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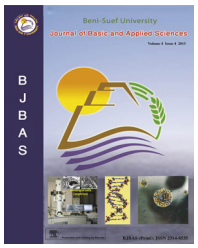

Full Length Article

Effect of *Commiphora mukul* gum resin on hepatic and renal marker enzymes, lipid peroxidation and antioxidants status in pancreas and heart in fructose fed insulin resistant rats

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ABSTRACT

This work aims to study the antioxidant efficacy of *Commiphora mukul* (*C. mukul*) gum resin ethanolic extract in high fructose diet (HFD) insulin resistant rats. The male Wistar albino rats were randomly divided into four groups of eight animals each; two of these groups (Control group [C] and Control treated with *C. mukul* [C + CM]) were fed with standard pellet diet and the other two groups (Fructose fed rats [F-group] and fructose fed with *C. mukul* treated group [F + CM]) were fed with high fructose diet (HFD) (66%). *C. mukul* gum resin ethanolic extract (200 mg/kg body weight/day) was administered orally to group C + CM and group F + CM. At the end of 60-day experimental period biochemical parameters related to antioxidant, oxidative stress marker enzymes and hepatic and renal marker enzymes of tissues were performed. The fructose fed rats showed increased level of enzymatic activities aspartate aminotransminases (AST), alanine aminotransminases (ALT) in liver and kidney and oxidative markers like lipid peroxidation (LPO) and protein oxidation (PO) in pancreas and heart. Antioxidant enzyme activities were significantly decreased in the pancreas and heart compared to control groups. Administration of *C. mukul* (200 mg/kg bwt) to fructose fed insulin resistant rats for 60 days significantly reversed the above parameters toward normal. In conclusion, our data indicate the preventive role of *C. mukul* against fructose-induced insulin resistance and oxidative stress; hence this plant could be used as an adjuvant therapy for the prevention and/or management of chronic diseases characterized by hyperinsulinemia, insulin resistance and aggravated antioxidant status.

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1. Introduction

Free radicals may play a pivotal role in the pathogenesis of a number of diseases, including diabetes mellitus (DM) (Feillet-Coudray et al., 1999). DM is a chronic metabolic disorder that continues to be a major health problem worldwide. It is characterized by absolute or relative deficiencies in insulin secretion and/or insulin action associated with chronic hyperglycemia and disturbances in carbohydrate, lipid, and protein metabolism (Dukworth, 2001). In addition to hyperglycemia, several other factors such as dyslipidemia or hyperlipidemia are involved in the development of diabetes related cardiovascular complications which are the major causes of morbidity and death (Markku, 1995).

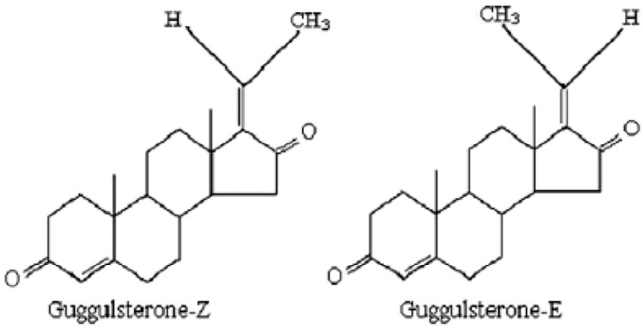
Rats fed with a high-fructose diet form a model of diet-induced insulin resistance, associated with hyperinsulinemia, hypertriglyceridemia and glucose intolerance (Thorburn et al., 1989). Recently, antioxidants are found to be effective in preventing a majority of the abnormalities induced by high-fructose diet (Faure et al., 1999).

Over the past few decades there has been increasing scientific and public interest in so called antioxidant hypothesis. Therefore, in addition to control of blood glucose levels, control of oxidative stress offers another avenue for the treatment of the disease. Chemicals with antioxidant properties and free radical scavengers may help in the regeneration of β-cells and protect pancreatic islets against the cytotoxic effects of STZ.

