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Original Research Paper

Antidiabetic activity of methanolic extract of *Polyalthia longifolia* seeds ameliorating the oxidative stress induced in diabetic rats

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ABSTRACT

Background: Oxidative stress is a disturbance in the equilibrium between free radicals and the body's protective mechanisms. In the present investigation the modulatory effect of a Methanolic Extract of *Polyalthia longifolia* seed (MEPLS) on oxidative stress and antioxidant enzymes in diabetic Sprague Dawley rats.

Methods: The plant seeds were collected, and identified then; Methanolic extract was obtained the *Polyalthia longifolia* seeds. Diabetes mellitus was induced with a single dose of 65 mg/kg Streptozotocin. The effect of *Polyalthia longifolia* seeds (50, 100, 200 mg/kg p.o.) was investigated against Streptozotocin induced Diabetic animals. Antioxidant status of biomarkers like Superoxide diamutase (SOD), Catalase, Malondialdehyde (MDA), Total Glutathion (GSH) were estimated in pancreas. Blood glucose level also investigsted.

Results: The study tested the effect of *Polyalthia longifolia* seed extract on certain biochemical markers in Streptozotocin-induced diabetic rats. The outcome showed a decreasing trend in fasting blood glucose in all groups under treatment. Glucose was reduced significantly by Metformin and *PLS* extract on day 28, with the maximum reduction being in the *PLS* high-dose group. Metformin and *PLS* treatment effectively reduced SOD activity, with the *PLS* medium-dose group showing the highest reduction. Treatment with Metformin and *PLS* extracts reduced MDA levels, with the *PLS* medium-dose group showing the greatest reduction (73%). Metformin and *PLS* extract treatments showed variable effects, with high-dose *PLS* significantly restoring Catalase activity (+13.23%) compared to the control. GSH activity was significantly lower in the STZ control group compared to normal, with *PLS* treatment at low and medium doses further decreasing it.

Conclusion: The results showed that MEPLS reduces oxidative stress and enhances the activities of antioxidant enzymes in STZ-diabetic Sprague Dawley rats. As such, MEPLS could be useful in the management of oxidative stress- mediated diabetic complications.

Keywords: Oxidative stress Antioxidants, *Polyalthia longifolia*, Diabetes mellitus Hyperglycemia

1. Background

Diabetes mellitus, or chronic hyperglycemia, worsens several organs or tissues and can cause life-threatening and disabling diseases when associated with other metabolic diseases like fatty liver disease and cardiovascular disease (CVD) [1]. Diabetes influences virtually all tissues and organs and is characterized by a multifarious etiology. A relative or absolute deficiency of insulin secretion or insulin action is coupled with disturbances in the metabolism of protein, fat, and

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carbohydrate resulting from insulin resistance or destruction of pancreatic beta-cells. In addition, obesity, hereditary susceptibility, physical inactivity, and inappropriate diet are classic risk factors for the development of type 2 diabetes mellitus (T2DM) [2].

Approximately 6.7 million deaths worldwide are caused by diabetes annually, and half of all people with the condition remain untreated. Three out of four adults in low- and middle-income countries have diabetes [3]. Damage to different molecular species, such as lipids, proteins, and nucleic acids, is associated with oxidative stress, which arises from an imbalance between the production of antioxidant defenses and oxidative defenses [4]. Oxidative stress has been linked to numerous diseases, including arthritis, vasculitis, glomerulonephritis, stomach ulcers, muscular dystrophy, ischemic disease, hypertension, Alzheimer's disease, diabetes mellitus, atherosclerosis and declining antioxidant status [5, 6]. Since herbal medicines are thought to have less harmful effects, there is a rising interest in analyzing them. Oral hypoglycemic drug sold in the market have side effect like Gastrointestinal upset such as diarrhea, nausea and vomiting, Weight loss, hepatic dysfunction [7].

