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# Research Article
# Alpha Mangostin Ameliorates Gestational Diabetes in Rats via Alteration of Oxidative Stress and Inflammation Reaction

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## Abstract

**Background and Objective:** Diabetes mellitus and impaired glucose tolerance discovered during pregnancy without a previous history of the disease are referred to as Gestational Diabetes Mellitus (GDM). GDM is known to have a high chance of causing type 2 diabetes. GDM is becoming more common around the world and it has a significant impact on patient's quality of life and raises the risk of pregnancy. The current study scrutinized the protective effect of alpha mangostin against streptozotocin (STZ) induced Gestational Diabetes Mellitus (GDM) in rats. **Materials and Methods:** Wistar rats were used in this experimental study. The STZ was used for the induction of GDM. The rats received the oral administration of alpha mangostin (5, 10 and 15 mg $kg^{-1}$). Blood glucose level, fetal weight, body weight, placental weight and plasma insulin were estimated. Intraperitoneal Insulin Tolerance Test ( IpITT) and Oral Glucose Tolerance Test (OGTT) were determined. The mRNA expression of SREBP-1 and its targeted genes. **Results:** Alpha mangostin significantly ($p<0.001$) improved the plasma insulin level and body weight and reduced blood glucose level. Alpha mangostin significantly ($p<0.001$) improved the insulin level in IPTT and reduced the blood glucose level in the OGTT test. Alpha mangostin treatment considerably improved fetal weight and suppressed placental weight. Alpha mangostin significantly ($p<0.001$) altered the lipid, antioxidant and inflammatory cytokines. Alpha mangostin significantly ($p<0.001$) suppressed the mRNA expression of SCD-1, SREBP-1, FAS and ACC. **Conclusion:** Taken together, alpha mangostin can be considered an alternative treatment for gestational diabetes.

Key words: Alpha mangostin, gestational diabetes mellitus, SREBP-1 expression, antioxidant, inflammation, hyperglycemia, fetal macrosomia

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Gestational diabetes mellitus is a common metabolic dysfunction that occurs during pregnancy[1]. GDM is observed in around 1-18% of total pregnancies. GDM is characterized by glucose intolerance or hyperglycemia during pregnancy[2,3]. The resultant causes defects in insulin action and insulin secretion. Hyperglycemia during pregnancy is attributed to long-term dysfunction and affects the mother's and offspring's vital organs as well as raising the risk of fetal-maternal morbidity[4-6]. Moreover, the offspring of women who suffered from GDM have more chances to expand their diminished glucose tolerance, obesity and metabolic dysfunction in later life[2,7,8].

The GDM is the abnormal rise in blood sugar levels during pregnancy that can have serious consequences for both the mother and the baby[9]. GDM is a major pregnancy complication and the incidence of this disease has increased in the number of pregnancy cases in Asia, especially in China[10]. GDM is commonly found in women who have advanced maternal age with obesity and abnormal body weight[11]. During the GDM, it increases the blood sugar level and causes gestational hypertension related to vital organ injuries such as the kidneys and liver and related complications in the baby's birth due to fetal macrosomia[12,13]. During pregnancy, it is commonly observed hormonal alteration develops insulin resistance and type II diabetes mellitus (DM) and its related complications[14]. Changes in hormones that promote subclinical inflammation during pregnancy and inflammatory reactions are boosted due to the production of oxidative stress[12,15]. It is well proven that enhanced inflammatory markers and insulin resistance increase the level of oxidative stress during DM[16,17].

According to a previous study, intrauterine oxidative stress caused negative consequences and the development of metabolic illnesses, which altered the development of fetal pregnancies[12,16]. According to a previous study, excessive oxidative stress plays an essential role in the development and progression of GDM[16,18]. Though, the underlying mechanism of diabetic complications is complex and not fully understood, clinical and preclinical research has shown that GDM is linked to oxidative stress, which causes a decrease in the endogenous antioxidant defense system and increases reactive oxygen species generation[19,20]. Consequently, it has been speculated that antioxidant therapy showed a beneficial effect on diabetes complications such as GDM via the reduction of ROS. Therefore, there is an urgent need to develop a more protective drug for the treatment of GDM[12,21].

In general, medications from various categories were used to alleviate the majority of the difficulties that had emerged. These medicines are known to have a direct or indirect effect on the foetus[15,22]. As a result, the use of phytochemical-based medications with no adverse effects is being considered for supersensitive disorders such as GDM. Traditional herbal medicinal and food products have been used for a long time[19,22].

Traditional herbal medicine and dietary products have high antioxidant activity and are frequently utilized as a complementary therapy for reducing oxidative stress in people with diabetes[23-25]. Alpha mangostin (AM) showed antioxidant and anti-inflammatory effects on various animal models[26-29]. Due to its suppression activity against inflammation, insulin resistance and oxidative stress, alpha mangostin has been shown to alleviate diabetic complications in various *in vivo* models[30-32]. Because of the similar symptoms and aetiology between GDM and DM, alpha mangostin, with its effects on DM, is highly likely to have similar pharmacological and physiological effects on alleviating GDM. Due to the potent anti-inflammatory and antioxidant activity of alpha mangostin against various rodent models.

In this experimental study, the authors try to explore the protective effect of alpha mangostin against STZ-induced GDM in rats and explore the underlying mechanism.

## MATERIALS AND METHODS

**Study area:** The current experimental study was carried out at China Three Gorges University, China from November to December, 2020.

### Chemical

**Experimental rodent:** Total of 40 Swiss albino Wistar rats aged 8-10 weeks, sex: Both, weight: Male (200-220 g) and female (180-200 g) were procured from the animal house and kept in standard laboratory conditions. The rats were kept at a constant temperature (205°C) and relative humidity (50-70%) and provided a light cycle of 12/12 hrs (light and dark). The rats were kept in the animal house for 7 days before the experimental study to adopt the laboratory conditions. All of the experiments were carried out following the institute's approved animal procedure.

**Induction of pregnancy:** The rats (both female and male) were free to mate after acclimating. The presence of a copulatory plug the next morning verified the female rat's pregnancy. That day was counted as a gestational day (GD) of 0 after confirmation[9].

