***Original Research Article***

**Antidiabetic, Antidyslipidemic, Hepatoprotective Effects and Histopathological Analysis of Aqueous Extract of *Tamarindus Indica* (*Fabaceae*) on streptozotocin Induced Diabetic Rats**

**ABSTRACT**

**Aims**

Diabetes is global public health concerns, imposing a heavy global burden on public health as well as socio-economic development. This study investigated the antidiabetic, antidyslipidemic and hepatoprotective effects of the aqueous leaves extract of *Tamarindus indica*.

**Methodology**

The present study was designed to investigate the anti-hyperglycemic, antidyslipidemic and hepatoprotective effects of the fixed dose of linagliptin [5mg/kg body weight (BW)] and *Tamarindus Indica* [200mg/kg body weight] for four week treatment on streptozotocin [45 mg/kg (BW)] induced diabetic rats.

**Results**

In streptozotocin induced diabetic rats, there was a significant decrease in blood glucose level from (20.04±0.480 mmol/L to 18.94± 0.397 mmol/L). After daily treatment for four weeks, *Tamarindus indica* reduced blood glucose level (19.8±0.265 mmol/L to 7.94± 0.214 mmol/L). In case of dyslipidemic effect, *Tamarindus indica* reduced total cholesterol (197.06±0.542 mg/dl), triglyceride (134.18 ±0.309 mg/dl) and LDL-cholesterol (86.18 ±0.307 mg/dl) levels significantly and increased HDL-cholesterol level (30.24 ±0.406 mg/dl) in comparison with diabetic control group. Liver dysfuction parameter significantly decresed SGPT (33.76 ±0.206 U/L) and SGOT (44.46 ±0.607 U/L) compared to diabetic control group was observed.Our findings show that tamarind extracts improve biochemical markers and restore normal histological architecture in treated groups.

**Conclusion**

The results of the present study suggest that, the fixed dose of *Tamarindus indica* leaves exhibits significant antidiabetic, antidyslipidemic, hepatoprotective properties, enhancing the potential effect for liver health as an adjunct in dietary management of these metabolic disorders. So aqueous leaves extract of *Tamarindus indica* might be efficacious in patients with diabetic dyslipidemia. It showed safer, synergistic and promising hypoglycemic properties and reduced dose level of oral hypoglycemic agents, while giving better glycemic control.

**Keywords:** *Tamarindus indica*, antidiabetic, antidyslipidemic, aqueous extract, liver dysfuction.

**1. Introduction**

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels resulting from inadequate insulin action or secretion. The World Health Organization (WHO) estimates that the global prevalence of diabetes will rise substantially, impacting millions and leading to significant morbidity and mortality associated with diabetes-related complications, such as cardiovascular disease, kidney failure, and liver dysfunction (Ali et al., 2020; International Diabetes Federation, 2021). In the quest for effective management strategies, there is growing interest in the therapeutic potentials of natural products, particularly those derived from medicinal plants, which have shown promise in improving glycemic control (Kumar et al., 2021).

*Tamarindus indica*, commonly known as tamarind, is a tropical tree native to Africa and widely distributed in Asia and other parts of the world. Its leaves are rich in bioactive compounds such as polyphenols, flavonoids, and antioxidants, which have been utilized in traditional medicine for various purposes, including the management of diabetes, dyslipidemia, and liver ailments (Abdulkhaleq et al., 2021; Anwar et al., 2020). Previous studies have highlighted the hypoglycemic effects of *Tamarindus indica*, suggesting that it may enhance insulin sensitivity and promote glucose utilization in adipose tissues and skeletal muscles (Haidar et al., 2019; Ghosh et al., 2018). Furthermore, research indicates that the consumption of tamarind leaves may positively influence lipid metabolism, showing promise as a potential antidyslipidemic agent (Ali et al., 2021; Singh et al., 2018).

Chronic diabetes is frequently associated with dyslipidemia, characterized by abnormal lipid profiles that exacerbate the risk of cardiovascular complications (Nishida et al., 2019; Boucher et al., 2020). The interplay between dyslipidemia and insulin resistance is well documented, and the modulation of lipid levels is critical in the management of diabetic patients (Pérez-Moreno et al., 2021). A study discusses the crucial role of natural products in managing lipid profiles in diabetic models, reinforcing the need for therapeutic interventions targeting these pathways (Rwegerara et al., 2017).

