Innovare Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 7, Issue 9, 2015

Original Article

PROTECTIVE EFFECT OF *COMMIPHORA MUKUL* GUM RESIN ON BRAIN IN STREPTOZOTOCIN-INDUCED DIABETIC RATS

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Received: 11 Jun 2015 Revised and Accepted: 27 Jul 2015

ABSTRACT

Objective: The present study was undertaken to investigate the hypolipidemic activity of ethanolic extract of *Commiphora mukul* gum resin (EtCMGR) on the brain of streptozotocin (STZ) induced diabetic Wistar rats.

Methods: Thirty two rats, included for the study, were divided into four groups: control (C), control treated with EtCMGR (C+CM), diabetic (D) and diabetic treated with EtCMGR (D+CM). Diabetes was induced by single intraperitonial injection of STZ (55 mg/kg b.w.).

Results: Diabetic rats showed significant reduction in the levels of total lipids, phospholipids, cholesterol, glycolipids and protein level and significant decrease in the activity of acetylcholinesterase while the levels of triglycerides, acetylcholine and the activities of glutamate pyruvate transaminases **(**GPT) and glutamate oxaloacetate transaminases **(**GOT) increased significantly when compared to control group. Oral administration of EtCMGR (suspended in 5% Tween-80 in distilled water prior to use) daily at a concentration of 200 mg/kg b.w. to group-D+CM rats for 60 days reversed the above changes significantly.

Conclusion: These results suggest that EtCMGR exhibits hypolipidemic effect in the STZ-induced diabetic rats.

Keywords: Acetylcholinesterase, *Commiphora mukul*, Hypolipidemic activity, Streptozotocin.

INTRODUCTION

Diabetes induced in experimental animals by administration of drugs like STZ is a widely used model system with many correlations to insulin-dependent diabetes mellitus in humans [1]. This disorder is characterized by elevated blood glucose levels and metabolic abnormalities, resulting from decreased levels of circulating insulin to target organs, including the brain [2, 3]. Brain is the most sensitive organ susceptible to oxidative stress due to its great oxygen consumption, high lipid content and poor antioxidant defences. One of the mechanisms of diabetes enhanced brain injury is oxidative stress caused by hyperglycemia. High oxidative stress can lead to microvascular cerebral diseases, e. g., stroke, cerebral haemorrhage, and brain infraction [4, 5]. Under experimental conditions, hyperglycemia dramatically increases neuronal alterations and glial cell damage caused by temporary ischemia [6]. Free radical species impair the central nervous system, attacking neurons and Schwann cells and the peripheral nerves [7]. Because of their high poly unsaturated lipid content, Schwann cells and axons are particularly sensitive to oxygen free radical damage; lipid peroxidation may increase cell membrane rigidity and impair cell function. Lipid peroxidation of the neuronal membrane causes loss of membrane fluidity and inhibition of membrane linked enzymes, increased neurolipofuscin deposition leading to diminished neurotransmitter uptake and loss of membrane asymmetry [8, 9], but also affects the activities of various membrane-bound enzymes, including acetyl cholinesterase (AchE) and ATPases. Streptozotocin is a valuable agent for experimental induction of diabetes. Its diabetogenic effect is a direct result of irreversible damage to the pancreatic β-cells, resulting in degranulation and loss of insulin secretion [10]. Insulin has been shown to stimulate both glucose uptake by tissues and tissue protein synthesis [11]. The major source of energy in the brain is glucose and morbid changes in nerves lead to diabetes [12]. Insulin deficiency will result in decreased activity of lipoprotein lipase and increased mobilisation of free fatty acids from peripheral fat depots. The STZ induced diabetic animal is thus considered as an animal model of Type-I diabetes mellitus and hyperlipidemia [13]. Diabetes has also been associated with an increased risk for developing premature arteriosclerosis due to increase in triacylglyceroles and low density lipoproteins and decrease in light density lipoprotein levels [14]. Additionally, free radical scavengers have been shown to protect neurons against a variety of experimental neurodegenerative conditions [15], as well as attenuation of the oxidative stress and diabetic state induced by STZ [16, 17]. The brain is especially susceptible to free radical injury because of its elevated metabolic rate and rich lipid composition. Therefore, any toxicity on the brain can be predicted by evaluating antioxidant system and lipid peroxidation [7].