Table 1: Treatment group of the study

| Group | Treatment |
|---|---|
| Normal group | 1% CMC |
| GDM | 1% CMC |
| GDM+AM | 5 mg $kg^{-1}$ |
| GDM+AM | 10 mg $kg^{-1}$ |
| GDM+AM | 15 mg $kg^{-1}$ |

Table 2: List of mRNA expression

| | Primer (5'-3') | |
|---|---|---|
| Gene | Forwarded | Reverse |
| ACC | ACACTGGCTGGCTGGACAG | CACACAACTCCCAACATGGTG |
| SCD-1 | TGCTGATCCCCACAATTCCC | CTTTGACGGCTGGGTGTTTG |
| SREBP-1C | CCCTGCGAAGTGCTCACAA | GCGTTTCTACCACTTCAGGTTTCA |
| FAS | GGCCACCTCAGTCCTGTTAT | AGGGTCCAGCTGAGGGTACA |
| GAPDH | GAACGGGAAGCTCACTGGC | GCATGTCAGATCCACAACGG |

**Induction of diabetes:** Briefly, an intraperitoneal injection of STZ (40 mg $kg^{-1}$) was prepared in citrate buffer (0.1 mol $L^{-1}$, pH = 4.5) for the induction of diabetes. Diabetic rats were defined as those with a fasting blood glucose level higher than 16.7 mmol $L^{-1}$ and were employed in the current study. The rats received injections of STZ at regular intervals (GD 6, 7 and 8). A similar amount of citrate buffer was injected intraperitoneally into normal rats.

**Preparation of test drugs:** The alpha mangostin was used to scrutinize the protective effect against GDM in rats. Briefly, the preparation of alpha mangostin was done using a 1% suspension of carboxymethylcellulose sodium (CMC). The rats were given alpha mangostin orally through oral gavage.

**Experimental protocol:** After the successful induction of GDM, the rats were divided into 5 groups and each group contained 8 rats. The groups were presented in Table 1.

The rats in the normal and GDM control groups were given 1% CMC orally via oral gavage. AM (5, 10 and 15 mg $kg^{-1}$) was given to the rats orally. The dose selection of alpha mangostin was done in our pilot study using the previously disclosed method[30]. The results of the pilot study revealed that a 200 mg $kg^{-1}$ dose of alpha mangostin was sufficient to exert the hypoglycemic effect in the current study.

The rats were starved at the end of the experiment (GD 18) and blood samples were taken by puncturing the orbital venous plexus and maintained in the pre-incubated test tube. The blood samples were centrifuged at 15000 rpm to separate the serum. The rats were euthanized using light anaesthesia (diethyl ether) and the placentas, fetuses and liver tissue was quickly removed and weighed and finally stored at -80°C for further analysis. The liver tissue was pulverized and homogenized in a solution of ice-cold saline and centrifuged at 10000 rpm for 15 min at 4°C to separate the supernatant. The supernatant was separated and kept at -20°C for further analysis[9].

**Biochemical parameters:** The blood glucose level, plasma insulin, glycated haemoglobin and hepatic glycogen were estimated using the previously reported method with minor modifications. The lipid parameters LDL-C, total cholesterol (TC), High-Density Lipoprotein cholesterol (HDL) and triglyceride (TG) were calculated using a commercially available kit (Nanjing Jiancheng Bioengineering Institute, Jiangsu, China) following the manufacturer's instructions.

Malonaldehyde (MDA), catalase (CAT), glutathione peroxidase (GPx) and superoxide dismutase (SOD) were assessed using the previously published method with minor modifications[16,19,22].

Interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-10 (IL-10) and Tumour Necrosis Factor-α (TNF-α) levels were measured using ELISA kits (Nanjing Jiancheng Bioengineering Institute, Jiangsu, China) according to the manufacturer's instructions.

**Oral Glucose Tolerance Test (OGTT) and Intraperitoneal Insulin Tolerance Test (IpITT):** The IPTT and OGTT tests were carried out on GD17. Briefly, the rats fasted overnight. For IPTT, an intraperitoneal injection of insulin (2 units $kg^{-1}$, b.wt.,) was administered to the rats[9]. For the OGTT test, the rats orally received glucose administration (2 g $kg^{-1}$, b.wt.,). After successfully developing the IPTT and OGTT models, the blood glucose level was measured at a regular time interval (every 30 min interval) using the blood glucose kits.

**RNA isolation and Real-Time Polymerase Chain Reaction (RTPCR):** The manufacturing procedure was used to extract total RNA from liver tissue using the Trizol kit (Invitrogen, CA, USA). The First Strand cDNA synthesis kit was used to make the cDNA using reverse transcription (Thermo, USA). Following the manufacturer's instructions, the SYBR Green qPCR Master Mix kit (Thermo, USA) was used for RT-PCR amplification. All of the procedures were performed under normal RT-PCR amplification settings (95°C for 10 sec, 60°C for 30 sec and 72°C for 30 sec), with primer sequencing (presented in Table 2). Transcripts from target genes were found to be connected to the expression of a reference gene (GAPDH). The results were expressed using control folds.

**Statistical analysis:** All of the data is presented as a mean and standard deviation. The statistical analysis was performed

using GraphPad Prism 7 (GraphPad Software, Inc., St., Louis, USA). The One-way ANOVA was used to evaluate the difference between the groups, followed by Tukey's multiple comparison test for *post hoc* analysis. Where, $p<0.05$ was considered significant.

## RESULTS

**Fetuses status:** The total number of liver fetuses, number of dead fetuses and percentage of dead fetuses were exhibited in Table 3. Normal rats showed the maximum number of liver fetuses with 3.67% of dead fetuses. The GDM group showed a smaller number of live fetuses (46) and dead fetuses (29) with 38.83% of dead fetuses. The GDM rats who, received alpha mangostin (5 and 10 mg $kg^{-1}$) showed a greater number of live fetuses (58, 79) and a smaller number of dead fetuses (24, 13) with 29.32 and 14.14% dead fetuses. The GDM rats treated with alpha mangostin (15 mg $kg^{-1}$) exhibited 96 live fetuses and 6 dead fetuses with 5.88% of dead fetuses.

**Blood glucose, body weight and insulin:** In the GD 0, the blood glucose level of all group rats was almost the same. At GD 9, the blood glucose level in the normal rats was almost similar to the initial blood glucose level. GDM group rats exhibited an increased blood glucose level, which was remain increased till GD 18. GDM rats treated with the alpha mangostin significantly ($p<0.001$) reduced their blood glucose level (Fig. 1a).

