

Comparative Assessment of the Effect of Lemongrass (*Cymbopogon citratus*) Ethanolic Extract, Aqueous Extract and Essential Oil in High Fat Diet and Fructose Induced Metabolic Syndrome in Rats

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ABSTRACT

Background: Lemongrass (*Cymbopogon citratus*) is widely used as a folklore medication for treating obesity and diabetes. The present study evaluates the comparative effect of ethanolic and aqueous extract and essential oil of lemongrass on various conditions associated with the metabolic syndrome. **Materials and Methods:** High fat diet and fructose (20% w/v) were given for 60 days to induce the metabolic syndrome in Wistar rats. Body weight and BMI were assessed weekly and fasting blood sugar was estimated at 15 days interval. Lemongrass ethanolic extract (LGEE) and aqueous extract (LGAE) were prepared and lemongrass oil (LGEO) was extracted. LGEE, LGAE and LGEO were given to the animals for 42 days. Various biochemical, hormonal and tissue parameters were assessed after completion of treatment protocol. Histopathology of pancreas and liver was performed. **Results:** Phytochemical analysis disseminated that total flavonoid, phenolic and alkaloid content are present in LGEE and LGAE, with maximum level of terpenoids in LGEO. Treatment of HDR with LGEE and LGEO caused significant reduction ($p < 0.001$) while LGAE exhibited moderate reduction ($p < 0.01$) in the body weight, BMI, and fasting blood sugar. LGEE and LGEO treatment also normalized abnormalities in serum insulin, insulin resistance, leptin, lipid profile and CRP level in hyperlipidaemic diabetic rats. A significant ($p < 0.001$) level of reduction in liver enzymes and improvement in oxidative stress parameters was observed after treatment with LGEE and LGEO. Histopathology showed improved histoarchitecture after treatment. **Conclusion:** Results concluded that administration of LGEE and LGEO exhibited better protection in conditions associated with metabolic syndrome than LGAE.

Key words: C-reactive protein, Hyperlipidaemia, Insulin resistance, Lemongrass, Metabolic syndrome, Obesity.

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INTRODUCTION

Metabolic syndrome (MetS) is now being considered as an epidemic due to its increased incidence and associated mortality. It is not a disease, rather a term used to describe a congregate of disorders; majorly visceral obesity, hyperglycaemia, dyslipidaemia that precipitate occurrence of type II diabetes mellitus, cardiovascular complications and several other associated disorders. The sedentary lifestyle and poor eating habits of the modern era is hypothesized as the basic reason behind precipitation of MetS.¹

There is an approximate MetS prevalence of about 25% in US, 30% in Iran, 40% in Asian Pacific region and 36% in Europe and is rising at an alarming pace with increasing westernized culture around the globe.²

The etiological cascade is complex and not clearly defined, but mainly the visceral obesity forms the basis for the development of further complexities. Obesity caused due to the ingestion of energy, excess diet, and physical inactivity results in an increased free fatty acid (FFA) level in the

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blood stream. This elevated levels of FFA results in dysfunctional adipocytes which tend to raise the level of inflammatory mediators and cause oxidative stress, thus leading to an insulin resistant state in the peripheral tissues. Furthermore, the lipid profile gets altered thereby increasing the risk of cardiovascular complications. All this consequently leads to the development of several correlated disorders.³

The complexity of MetS makes its treatment even more challenging. Medicinal plants find folklore application in the treatment of various disorders. The complex phytochemical makeup of medicinal plants comprising numerous components with different targets such as flavonoids, polyphenols, essential oils etc. make it easier to treat several disorders simultaneously and thus can be employed for treatment of MetS.⁴

Cymbopogon citratus (DC.) Stapf belongs to family *Poaceae*. It is a perennial aromatic herb having long thin leaves, native to southwest Asia and commonly known as lemongrass or citronella grass. Tea prepared by lemongrass is quite popular in various countries of the world for nutritional purposes as well as for treating obesity and hypertension.⁵

The studies done previously to establish the phytochemistry of lemongrass states the presence of variety of essential oils, tannins, phenols, flavonoids, vitamins and minerals.⁶ The aqueous extract of lemongrass contains gallic acid, rutin, tannic acid, quercetin hydroquinone, isoquercetin, catechin in abundance. Traditionally, Lemongrass has been used for the treatment of several disorders like cough, flu, headache, pneumonia, elephantiasis, malaria, gingivitis, leprosy, and several other disorders of ophthalmic and vascular origin. Several studies have successfully established the anti-oxidant and anti-inflammatory activity,⁷ and ameliorative effect on hyperglycemia and altered lipid profile^{8,9} of essential oil and aqueous extract of lemongrass. Study done by Bharti *et al.*, 2013 concluded that lemongrass essential oil was responsible for the hypoglycemic and hypolipidemic effect¹⁰ while Garba *et al.*, 2020 reported that the lemon grass tea produced significant antidiabetic effect in type 2 diabetic rats.⁵ However, no data is yet available on the ameliorative effect of lemongrass extract on the parameters of metabolic syndrome despite its use in obesity and hypertension. Some of the previous studies stipulate the potency of aqueous and ethanolic extracts whereas few studies established the potency of lemongrass essential oil.¹¹

Therefore, the present study aimed to compare the effect of ethanolic extract, aqueous extract, and essential oil of lemongrass on a high fat diet and fructose-induced metabolic syndrome in rats.

MATERIALS AND METHODS

Drugs and chemicals: Chemicals of analytical grade were employed for the research. Chemicals were procured from Sigma Chemical Co., St Louis, Missouri, USA and Himedia Laboratories, Mumbai, India. ERBA diagnostic kits (Mumbai, India) and ELISA kits (Cell Biolabs, Inc., USA) were utilized for the biochemical estimation.

Collection of plant material and its authentication:

Fresh lemongrass leaves were accumulated from a local garden of Dehradun region of Uttarakhand for the purpose of this study. Plant authentication was done by Botanical Survey of India (BSI), Dehradun (269).