Additionally, the hepatoprotective properties of *Tamarindus indica* have garnered attention; their antioxidant constituents may protect hepatic tissue from damage associated with hyperglycemia and the toxic effects of lipid peroxidation (Sarma et al., 2019; Jabeen et al., 2019). Animal models, such as the streptozotocin (STZ)-induced diabetic rat model, are widely used to mimic the pathophysiology of human diabetes, providing essential insights into the efficacy of therapeutic interventions (Gao et al., 2019; Masudaet al., 2020).

This study aims to evaluate the antidiabetic, antidyslipidemic, and hepatoprotective effects of *Tamarindus indica* in STZ-induced diabetic rats. By assessing biochemical parameters alongside histopathological examinations. Ultimately, this research seeks to contribute to the understanding of *Tamarindus* *indica* as a viable, natural therapeutic option for managing diabetes and its related disorders.

**2. MATERIAL AND METHODS**

**2.1 Chemicals**

Streptozotocin was obtained from the Sigma-Aldrich Chemical Company, located in Saint Louis, Missouri, USA. Biochemical analyses were performed using commercial kits from RANDOX. All other reagents and compounds utilized throughout the study were of analytical grade. The antidiabetic medication linagliptin was sourced from Square Pharmaceuticals Ltd., Bangladesh.

**2.2 Preparation of Aqueous Leaves Extract of *Tamarindus indica***

The leaves of *Tamarindus indica*, sourced from the local market in Rajshahi city, Bangladesh, were dried under direct sunlight. In order to make the aqueous leaves extract, 500 g of the dried leaves of *Tamarindus indica* were crushed in an electrical grinder and soaked in 2.5 L distilled water. Following this, the mixture was filtered through a fine sieve to obtain the crude extract, which was then allowed to air-dry for three days as per established procedures (Gohil et al.,2010; Amin et al.,2013).

**2.3 Experimental Animals**

A total of 20 male Wistar rats, weighing between 150-200 grams, were procured from the Pharmacology Research Laboratory at the Department of Pharmacy, Jahangirnagar University. The rats were acclimatized to their new environment for one week. They were housed in a well-ventilated animal facility, maintained at a temperature of approximately 25°C, and were provided with standard ICDDRB pellets and clean drinking water. The rats were kept in cages under a controlled 12-hour light/dark cycle. Ethical approval for the study was obtained from the Institutional Ethical Committee of Varendra University, Bangladesh.

To evaluate the effects of linagliptin and the aqueous leaves extract of *Tamarindus indica*, on blood glucose levels, lipid profiles, and hepatoprotective activity in streptozotocin (STZ)-induced diabetic rats. 20 Wistar rats were randomly divided into four groups (A, B, C and D), with five rats in each group. The groups were treated for four weeks as follows:

* **Group A (Normal):** Normal control group receiving 0.5 mL of distilled water.
* **Group B (STZIDRs):** Diabetic control group receiving 0.5 mL of distilled water.
* **Group C (STZ + Linagliptin):** Diabetic group receiving linagliptin at a dose of 1 mL corresponding to 5 mg per 70 kg body weight.
* **Group D (STZ** + ***Tamarindus indica*):** Diabetic group treated with the aqueous leaves extract of *Tamarindus indica* at a dosage of 1 mL corresponding to 200 mg per kg body weight.

**2.4 Experimental Induction of Diabetes**

Except for Group A, all animals were subjected to a fasting period of 16 hours before receiving a freshly prepared intraperitoneal injection of streptozotocin (STZ) at a dose of 45 mg/kg body weight to induce diabetes. The STZ was dissolved in a 0.01 M citrate buffer, which was freshly prepared and adjusted to a pH of 4.5. To mitigate early mortality that might arise from the release of insulin reserves from damaged pancreatic islets, rats received drinking water supplemented with sugar (15 g/L) for 48 hours post-injection (Choudhury et al., 2017).

**2.5 Evaluation Parameters**

Three days following the STZ injection, diabetes was confirmed by measuring blood glucose levels with a glucose test meter (Bioland G-423S Test Strip, Germany) using blood samples obtained from the tail vein. Animals with blood glucose levels exceeding 11.1 mmol/L were selected for inclusion in the study (Ghosh et al., 2012).