Insulin sensitizers and antioxidants are found to be effective in preventing not all but at least a majority of the abnormalities induced by fructose (Faure et al., 1999). Current treatment with thiazolidinediones and particularly metformin does not adequately address the issue of IR (Hollenberg, 2003). Hence, there is a need to search for new agents with better efficacy and minimal side effects. Plants and herbs are mines of a large number of bioactive phytochemicals that might serve as lead for the development of effective, safe, cheap novel drugs.

Traditional (India) uses of *Commiphora mukul* (CM) are for its anti-inflammatory, antispasmodic, carminative, emmenagogue, hypoglycemic, alternative, antiseptic, and astringent, a thyroid stimulant, anthelmintic and antihyperlipidemia properties. It is an important herb used also in the treatment of several degenerative disorders in modern medicine and established as a hypolipidemic drug (Ulbricht et al., 2005). Ayurvedic medicines containing gum guggul often contain guggul in their names, such as in Shunthi-guggul and Yogaraja guggul. All the formations used for traditional Ayurvedic treatments for obesity contained gum guggul among its herbal ingredients.

Guggulipid, an ethyl acetate extract of the resin of plant *C. mukul* is an established hypolipidemic agent. The hypolipidemic effect of guggulipid and guggulsterone has been consistently demonstrated in various animal species, including rat, mouse, rabbit, chicken (Baldwa et al., 1981), domestic pig (Khanna et al., 1969), dog and monkey (Dixit et al., 1980). In addition, it was found that guggulsterone treatment increased lipolytic enzyme activity as well as receptor-mediated catabolism of LDL (Chander et al., 1996). Two stereo isomers, E- and Z-guggulsterone (cis- and trans-4, 17(20)-pregnadiene-3, 16-dione, respectively), are the most important constituents studied in detail for their therapeutic potential from *C. mukul*. Various studies have been conducted to understand and illustrate the mechanism of action and potential of guggulsterone as a therapeutic agent using synthetic E and Z isomers (Ichikawa and Aggarwal, 2006).



The mechanisms implicated for lipid-lowering effect of guggulipid are stimulation of hepatic lipases and receptor mediated catabolism of low-density lipoproteins, and suppression of hepatic cholesterol biosynthesis (Nityanand and Kapoor, 1973). Guggulsterones inhibited cholesterol synthesis in the liver via antagonism of the forsenoid X receptor and the bile acid receptor (Nagarajan et al., 2001). A number of clinical trials have been conducted to evaluate the hypolipidemic effect of guggulipid. Most of these studies were carried out in India and one in the United States. Consistent with the preclinical data, most of these studies demonstrated polipidemic activity of guggul or guggulipid with an average of 10–30% and 10–20% decrease in total cholesterol and triglyceride, respectively. With proven hypolipidemic efficacy in rats, guggulsterone was used as a positive control to assess the hypolipidemic activity of other chemical compounds (Kumari and Augusti, 2007). Our previous work demonstrated that *C. mukul* gum resin ethanol extract has antidiabetic activity in streptozotocin (STZ)-induced insulin-dependent diabetes mellitus and fructose-induced insulin resistance in animals (Ramesh et al., 2011, Ramesh and Saralakumari, 2012). We are presently experimenting with the fructose-enriched diet rat model, and the aims of the present work were to characterize its efficacy against fructose-induced alterations in antioxidant enzymes, oxidative stress and hepatic and renal marker enzymes.

2. Materials and methods

2.1. Chemicals

Thiobarbituric acids and pyrogallol were obtained from the Sigma Chemical Co., St. Louis, MO, USA. All other chemicals and solvents were of analytical grade and procured from Sisco Research Laboratories (P) Ltd., Mumbai, India.

2.2. Plant material

Ethanolic extract of *C. mukul* gum resin (CMEE; brown, dry powder with Lot No. L5111031) was obtained from the manufacturers and exporters of herbal extracts, Ms Plantex Pvt. Ltd.,