Table 3: Effect of alpha mangostin on the total number of fetuses, number of live, dead fetuses and dead the fetus (percentage) in pregnant rats

| Groups | Total | Live | Dead | Dead fetuses (percentage) |
|---|---|---|---|---|
| NC | 109 | 105 | 4 | 3.67 |
| GDM | 75 | 46 | 29 | 38.83 |
| GDM+Alpha mangostin (5 mg $kg^{-1}$) | 82 | 58* | 24* | 29.32* |
| GDM+Alpha mangostin (10 mg $kg^{-1}$) | 92 | 79** | 13** | 14.14** |
| GDM+Alpha mangostin (15 mg $kg^{-1}$) | 102 | 96*** | 6*** | 5.88*** |

Data are presented as Mean±SD, where, the tested group was treated with GDM group rats, where, *p<0.05, **p<0.01 and ***p<0.001

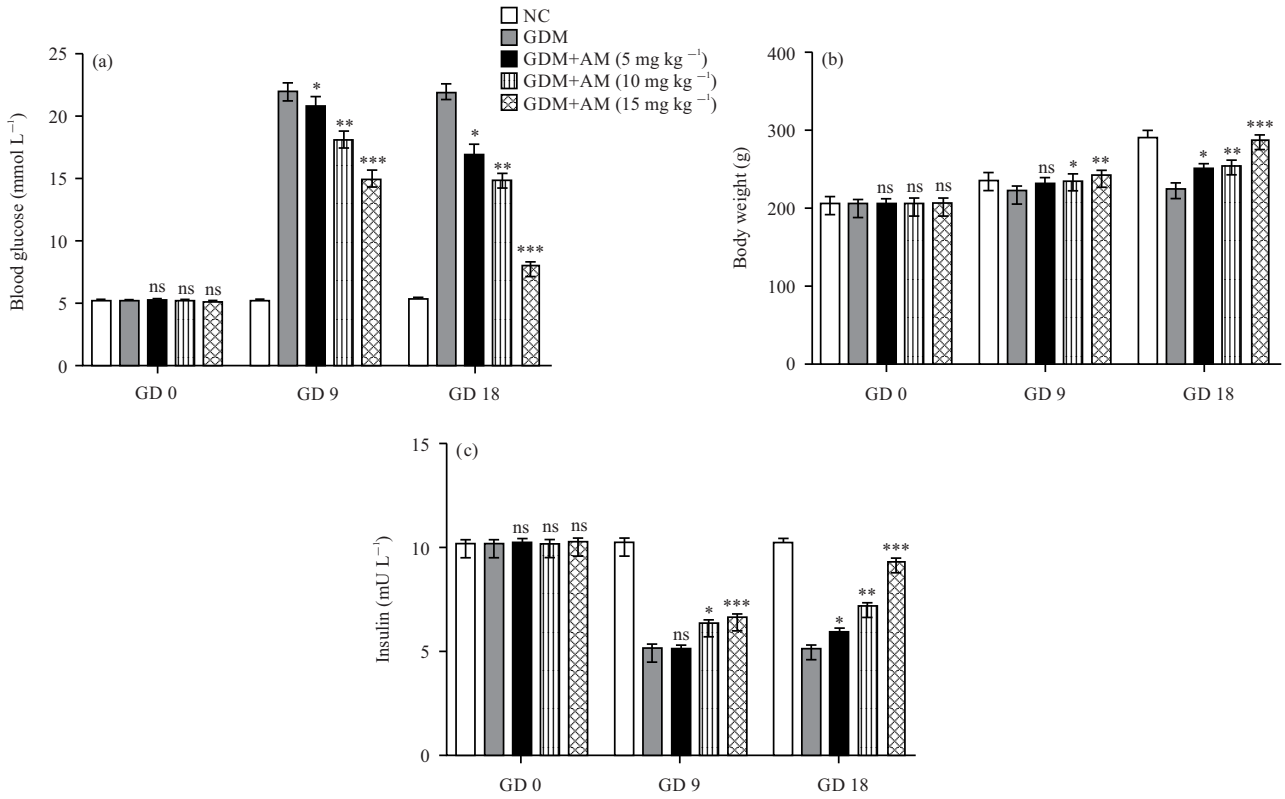


Fig. 1(a-c): Effect of alpha mangostin on the level of blood glucose, body weight and plasma insulin in the STZ-induced GDM in rats, (a) Blood glucose level, (b) Body weight and (c) Plasma insulin

Data are presented as Mean±SD, where, the tested group was treated with GDM group rats, where *p<0.05, **p<0.01 and ***p<0.001 and X-axis: Gestational diabetes day

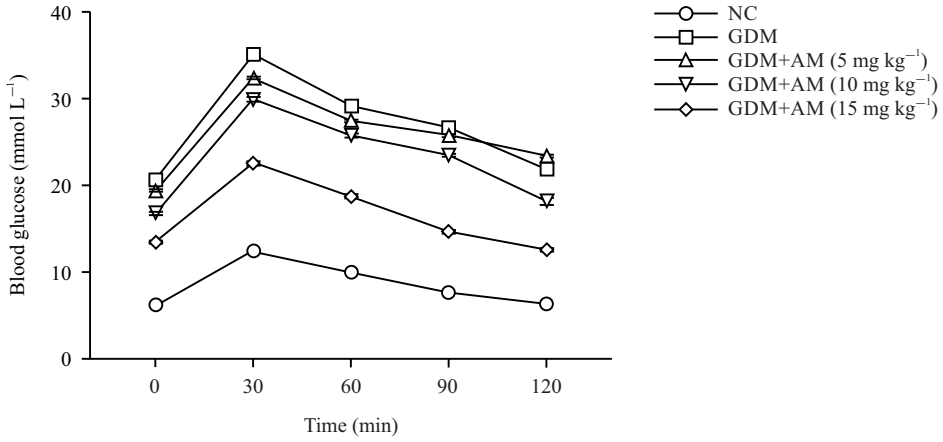


Fig. 2: Effect of alpha mangostin on the oral glucose tolerance test in the STZ-induced GDM in rats
Data are presented as Mean±SD, where, the tested group was treated with GDM group rats, where *p<0.05, **p<0.01 and ***p<0.001

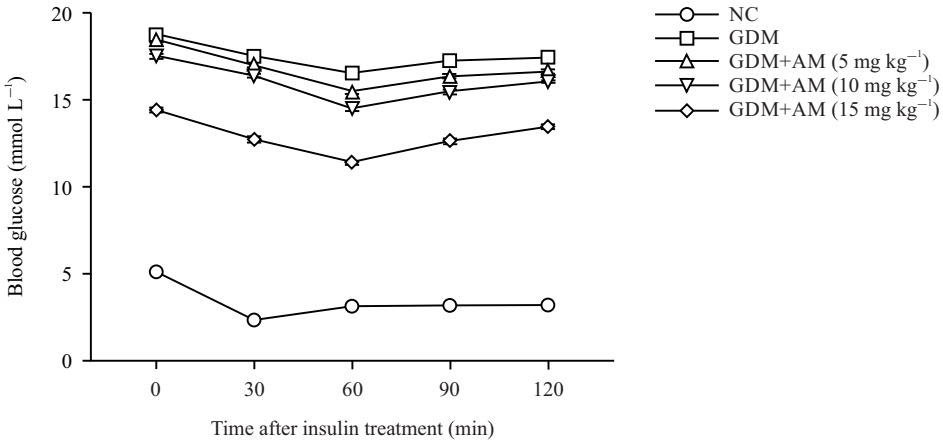


Fig. 3: Effect of alpha mangostin on blood glucose in intraperitoneal insulin tolerance test in the STZ-induced GDM in rat.
Data are presented as Mean±SD, where the tested group was treated with GDM group rats, where *p<0.05, **p<0.01 and ***p<0.001

Figure 1b demonstrated the effect of alpha mangostin on the body weight of GDM group rats. Normal rats displayed the augmented body weight at different time intervals (GD 9 and GD 18). The GDM group rats demonstrated a reduced body weight at GD 9 and GD 18. The GDM rats treated with alpha mangostin significantly ($p<0.001$) improved their body weight.