Preparation of Lemongrass aqueous extract (LGAE):

Fresh lemongrass leaves (100 g) were taken and cut into small pieces and washed thoroughly with normal saline followed by a final washing with distilled water. The chopped leaves were then simmered for 1 hr in distilled water (500 ml) and after it cooled down was filtered using cotton cloth. The filtrate obtained was then evaporated until a chocolate-coloured sweet-scented solid residue was obtained. It was stored in an air-tight container till used.⁸

Preparation of Lemongrass ethanolic extract (LGEE):

The crude powdered lemongrass leaves (50 g) were refluxed with 200ml methanol thrice. The ethanolic extracts were combined and evaporated to complete dryness. The dry powder obtained was stored at 4°C in dark till needed.¹²

Isolation of Lemongrass essential oil (LGEO):

Fresh leaves of lemongrass were washed thoroughly, chopped into small pieces and added to 200 ml of distilled water in round bottom flask. Clevenger apparatus was used for distillation for about 4 hr. The floating essential oil was collected and dried using anhydrous Sodium and stored at -20°C till used.¹³

Determination of Phytoconstituents

Total Flavonoid content: Total flavonoid content was determined using colorimetric assay. To 1ml of extract added 4 ml of distilled water and 0.3ml each of 5% NaNO₂ and 10% AlCl₃, and were allowed to incubate at room temperature for 5 min. This was followed by addition of 2 ml 1M NaOH to the mixture and finally made up the volume up to 10 ml with distilled water. The reaction mixtures were then vortexed and measured its absorbance at 510 nm using UV spectrophotometer.¹⁴

Total Phenolic Content: Colorimetry was used to determine the total phenolic content of the extracts. 5 g of the extract was mixed with 50 ml of ether and boiled for 5 min. Added 2 ml of ammonium hydroxide solution

and 5 ml of amyl alcohol to 5 ml of the aforementioned reaction mixture and finally made up the volume to 50 ml using distilled water and was kept standing for 30 min. The absorbance of the mixture was read at 550 nm using UV spectrophotometer. For calibration standard curve of gallic acid was utilized.¹⁵

Total Alkaloid content: In a 250 ml beaker took 5 g of the extract and 200 ml of 10% acetic acid in ethanol, and covered the mixture and allowed it to standstill for 4 hr. Afterwards filtered the mixture and concentrated the filtrate to quarter of the original volume followed by addition of conc. NH_4OH drop wise until complete precipitation. The precipitate collected was washed with dil. NH_4OH , filtered and the residue was weighed and recorded as alkaloid content.¹⁶

Terpenoid content: 100 mg (w) dried plant extract was immersed in 9 ml ethanol for 24 hr. After filtration the mixture was extracted with 10 ml petroleum ether with help of separating funnel.¹⁷ The ether extract obtained was evaporated to complete dryness (w) and the terpenoid yield (%) was reported using following formula:

$$(w_i - w_f)/w_f \times 100$$

Animals: Wistar rats (male) having weight between 225-250 g and age around 6-7 weeks were obtained from Indian Veterinary Research Institute, Bareilly, Uttar Pradesh. Standard propylene cages were used to house the rats in groups of four to five per cage under optimally adjusted room temperature and humidity. A period of one week prior to initiation of experimental protocol was given to animals for acclimatization with the laboratory environment. The experimental protocol was approved by Institutional Animal Ethical Committee (IAEC approval number CPCSEA/IAEC/SBS/2019/011) and guidelines specified by Committee for the Purpose of Control and Supervision of Experimental Animals (CPCSEA) of the Govt. of India for humane care of experimental animals were taken into consideration throughout the study.

Induction of Metabolic Syndrome: Obesity and hyperlipidaemia were induced in experimental animals using hyperlipidaemic diet for a duration of 60 days. Freshly prepared fructose (20% w/v in distilled water) was given in the form of drinking water to all the test groups for induction of diabetes.¹⁸ The weight and fasting blood sugar (FBS) level of the experimental rats were estimated and those animals having body weight greater than 350g and FBS levels greater than 200mg/dl were supposed to be hyperlipidaemic diabetic rats (HDR) and chosen for the study.

Selection and Preparation of doses: Based on studies done previously on lemongrass, two doses of aqueous extract (125 and 250 mg/kg body weight),¹¹ two doses of ethanolic extract (100 and 200 mg/kg body weight)⁸ and two doses of essential oil (150 and 300 mg/kg/day body weight)¹⁹ were selected for the pharmacological activity. The selected doses were given to the different groups of hyperlipidemic diabetic animals for 42 days duration. LGAE and LGEE were given as suspension in 1% CMC in distilled water whereas LGEO was given as emulsion using 0.001% Tween 80.

Experimental Design

The HDR were distributed into seven groups each having six animals along with one group having normal animals (disease free) were administered the following treatment for 42 days.

Group I (Normal control): Normal animals were administered distilled water (1 ml/kg, p.o.).

Group II (Toxicant control): Hyperlipidaemic diabetic rats were administered distilled water 1 ml/kg, p.o.

Group III: HDR animals were administered lemongrass ethanolic extract 100 mg/kg/day p.o.

Group IV HDR animals were administered lemongrass ethanolic extract 200 mg/kg/day p.o.

Group V: HDR animals were administered lemongrass aqueous extract 125 mg/kg/day p.o.

Group VI: HDR animals were administered lemongrass aqueous extract 250 mg/kg/day p.o.

Group VII: HDR animals were administered lemongrass essential oil 150 mg/kg/day p.o.

Group VIII: HDR animals were administered lemongrass essential oil 300 mg/kg/day p.o.

Body weight was recorded weekly from the start till the end of study. BMI was calculated using the formula given below. Fasting blood sugar (FBS) was estimated at 15 days interval. After the 42 days treatment period all the animals were kept on overnight fasting. Under ether anaesthesia blood sample was withdrawn from the retro-orbital plexus. Serum was obtained by centrifuging the blood sample in cooling centrifuge (Remi, C24, India) at 2500 rpm for 15 min at 3°C temperature and was further utilized for lipid, Insulin, C- reactive protein, leptin, AST and ALT level estimation. At the end, animals were euthanised (Phenobarbitone 150 mg/kg, i.p.) and immediately excised pancreas and liver from all the group of animals and utilized for histopathological examination and assessment of oxidative stress parameters. Pancreatic tissue was washed with ice cold saline, weighed and then homogenized in phosphate buffer (50mM, pH 7.4) so as to prepare a 10% (w/v)

solution, followed by centrifugation of homogenate at $7000 \times g$ at 4°C for 10 min. The supernatant derived was utilized for the assay of lipid peroxidation (LPO), superoxide dismutase (SOD) and reduced glutathione (GSH).

Assessment of body weight and body mass index (BMI): After the high fat diet and the initiation of treatment, body weight and BMI were estimated at weekly interval.

$$\text{BMI} = \text{Mass (kg)} / \text{height (m}^2\text{)}$$

$$\text{BMI} = \text{Mass (lbs.)} / \text{height (inch}^2\text{)} \times 703$$

Where m and h are the weight and height of subject respectively.

Serum biochemical analysis

Estimation of FBS: FBS was estimated from serum by GOD-POD method on 0, 15th, 30th and 42nd day of the treatment using Erba diagnostic kit and sample was analysed in Chem 5X Clinical Chemistry Analyser, Mannheim, Germany.²⁰

Estimation of lipid profile: CHOD-PAP method,²¹ phosphotungstic acid method²² and GPO-Trinder method²³ were used to determine the serum level of total cholesterol, HDL and triglyceride in the serum respectively with the help of Erba diagnostic kits using Erba Chem 5X Clinical Chemistry Analyser, Mannheim, Germany.

The atherogenic index was calculated by using the formula:

$$\text{AI} = \log_{10} (\text{TG}/\text{HDL})$$

Friedewald's equation was used to estimate the VLDL and LDL level as follows:

$$\text{VLDL} = \text{Total serum triglycerides} / 5$$

$$\text{LDL} = \text{Total serum cholesterol} - \text{VLDL} - \text{HDL}$$

Estimation of Uric acid: The serum uric acid level was estimated with help of Trinder peroxidase method²⁴ using TBHB using Erba Chem 5X Clinical Chemistry Analyser, Mannheim, Germany.