Regions with greatest potential, where diabetes mellitus rates could rise to 2-3 fold than the present rates are Asia and Africa [18]. Many herbal medicines have been recommended for the treatment of diabetes [19, 20]. Plant drugs are frequently considered to be less toxic and more free from side effects than synthetic ones [21]. Many minor components of foods such as secondary plant metabolities have shown to alter biological processes, which may reduce the risk of chronic diseases in human such as diabetes mellitus and myocardial infarction [22].

Commiphora mukul (C. mukul) (family Burseraceae) is indigenous to western India and has been in use as a valued herb in Ayurvedic medicine for over 2500 years. Gum guggul is the oleoresin of *C. mukul*, a plant that is native to India, and its extracts include compounds known for their hypolipidemic properties—the Z-and E-isomers of guggulsterone and its related guggulsterols. Lipid lowering activity of guggul however, was first reported by Satyavati [23] which was further confirmed in many experimental models [24]. *C. mukul* has been used as an inactive pharmaceutical ingredient, binding agent, anti-obesity agent, and cholesterol-reducing agent. The resin secreted by the plant *C. mukul* known as guggul is one of the widely used drugs in Ayurveda for the treatment of several disorders such as gout arthritis, rheumatism, atherosclerosis, ulcers and inflammation [25]. Early research looking at the effect of gugglesterone appeared to have positive effects. Studies, in both animal and humans demonstrated that guggul sterone may significantly lower blood lipid levels [26, 27] and may lower cholesterol levels [28, 29]. In addition, our earlier studies proved hypolipidemic activity of *C. mukul* seen in insulin deficient Wistar rats [30] and hypolipidemic activity of *C. mukul* in fructose fed Wistar rats [31]. The presence of strong antioxidant principles in *C. mukul* thus prompted us to design the present study to investigate whether management with *C. mukul* has any

protective effect on brain lipids and activities of transaminases and acetyl cholinesterase in STZ induced diabetic rats.

MATERIALS AND METHODS

Chemicals

STZ was obtained from the Sigma (St. Louis, MO, USA) and 2,4-dinitro phenyl hydrazine (DNPH) was procured from Sd-Fine Chemical, India. All other chemicals and solvents of analytical grade were procured from Sisco Research Laboratories Ltd., Mumbai, India.

Collection of plant material

EtCMGR (brown, dry powder, and cream colour) was purchased from Chemiloids (manufactures and exporters of herbal extracts) Vijayawada, Andhra Pradesh, India. Herb to product ratio was 8:1 and the extract was suspended in 5% Tween-80 in distilled water prior to use.

Induction of diabetes

Two-three week-old male Wistar rats of body weight 125–150 g procured from Sri Raghavendra Enterprises (Bangalore, India), were acclimatized for 7 days to our animal house, and maintained at standard conditions of temperature and relative humidity, with a 12 h light/dark cycle. Water and commercial rat feed were provided ad libitum. The current work was carried out with a prior permission from our institutional animal ethical committee (Regd. no. 470/01/a/CPCSEA, dt. 24th August 2001). Diabetes was induced in overnight fasted rats by a single intraperitoneal injection of freshly prepared STZ solution (55 mg/kg b.w., in ice cold 0.1 M citrate buffer, pH 4.5 in a volume of 0.1 ml per rat). After 72 h of STZ administration, the plasma glucose level of each rat was determined for confirmation of diabetes. Rats with plasma glucose level above 250 mg/dl were considered as diabetic and used in the experiment.

Experimental design

In the present experiment, a total of 32 rats (16 diabetic rats; 16 normal rats) were used. The rats were divided into four groups of 8 each: control (C); control rats treated with EtCMGR (C+CM); diabetic (D); and diabetic rats treated with EtCMGR (D+CM). The dose of EtCMGR in the current study is based on the earlier reports on the extract [32]. Diabetic treated group and control treated groups received EtCMGR (2 ml of 5% Tween-80) by orogastric tube at a dose of 200 mg/kg b.w. for 60 days, whereas, 2 ml of distilled water was administered to control and diabetic rats. Based on results of the preliminary experiment on dose-dependent antihyperlipidemic effect of EtCMGR, a dose less than 200 mg/kg b.w. was not expected to be effective in rats [32].

Animal sacrifice and organ collection

After the experimental period of 60 days, the animals from each experimental group were starved for 12 h and sacrificed by cervical dislocation and immediately the whole brain was dissected out and washed with ice-cold saline and used for analysis.