The plasma insulin level of the different group's rats was shown in Fig. 1c. The GDM rats demonstrated a reduced plasma insulin level at GD 9 and GD 18. The GDM rats received the alpha mangostin significantly ($p<0.001$) and improved their insulin level.

**OGTT and IpITT:** The blood glucose level in normal rats was normal. After 30 min of glucose injection, GDM rats had higher blood glucose levels, which remained higher until the completion of the trial. The GDM rats given alpha mangostin had significantly lower blood glucose levels ($p<0.001$) (Fig. 2).

Throughout, the trial, normal rats had a typical pattern of plasma insulin. Until the completion of the experimental investigation, GDM rats showed a decrease in glucose levels. GDM rats given alpha mangostin had significantly ($p<0.001$) lower glucose levels (Fig. 3).

**Fetus and placental:** Figure 4 exhibited the effect of alpha mangostin on fetal weight and placental weight. The GDM rats showed decreased fetal body weight (Fig. 4a) and increased placental weight (Fig. 4b). Alpha mangostin significantly ($p<0.001$) enhanced the fetal body weight and suppressed the placental weight.

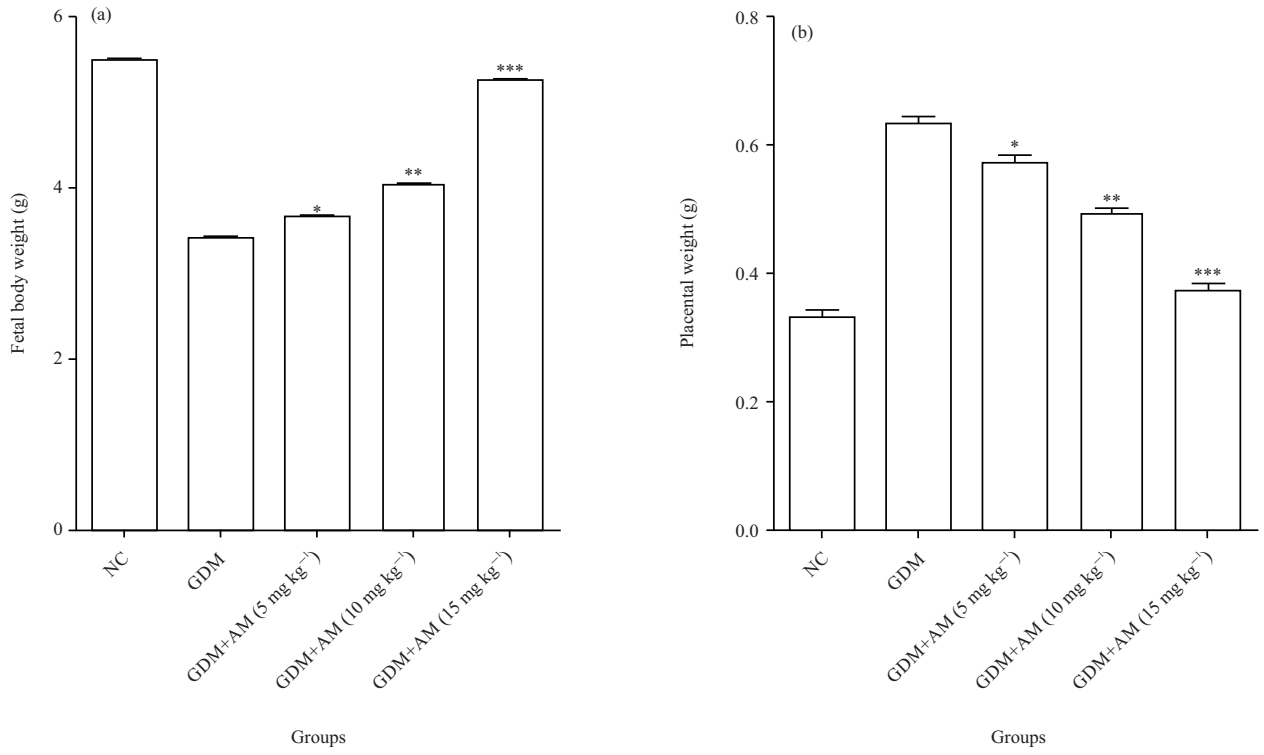


Fig. 4(a-b): Effect of alpha mangostin on the fetal weight and placental weight of STZ-induced GDM in rats, (a) Fetal weight and (b) Placental weight

Data are presented as Mean±SD, where, the tested group was treated with GDM group rats, where *p<0.05, **p<0.01 and ***p<0.001

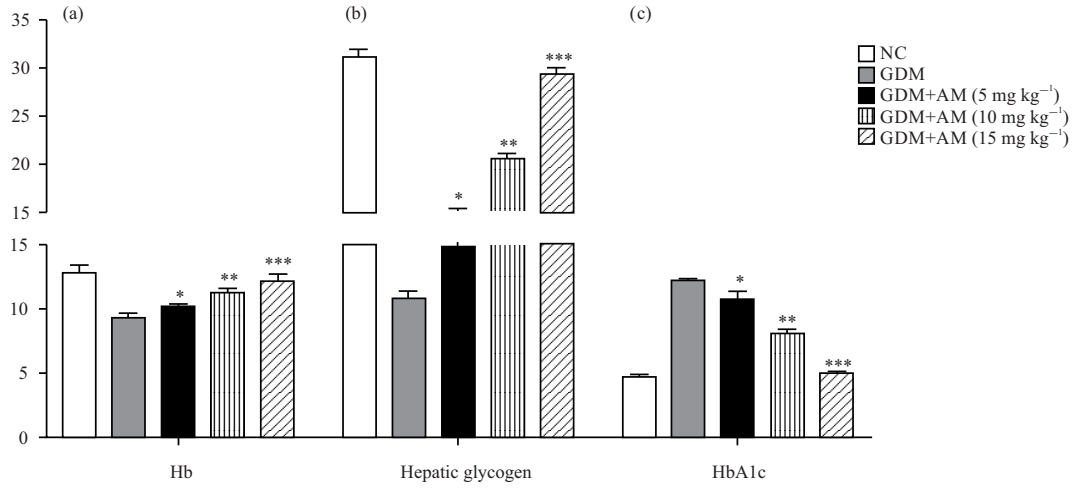


Fig. 5: Effect of alpha mangostin on the level of Hb, HbA1c and hepatic glycogen in the STZ-induced GDM in rats, (a) Hb, (b) Hepatic glycogen and (c) HbA1c

Data are presented as Mean±SD, where, the tested group was treated with GDM group rats, where *p<0.05, **p<0.01 and ***p<0.001 and X-axis: Biochemical parameters

**Hb, HbA1c and hepatic glycogen:** GDM rats showed a reduced level of Hb (Fig. 5a), hepatic glycogen (Fig. 5b) and an increased level of HbA1c (Fig. 5c). The GDM rats treated with alpha mangostin significantly ($p<0.001$) improved the level of Hb and hepatic glycogen and suppressed the level of HbA1c.