Hepatic enzyme assay: AST and ALT enzyme level in the serum was assessed by IFCC kinetic method.²⁵

Hormonal analysis

Insulin Assay and Insulin Resistance: Insulin level in the serum was estimated with the help of method of MacDonald 1989²⁶ using an ELISA kit (Cell Biolabs, Inc., USA). Insulin resistance extent was reported by estimating the HOMA-IR (Homeostasis Model Assessment of insulin resistance) index²⁷ using the following formula:

$$\text{HOMA-IR} = \frac{(\text{fasting insulin} (\mu\text{U/mL}) \times \text{fasting glucose (mmol/L)})}{22.5}$$

Leptin Assay: The serum leptin level was determined with help of Sandwich ELISA assay method²⁸ using leptin ELISA kit (Cell Biolabs, Inc., USA).

Measurement of CRP: The CRP level in the serum was determined using latex agglutination test method²⁹ and kit from Spectrum Diagnostics, Egypt.

Oxidative stress markers analysis

Malondialdehyde (MDA) assay: Estimation of MDA was done from the tissue supernatant of pancreas by spectrophotometrically estimating the amount of lipid peroxides in the tissue using thiobarbituric acid.³⁰

Superoxide dismutase (SOD) assay: SOD was determined in the pancreatic supernatant spectrophotometrically with help of method given by Sun and Zigman, 1978.³¹

Reduced glutathione assay: Reduced glutathione was assayed spectrophotometrically from the pancreatic supernatant with the help of method of Moron *et al.*, 1979.³²

Histopathology: The isolated pancreas and liver were stored in 10% formalin and were then embedded in paraffin. 5 μm thick tissue sections were cut, stained using eosin and haematoxylin and observed under light microscope (100X magnification) for histoarchitectural study.

Statistical analysis: Graph pad prism 7.0 software was used for the statistical analysis of the results expressed as mean \pm SEM for each group of six animals. Students *t*-test was used to compare two groups while for multiple comparisons in between different groups one way ANOVA (Analysis of Variance) followed by Dunnett's multiple comparison was utilized. Results having *P* value less than 0.05 were considered as significant.

RESULTS

Phytochemical Analysis of LGEE, LGAE and LGEO for Total Flavonoid, Total Phenolic, Total Alkaloid and Total Terpenoid content: The quantitative analysis of phytochemicals in LGAE, LGEE and LGEO have been summarized in Table 1. The total phenolic and flavonoid content was found in greater amounts in LGEE, except alkaloid content, which was found more in LGAE, though the difference was insignificant. The terpenoid content was found to be higher in LGEO as compared to other phytochemicals.

Effect of LGEE, LGAE and LGEO on the body weight and BMI of hyperlipidemic diabetic rats: Feeding HFD and fructose to rats for 60 days caused significant ($p < 0.01$) increase in body weight on the 30th day and most significant ($p < 0.001$) on the 60th day of

the study in all the treatment groups in comparison to the initial day, indicating induction of hyperlipidaemic state. BMI also increased significantly ($p<0.001$) on the 30th and the 60th day of the study in comparison to the initial day.

Table 2 summarizes the effect of LGAE, LGEE and LGEO administration on the body weight and BMI of HDR. Results clearly demonstrated that administration of LGEE at 200 mg/kg caused most significant ($p<0.001$) decrease in body weight and BMI (adiposity index) of HDR in comparison to the toxicant control as well as to the first day of the treatment. LGAE 250 mg/kg and LGEO 300 mg/kg produced significant decrease ($p<0.01$) in the body weight and BMI of HDR as compared to day 1 of the study. Lower doses of LGEE and LGAE did not cause significant ($p<0.1$) reduction in body weight and BMI of HDR. Administration of LGEE, LGAE and LGEO also resulted in gradual reduction in BMI of HDR. No significant decrease in body weight and BMI of vehicle control group was observed.

Effect of LGEE, LGAE and LGEO on FBS of the hyperlipidemic diabetic rats: The results of LGEE, LGAE and LGEO administration on FBS level at

different time interval are indicated in Table 3. Results show that HFD and fructose (20% w/v) administration for 60 days duration resulted in significant ($p<0.001$) elevation in plasma FBS in all the groups as compared to that on the day 0 of the study. Treatment of hyperlipidaemic diabetic rats with higher doses of LGEE, LGAE and LGEO for 42 days significantly ($p<0.001$) reduced FBS level to normal in all the treatment groups in comparison to day 1 of treatment. Lower doses of LGEE (100 mg/kg), LGAE (125 mg/kg) and LGEO (150 mg/kg) produced slight decrease ($p<0.05$) in FBS level in HDR in comparison to day 1 of treatment. No significant reduction in plasma FBS level was seen in the vehicle control group.

Effect of LGEE, LGAE and LGEO on the lipid profile and atherogenic index (AI) in hyperlipidemic diabetic rats

HFD and fructose (20% w/v) administration to rats for 60 days duration caused significant decrease ($p<0.001$) in level of HDL and significant increase ($p<0.001$) in total cholesterol (TC), triglyceride (TG), LDL and VLDL and atherogenic index. The effect of LGEE, LGAE and LGEO administration on lipid profile of HDR are summarized in Table 4. Results indicated that LGEE (200 mg/kg) and LGEO (300 mg/kg) produced significant increase ($p<0.001$) in plasma HDL and significant reduction in TC, TG, LDL and VLDL levels followed by LGAE (250 mg/kg) ($p<0.001$) as compared to toxicant control group. LGEO lower dose 150 mg/kg brought moderate improvement ($p<0.05$) in lipid profile but the lower doses of LGEE and LGAE caused improvement only in the level of HDL, LDL and VLDL in comparison to toxicant control group.

Table 1: Quantitative phytochemical analysis of lemongrass extract.

Phytochemicals	LGAE	LGEE	LGEO
Flavonoids (mg/g)	54.3±6.1	68.5±4.8	21.4±1.3
Total Phenolics (mgGAE/g)	78.6±4.3	121±5.9	32.8±7.6
Alkaloids (mg/g)	38.2±2.1	37.8±4.1	12.6±3.6
Terpenoid content (%)	20.5±5.2	24.7±6.2	93.2±2.7

Index: LGAE: lemongrass aqueous extract; LGEE: lemongrass ethanolic extract; LGEO: lemongrass essential oil.

Table 2: Effect of LGEE, LGAE and LGEO on body weight and BMI of hyperlipidaemic diabetic rats.