**2.6 Biochemical Analysis**

Blood glucose levels in serum samples from each rat were determined via the glucose oxidase method using the Bioland G423S Test Strip (Germany). The levels of serum total cholesterol (TC), triglycerides (TGs), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, SGPT and SGOT were analyzed using UV spectrophotometric methods with diagnostic kits (Human, Germany) (Alfawaz et al., 2022).

**2.5 Statistical Analysis**

Data analysis was conducted using IBM SPSS Statistics 23 and Microsoft Office Excel 2007, with results expressed as mean ± SEM. A one-way analysis of variance (ANOVA) was performed, and when applicable, Dunnett's post-hoc test or Student's paired and unpaired t-tests were implemented. Each *figure* contained a description of the statistical methods applied in the analysis. Significance was defined at p values less than 0.05 (p < 0.05 and p < 0.01).

**3. RESULTS**

**3.1** **Effect on Blood Glucose Level**

Fig.1 illustrates the blood glucose levels measured in mmol/L before and after four weeks of treatment across different experimental groups. The normal group maintained stable glucose levels, with values of 5.62±0.097 and 5.54±0.081 mmol/L, respectively. In contrast, the STZIDRs group (diabetic rats with no treatment) exhibited a significant reduction from 20.04±0.480 to 18.94±0.397 mmol/L. Notably, both the STZ + Linagliptin and STZ + *Tamarind indica* groups showed dramatic decreases in glucose levels, dropping from 19.56±0.312 to 7.78±0.198 mmol/L and from 19.80±0.265 to 7.94±0.214 mmol/L, respectively.

**Fig.1. Effect of *Tamarindus indica* on Blood Glucose Level at Day 1 and after four week in STZIDs.** *Data were represented as mean ± SEM and n=5 in each group. #p<0.05 when compared with normal group, \*p˂0.05 when compared with diabetic control group.*

**3.2 Effect on Lipid Profile**

The extract significantly decreased total cholesterol, triglycerides, and LDL levels while enhancing HDL levels, indicating its antidyslipidemic effects.

**3.2.1 Effect on Total Cholesterol**

The results are presented in Fig.2, showing the serum total cholesterol levels of mg/dl across different experimental groups. The normal group exhibited a mean serum level of 145.82±0.285 mg/dl, whereas the STZIDRs group showed a significant increase to 229 mg/dl. Treatment with Linagliptin and *Tamarind indica* resulted in mean levels of 186.44±0.341 mg/dl and 197.06±0.542 mg/dl, respectively. Error bars represent the standard error of the mean (SEM) for each group.

**Fig. 2. Effect of *Tamarindus indica* on serum Total Cholesterol level in STZIDs.** *Data were represented as mean ± SEM and n=5 in each group. #p<0.05 when compared with normal group, \*p˂0.05 when compared with diabetic control group.*

**3.2.2 Effect on Triglyceride**

The results are presented in Fig.3, illustrating the serum triglyceride (TG) levels measured in mg/dl across different experimental groups. The normal group exhibited a mean serum TG level of 118.56±0.483 mg/dl, serving as the control. In contrast, the STZIDRs group showed a significant increase in serum TG levels, reaching 182.18±0.188 mg/dl. Treatment with Linagliptin led to a reduction in TG levels, with a mean of 133.3±0.266 mg/dl. Additionally, the administration of *Tamarindus indica* resulted in a similar mean TG level of 134.18±0.309 mg/dl. Error bars represent the standard error of the mean (SEM) for each group, emphasizing the variability within the data.

**Fig.3. Effect of *Tamarindus indica* on serum Triglyceride level in STZIDs.** *Data were represented as mean ± SEM and n=5 in each group. #p<0.05 when compared with normal group, \*p˂0.05 when compared with diabetic control group.*

**3.2.3 Effect on LDL level**

The results are summarized in Fig.4, which displays the serum low-density lipoprotein (LDL) levels measured in mg/dl across different experimental groups. The normal group recorded a mean LDL level of 66.38±0.306 mg/dl. The STZIDRs group exhibited a significant increase in LDL levels, reaching 113.9±0.315 mg/dl, indicating the impact of diabetes on lipid metabolism. In contrast, treatment with Linagliptin and *Tamarind indica* resulted in reduced LDL levels, with means of 83.84±0.445 mg/dl and 86.18±0.307 mg/dl, respectively. These findings suggest that both treatments may effectively lower LDL levels in the context of STZ-induced diabetes.