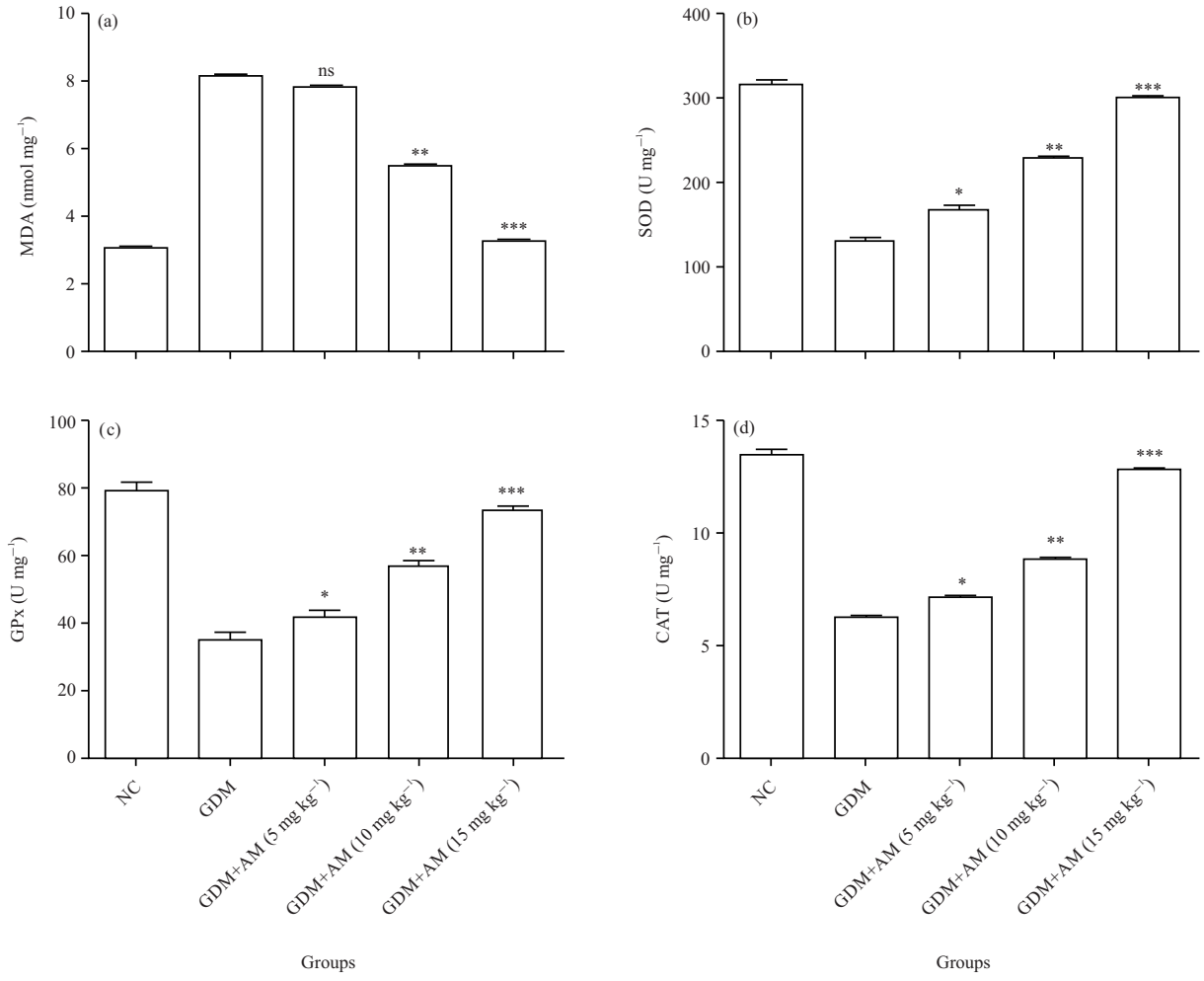


Fig. 6(a-d): Effect of alpha mangostin on the antioxidant parameters in the STZ-induced GDM in rats, (a) MDA, (b) SOD, (c) GPx and (d) CAT

Data are presented as Mean±SD, where the tested group was treated with GDM group rats, where, *p<0.05, **p<0.01 and ***p<0.001

**Antioxidant parameters:** Antioxidant parameters such as MDA (Fig. 6a), SOD (Fig. 6b), GPx (Fig. 6c) and CAT (Fig. 6d) were estimated in a different group of rats. The GDM rats demonstrated an enhanced level of MDA and suppressed levels of SOD, GPx and CAT. The GDM rats treated with alpha mangostin significantly ($p<0.001$) suppressed the level of MDA and enhanced the level of SOD, GPx and CAT.

**Lipid parameters:** The GDM rats exhibited an enhanced level of TG (Fig. 7a), TC (Fig. 7b), LDL (Fig. 7c) and decreased level of HDL (Fig. 7d) as compared to normal and tested group rats. GDM rats received alpha mangostin significantly ($p<0.001$) suppressed the level of TG, TC and LDL and enhanced the level of HDL.

The ratio of TC/HDL (Fig. 8a) and LDL/HDL (Fig. 8b) was increased in the GDM group of rats. The GDM rats treated with the alpha mangostin significantly ($p<0.001$) down-regulated the TC/HDL and LDL/HDL ratios.

**Pro-inflammatory cytokines:** Figure 9 demonstrated the level of pro-inflammatory cytokines in a different group of rats. The GDM group rats demonstrated an increased level of TNF-α (Fig. 9a), IL-1β (Fig. 9b), IL-6 (Fig. 9c) and decreased level of IL-10 (Fig. 9d). GDM rats treated with alpha mangostin significantly ($p<0.001$) altered the level of inflammatory cytokines.