Groups	Body weight (grams)			BMI (gm/cm ²)		
	0 Day	21 st Day	42 nd Day	0 Day	21 st Day	42 nd Day
Normal Control	243 ± 1.7	242 ± 1.1	239 ± 0.8	0.59 ± 0.1	0.59 ± 0.1	0.6 ± 0.1
Toxicant control HDR given distilled water (1ml/kg p.o)	402 ± 0.6	396 ± 0.4	390 ± 2.2 ^a	0.9 ± 0.1	0.9 ± 0.2	0.9 ± 0.2 ^a
HDR received LGEE (100 mg/kg p.o.)	409 ± 0.2	398 ± 0.6	346 ± 0.9 [*]	0.9 ± 0.2	0.9 ± 0.3	0.8 ± 0.3
HDR received LGEE (200 mg/kg p.o.)	405 ± 0.4	371 ± 0.3	250 ± 0.6 ^{***}	0.9 ± 0.1	0.8 ± 0.2	0.6 ± 0.1 ^{***}
HDR received LGAE (125 mg/kg p.o)	407 ± 0.5	385 ± 0.8	377 ± 0.5	0.95 ± 0.1	0.9 ± 0.3	0.8 ± 0.2
HDR received LGAE (250 mg/kg p.o)	409 ± 0.5	367 ± 0.1	274 ± 0.2 ^{**}	1.0 ± 0.1	0.9 ± 0.3	0.6 ± 0.2 ^{***}
HDR received LGEO (150 mg/kg p.o)	405 ± 0.5	375 ± 0.3	380 ± 0.5 [*]	0.9 ± 0.1	0.9 ± 0.2	0.9 ± 0.2
HDR received LGEO (300mg/kg p.o)	407 ± 0.4	356 ± 0.1	275 ± 0.1 ^{**}	0.9 ± 0.2	0.8 ± 0.3	0.7 ± 0.1 ^{**}

All values are expressed as mean ± SEM and $n=6$ in each group.

P values: ^{*} $p<0.05$, ^{**} $p<0.01$, ^{***} $p<0.001$ when results on day 42 of treatment were compared with results on day 0 of each group. ^a $P<0.001$ when the results of toxicant control group were compared with normal control on day 42.

LGAE: Lemongrass aqueous extract; LGEE: Lemongrass ethanolic extract; LGEO: Lemongrass essential oil; HDR: Hyperlipidemic diabetic rat

Table 3: Effect of LGEE, LGAE and LGEO on Fasting Blood Sugar level of hyperlipidaemic diabetic rats.

Groups	Fasting Blood Sugar (mg/dL)			
	0 Day	15 th Day	30 th Day	42 nd Day
Normal Control	97.2 ± 0.5	99.9 ± 0.8	99.8 ± 0.8	97.0 ± 3.3
Toxicant control HDR given distilled water (1ml/kg p.o)	234.6 ± 1.5	231.7 ± 1.1	227.2 ± 1.2	224.9 ± 1.6
HDR received LGEE (100 mg/kg p.o.)	237.8 ± 0.2	235.2 ± 0.9	223.3 ± 1.1	215.9 ± 0.2 [*]
HDR received LGEE (200 mg/kg p.o.)	243.9 ± 0.3	182.1 ± 2.4	148.5 ± 1.0	111.8 ± 0.4 ^{***}
HDR received LGAE (125 mg/kg p.o)	238.9 ± 0.7	231.2 ± 0.8	218.7 ± 0.6	210.5 ± 0.6 [*]
HDR received LGAE (250 mg/kg p.o)	237.7 ± 3.1	163.8 ± 0.7	149.8 ± 1.1	127.5 ± 0.2 ^{***}
HDR received LGEO (150 mg/kg p.o)	237.9 ± 4.1	231.0 ± 0.3	225.9 ± 0.8	209.6 ± 0.9 [*]
HDR received LGEO (300mg/kg p.o)	244.4 ± 0.6	161.8 ± 0.8	130.3 ± 1.0	111.6 ± 0.2 ^{***}

All values are being expressed as mean ± SEM; n=6 in each group.

P values: ^{*}p<0.05, ^{**}p<0.01 ^{***}p<0.001 when results on day 42 of treatment were compared with results on day 0 of each group.

LGAE: lemongrass aqueous extract; LGEE: lemongrass ethanolic extract; LGEO: lemongrass essential oil; HDR: hyperlipidemic diabetic rats.

Table 4: Effect of LGEE, LGAE and LGEO on lipid profile of hyperlipidaemic diabetic rats.

Groups	HDL (mg/dL)	Total Cholesterol (mg/dL)	Triglyceride (mg/dL)	LDL (mg/dL)	VLDL (mg/dL)
Normal Control	54.2 ± 1.9	102.6 ± 2.8	88.3 ± 0.3	40.8 ± 0.5	17.6 ± 0.6
Toxicant control HDR given distilled water (1ml/kg p.o)	21.8 ± 1.8 ^a	189.9 ± 2.0 ^a	186.2 ± 0.4 ^a	130.8 ± 3.2 ^a	37.2 ± 0.9 ^a
HDR received LGEE (100 mg/kg p.o.)	27.3 ± 2.5 [*]	166.6 ± 0.8	154.5 ± 0.6 [*]	113.1 ± 1.8 [*]	25.7 ± 1.1 [*]
HDR received LGEE (200 mg/kg p.o.)	48.7 ± 1.1 ^{***}	108.5 ± 0.4 ^{***}	89.7 ± 0.3 ^{**}	57.9 ± 0.4 ^{***}	18.9 ± 0.5 ^{***}
HDR received LGAE (125 mg/kg p.o)	27.9 ± 1.6	165.1 ± 0.8 [*]	166.4 ± 0.1	92.6 ± 0.5 [*]	25.7 ± 0.6 [*]
HDR received LGAE (250 mg/kg p.o)	41.2 ± 1.2 ^{**}	118.8 ± 0.4 ^{***}	99.3 ± 0.3 ^{**}	71.8 ± 0.6 ^{***}	20.7 ± 1.2 ^{**}
HDR received LGEO (150 mg/kg p.o)	32.7 ± 1.3 [*]	166.7 ± 0.3 [*]	138.8 ± 0.9 [*]	90.7 ± 0.2 [*]	24.7 ± 0.4 [*]
HDR received LGEO (300mg/kg p.o)	42.5 ± 0.7 ^{**}	117.9 ± 0.5 ^{***}	83.6 ± 0.3 ^{***}	61.5 ± 2.3 ^{***}	16.7 ± 0.5 ^{***}

All values are expressed as mean ± SEM; N=6 in each group.

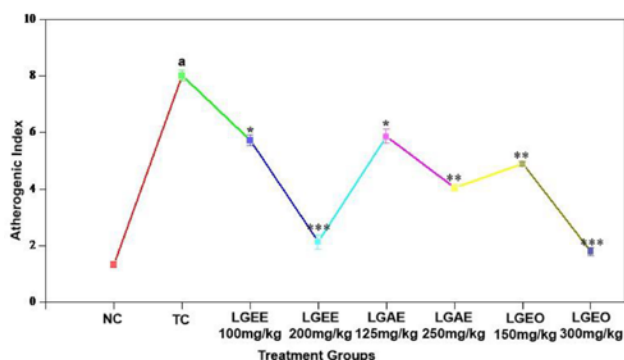
P values: ^{*}p<0.05, ^{**}p<0.01 ^{***}p<0.001 when results of treatment group were compared with toxicant control group on day 42.