Extraction of lipids from brain tissue

Tissue (250 mg) homogenate was prepared in Folch reagent (2:1 chloroform-methanol) using Potter-Elvehjem homogenizer and centrifuged at 3000 rpm. Five ml of the supernatant was mixed with 3 ml of distilled water and again centrifuged at 3000 rpm and resulting organic phase was used for total lipids, triglycerides, cholesterol, phospholipids and glycolipids analysis by the method of Folch *et al.* [33]. Total lipids were estimated by gravimetric method.

Estimation of triglycerides

Triglycerides (TG) were estimated by GPO-PAP enzymatic method using Liquid Gold Diagnostic kit according to the method of Foosati *et al.* [34]. Sixty µl of the lipid extract, taken in an eppendorf tube, was allowed to evaporate in an incubator. To this 1.0 ml of the triglyceride reagent was added, mixed and incubated at 37 ˚C for 10 min. Triglyceride standard (200 mg%) and water blank were also treated in a similar manner. After incubation, absorbance was read at 505 nm and values are expressed as mg/g tissue.

Estimation of cholesterol

Total cholesterol was estimated by CHOD-PAP enzymatic method using Liquid Gold Diagnostic kit [35]. Sixty µl of lipid extract, taken in an eppendorf tube, was allowed to evaporate in an incubator. To this 1.0 ml of the cholesterol reagent was added, mixed and incubated at 37 ˚C for 10 min. Cholesterol standard (200 mg%) and water blank were also treated in a similar manner. After incubation, absorbance was read at 510 nm and values are expressed as mg/g tissue.

Estimation of phospholipids

Phospholipids (PL) were estimated by the method of Connerty *et al.* [36]. Phospholipids were digested with H_2SO_4 and the liberated inorganic phosphate was estimated by the method of Fiske and Subbarow method [37]. Two hundrend µl of lipid extract sample was subjected to evaporation and 1 ml of 10 N H_2SO_4 was added and digested for 1 h in a boiling water bath. Then 20 µl of H_2O_2 was added and the solution was boiled until the liquid becomes colourless. The tubes were cooled and phosphorus was estimated by Fiske Subbarow method. To the above digest 1.0 ml of molybdate II, 0.4 ml of ANSA (1-amino-2-napthol-4-sulfonic acid) reagents were added and the volume was made up to 10 ml with distilled water. After an incubation period of 15 min, the blue colour formed was read at 660 nm. The phospholipid content is calculated by multiplication of phosphate value by 25. The results are expressed as mg/g tissue.

Estimation of glycolipids

Glycolipids (GL) were estimated based on the method of Roughan and Batt [38]. Two hundrend µl of brain homogenate was subjected to evaporation and 2 ml of 2 N sulphuric acid was added and digested for 2 h in a boiling water bath. After hydrolysis, 4 ml of chloroform was added and centrifuged. The aqueous layer was separated and 50 µl of 80% phenol was added followed by 4 ml of concentrated H_2SO_4. The orange colour was measured at 480 nm. A series of galactose standards (20-200 µg) were treated in similar manner. Glycolipid concentration was estimated by multiplying galactose content with 4.45. The values are expressed as mg/g tissue.

Preparation of brain homogenate for activities of enzymes (protein and acetyl choline and activities of acetylcholine esterase and transaminases)

Ten per cent brain homogenate was prepared in 0.15 M potassium chloride by using Potter-Elvehjem homogenizer at 0 ˚C and centrifuged at 12,000 rpm for 45 min at 0-4 ˚C. The supernatant thus obtained was distributed into eppendorf tubes, labelled and stored at-20 ˚C and used for enzyme assays.

Determination of protein content

The protein content of tissue homogenates was determined by the Lowry protein assay using bovine serum albumin as the standard [39].

Estimation of acetyl choline

Acetyl choline (Ach) content was estimated by the method of Metcalf [40] as described by Augustinson [41]. In this method the acetyl group reacts with alkaline hydroxylamine to form acetyl hydroxamate, which then reacts with ferric chloride in acidic medium to form a brown coloured complex which was measured spectrophotometrically at 540 nm against reagent blank. The acetyl choline content is expressed as µmoles of Ach/g of tissue.

Estimation of Acetylcholinesterase activity

The activity of Acetycholinesterase (AchE) was estimated by the method of Ellman *et al.* [42]. Thio-choline, released from acetyl thio-choline by the action of enzyme, reacts with–SH group of DTNB (5, 5'-Dithio-Bis (2-Nitrobenzoic Acid)) reducing it to thiol, which has maximum absorbance at 412 nm. The activity was calculated by using molar extinction coefficient of SH group of DTNB as $14.3x10^3$ and expressed as µmoles of Ach hydrolysed/min/mg protein.

