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Studies on the evaluation of antidiabetic and antioxidant activities using some selected medicinal plants

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Abstract
Diabetes mellitus defined as metabolic disorder of multiple etiology characterized by chronic hyperglycemia along with disturbances of carbohydrate, fat and protein metabolism resulting due to the defects in insulin secretion, insulin action, or both. The effects of diabetes mellitus include long– term damage, dysfunction and failure of various organs. Medicinal plants are the plants which are attributed as safe, natural, non-narcotic, having no side effects, cost effective and are primarily aimed for health of all. Ancient to modern times, medicinal plants have been used in virtually all cultures as a source of medicine. Around 20,000 medicinal plants are identified in India till today and are recorded in the literature. Today, only one-third of the identified medicinal plants are explored and are leveraged for curing various diseases. This paper discusses and presents studies in focus with the treatment of diabetes mellitus using some selected medicinal plants.

Keywords: antidiabetic activities, antioxidant activities, medicinal plants, herbal drugs

1. Introduction
Diabetes mellitus is a chronic metabolic disorder attributed by hyperglycemia, glucosuria and negative nitrogen balance and is primarily caused due to absolute deficiency or deprecated production of insulin. It is the most prevalent disease in the world affecting 25% of the population and afflicts 150 million people and is predicted to rise to 300 million by 2025 [1]. Even today no treatment has ensured for permanent cure of diabetes. In spite of few drawbacks like anorexia, brain atrophy and fatty lever etc., still insulin therapy is the only accepted treatment for diabetes. Continuous research is pursued to identify efficient and effective hypoglycemic agents since the existing agents show more or less adverse effects during anti-diabetic therapy. At present extracts from more than 150 plants are used to treat diabetes. This leads to an active gain in popularity of using herbal drugs to control this disease. The major qualities of using herbal medicines seem to be their supposed efficacy, low incidence of serious adverse effects and low cost [9].

