Introduction

Obesity is a medical condition involving an excess accumulation of body fat. The prevalence of obesity is increasing not only in adults, but also among children and adolescents. The prevalence of obesity has increased steadily over the past five decades, and may have a significant impact on the quality adjusted life years (Pi-Sunyer, 2009). The national family health survey (NFHS-3) conducted in 2005-2006 indicates that obesity has increased significantly in India. Particularly among women, and needs the attention of the people concerned. It was found that 51% of the women tested, of age 15 - 49 years were obese. The percentage prevalence of obesity among Indians is still less in comparison with the global context, but being the second most populated country in the world, urgent attention is required towards this issue; otherwise, India would be one of the first nations, from the developing countries in Asia (Garg et al., 2010).

Obesity has reached epidemic proportions globally. More than 1 billion adults are overweight and at least 300 million of them are clinically obese. Significantly, obesity is increasing rapidly in developing countries undergoing rapid nutrition and lifestyle transition, and it often co-exists with under nutrition. The rising prevalence of obesity in developing countries is largely due to rapid urbanization and mechanization which has led to reduction in the energy expenditure along with an increase in energy intake due to increased purchasing power and availability of high fat, energy dense fast foods.

Obesity incidence has increased rapidly over the last two decades, reaching an epidemic state. An incidence of above 20% has been observed in most Western countries (WHO, 2007). According to the World Health Organization (WHO), in 2010, around 43 million children under five were overweight. Once considered a high income country problem, overweight and obesity are now on the rise in low and middle income countries, particularly in urban settings. Close to 35 million overweight children are living in developing countries and 8 million in developed countries. Obesity is defined as a body mass index (BMI) of 30 kg/m² or more and overweight is defined as a BMI of 25 kg/m² or more by the World Health Organization (WHO 2005). However, BMI is not necessarily the best parameter in defining obesity, and in particular not for predicting obesity associated metabolic problems.
Obesity is a chronic metabolic disorder characterized by increased fat accumulation, such as increases in the cell number and/or cell size in adipose tissue and elevated lipid concentrations in the blood (Fujioka, 2002). Obesity results from an imbalance between energy intake and expenditure. It is also known to be caused by altered lipid metabolic processes, including lipogenesis and lipolysis (Pagliassotti et al., 1997). Lipogenesis is the process that stores free fatty acids in the form of triglyceride (TG) within lipid droplets, and thus changes in the cell size reflect the amount of stored TG (Mandrup and Lane, 1997). On the other hand, lipolysis is the process whereby TG stored within lipid droplets is metabolized to free fatty acids and glycerol (Ducharme and Bickel, 2008). Consequently, an imbalance in lipid metabolism is a related factor that leads to obesity.

Obesity is reaching epidemic proportions worldwide; it is correlated with various comorbidities, among which the most relevant are dyslipidemia (Fried et al., 2008), diabetes mellitus (Pagotto et al., 2008), fatty liver (Marovic, 2008), cardiovascular diseases such as heart failure and coronary heart disease (Lavie et al., 2008).

The rising prevalence of these lifestyle disorders in India is of concern as singly or in combination, which act as major risk factor for Coronary Artery Diseases (CAD). Increased predisposition to diabetes and premature CAD in Indians has been attributed to the “Asian Indian Phenotype” characterized by less of generalized obesity measured by Body Mass Index (BMI) and greater central body obesity as shown by greater Waist Circumference (WC) and Waist to Hip Ratio (WHR). Many Indians fit into the category of metabolically obese, normal weight individuals. Although having lean BMI an adult Indian has more chances of having abdominal obesity (Carly et al., 1997; Banerji et al., 1999). The body fat percentage of an Indian is significantly higher than a western counterpart with similar BMI and blood glucose level. It has been hypothesized that excess body fat and low muscle mass may explain the high prevalence of hyperinsulinemia and the high risk of type 2 diabetes in Asian Indians (Misra et al., 2001; Mohan et al., 2005).

Obesity, especially abdominal obesity, is among the strongest risk factors for type 2 diabetes mellitus (T2DM). In children, T2DM has been increasingly reported globally. T2DM was reported exclusively in overweight or obese Asian children with family origin in Pakistan, India or Middle-Eastern countries in UK (Ehtisham
et al., 2000). We have reported that generalized obesity and abdominal obesity were significantly higher in children and adolescents with T2DM in North India (Vikram et al., 2006). Important independent risk factors for development of T2DM in Asian Indian adolescents and young adults were hypertriglyceridemia, high waist-to-hip ratio and family history of diabetes (Vikram et al., 2003).

Non alcoholic fatty liver disease (NAFLD) is the most common liver disorder in the world, and in obesity, type 2 diabetes and related metabolic diseases, its incidence reaches 70-90% (Adams and Angulo, 2005). The disease is characterized by the accumulation of triacylglycerols (TG) inside liver cells, and the condition can progress into more serious liver disease, such as non alcoholic steatohepatitis (NASH), liver fibrosis, cirrhosis, and more rarely, liver carcinoma (Adams and Angulo, 2005). Although it is known that progression of the disease is more likely to occur in patients with metabolic diseases (Svegliati et al., 2006), the factors involved are not well understood. However, oxidative stress coupled with insulin resistance is believed to play an important role (Videla et al., 2006).

The dramatic rise in obesity and the metabolic syndrome are a consequence of several lifestyle factors in modern societies. Factors such as nutrition, physical activity, smoking, alcohol and stress are well known lifestyle components associated with the development of obesity associated diseases (Ueno et al., 1997). Modern Western lifestyle involves a reduced need for physical activity, due to the sedentary nature of many jobs with technological developments and the increasing use of computers for everyday tasks as well as readily available, high calorie, readymade diets.

