nutritional and metabolic benefits that are equal to and sometimes greater than those observed with a high-carbohydrate diet.

Today, numerous drugs and herbs are used in treating obesity such as, when administered with a meal, orlistat acts locally in the gastrointestinal tract because its systemic absorption is negligible**.** The drug therefore acts specifically on digestive lipases in vivo, although it can inhibit other human lipases such as lipoprotein lipase and hormone-sensitive lipase in vitro **(Smith et al., 1996 and Zhi et al., 1995)**.

The Food and Drug Administration has approved orlistat, a new drug to treat obesity. Orlistat is the first drug in a new class of non-systemically acting anti-obesity drugs known as lipase inhibitors **(FDA,1999)**.

Orlistat acts as an inhibitor of pancreatic, gastric, and carboxyl ester lipase, consequently results in both a decreased absorption of fat and the emission of unabsorbed cholesterol and triglycerides **(Pi-Sunyer, 1996)**.

Orlistat is a new inhibitor of pancreatic lipase enzyme. At doses of 120 mg three times per day with meals, it results in a 30% reduction in dietary fat absorption, which equals approximately 200 kcal daily energy deficit **(Matti, 2000).**

Chitocal (Chitosan) is an extraordinary fat binder and carbohydrate bluster. It is an amino polysaccharide that has the ability to bind the lipid in the intestine so it reduces the absorption of fat, in return it reduces the blood lipid profile and prevents obesity and heart diseases **(Keiji et al ., 1994)**. Under optimal conditions, chitosan can bind an average of 8 to 12 times its weight with all the lipid aggregates tested **(Nauss et al., 1993)**.

Neopuntia is a natural fiber made from dehydrated leaves of a cactus (*Opuntia ficus indica*) . NeOpuntia is a complex of insoluble dietary fibers " Neofibers " and soluble polysaccharide dietary fibers " Neomicel " **(Stintzing and Carle, 2005)**.

An experiment test using 2 grams of NeOpuntia prevented the absorption of 2.7grams of fatty acids during the 4 hours of experiment. The percentage bound to the NeOpuntia was similar for each individual fatty acid (72 ±7%), this indicates that the binding is not selective for specific fatty acids **(Smeets-Peeters and Minekus , 2001)**.

Jamu Tea is extracted from plant essence taken from roots, foliage, barks and other ingredients that contain vitamins and minerals which have traditionally been used in the Far East for centuries and have been passed on through generations. The ingredients of Jamu tea is from, folium extract (80%), parameriae extract (6%), guazumae extract (6%), Foeniculum vulgars (4%), and curcumae extract (4%) **(Lily and Judith,1999)**.

According to the clinical studies conducted by **Tomoyoshi (2005)**, Jamu tea reduces serum lipid peroxide (LPO), glucose and fructose – loaded mice (reduces sugar level) and serum triglycerides. It reduces glucose level by 22% after 60 minutes in glucose tolerance mice, reduces the weight of epididymal fat pads/mouse by 28.7%, and it prevents lipogenesis, especially under highly lipogenic condition such as large amounts of fructose so helps to reduce total cholesterol.

Aim of The Study

The present investigation aims to study the effect of feeding obese rats with different portions of essential nutrients (protein, carbohydrate and fat) in enhancing the effect of some drugs and herbs used in weight loss of obese rats. Amount of food intake, internal organs weight, blood glucose levels, lipids profile, liver & kidney functions and thyroid hormones were determined. Moreover, the histological studies were conducted on some internal organs (liver and kidney) of normal non-treated and treated obese rats.

REVIEW OF LITERATURE

Obesity, Complications and Management:

Excess caloric intake and sedentary life style have led to an increase prevalence of obesity and its life shortening consequence, including cardiovascular disease , diabetes and hypertension **(Beeson, 1979)**.

Obesity is generally defined as condition in which there is an abnormal accumulation of fat in body tissue **(Bray, 1985)**. Thus, the people have turned to plants for healing. It is rather ironic that this form of medicine , the oldest, and still the most important in many parts of the world **(Bremness 1993).**

Increased cholesterol and saturated fatty acid (SFA) intake has been associated with increased CHD mortality. The intake of excess dietary fat is one of the leading causes of obesity, and the above described systemic effect should facilitate weight loss in obese subjects. Given that weight loss in overweight persons is known to be associated with an improvement in the serum lipid profile **(Kromhout et al., 1995 and Pi-Sunyer, 1996)**.