^aP<0.001 when results of toxicant and vehicle control compared with the normal control group.

LGAE: lemongrass aqueous extract; LGEE: lemongrass ethanolic extract; LGEO: lemongrass essential oil; HDR: hyperlipidemic diabetic rats

The effect of LGEE, LGAE and LGEO administration on AI of HDR is summarized in Figure 1. Results indicated LGEE, LGAE and LGEO at high dose levels for 42 days produced significant ($p<0.001$) decrease in AI of HDR in comparison to toxicant control group.

Effect of LGEE, LGAE and LGEO on level of insulin, insulin resistance, uric acid and leptin in hyperlipidemic diabetic rats: The outcome of 42 days administration of LGEE, LGAE and LGEO on insulin, uric acid and leptin level in serum of HDR is summarized in Table 5. Result indicated significant ($p<0.001$) increase in level of insulin, leptin and uric acid in all the groups after administration of HFD and fructose (20% w/v) for 60-days. LGEE, LGEO and LGAE caused significant and dose dependent reduction in serum insulin, leptin and uric acid level in HDR in comparison to toxicant control group.

**Figure 1: Effect of LGEE, LGAE AND LGEO on atherogenic index (AI) in hyperlipidemic diabetic rats.**

All values are expressed as mean ± SEM; N=6.

P values: ^{*}P<0.05, ^{**}P<0.01, ^{***}P<0.001 when the results of treatment groups were compared with the toxicant control groups.

^aP<0.001 when the results of toxicant control group were compared with the normal group of animals.

LGAE: lemongrass aqueous extract; LGEE: lemongrass ethanolic extract; LGEO: lemongrass essential oil; HDR: hyperlipidaemic diabetic rats.

Table 5: Effect of LGEE, LGAE and LGEO on serum insulin, leptin, uric acid, AST and ALT level in hyperlipidaemic diabetic rats.

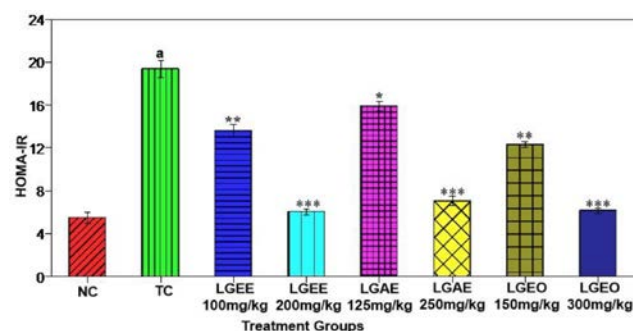
Groups	Insulin (mIU/ml)	Leptin (ng/mL)	Uric acid (mg/dL)	AST (IU/L)	ALT (IU/L)
Normal Control	22.6 ± 1.3	8.4 ± 0.6	4.7 ± 0.8	70.3 ± 1.2	37.3 ± 0.6
Toxicant control HDR given distilled water (1ml/kg p.o)	34.9 ± 1.8 ^a	14.1 ± 0.8 ^a	15.8 ± 0.9 ^a	91.8 ± 2.7	64.2 ± 2.0
HDR received LGEE (100 mg/kg p.o.)	29.5 ± 0.6 [*]	12.2 ± 0.2 [*]	9.6 ± 0.8 [*]	85.0 ± 2.0	56.0 ± 1.4 [*]
HDR received LGEE (200 mg/kg p.o.)	22.8 ± 1.7 ^{***}	8.7 ± 0.2 ^{***}	5.1 ± 0.5 ^{***}	73.8 ± 2.9 ^{**}	39.3 ± 1.1 ^{***}
HDR received LGAE (125 mg/kg p.o)	30.5 ± 2.1 [*]	12.6 ± 0.7 [*]	10.5 ± 0.6 ^{**}	84.3 ± 2.6	57.3 ± 2.2 [*]
HDR received LGAE (250 mg/kg p.o)	25.5 ± 0.9 ^{***}	8.9 ± 1.1 ^{***}	6.97 ± 0.1 ^{***}	78.7 ± 2.7 ^{***}	43.8 ± 1.6 ^{**}
HDR received LGEO (150 mg/kg p.o)	28.5 ± 0.5 [*]	10.8 ± 1.6 ^{**}	8.67 ± 1.2 ^{**}	81.3 ± 3.2 [*]	55.7 ± 2.5 ^{**}
HDR received LGEO (300 mg/kg p.o)	20.7 ± 0.9 ^{***}	8.6 ± 0.73 ^{***}	5.39 ± 1.1 ^{***}	71.5 ± 2.1 ^{***}	40.0 ± 1.4 ^{***}

All values are expressed as mean ± SEM; N=6 in each group.

P values: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ when results of treatment group were compared with toxicant control group on day 42.

^a $p < 0.001$ when results of toxicant and vehicle control compared with the normal control group

LGAE: lemongrass aqueous extract; LGEE: lemongrass ethanolic extract; LGEO: lemongrass essential oil; HDR: hyperlipidaemic diabetic rats

**Figure 2: Effect of LGEE, LGAE and LGEO on HOMA-IR in hyperlipidemic diabetic rats.**

All values are expressed as mean ± SEM; N=6.

P values: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ when the results of treatment groups were compared with the toxicant control groups.

^a $P < 0.001$ when the results of toxicant control group were compared with the normal group of animals.

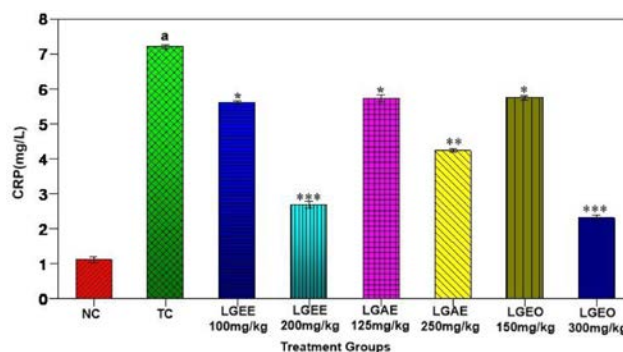
LGAE: lemongrass aqueous extract; LGEE: lemongrass ethanolic extract; LGEO: lemongrass essential oil; HDR: hyperlipidaemic diabetic rats.

However, the results produced by LGEE (200 mg/kg) LGAE (250mg/kg) and LGEO (300 mg/kg) were most significant ($p < 0.001$) and brought about remarkable reduction in insulin, leptin and uric acid level.

The effect of LGEE, LGAE and LGEO on HOMA-IR score as evident from Figure 2, decreased in all the treatment groups except in vehicle control group after 42 days treatment protocol in comparison to toxicant control. Results were more significant ($p < 0.001$) at higher doses of LGEE, LGAE and LGEO than the respective lower doses.