**Fig.4. Effect of *Tamarindus indica* on serum LDL Cholesterol level in STZIDs.** *Data were represented as mean ± SEM and n=5 in each group. #p<0.05 when compared with normal group, \*p˂0.05 when compared with diabetic control group.*

**3.2.4 Effect on HDL level**

The serum high-density lipoprotein (HDL) levels measured in mg/dl across the experimental groups are presented in Fig.5. The normal group exhibited a mean HDL level of 38.62±0.402 mg/dl. The STZIDRs group displayed a marked reduction in HDL levels, with a mean of 24.84±0.515 mg/dl. Treatment with Linagliptin resulted in a higher HDL level of 32.7±0.327 mg/dl, while administration of *Tamarind indica* led to a mean HDL level of 30.24±0.406 mg/dl. These results indicate that both drug treatments improved HDL levels compared to the STZIDRs group, suggesting potential beneficial effects on lipid profile modulation in the context of STZ-induced conditions.

**Fig. 5. Effect of *Tamarindus indica* on serum HDL Cholesterol level in STZIDs. Data** *were represented as mean ± SEM and n=5 in each group. #p<0.05 when compared with normal group, \*p˂0.05 when compared with diabetic control group.*

**3.3 Effect on liver dysfunction**

**3.3.1 Effect on SGPT level**

As illustrated in Fig.6, serum levels of serum glutamate pyruvate transaminase (SGPT) (U/L) were evaluated across different experimental groups. The normal group exhibited a mean SGPT of 23.86±0.349 U/L. Conversely, the STZIDRs group demonstrated a significant elevation in SGPT levels, with a mean of 45.74±0.594 U/L, indicative of liver dysfunction. Treatment with Linagliptin resulted in a marked reduction in SGPT levels to 31.3±0.421 U/L, while the *Tamarind indica* group showed a mean SGPT of 33.76±0.206 U/L. These data suggest that both Linagliptin and *Tamarind indica* treatments effectively reduced SGPT levels compared to the STZIDRs group, highlighting their potential hepatoprotective effects in the context of STZ-induced metabolic disturbances.

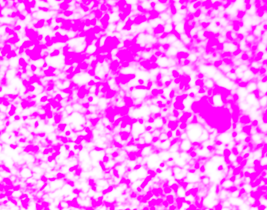
**Fig. 6. Effect of *Tamarindus indica* on serum SGPT level in STZIDs***. Data were represented as mean ± SEM and n=5 in each group. #p<0.05 when compared with normal group, \*p˂0.05 when compared with diabetic control group.*

**3.3.2 Effect on SGOT level**

Fig.7 presents the serum levels of serum glutamate oxaloacetate transaminase (SGOT) (U/L) across the different experimental groups. The normal group recorded a mean SGOT level of 31.24±0.522 U/L. In contrast, the STZIDRs group exhibited a significant increase, with mean SGOT levels reaching 58.8±0.322 U/L, indicating substantial liver enzyme elevation. Treatment with Linagliptin resulted in a reduction of SGOT levels to 41.84±0.483 U/L, while the *Tamarindus indica* group showed a mean level of 44.46±0.607 U/L. These findings indicate that both Linagliptin and *Tamarindus indica* effectively lower SGOT levels compared to the untreated STZIDRs group, suggesting their potential roles in mitigating liver damage in the context of STZ-induced metabolic changes.

**Fig.7. Effect of *Tamarindus indica* on serum SGOT level in STZIDs.** *Data were represented as mean ± SEM and n=5 in each group. #p<0.05 when compared with normal group, \*p˂0.05 when compared with diabetic control group.*

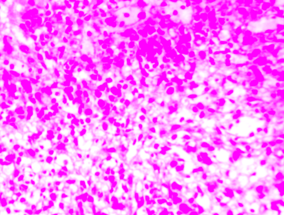
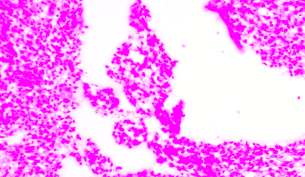
**3.4 Effect on Histopathological Analysis**



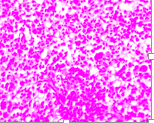
1. Normal

B. STZIDRs

D. STZ+ *Tamarind indica*



C. STZ + Linagliptin



**Fig.8. Histopathology of Pancreases in STZIDs. Microscopic view of pancreatic islets of Langerhans cells at 10× magnification after four weeks’ treatment with *Tamarind indica* in STZIDRs.**

Histological analysis of pancreatic tissue showing islet architecture. (A) Normal control group illustrating healthy islet structure and density of insulin-positive beta cells. (B) Untreated diabetic controls exhibit atrophied islets with leukocytic infiltration. (C) The STZ + Linagliptin group shows intact and well-preserved islets. (D) The STZ + *Tamarindus indica* group demonstrates preserved islets with reduced inflammatory response.