Estimation of transaminases activities [(glutamate pyruvate transaminases (GPT) and glutamate oxaloacetate transaminases (GOT)]

Pyruvate gives a brown colored compound with 2, 4-Dinitrophenyl hydrazine (DNPH) which is measured chromatically at 520 nm [43]. The enzyme activities are expressed as µg of pyruvate liberated/min/mg protein.

Statistical analysis

The results were expressed as mean±SEM. for eight rats in each group. Data were analysed for significant difference using Duncan's multiple range test ($P<0.05$) [44].

RESULTS

Effect of EtCMGR on brain lipid profiles

Table 1 represents data on total lipids constitute phospholipids, glycolipids, cholesterol, triglycerides and also the brain lipids profile of groups-C, C+CM, D and D+CM rats at the end of experimental period. STZ induced diabetic rats showed significant decrease in phospholipids, glycolipids, and cholesterol (29%, 72.5% and 25%) and significant increase intriglycerides (33.6%) when compared with group-C.

EtCMGR treatment for 60 days caused significant increase in phospholipids, glycolipid, and cholesterol (12%, 114% and 16%) and significant decrease in triglycerides (22%) in group-D+CM rats when compared to group-D. But this significant increase in phospholipids, glycolipids, and cholesterol could not reach the control values whereas triglycerides levels were normalized. Thus phospholipids, glycolipids, and cholesterol levels (20%, 41% and 13%) in group-D+CM rats were still significantly lower (25%, 40% and 14%) when compared to group-C whereas EtCMGR treatment for 60 days to group-C+CM rats showed slight increase in glycolipids (54 %) and decrease in cholesterol and phospholipids (10% and 5%) and no significant change in triglycerides levels when compared to group-C.

Effect of EtCMGR on acetylcholine and acetylcholine esterase

Table 2 illustrates the concentration of Ach and the activity of AchE in the brain of four experimental groups. Diabetic group showed significant decrease in the activity of AchE (8%) and increase in Ach (29%) content when compared with group-C. EtCMGR treatment for 60 days resulted in significant increase in the activity of AchE (40%) and significant decrease in Ach (48%) content in group-D+CM rats when compared to group-D. At 60 days, group-C+CM rats showed significantly higher activity of AchE (68%) and slight decrease in Ach (36%) content when compared to group-C. Thus, the present study indicates the protective effect of EtCMGR treatment in maintaining the normal level of neurotransmitter i.e., Ach even under STZ induced diabetic state.

Table 1: Effect of EtCMGR administration on brain lipid profile in diabetic rats

Experimental groups	Total lipids (mg/g tissue)	Phospholipids (mg/g tissue)	Triglycerides (mg/g tissue)	Cholesterol (mg/g tissue)	Glycolipids (mg/g tissue)
Group C	330.65±14.70^{d}	64.80±1.42^{c}	8.44±0.22^{a}	32.52±0.97^{d}	3.49±0.22^{c}
Group C+CM	300.21±6.27^{c}	61.76±1.29^{c}	7.63±0.32^{b}	29.21±0.36^{c}	4.39±0.27^{d}
Group D	135.16±15.76^{a}	46.21±2.06^{a}	11.28±0.24^{d}	24.42±1.39^{a}	0.96±0.11^{a}
Group D+CM	220.00±6.53^{b}	51.69±1.53^{b}	8.84±0.44^{c}	28.31±0.80^{c}	2.06±0.22^{b}

C: control, C+CM: control rats treated with EtCMGR, D: diabetic, D+CM: diabetic rats treated with EtCMGR. Values are expressed as mean±SEM (n=8 animals). Means with different superscripts within the column are significantly different at $P<0.05$ (Duncan's multiple range test).

Table 2: Effect of EtCMGR administration on brain acetylcholine content and activity of acetylcholinesterase in diabetic rats

Experimental groups	Acetylcholinesterase (µmoles of Ach hydrolysed/min/mg protein)	Acetylcholine (µmoles of Ach/g tissue)
Group C	0.296±0.019^{a}	3.59±0.17^{a}
Group C+CM	0.498±0.026^{d}	2.28±0.11^{b}
Group D	0.274±0.009^{a}	5.39±0.18^{c}
Group D+CM	0.382±0.023^{b}	2.80±0.18^{b}

C: control, C+CM: control rats treated with EtCMGR, D: diabetic, D+CM: diabetic rats treated with EtCMGR. Values are expressed as mean±SEM (n=8 animals). Means with different superscripts within the column are significantly different at $P<0.05$ (Duncan's multiple range test).