Effect of LGEE, LGAE and LGEO on C-reactive protein (CRP) in hyperlipidemic diabetic rats

Administration of HFD and fructose (20% w/v) for 60 days produced significant ($p < 0.001$) increase in CRP level in serum of all HDR groups in comparison to normal control as indicated in Figure 3. HDR treated

**Figure 3: Effect of LGEE, LGAE and LGEO on C-reactive protein level in hyperlipidemic diabetic rats.**

All values are expressed as mean ± SEM; N=6.

P values: * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ when the results of treatment groups were compared with the toxicant control groups.

^a $P < 0.001$ when the results of toxicant control group were compared with the normal group of animals.

LGAE: lemongrass aqueous extract; LGEE: lemongrass ethanolic extract; LGEO: lemongrass essential oil; HDR: hyperlipidaemic diabetic rats.

with LGEE (200 mg/kg) and LGEO (300 mg/kg) for 42 days resulted in significant ($p < 0.001$) decrease in CRP level in comparison to the toxicant control group. Administration of LGAE (250 mg/kg) exhibited moderately significant ($p < 0.01$) reduction in CRP level. Lower doses of LGEE, LGEO and LGAE did not precipitate any significant ($p \geq 1$) decrease in the CRP level of HDR.

Effect of LGEE, LGAE and LGEO on AST and ALT level in hyperlipidemic diabetic rats

Administration of HFD and fructose (20% w/v) for 60 days caused significant ($p < 0.01$) elevation in AST and ALT levels in serum of all HDR groups in comparison to the normal control as indicated by results given in Table 5. In hyperlipidaemic diabetic rats, significant improvement was seen in AST and ALT levels after

administration of LGEE (200 mg/kg) and LGEO (300 mg/kg) for 42 days duration. LGAE also precipitated significant reduction ($p<0.001$) in the level of AST but moderate decrease ($p<0.01$) in ALT level in HDR in comparison to the toxicant control group. LGEE (100 mg/kg), LGAE (125 mg/kg) and LGEO (150 mg/kg) at lower dose caused slight reduction in the hepatic enzymes level in HDR. The vehicle control group did not show significant effect in reducing the levels of plasma AST and ALT in HDR when compared to toxicant control.

Effect of LGEE, LGAE and LGEO on the level of oxidative stress and antioxidant enzymes in the hyperlipidemic diabetic rats

Administration of HFD and fructose (20% w/v) for 60-days period significantly ($p<0.001$) increased the amount of malondialdehyde, a marker of lipid peroxidation and decreased the quantity of antioxidant enzymes GSH and SOD. Results in Table 6 indicated that HDR treated with LGEE, LGEO and LGAE for 42 days indicated dose dependent alleviation in MDA levels and improvement in GSH and SOD level. Higher doses caused significant ($p<0.001$) improvement in

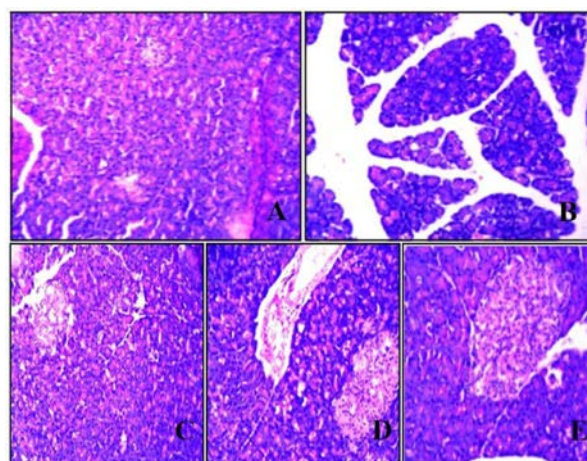


Figure 4: (A) Microscopic sections of rat pancreas of normal control group (Hematoxylin-eosin, magnification X 100 (H&E, X 100)). (B) Microscopic section of rat pancreas of toxicant control group (H&E, X 100). (C) Microscopic section of pancreas of rat treated with LGEE 200 mg/kg (H&E, X 100). (D) Microscopic section of pancreas of rat treated with LGAE 250 mg/kg (H&E, X 100). (E) Microscopic section of pancreas of rat treated with LGEO 300 mg/kg H&E, X 100).

comparison to the toxicant control group, while vehicle control group produced insignificant changes.

Effect of LGEE, LGAE and LGEO on the histopathology of pancreas and liver of the hyperlipidemic diabetic rats

Figure 4 shows the histopathological examination of tissue of pancreas of rats. Figure 4A revealed a normal histo-architecture with intact β -cells in the normal group of animals. Figure 4B showed the pancreatic tissues of the toxicant control group with small and atrophic islets of Langerhans. Slight inflammatory cells are also noted in the toxicant control group. Treatment with LGAE 250 mg/kg (Figure 4D) showed little improvement on the histology of pancreatic tissue of HDR. LGEE at 200 mg/kg (Figure 4C) showed marked improvement in the histoarchitecture of pancreatic β cells with normal acinar cells. Figure 4E showed the effect of LGEO 300 mg/kg on rat pancreatic tissue and indicated maximal protection having histo-architecture comparable to that of normal animals.

Figure 5 shows microscopic examination of the tissues of rat liver. Figure 5A reflected histologically unremarkable and normal liver tissue without any inflammation in the normal group of rats. Significant hepatocytic degeneration mainly in periportal area, acute inflammatory exudate along with congestion and periportal mononuclear cells infiltration was noted in the toxicant control group (Figure 5B). Rats administered LGAE 250 mg/kg presented little improvement in the histology of the liver (Figure 5D). Figure 5C

Table 6: Effect of LGEE, LGAE and LGEO on oxidative stress parameters in hyperlipidaemic diabetic rats.

Group	MDA (nmol/mg)	GSH (microgram/mg protein)	SOD (EU/mg protein)
Normal Control	3.7 \pm 0.5	70.2 \pm 3.5	25.8 \pm 1.4
Toxicant control HDR given distilled water (1ml/kg p.o)	10.9 \pm 0.8 ^a	40.0 \pm 2.9 ^a	10.6 \pm 0.8 ^a
HDR received LGEE (100 mg/kg p.o.)	7.8 \pm 0.3 [*]	51.6 \pm 1.3 [*]	15.3 \pm 1.2 [*]
HDR received LGEE (200 mg/kg p.o.)	4.1 \pm 0.2 ^{***}	69.7 \pm 2.5 ^{***}	23.2 \pm 0.9 ^{***}
HDR received LGAE (125 mg/kg p.o)	7.2 \pm 0.8 [*]	50.1 \pm 1.5 [*]	16.1 \pm 0.8 [*]
HDR received LGAE (250 mg/kg p.o)	4.6 \pm 0.8 ^{***}	68.2 \pm 2.7 ^{***}	22.2 \pm 0.5 ^{***}
HDR received LGEO (150 mg/kg p.o)	8.7 \pm 0.3 [*]	52.7 \pm 2.4 [*]	14.5 \pm 0.9 [*]
HDR received LGEO (300 mg/kg p.o)	4.8 \pm 0.6 ^{***}	69.9 \pm 1.6 ^{***}	24.7 \pm 1.2 ^{***}

All values are expressed as mean \pm SEM; N=6 in each group.