**4. DISCUSSION**

The findings suggest that the aqueous leaves extract of *Tamarindus indica* possesses noteworthy antidiabetic, antidyslipidemic, hepatoprotective and histopathological effects, possibly due to the presence of bioactive compounds such as flavonoids and polysaccharides (Nagoor et al., 2020; Yagupsky et al., 2016), which have been documented for their therapeutic efficacy in various studies (Rafiq et al., 2016; Khong et al., 2019).

The antidiabetic potential of *Tamarindus indica* has been well-recognized in traditional medicine. Our findings are consistent with previous studies where tamarind extracts demonstrated a reduction in blood glucose levels in diabetic models (Shan et al., 2016). Flavonoids, such as quercetin and kaempferol, have shown the ability to enhance insulin sensitivity and promote glucose uptake in peripheral tissues (Khan et al., 2022). Moreover, the polysaccharides present in tamarind may act to modulate carbohydrate digestion and absorption, resulting in improved glycemic control (Paredes-López et al., 1991).

In addition to its antidiabetic properties, *Tamarindus indica* exhibits a significant antidyslipidemic effect. Dyslipidemia is a common complication associated with diabetes, characterized by abnormal lipid profiles that contribute to cardiovascular diseases. Recent studies have reported that herbal extracts, including those from tamarind, can effectively reduce total cholesterol and triglyceride levels (Kumar et al., 2018). The mechanism underlying these lipid-lowering effects may involve the modulation of lipid metabolism and the enhancement of hepatic lipid clearance, potentially mediated by the antioxidant properties of the flavonoids found in the leaves (Mokhtar et al., 2019; Moghadam et al., 2020).

The hepatoprotective effects observed in this study further validate the therapeutic applications of *Tamarindus indica*. The liver plays a crucial role in glucose and lipid metabolism, and its impairment can exacerbate metabolic disorders. Several studies have reported that tamarind extracts can protect against chemically induced hepatotoxicity, likely due to their antioxidant and anti-inflammatory properties (Dixit et al., 2020). The flavonoid content, particularly its ability to scavenge free radicals, is thought to contribute to the observed hepatoprotection by preventing oxidative stress and subsequent liver damage (Kumar et al., 2019).

The histopathological analysis provided additional insights into the therapeutic mechanisms of *Tamarindus indica* leaves. Previous investigations have suggested that the structural integrity of pancreatic cells and liver tissues can be significantly improved by the administration of herbal extracts rich in bioactive (Ali et al., 2014; Kadi et al., 2017). Our findings indicated a restoration of normal histological architecture in treated groups, further supporting the notion that the therapeutic properties of tamarind extracts extend beyond biochemical markers to tangible histological improvements.

The present study underscores the multifaceted therapeutic benefits of *Tamarindus indica*, supporting traditional uses for diabetes and related metabolic disorders. Additionally, clinical trials are imperative to validate these findings in human populations, with a focus on dosage optimization and long-term safety. Future studies should also explore the synergistic effects of *Tamarindus indica* with other medicinal plants, which could pave the way for novel integrated therapeutic approaches in managing diabetes and its complications.

**5. CONCLUSION**

The present study highlights the significant medicinal properties of the aqueous extract of *Tamarindus indica* leaves, demonstrating their potential as a natural adjunct in the management of diabetes and its associated complications. The observed antidiabetic, antidyslipidemic, and hepatoprotective effects suggest that this plant may serve as a valuable therapeutic agent, contributing to improved metabolic health and liver function. In addition, further exploration of the synergistic effects of *Tamarindus indica* in combination with other medicinal plants may yield innovative strategies for enhancing therapeutic efficacy and addressing the multifaceted nature of diabetes management. This holistic approach aligns with the principles of integrative medicine, incorporating traditional knowledge with modern scientific validation.

**ETHICAL APPROVAL**

Animal Ethical committee approval has been collected and preserved by the author(s).

**COMPETING INTERESTS DISCLAIMER:**

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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