Table 3: Effect of EtCMGR administration on protein content and activities of transaminases in diabetic rats

Experimental groups	Protein (mg/g tissue)	GPT (µg of Pyruvate formed/min/mg protein)	GOT (µg of Pyruvate formed/min/mg protein)
Group C	28.11±0.79^{a}	3.58±0.22^{a}	2.89±0.20^{a}
Group C+CM	22.57±0.52^{b}	3.50±0.16^{a}	3.01±0.11^{b}
Group D	20.26±0.62^{d}	4.45±0.07^{b}	4.83±0.15^{d}
Group D+CM	23.88±0.70^{b}	3.79±0.13^{b}	3.53±0.11^{c}

C: control, C+CM: control rats treated EtCMGR, D: diabetic, D+CM: diabetic rats treated with EtCMGR. Values are expressed as mean±SEM (n=8 animals). Means with different superscripts within the column are significantly different at $P<0.05$ (Duncan's multiple range test).

Effect of EtCMGR on transaminases

Data presented in table 3 indicate total protein content and activities of transaminases (GOT and GPT) measured in the four experimental groups. STZ induced diabetic rats showed significant decrease in protein content (28%) with significantly increased activities of GOT (67%) and GPT (24%) in brain when compared with group-C. EtCMGR treatment for 60 days in group-D+CM rats resulted in significant increase in protein content (18%) with significantly decreased activities of GOT (27%) and GPT (15%) in brain compared to group-D. But this change in protein content and transaminases in group-D+CM rats could not reach the control values. However group-C+CM rats showed no significant variation in protein content and activities of GPT and GOT when compared to group-C.

DISCUSSION

Diabetes mellitus is a chronic disease which cannot be completely cured and may lead to development of complications if not properly

regulated. Diabetes is primarily characterized by hyperglycaemia which results from lack of insulin or a weak response of tissues to this hormone. It is associated with long-term complications affecting the eyes, kidneys, cardiovascular system and nervous system [45-47].

In the current study, the significant decrease in total lipid content of group-D rats may be due to increased catabolism of lipids and/or enhanced LPO due to oxidative stress observed under diabetic conditions. Earlier studies in our laboratory demonstrated a defective metabolism of lipid peroxides in brain tissue of diabetic animals [48]. EtCMGR treatment for 60 days showed partial recovery from diabetic induced decrease in total lipid content of group-D+CM which may be due to its protective effect against diabetic induced alterations in lipid metabolism.

In STZ induced diabetic rat brain alterations may be responsible for demyelization and nerve degeneration. The alterations in brain lipids lead to changes in physiological properties of membranes, in enzyme activities, receptors, transport, and cellular interactions and activities of membrane bound proteins [49]. These physiological changes are accompanied by learning and behavioural deficits in rats and mice [50, 51]. Brain is considered the richest organ of the body in cholesterol. It is an important constituent of brain and is used for membrane synthesis and for many other activities by cells through the body and phospholipids and glycolipids are essential components of myelin, microsomal and mitochondrial fractions of brain. It was suggested that a number of neurological and chemical changes occur in the brain tissue due to the decrease in cholesterol synthesis in the diabetes [52]. In our study, the cholesterol level decreased in the brain tissue of group-D rats. In contrast, its level was increased and close to the control group values as a result of the EtCMGR administration in the group-D+CM. The resulting increase in the level of the cholesterol can be caused by the protective effects of the EtCMGR on the neurological and metabolic changes in the brain tissue of diabetic rats. The decreased phospholipids and glycolipids and increased triglyceride content of group-D rats compared to group-C rats indicate the presence of lipid damage or oxidation. Our reports of decreased phospholipids and cholesterol content in diabetic rats are in agreement with earlier studies [53] suggesting that membrane function may be altered and in addition to physicochemical alterations, the specific activities of several membrane bound enzymes (AchE, Mg^{2+}-ATPase, and Na^{+}, K+-ATPase) are significantly decreased and play a role in the development of diabetic complications in brain. Similar results were also reported with regard to the effect of morphine sulphate on brain [54]. Very few studies are available on the protective effect of plants on altered lipid components in diabetic animals. Guggulipid, an alkaloid of *C. mukul* [55], dried flowers of *Adenocalymma alliaceum* [56], *Trigonella graceum* [57]were reported to possess hypolipidemic activity in hypercholesterolaemic rats and in type 1 diabetic animals. The present study is the first to demonstrate the neuroprotective effect of EtCMGR against diabetes induced lipid alterations in the brain of rats.