P values: * $p<0.05$, ** $p<0.01$ *** $p<0.001$ when results of treatment group were compared with toxicant control group on day 42.

^a $P<0.001$ when results of toxicant and vehicle control compared with the normal control group

LGAE: lemongrass aqueous extract; LGEE: lemongrass ethanolic extract; LGEO: lemongrass essential oil; HDR: hyperlipidaemic diabetic rats

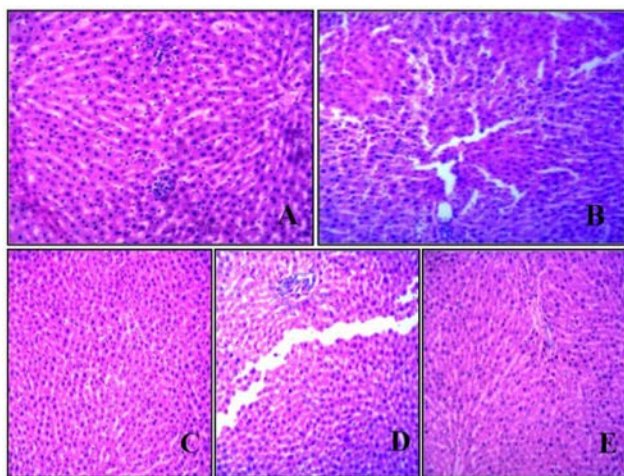


Figure 5: (A) Microscopic sections of rat liver showing normal tissue (Hematoxylin-eosin, magnification X 100 (H&E, X 100)). (B) Microscopic section of rat liver of toxicant control group (H&E, X 100). (C) Microscopic section of liver of rat treated with LGEE 200 mg/kg (H&E, X 100). (D) Microscopic section of liver of rat treated with LGAE 250 mg/kg (H&E, X 100). (E) Microscopic section of liver of rat treated with LGEO 300 mg/kg H&E, X 100).

and Figure 5E treated with LGEE 200 mg/kg and LGEO 300 mg/kg exhibited significant regeneration of hepatocytes and decrease in inflammation.

DISCUSSION

Present study presented that administration of HFD with fructose (20% w/v) for 60 days increased the body weight, white adipose tissue mass and BMI of normal animals. HFD and fructose provides excessive energy that is not fully utilized by the animals and consequently accumulates up in the adipocytes leading to adipocyte hypertrophy and increase in white adipose tissue mass.³³ LGEE had higher amounts of flavonoids, phenolic acids, and alkaloids than LGAE, while LGEO had higher amount of terpenoids than other phytochemicals. The administration of LGEE and LGAE caused significant reduction in body weight of treated rats probably owing to lipid lowering and anorexic effect of extracts of lemongrass; as previously established by Adeneye, Agbaje, 2007.⁸ This weight loss consequently decreased the BMI of HDR. LGEO administration also decreased the body weight of the HDR rats as indicated by the results of the study. Modak *et al.*, 2011 in their study proclaimed that citral administration decreased the body weight without affecting the food intake by reducing absorption of fat and enhancing fat metabolism.³⁴ Thus, we can correlate that the decrease in the body weight and BMI by LGEO might be possible due to the presence of citral.

LGEO, LGEE and LGAE administration for 42 days caused significant decrease in FBS level in HDR. High amount of phytochemicals like flavonoids, phenols, tannins, anthocyanins present in LGEE and LGAE and essential oils present in LGEO might be responsible for this effect, as it is well known that polyphenols and essential oils are responsible for antidiabetic effects of many plants.³⁵ Studies done in past on various flavonoids have also shown to improve insulin signalling pathways like cAMP/PKA and PLC/PKC and β cell function by inhibition of NF- κ B and activation of PI3K/AKT pathways which might be the possible mechanism behind increased glucose utilization and decrease in FBS.³⁶ The results of our study are well supported by a recent study done on lemongrass tea to demonstrate its anti-hyperglycaemic effect associated with increased hepatic glucokinase activity and subsequent increased glucose utilization.⁵ Another study demonstrated that the hypoglycaemic activity of lemongrass extract is attributed to its ameliorative effect on ER stress by upregulating the Nrf2 signalling pathways.³⁷ The anti-diabetic effect of LGEO can be attributed to the PPAR- γ activating and DPP-IV inhibiting action owing to various constituents in the essential oil as suggested by the work of Bharti *et al.*, 2013.¹⁰

In this study, administration of LGEE, LGEO and LGAE positively altered the lipid profile as well as lowered the atherogenic index, a marker of cardiovascular complications in HDR. However, among the three extracts, LGEO and LGEE at higher dose produced most significant improvement in lipid profile followed by LGAE. Presence of various alkaloids and flavonoids may contribute to the lipid lowering effect of LGEE and LGAE.⁹ The reduction of cholesterol levels by LGEO can be substantiated by previous studies done on lemongrass essential oil with citral as the main component that activates PPAR- α , primary involved in enhancing fatty acid metabolism.³⁸

The administration of HFD and fructose led to an increased circulating FFA levels that ultimately resulted in the state of insulin resistance and hyperinsulinemia, a characteristic feature of metabolic syndrome. LGEE and LGAE administration to HDR resulted in decrease in the level of insulin and improved insulin sensitivity as indicated by a decrease in insulin resistance. This might be due to the rich alkaloid and flavonoid content of lemongrass. Comparable results were obtained from a past study on ovariectomized rats using a different plant with similar flavonoids.³⁹ Previous studies done on flavonoids indicated that by improving phosphorylation of IR β and IRS1, insulin sensitivity was improved.⁴⁰ LGEO administration also decreased insulin level and

improved HOMA-IR in HDR. Bharti *et al.*, 2013 also reported similar results and concluded that activation of PPAR- γ , an enzyme involved in the lipid metabolism and insulin signalling by citral, may be responsible for this effect.¹⁰

In the present study, HFD and fructose given to animals also caused hyperleptinemia in HDR. LGEE and LGAE caused significant decrease in serum leptin level. LGEO administration also reduced the level of leptin in HDR. Our study showed an increase in serum CRP levels after HFD and fructose administration. Released by hepatocytes, in response to pro-inflammatory cytokines, CRP is employed as an inflammatory biomarker. The oxidative stress developed in response to the lipid accumulation in adipocytes and hepatocytes initiates migration of inflammatory cytokines to these cells.⁴¹ HFD and fructose administration also resulted in an elevated level of serum uric acid, a biomarker for the metabolic syndrome. Fructose in the hepatocytes is metabolized by consuming ATP, thus producing AMP and ADP. The increased AMP levels activates the AMP deaminase which consequently triggered the hypoxanthine pathway associated with the formation of uric acid and oxidative stress. Uric acid further by activating ERK 44/42 and p-38 MAPK pathways results in increased expression of CRP as concluded by Kang *et al.*, 2005.⁴² Administration of LGEE caused significant decrease while LGAE resulted in moderate decrease in the levels of both CRP and uric acid in HDR. The high content of rutin and quercetin present in lemongrass might cause attenuation of expression of various proteins like rSLC2A9v2 involved in the regulation of serum uric acid levels that gets dysregulated due to fructose administration.⁴³ The administration of LGEO also precipitated significant reduction in uric acid level and the inflammatory marker CRP. Results of our study are supported by the Study done by Mirghani *et al.*, 2012 substantiate the results of our study by concluding that inhibition of xanthine oxidase by the LGEO led to decrease in uric acid level.⁴⁴