Polyalthia longifolia seeds (Family: Annonaceae) are commonly referred to as "Ashoka" or "Asoka" (Saraca indica), the latter belonging to the Caesalpiniaceous family. English refers to it as "false Ashoka," and in Hindi, as Devadari, Nakali Ashoka. Saraca refers to "one without sorrow," and *Polyalthia* is "many cures." Indigenous traditional medicine has used *Polyalthia longifolia* as an antipyretic in reducing fevers of unknown cause [8, 9]. Saraca indica root, bark, and seed extracts have been used to treat dermatological conditions like herpes- kushta/visarpa, psoriasis, acne, eczema, dermatitis, and carcinomas. The Visarpa Chikitsa medical system is recorded in detail in the Charak Samhita, a well-known and widely read compilation of centuries-old indigenous traditional knowledge [10, 11].

In Ayurveda, Ashoka has also been utilized successfully to relieve clinicopathological symptoms brought on by an imbalance in medas, mamsadhatus, and ama. The early stage of any ailment is represented by ama, whereas medas and mamsadhatu are associated with muscles and skin oil (sebum), respectively. In addition to its pharmacological properties, *Polyalthia longifolia* is said to possess cytotoxic, antibiotic (antibacterial and antifungal), and anticancer properties [12, 13]. Further, antiplasmodial activity of *Polyalthia longifolia* was suggested by Bankolé [14] due to presence of several Flavonoids and other similar compounds. *Saraca indica*, bearing resemblance to *Polyalthia*, has been reported to possess promising pharmacological activities, namely anti-inflammatory [15], antidiabetic [16], antioxidant [15], antimicrobial [17] and anticancer [18] activities. Different extract of *P. Longifolia* seed extracts have indeed shown varying medicinal potentials. It was hypothesized that methanolic extract of *Polyalthia longifolia* extract could improve the antioxidant status of Sprague Dawley rats with STZ-induced diabetic rats.

2. Methods

Plant Material collection, Identification and extraction

Polyalthia longifolia mature, ripe fruits were gathered at the Botanical Garden of DCS's A. R. A. College of Pharmacy in Dhule, India. A voucher specimen has been submitted after the fruiting stage plant was verified at S.S.V.P.S. College, Dhule, in the Department of Botany, Faculty of Science. After cutting open the mature fruits, the seeds were transferred and let a week to air dry before being crushed into a fine powder and put away for later use.

Five hundred grams of dried *Polyalthia longifolia* seed powder were packed individually in the Soxhlet apparatus and extracted using methanol until the extraction process was finished. After the extract was filtered while still hot, it was distilled at decreased pressure in a vacuum to eliminate all of the solvent, and it was then dried in dedicators. Following that, the methanolic seed extract was stored for future research in an airtight container.

Experimental animals: Collection of experimental animals

We used 36 female Sprague Dawley rats, weighing between 180 and 270 grams. For two weeks, the animals were kept at the animal house of the pharmacology department of DCS's A. R. A. College of Pharmacy in Dhule, India, under a 12-hour light/dark cycle with typical humidity and temperature levels. The use of animals received ethical approval, with the number being ARACOP/IAEC/24/10. Standard pellets and unlimited water were given to the animals.

Experimental design

Diabetes mellitus was induced by intraperitoneal injection of a single dosage of Streptozotocin (STZ) (65mg/kg bwt) in 0.1 M sodium citrate buffer, pH 4.4 [19, 20]. Female Sprague Dawley rats were fed with standard pellets and watered *ad libitum* with 10 % (w/v) fructose in drinking water for two weeks. The diabetic-induced groups were further monitored without treatment for 21 days with routine checks for glucose levels at 7-day intervals using an One touch Glucometer. The experimental animals were administered single doses of the extract (50 mg/kg MEPLS, 100 mg/kg MEPLS and 200 mg/kg MEPLS) and metformin daily for 28 days 8. The experimental rats were divided into six groups of six rats in each group.

Group1: Non-diabetic control rats (Normal group)
Group 2: Diabetic control rats (Control group)
Group 3: Diabetic rats + 100 mg/kg Metformin (Standard group)
Group 4: Diabetic rats + 50 mg/kg MEPLS (Low Dose)
Group 5: Diabetic rats + 100 mg/kg MEPLS (Medium Dose)
Group 6: Diabetic rats + 200 mg/kg MEPLS (High Dose)

Preparation of tissue homogenates and blood samples

The blood sample is collected by retro orbital puncture on 7, 14, 21, 28th days and check the Fasting glucose level.