It has been reported that increased intake of foods with high energy and dietary fat content promotes body fat storage, and that diets that consistently contain high levels of fat lead to increased caloric intake and therefore body weight and adiposity in humans and animals (Bray and Popkin, 1999). Western diets are high in fat and tend to promote obesity, and the pharmacologic inhibition of the digestion and absorption of dietary fat has been used as a strategy to treat obesity (Ballinger and Peikin, 2002).
Currently there is a great need for effective therapies. Numerous medical and
behavioural interventions have been tried to treat obese patients but only a few were
successful. Pharmacological compounds frequently had to be inhibited, due to
severe undesired side effects (Farrigan and Pang, 2002). Bariatric surgery is
considered the most successful treatment in highly obese patients but the significant
risk of complications does not allow its wide-range use (Sjostrom et al., 2004).

Therefore, there is a huge challenge for the scientific community to search
for more effective and better acceptable treatment against obesity.

Two different types of obesity treatment drugs are currently available on the
market (Chaput et al., 2007). One of these is orlistat (Xenical), which reduces
intestinal fat absorption through inhibition of pancreatic lipase (Ballinger and
Peikin, 2002; Drew et al., 2007; Thurairajah et al., 2005). The other is sibutramine
(Reductil), which is an anorectic, or appetite suppressant (Lean, 2001; Poston and
Foreyt, 2004; Tziomalos et al., 2009). Both drugs have side-effects, including
increased blood pressure, dry mouth, constipation, headache, and insomnia (de
Simone and D’Addeo, 2008; Karamadoukis et al., 2009; Thurairajah et al., 2005).
A number of anti-obesity drugs are currently undergoing clinical development,
including centrally-acting drugs (e.g. radafaxine and oleoyl-estrone), drugs targeting
peripheral episodic satiety signals (e.g. rimonabant and APD356), drugs blocking fat
absorption (e.g. cetilistat and AOD9604), and human growth hormone fragments
(Halford, 2006).

At present, because of unhappiness with high costs and potentially hazardous
side effects, the potential of natural products for treating obesity is under
investigation, and this may be an excellent alternative strategy for developing future
effective, safe antiobesity drugs (Mayer et al., 2009; Nakayama et al., 2007; Park et
al., 2005). A variety of natural products, including crude extracts and isolated
compounds from plants, can induce body weight reduction and prevent diet-induced
obesity. Therefore, they have been widely used in treating obesity (Hian et al.,
2005a; Rayalam et al., 2008).

In particular, many therapeutic herbs have far fewer side effects and may
provide an alternative treatment or could be used to enhance the effect of
prescription medications. Although such treatments are widely used, none has been convincingly demonstrated to be safe and effective (Allison et al., 2001). Under the guidelines of the US Food and Drug Administration, botanical drugs can be developed faster and cheaper than conventional single entity pharmaceuticals. Many botanicals may provide safe, natural, and cost effective alternatives to synthetic drugs (Raskin et al., 2002; Zdunczyk et al., 2002).

Currently there is an increased demand for using plants in therapy instead of using synthetic drugs which may have adverse effects. Traditional medicinal plants are often cheaper, locally available, and easily consumable. These simple medicinal preparations often mediate beneficial responses due to their active chemical constituents.

In view of wide occurrence of saponins in medicinal plants and our interest about antiobese agents from herbs resources, aimed to investigate the anti-obese prospective of a known source of saponins from Gymnema sylvestre (Ye et al., 2001).

Gymnema sylvestre R. Br, a member of family Asclepiadaceae is a large woody climbing plant species found throughout India, in dry forests up to 600 m, common throughout the Asia and tropical Africa and Australia. G. sylvestre has been used in Indian traditional medicine ("Ayurvedic medicine") and is considered to be effective in improving urination, stomach stimulation and diabetes (Abe, 1993; Ota et al., 1998). In addition, the metabolism of carbohydrates and lipids play a considerable part in obesity. Various effects have been reported, such as suppression of glucose absorption in the small intestine of rats, reduction of plasma glucose increment in the oral sucrose tolerance test, significantly lowered blood glucose and insulin values in dogs as well as suppression of insulin increase in glucose tolerance tests in men and the alleviation of diabetic symptoms in patients with non-insulin-dependent diabetes mellitus (Hirata et al., 1992). As for the active substances involved in G. sylvestre, the triterpenoid saponin and its derivatives have been identified. These are glycosides where gymnemagenin is formed by attachment of glucuronic acid to the triterpenoid structure as aglycone. This glycoside and its derivatives are referred to as gymnemic acids (Yoshikawa et al., 1997). Other than
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these glycosides, conduritol A with a tetrahydroxyhexene structure has been also confirmed to be involved in glucose absorption. Moreover, the peptide grumarin, which is a peptide consisting of 35 amino acids has been shown to be involved in suppression of sweetness (Ota et al., 1998).

In this study, we examined the effects of saponins from G. sylvestre aqueous leaf extract on obesity induced in rats fed on cafeteria and high-fat diets, respectively.

Objectives of the present study

➢ To evaluate the protective role of saponins from Gymnema sylvestre leaf extract against cafeteria and high-fat diets induced obese rats.

➢ To investigate the effects of saponins from Gymnema sylvestre leaf extract on body weight parameters in cafeteria and high-fat diets induced obese rats.

➢ To study the effects of saponins from Gymnema sylvestre leaf extract on serum and tissue biochemical parameters in cafeteria and high-fat diets induced obese rats.

➢ To determine the role of saponins from Gymnema sylvestre leaf extract on oxidative stress in cafeteria and high-fat diets induced obese rats.