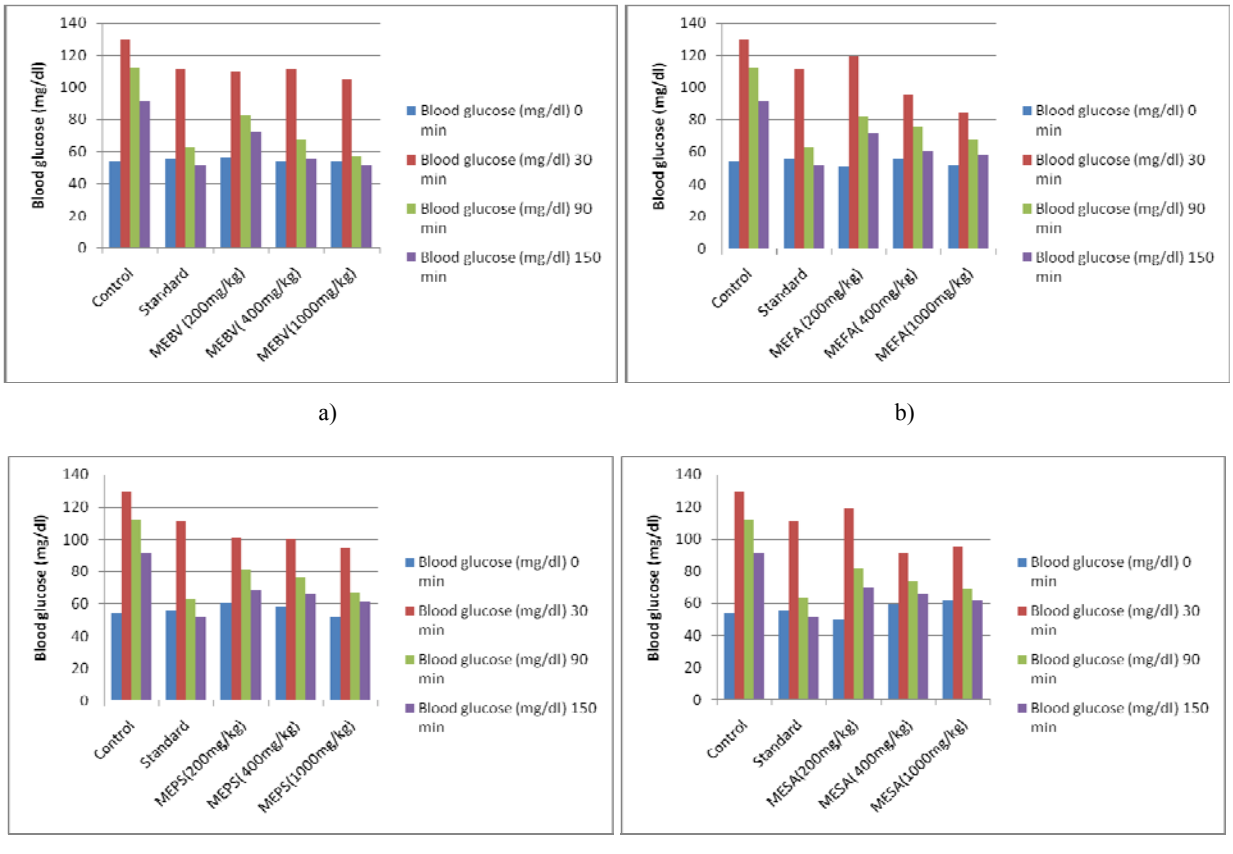
2. Materials and Methods
The use of rats as an experimental animal in the present study is done due to their close resemblance of physiology and genetic makeup to that of humans [2]. Especially male rats are used in the present study. In the oral glucose tolerance test, at 90 & 150 min, a significant decrease in blood glucose levels is observed in animals treated with methanolic extract of *Bauhinia variegate* (MEBV), methanolic extract of *Ficus arnottiana* (MEFA), methanolic extract of *Pterocarpus santalinus* (MEPS) and methanolic extract of *Syzygium alternifolium* (MESA) when compared with the diabetic control animals. From the oral glucose tolerance test (OGTT) data, it is clear that administration of MEBV, MEFA, MEPS and MESA at different dose levels effectively decreased the serum glucose levels without causing a hypoglycemic state. Depending upon this data, further studies are carried out at the doses of 200 and 400 mg/kg, p.o., which showed 50%, decrease in the blood glucose levels after glucose load for the selected plants.
Streptozotocin (STZ) is an antibiotic obtained from *Streptomyces achromogenes*. STZ enters the pancreatic cells via a glucose transporter - GLUT2 and causes alkylation of deoxyribonucleic acid (DNA) leading to pancreatic damage. Its toxicity depends upon the potent alkylation properties combined with the synergistic action of nitric oxide and reactive oxygen species that continue to DNA fragmentation. As a result of STZ action, pancreatic cells are destroyed by necrosis. STZ not only damages the pancreatic cells but also impairs hepatocytes, nephrons and cardiomyocytes (Biswas; mythili). In the present study,

administration of STZ alone produced significant fasting hyperglycemia and body weight loss due to increased muscle wasting and loss of tissue proteins in diabetic control group. Treatment with MEBV, MEFA, MEPS and MESA showed significant and consistent reduction in fasting blood glucose levels and also significantly improved the body weight loss at different intervals throughout the period of experiment as compared to the vehicle treated diabetic controls indicating their potent anti-diabetic activity. The order of anti-hyperglycemic activity of the selected plants is found to be as follows at both the doses tested. During experimentation, the effect is observed to be dose dependent.

3. Results and Discussion

Figure 1 presents the effects of MEBV, MEFA, MEPS and MESA respectively. Results obtained from the present study are very much promising and comparable with glibenclamide, a standard drug used to treat diabetes mellitus. A similar study is done by Noor *et al*. [3] and has reported the antidiabetic activity of Aloe vera in streptozotocin induced diabetic rats. In their work authors have also mentioned two possible explanations for their observations. First explanation is as follows: Vera may exert its effect by preventing the death of pancreatic β cells. Second explanation is as follows: It may permit recovery of partially destroyed β cells. Burcelain *et al*. [4] also reported that the hypoglycemic action of the extract of herbal plants in diabetic rats may be possible through the insulin mimetic action or by other mechanism such as stimulation of glucose uptake by peripheral tissue, inhibition of endogenous glucose production or activation of gluconeogenesis in liver and muscles. It can also be noted that the antidiabetic activity of the selected plants during this experimentation may also be possible through the mechanism as reported by Noor *et al*. [3] and Burcelain *et al*. [4].