Acetylcholine is the primary neurotransmitter of the cholinergic system and its activity is regulated by acetylcholine esterase (AChE). Acetyl cholinesterase in brain is chiefly localized in neurons and belongs to a family of hydrolases. It hydrolyses acetylcholine and is used as a marker for cholinergic neural function. Degradation of acetylcholine is necessary to depolarize nerves so that it might repolarize in the next conduction event. The termination of nerve impulse transmission is accomplished through the degradation of acetylcholine into choline and acetyl CoA by AChE [58]. Significant decrease in the activity of AchE and increase in the content of acetylcholine was observed in the brain of group-D rats compared to group-C. The decreased AChE activity could be due to a decrease in the enzyme synthesis by the inhibitory action of the toxicants [59]. It was reported that AChE varies in different organisms responding to environmental stress [60]. Some studies suggested that rat brain AChE activity is not significantly altered by STZ [61, 62]. While some reports refer to reduced rat brain AChE activity occurs due to diabetes [63, 64]. Moreover, an increase in whole brain AChE activity due to diabetes. Our reports of increased concentration of Ach and decreased activity of AchE in diabetic rats are in agreement with earlier studies [65-67]. The increased activity of acetylcholine esterase by *C. mukul* treatment observed both in groups-D+CM and C+CM may be due to increased plasma insulin concentration and decreased blood glucose levels in group-D+CM compared to group-D and increased insulin sensitivity in group-C+CM. Similar to our studies it was demonstrated that decreased AchE activity in brain and heart can be reversed by insulin administration [68]. Thus restoration of Ach concentration and increased AchE activity in group-D+CM rats may be due to improved plasma insulin level by EtCMGR treatment. EtCMGR was reported to possess antihyperglycemic activity in STZ [48, 30] and fructose fed diabetic animals [31].

Measurements of tissue transaminases are useful to assess the tissue functions. Their activities are related to protein metabolism and the maintenance of amino acid homeostasis and might be an indicator of mitochondrial injury [69]. Further, enhanced protein glycation and oxidative stress under hyperglycemic conditions indicates altered protein metabolism in diabetes. Increased GOT activity may be related to an increased transport of NADH from the cytosol to mitochondria [70]. Matthews *et al.* [71] reported that both the enzymes degrade glutamate; though only GPT was able to reduce toxic (500 μM) levels of glutamate into the physiologic (<20 μM) range. The excitotoxic effect of glutamate is believed to be the cause of several neurodegenerative processes [72] and several enzymes with the capacity to degrade glutamate have been suggested as possible neuro-protectants [71]. Thus, enhanced transaminase activities in group-D rats indicate an adaptive mechanism to decrease the glutamate level in the brain. Our reports of decrease in protein content and increase in extent of GPT and GOT activities are supported by earlier studies on diabetic rats [73]. This may be due to increased protein turnover and also increased catabolism of amino acid in the brain of diabetic rats due to enhanced protein oxidation and protein glycation observed under hyperglycemic conditions [48]. The partial rectification of decreased protein content and enhanced transaminases activities observed in group-D+CM by EtCMGR treatment which may be due to its antihyperglycemic activity with enhanced insulin secretion. Thus *C. mukul* treatment to diabetic rats showed improved brain energy metabolism.

CONCLUSION

In summary, EtCMGR has been shown to have, besides hypoglycemic properties, strong hypolipidemic action on diabetic hypertriglyceridemia and hypercholestrolemic as well. This could be useful for prevention or early treatment of diabetic disorders. Further studies are in progress in identifying the active components in *C. mukul* and their role in controlling diabetes.

ACKNOWLEDGEMENT

The work is supported by a grant from Rajiv Gandhi National Fellowship, University Grants Commission, New Delhi and thanks are also due to Prof. Mahammad Akhtar, Sri Krishnadevaraya University, Anantapur, Andhra Pradesh for his help in statistical analysis.

CONFLICT OF INTERESTS

Declared None

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