**mRNA expression:** The level of mRNA expression of a different group of rats was exhibited in Fig. 10. The GDM rats

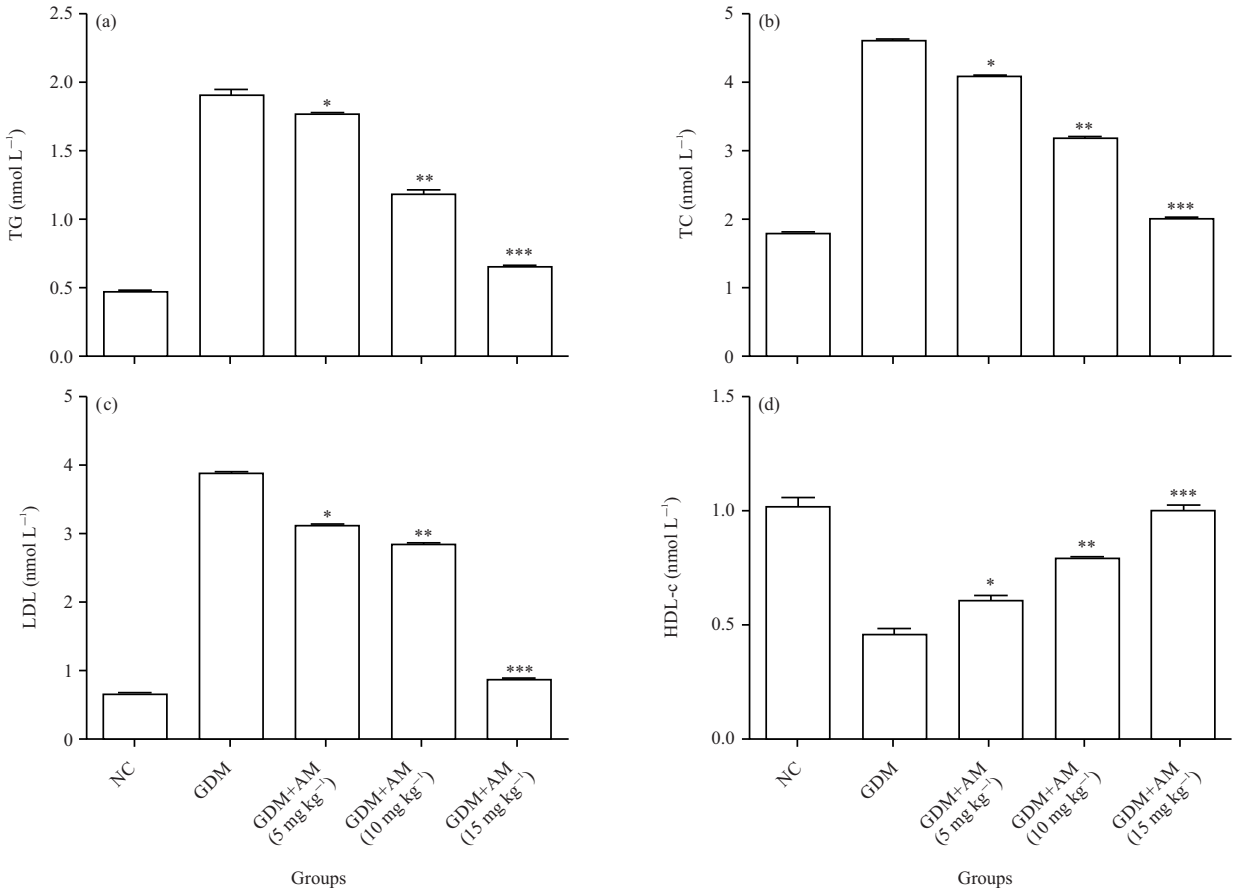


Fig. 7(a-d): Effect of alpha mangostin on the level of lipid parameters in the STZ-induced GDM in rats, (a) TG, (b) TC, (c) LDL and (d) HDL

Data are presented as Mean±SD, where the tested group was treated with GDM group rats, where *p<0.05, **p<0.01 and ***p<0.001

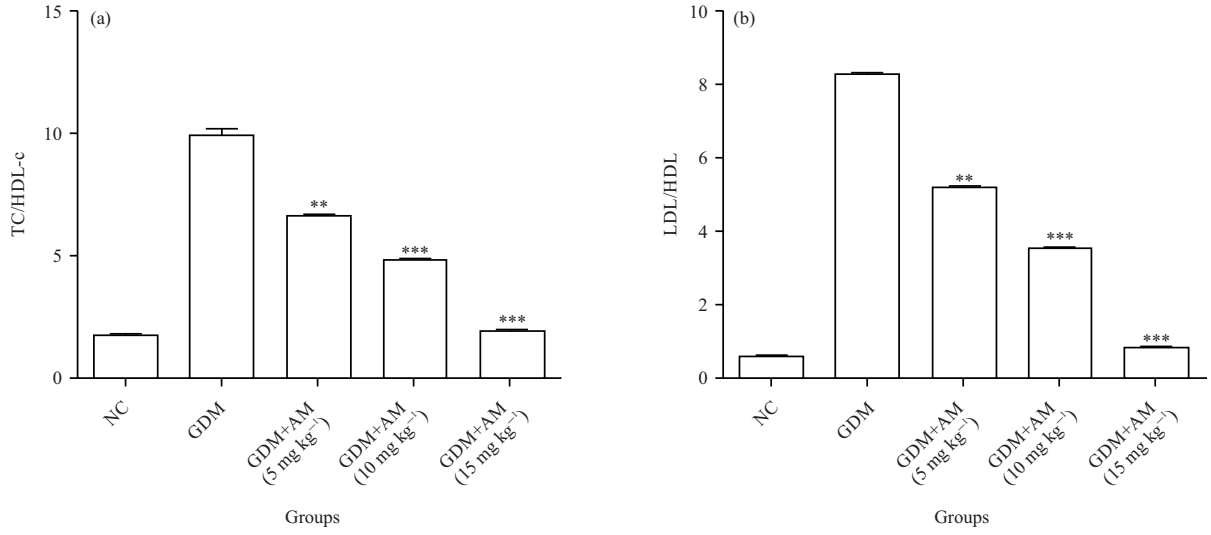


Fig. 8(a-b): Effect of alpha mangostin on the ratio of TC/HDL-c and LDL/HDL in the STZ-induced GDM in rats, (a) TC/HDL-c and (b) LDL/HDL

Data are presented as Mean±SD, where the tested group was treated with GDM group rats, where *p<0.05, **p<0.01 and ***p<0.001