The present study also showed increase in plasma triglycerides, total cholesterol and LDL cholesterol with decrease in HDL cholesterol supporting the findings of the other researchers. Figure 2 presents the effect of selected plants on blood glucose levels, Triglycerides (mg/dl), total cholesterol (mg/dl), HDL - Cholesterol (mg/dl), VLDL (mg/dl), LDL-Cholesterol (mg/dl), serum creatinine (mg/dl) and vivo antioxidant parameters. Potential of the selected plant extracts of MEBV, MEFA, MEPS and MESA extracts to decrease cholesterol and triglyceride levels could be helpful in improving lipid metabolism in diabetics which in turn will help to prevent diabetic complications. LDL- cholesterol being involved in the transport of cholesterol from liver to peripheral tissues is the key factor in atherogenesis. Potential of the MEBV, MEFA, MEPS and MESA extracts to reduce LDL-cholesterol thereby indicates its possible involvement in prevention of diabetes mellitus induced cardiovascular complications. The order of benefit of the selected plants against changes in lipid profile was found to be as follows at both the doses tested and effect was observed to be dose dependent.



a) b)

c) d)

Fig 1: Effect of a) MEBV b) MEFA c) MEPS d) MESA on OGTT respectively.

Insulin generally has anabolic effect on protein metabolism, stimulates protein synthesis and retards protein degradation which may be responsible for the decreased levels of haemoglobin in diabetic rats. In uncontrolled or poorly controlled diabetes, there is an increased glycosylation of a number of protein including haemoglobin and crystallization of lens. Glycosylated haemoglobin was significantly increased in diabetic animals and this increase was found directly proportional to the fasting blood glucose levels. During diabetes the excess glucose present in blood reacts with haemoglobin.