Administration of HFD and fructose to the experimental rats caused lipotoxicity in the hepatic cells due to lipid accumulation. The increased oxidative stress and inflammatory cytokines results in the damage to the hepatocytes and development of hepatic manifestation of MetS, non-alcoholic fatty liver disease (NAFLD). The damage caused to the hepatocytes results in the leakage of AST and ALT into plasma, and thus the elevated levels of these biomarkers are evidence of the hepatic damage. LGEE and LGAE administration to HDR attenuated the dysregulated levels of liver function biomarkers AST and ALT. The results are well supported

by a previous study indicating hepatoprotective effect of lemongrass water extract.⁴⁵ Eraj *et al.*, 2016 also reported that various bioactive components present in LGAE reduced oxidative stress and maintained hepatocyte membrane stability and provided hepatoprotective effect.⁴⁶ LGEO administration to experimental HDR resulted in decreased level of biomarkers of liver injury namely AST and ALT.

Administration of HFD and fructose increased the oxidative stress in the experimental animals. The excessive energy provided by HFD causes mitochondrial dysfunction due to increased oxidative activity. In hepatocytes, fructose mediated activation of hypoxanthine pathway leads to increase in oxidative stress. LGEE caused significant reduction in MDA level and elevation in GSH and SOD level followed by LGAE in the experimental HDR. The anti-oxidant status is mainly linked to the bioflavonoid content present in lemongrass and the results harmonize with outcomes of previous study done to assess the effect of LGAE on paracetamol induced oxidative stress.⁴⁷ Quercetin present in lemongrass shows potent anti-oxidant potential by inhibiting enzymes NADPH, xanthine oxidase and LOX-1 might explain the anti-oxidant potential of LGAE.⁴⁸ The level of LPO was decreased, while the GSH and SOD levels showed significant increase on the administration of LGEO to HDR. Citral, a major constituent of LGEO and a mixture of terpenoids might produce free radical scavenging property and decrease ROS consequently producing overall reduction in oxidative stress.

HFD and fructose administration in rats adversely affected the histo-architecture of rat pancreas and liver. The β -cell destruction due to increased ROS resulting from the lipotoxicity was evident from the histopathology of the HFD fed rats. Also, increased level of plasma lipids caused hepatocellular damage indicating development of NAFLD related to metabolic syndrome. The antioxidant property of ethanolic and aqueous extract of lemongrass due to the presence of polyphenols showed β -cell and hepato-protective effect. In the past, essential oil of lemongrass has shown to alleviate hepatocellular and β -cell damage probably because of its anti-inflammatory and free radical scavenging activity.¹³

CONCLUSION

The ethanolic and aqueous extracts and the oil of lemongrass (*Cymbopogon citratus*); all were effective in improving the comorbidities associated with metabolic syndrome, however LGEE (250 mg/kg) and LGEO

(300 mg/kg) fed to the HDR for 42 days were more effective than LGAE (250 mg/kg). The preventive activity of LGEE and LGAE in MetS may be by virtue of high content of flavonoids and polyphenols present. The reason for the enhanced activity of LGEE than LGAE may be a consequence of more phytochemicals (flavonoids and phenolic acids) in LGEE than LGAE. Presence of high content of terpenoids in LGEO may attribute to its ameliorative effect in MetS. In future, the active constituent responsible for the effect of lemongrass in MetS can be isolated and clinical studies could be performed to confirm the effects on human subjects.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

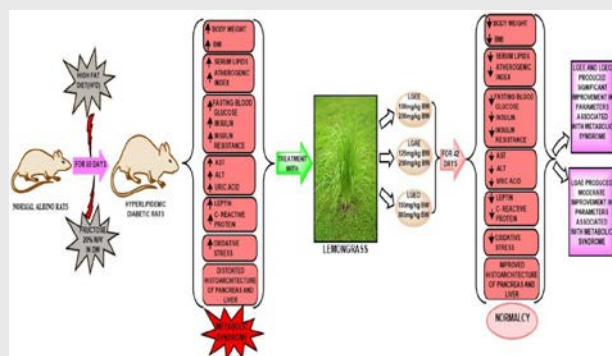
AI: Atherogenic index; **AKT:** Protein kinase B; **ALT:** Alanine aminotransferase; **AST:** Aspartate aminotransferase; **cAMP:** cyclic Adenosine Monophosphate; **CRP:** C- reactive protein; **ERK:** Extracellular signal regulated kinase; **FBS:** Fasting Blood Sugar; **HDR:** Hyperlipidemic Diabetic Rats; **HFD:** High Fat Diet; **HOMA-IR:** Homeostasis Model Assessment of Insulin Resistance; **LGAE:** Lemongrass Aqueous Extract; **LGEE:** Lemongrass Ethanolic Extract; **LGEO:** Lemongrass Essential Oil; **MetS:** Metabolic Syndrome; **MAPK:** Mitogen Activated Protein Kinase; **NAFLD:** Non-Alcoholic Fatty Liver Disease; **NF- κ B:** Nuclear Factor κ B; **Nrf2:** Nuclear factor erythroid 2 related factor 2; **PI3K:** Phosphoinositide -3- kinase; **PKA:** Protein kinase A; **PKC:** Protein Kinase C; **PLC:** Phospholipase C.

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PICTORIAL ABSTRACT



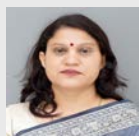
SUMMARY

This study is a comparative assessment of the ameliorative effect of ethanolic (LGEE), aqueous extract (LGAE) and essential oils (LGEOL) of Lemongrass (*Cymbopogon citratus*) on various parameters of HFD and fructose induced metabolic syndrome in rats. The phytochemical screening of ethanolic, aqueous extract and essential oil revealed that high content of total phenols and flavonoid were present in LGEE and high terpenoid content in LGEOL. The administration of HFD and fructose for a period of 60 days significantly increased the fasting blood sugar level, lipid profile and various other biomarkers like insulin, leptin, AST, ALT, CRP, uric acid thereby indicating a state of MetS. The effect of administration of LGEE, LGAE and LGEOL was assessed on the different biomarkers of MetS. The present study concludes that higher dose of LGEE and LGEOL has more significant effect on parameters of metabolic syndrome while LGAE produced moderate effects. It can be concluded that the lemon grass essential oil and extracts represents a potential treatment strategy for metabolic syndrome.

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