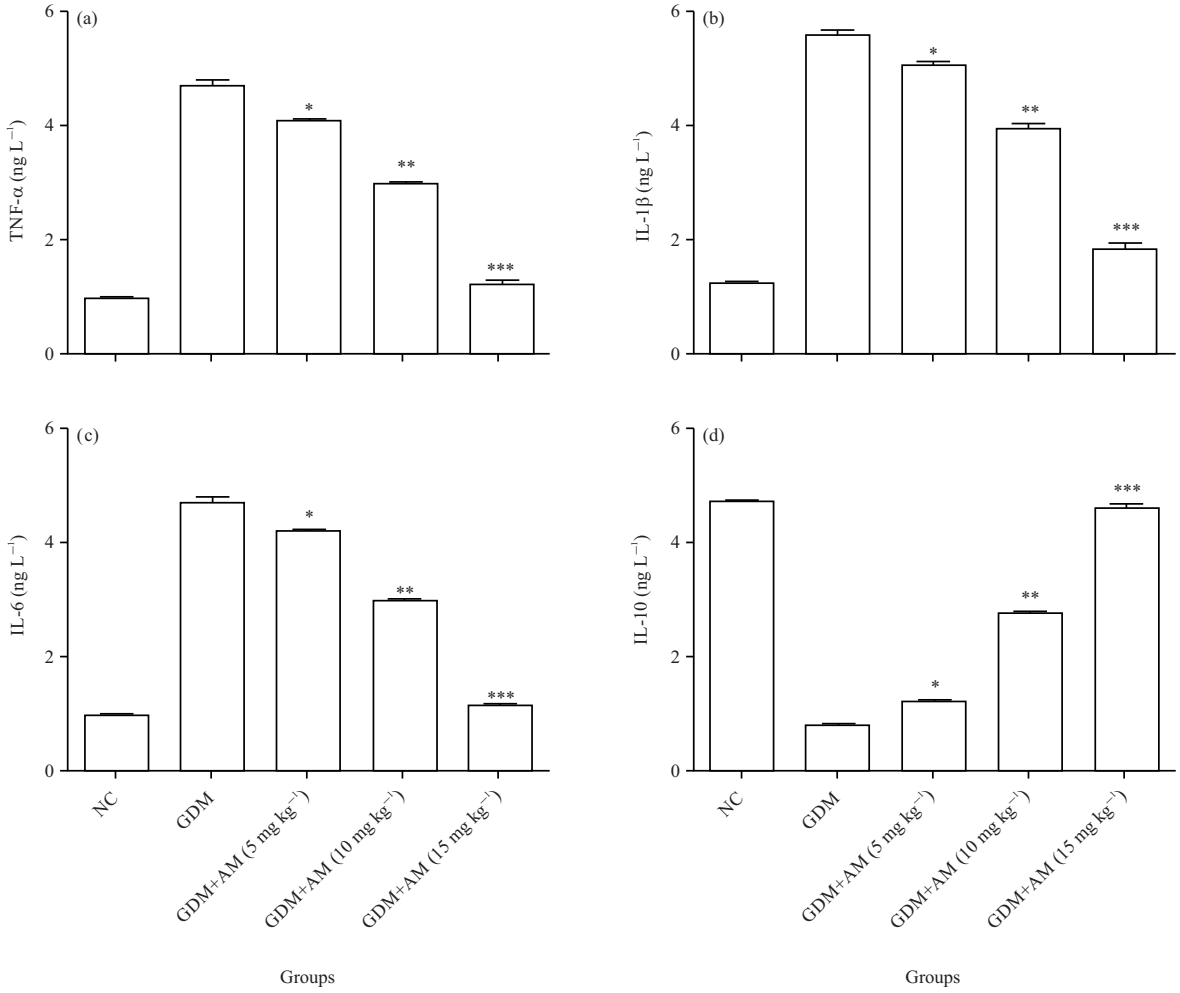


Fig. 9(a-d): Effect of alpha mangostin on the level of inflammatory cytokines in the STZ-induced GDM in rats, (a) TNF-α, (b) IL-1β, (c) IL-6 and (d) IL-10

Data are presented as Mean±SD, where tested group was treated with GDM group rats, where *p<0.05, **p<0.01 and ***p<0.001

demonstrated the enhanced mRNA expression of SREBP-1 (Fig. 10a), SCD-1 (Fig. 10b), ACC (Fig. 10c) and FAS (Fig. 10d). GDM rats treated with alpha mangostin significantly ($p<0.001$) down-regulated the expression of SCD-1, SREBP-1, FAS and ACC.

## DISCUSSION

The use of traditional herbal medicine and plant-based phytoconstituents has increased in the treatment of multifarious diabetes-related complications, due to fewer or no side effects as compared to synthetic drugs[12,13]. Recent investigation suggests that alpha mangostin has beneficial effects on diabetes. However, alpha mangostin preventive efficacy against STZ-induced GDM rats has not been completely studied. The protective effect of alpha mangostin against STZ-induced GDM is investigated in this experimental investigation as well as the likely mechanism.

Previous studies showed that STZ induces GDM in experimental rats, along with increasing embryo lethality incidence[12,20,33]. STZ-induced GDM rats demonstrated reduced fetal weight. In this study, alpha mangostin treatment significantly protected the embryo against STZ-induced embryo lethality under GDM and improved fetal weight[15,34]. The previous investigation showed a similar effect when the rats were treated with walnuts and improved the effect via its antioxidant nature[19,35]. The result showed that alpha mangostin had the antioxidant property to ameliorate diabetic embryopathy.

It is well proven that oxidative stress increases or expands the GDM and its related complications[12]. In this experimental study, we observed increased hepatic oxidative stress markers