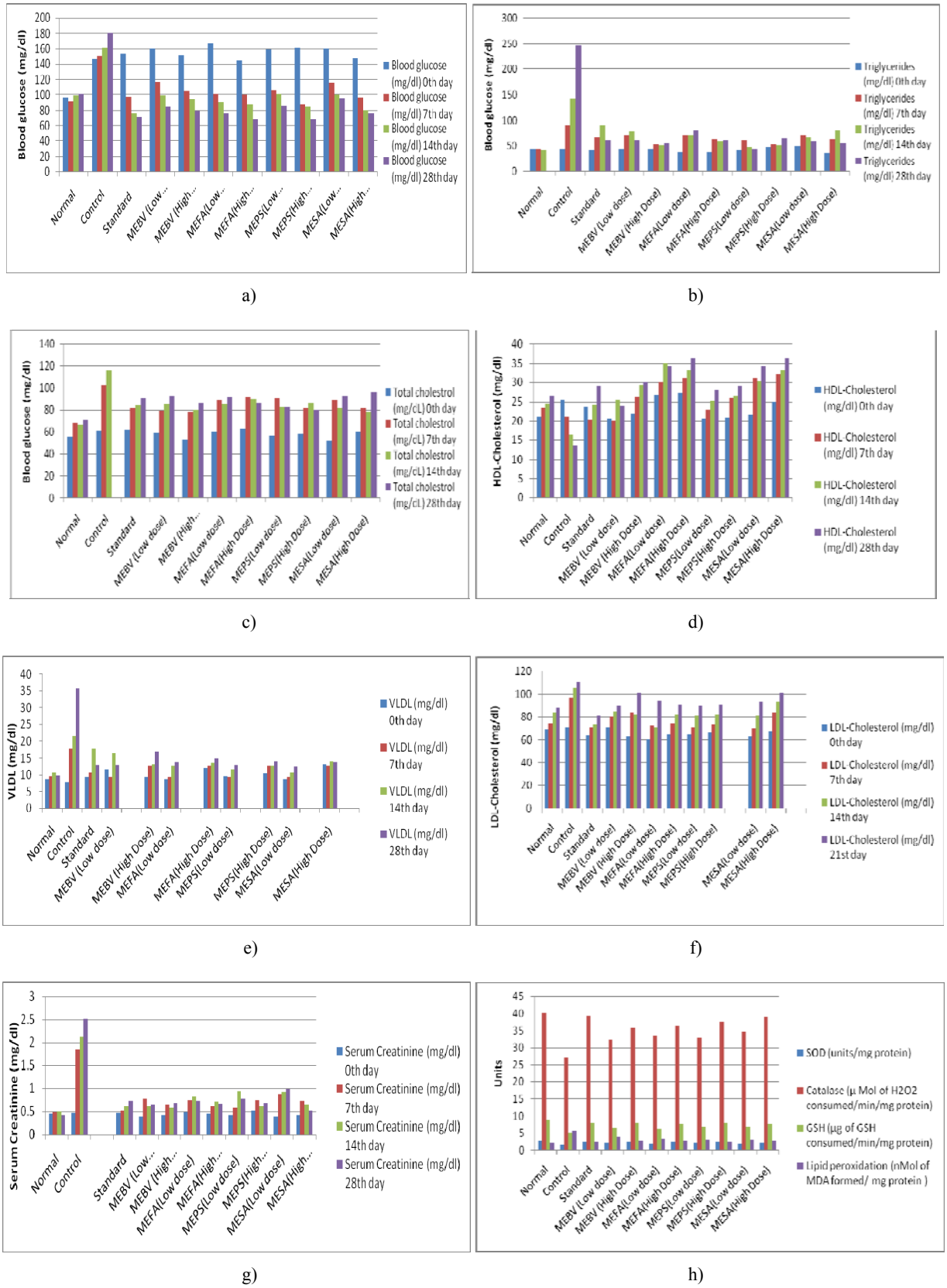


Fig 2: Effect of selected plants on a) blood glucose levels b) on Triglycerides (mg/dl) c) Total cholesterol (mg/dl) d) HDL - Cholesterol (mg/dl) e) VLDL (mg/dl) f) LDL-Cholesterol (mg/dl) g) serum creatinine (mg/dl) h) *vivo* antioxidant parameters

The antidiabetic activity of the selected plants in the present study might have contributed for the restoration of increased glycosylated levels back to normal in group of animals treated with methanolic extracts of B. variegate, F. arnnotiana, P. santalinus and S. alternifolium. In diabetes, oxidative stress is due to both an increased production of plasma free radical concentration and a sharp reduction of antioxidant defenses. The important mechanism implicated in the diabetogenic action of STZ is by increased generation of oxygen free radicals, which causes a decrease in plasma GSH concentration, and plasma GSH/GSSG ratio [1:4]. Hence, drugs that could prevent the generation of these oxygen free radicals or increase the free radical scavenging enzymes may be effective in STZ induced diabetes. Increase in SOD in groups treated with MEBV, MEFA, MEPS and MESA extracts may be the one of the good indication for their anti-

oxidant activity. Because it is stated that SOD is a ubiquitous cellular enzyme that dismutases super oxide radical to H2O2 considered as one of the cellular defensive mechanism [5]. Catalase is an enzymatic antioxidant actively involved in red blood cells and liver extensively, spread in all animal tissues. This antioxidant decomposes hydrogen peroxide and protects the animal tissues from highly reactive hydroxyl free radicals [6]. Depletion of catalase observed in diabetic control group was found to be restored in the animal groups treated wih MEBV, MEFA, MEPS and MESA extracts indicating the good antioxidant nature of the selected plants. The most important biomolecule against chemically induced toxicity is GSH which involves in elimination of reactive intermediates by reduction of hydroperoxides in the resence of Glutathione peroxidase [7]. This biomolecule also takes the role as a free radical scavenger [8].

4. Conclusion

MEBV, MEFA, MEPS and MESA extracts have reduced the oxidative stress by reduction in GSH perturbation. Lipid peroxidation is a free radical chain reaction which is triggered by hydroxyl radical and leads to membrane break down and leading to produce more number of free radicals. The flavonoid components of plant extracts are known to be efficient in scavenging the highly reactive hydroxyl radical and superoxide anion and inhibit the lipid peroxidation by quenching the peroxyl radicals. Hence, flavonoid and polyphenolic content of MEBV, MEFA, MEPS and MESA extracts might be responsible for the increase in SOD, catalase, GSH and thus lead to decrease in lipid peroxidation levels in STZ treated rats.

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