Considerable evidence suggests that weight loss of 5% to 10% of initial body weight substantially improves the health of obese patients **(Williamson et al.,1995).**

Some general causes may be heredity ; glandular and hormonal malfunction ; malnutrition ; emotion tension ; slow metabolism ; boredom ; habit and love of food . Obesity are a part of such conditions as heart disease ; kidney trouble ; diabetes ; gallstones (from saturated fat and cholesterol) ; high blood pressure ; malnutrition ; complications of pregnancy ; cancer and psychological problems **(Kirschmann , 1996).**

Obesity is major health problem in many developed countries and its prevalence is increased in developing countries. In the USA the prevalence of obesity (body mass index equal to or more than 30 kg/m2) is approximately 30% , and in most European countries the respective prevalence figures range from 10-20% . Even higher figures have been reported in the eastern European countries of the former Soviet Union **(WHO, 1997)** . Morbid obesity (body mass index at least 40 kg/m^2) is associated with a six- to 12-fold increase in mortality compared with normal weight, but the major impact of obesity on health in a population is because of co morbidities related to moderate or severe obesity.

Overweight and obesity are now major public health problem in many countries . Obesity is a major risk factor for many metabolic disorders and non-communicable diseases such as diabetes , cardiovascular diseases and certain types of cancer **(WHO , 1998)**. on the other hand, **McNeely and Goa, (1998)** reported that, Obesity has widespread impacts on the individual's physical and emotional well-being, as well as more distant repercussions on society as a whole through healthcare costs and reduced productivity. There are many co-morbid conditions associated with obesity , including hypertension, diabetes and hyperlipidemia, all of which contribute to the association of obesity with coronary heart disease (the major killer in the Western world).

Diet and exercise, the cornerstones of obesity treatment, have limited effectiveness with respect to long-term weight loss and maintenance **(Wing et al.,1998).**

The cornerstone of any management plan for obesity must be lifestyle modification, which should aim to reduce both weight and overall risks of morbidity and premature mortality. This package must therefore consist of appropriate dietary advice, encouragement of physical activity, and the removal of other co-morbid risk factors, as well as consideration of drug and , possibly, surgical treatments **(McNeely and Goa, 1998).**

Until recently , treatment of obesity has been based on diet , behavior therapy and physical exercise. For patients with morbid obesity or those with severe complicated obesity (e.g. hypertension, diabetes) different surgical treatment modalities have also been developed. As for drug treatment, the formerly used anorectic drugs or appetite suppressants are no longer available. They were withdrawn from the market because of their adverse effects on pulmonary circulation and cardiac values **(Grundy, 1998).**

Obesity is a primary risk factor for coronary heart disease (CHD) and mortality **(Must et al., 1999)**.

Serdula et al., (1999) reported that, 29% of men and 24% of women claim to be attempting to lose weight or maintain previously achieved weight losses.

Obesity is a major health concern because it is implicated in the development of many chronic diseases. Strategies recommended for weight control have generally recommended the adoption of low-fat dietary patterns, which facilitate energy restriction and cardiovascular disease risk reduction. However, studies of the role of a high dietary ratio of protein to carbohydrate in enhancing weight loss and disease risk management have emerged along with an increasing public

interest in weight control. From an epidemiologic perspective, a positive health benefit from a high protein intake was observed in the Nurses' Health Study, which found a 26% lower rate of cardiovascular disease in those women in the highest protein intake group than in those in the lowest protein intake group **(Hu et al., 1999).**

A higher protein intake during weight loss may also prevent some of the inevitable loss of lean body mass and, thus, may enhance insulin sensitivity **(Baba et al., 1999)**.

Obesity is a major risk factor for several chronic diseases. Studies have shown that obese subjects suffer increased mortality from diabetes mellitus, coronary heart disease and cancer . Obesity is an associated or recognized risk factor for other diseases, such as diabetes mellitus , hypertension, coronary heart disease , gallbladder disease, osteoarthritis and breast cancer **(Volek and Westman , 2002**).

In two studies in overweight men and women, with either insulin resistance or type 2 diabetes, it was shown that a high-protein weight-loss diet (28– 30% of energy from protein) from mixed sources enhances fat loss by 1–2 kg over 12 wk, particularly in women, compared with an isocaloric high-