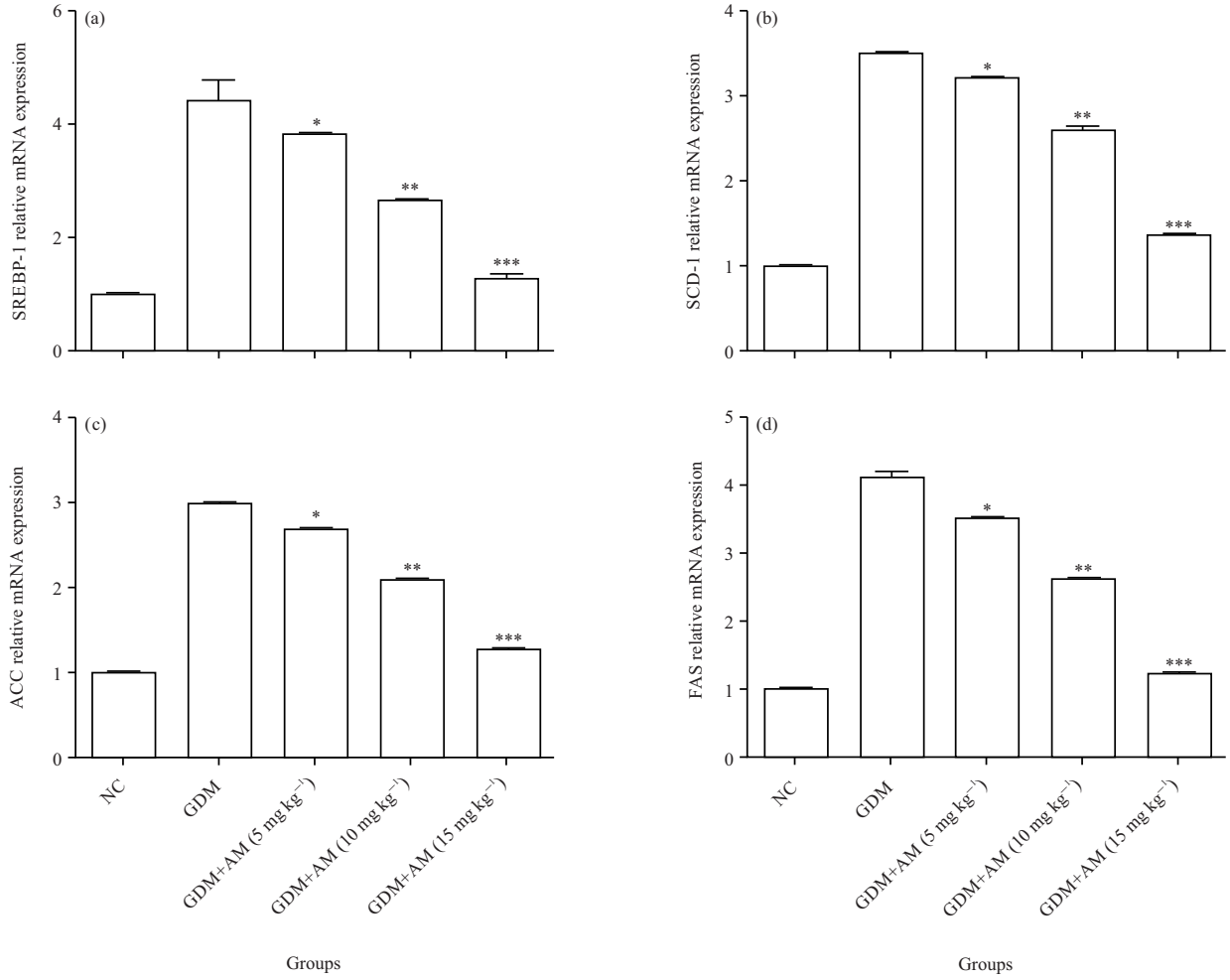


Fig. 10(a-d): Effect of alpha mangostin on the mRNA expression of SERBP-1 and its genes in the STZ-induced GDM in rats, (a) SERBP-1, (b) SCD-1, (c) ACC and (d) FAS

Data are presented as Mean±SD, where tested group was treated with GDM group rats, where *p<0.05, **p<0.01 and ***p<0.001

in diabetic rats, which showed a similar effect as presented by previous research. Our findings indicate that alpha mangostin countered STZ-induced oxidative stress in the liver tissue of pregnant rats, clearly indicating the antioxidant nature of alpha mangostin.

A prior study found that aberrant changes in lipid metabolism were associated with the development of GDM and increased oxidative stress[12,21]. Previous studies also suggest that the abnormal alteration in lipid metabolism in the liver tissue and plasma increases oxidative stress in the body[12,15,21]. STZ-induced rats had higher levels of TC and TG in this experimental investigation. A previous study showed that the increased TG and TC levels were due to enhanced lipoprotein synthesis and secretion[16,17]. The alpha mangostin treatment considerably lowered TG and TC levels, implying that it has lipid-lowering properties. Alpha mangostin can suppress lipid metabolism changes in GDM rats. The enhancement of HDL levels and suppression of TC, TG and LDL levels showed the strength of our findings. These results suggested that alpha mangostin ameliorates lipid metabolism disorder under the GDM condition.

It has been enhanced in GDM, owing to an increase in the expression of inflammatory cytokines like IL-1β and TNF-α, which create an inflammatory condition that leads to insulin resistance[12,16,21]. The STZ-induced GDM rats displayed an augmented inflammatory level and reduced antioxidant enzymes and increased the chance of preterm labour, preeclampsia, fetal complications and polyhydramnios of macrosomia in rats, which exhibited a slight effect on the litter numbers[12,13,15,18]. The STZ-induced GDM rats treated with alpha mangostin showed suppression of inflammatory cytokines due to its anti-inflammatory and antioxidant effect. Alpha

mangostin significantly ($p<0.001$) reduced inflammatory cytokines, protecting pups from inflammatory cytokine-related problems.

For the estimation of the underlying mechanism, we estimated the mRNA expression of fatty acid metabolism[9]. SREBP-1 (nuclear transcription factor) is thought to play a role in the control of lipid parameters like total cholesterol, triglycerides and fatty acid production by targeting genes like ACC, FAS and SDC-1, according to previous studies Li *et al.*[36], Ding *et al.*[37]. All the genes such as ACC, FAS and SDC-1 play a crucial role in the synthesis of fatty acids. SREBP-1 mRNA expression abnormalities have also been connected to diabetes pathogenesis[36-39]. In this study, we found that increased mRNA expression of FAS, SCD-1, SREBP-1 and ACC in the GDM group rats and alpha mangostin significantly reduced the expression. This is because omega-3 and omega-6 unsaturated long-chain fatty acids may reduce hepatic lipogenesis while increasing hepatic fatty acid oxidation, potentially improving hepatic insulin sensitivity[36,38,40,41]. As a result, our findings revealed that alpha mangostin can influence lipid metabolism gene expression and antioxidant enzymes, contributing to its glucose metabolism protection. The findings revealed that alpha mangostin protected pregnant rats from hyperlipidemia, inflammation and oxidative stress.

## CONCLUSION

The alpha mangostin lowered blood glucose levels and enhanced plasma insulin and body weight, according to our findings. It also improved the insulin level in IPTT and reduced the blood glucose level in the OGTT test. Alpha mangostin considerably improved the fetal weight and decreased the placental weight and also improved the live fetuses and reduced the percentage of death fetuses rate due to boosting the level of endogenous antioxidants. Alpha mangostin significantly suppressed the inflammatory cytokines and mRNA expression of SREBP-1 and related genes. Alpha mangostin exhibited a protective effect against GDM and more molecular-level study is needed to scrutinising the underlying mechanism.

## SIGNIFICANCE STATEMENT

The current investigation executes the protective effect of alpha mangostin against STZ-induced GDM in rats. Gestational diabetes mellitus arises during pregnancy. During the GDM, enhanced glucose level that affects the fetus and induces several dysfunctions. Alpha mangostin considerably suppressed the glucose level, improved the insulin and suppressed the various dysfunction in fetal. This investigation helps the researchers to uncover the critical complications related to gestational diabetes mellitus. Thus, a new beneficial therapy for gestational diabetes mellitus occurred during the pregnancy.

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