The rats were sacrificed on the 28th day after overnight fasting under mild anesthesia. The pancreas tissues of the experimental animals were removed aseptically into universal bottles under ice and rinsed in normal saline (0.9% w/v NaCl) before

processing while some parts were stored in 10% (v/v) formaldehyde (formalin) for histological investigations.

The centrifuged with a Bosch centrifuge, ModelR-8C-DX, at 4000rpm. The resulting plasma and tissue samples were kept in plane bottles labeled accordingly at - 20 ◦C further biochemical investigations.

Assay of activities of superoxide dismutase (SOD) in pancreas

The superoxide dismutase activity assay was conducted by the Nam [21] and Amini-Esfidvajani [22] method to measure the activity of the enzyme in the pancreas. The reaction mixture contained 75 mM Tris-buffer, pH 8.0, 30 mM EDTA, and 2 mM pyrogallol after the expansion of 2.5 ml of Tris-buffer and 100 l of EDTA. Next, the enzyme reaction was initiated with 300 ml of pyrogallol on 0.2 ml of tissue extract. Within 150 seconds, a rise in the absorbance at 420 nm was noted at 30-second intervals over a blank containing the same amount of distilled water as existed in samples. Variations of the absorbance per minute were calculated using the following equation:

$$Change\ in\ Absorbance\ per\ minute\ (\Delta Abs./min) = \frac{B6 - B2}{2.5}$$

Where, B_6 =Absorbance at 150 secs and B_2 =Absorbance at 30 sec. The percentage activity of SOD was calculated as:

$$\%\ enzyme\ activity = 100 - (100 \times \frac{Increased\ in\ absorbance\ of\ substrate}{Increased\ in\ absorbance\ of\ blank})$$

The activity of SOD was expressed as unit/mg of protein, where 1 unit of SOD activity is expressed as the amount of SOD required to cause 50% inhibition of oxidation of pyrogallol.

Evaluation of Malondialdehyde (MDA) activity in pancreas [23]

The reaction mixture comprised 0.1M, pH 7.4 phosphate buffer (0.58 ml), 100 mM (w/v) ascorbic acid (0.2 ml), 100 mM (w/v) ferric chloride (0.02 ml), 10% (w/v) tri-chloroacetic acid (TCA) (1 ml), and 0.67%(w/v) thiobarbituric acid (TBA) (1 ml). Malondialdehyde was measured by using the modified technique.

Assay activity of Catalase in pancreas [24]

The modified procedure was used to determine the Catalase activity. For each test tube, 2 ml of 30 mM hydrogen peroxide (H_2O_2) in 50 mM potassium phosphate buffer (pH 7.0) was made up to 3 ml with distilled water. The absorbance at 240 nm fell each 30 seconds for 2 minutes from that of the blank reagents. Plotting the absorbance against time allowed the quantification of the activity of the enzyme in units of H_2O_2 hydrolyzed per milliliter of material.

$$Catalase\ activity\ \left(\frac{Units}{ml}\right) = \frac{\Delta A/min}{SV \times 0.0436} \times df \times TV$$

ΔA/min = Slope of the graph; df= dilution factor; TV = Total reaction volume; SV = sample volume;

Destruction coefficient of hydrogen peroxide = 436 × 10^{-4} M^{-1} cm^{-1}.

Determination of total glutathione (GSH) concentrations in pancreas [25]

With slight alteration, the method was applied to obtain the concentrations of reduced glutathione in pancreas homogenate. The DTNB reagent (0.6m MDTNB in 0.2M, pH8.0 phosphate buffer) and 5% (w/v) TCA were added to the action mixture. A 10-fold stock solution of glutathione (GSH) was prepared by dissolving 0.1 mg of GSH in 1 milliliter of distilled water and 10-fold dilution. GSH was pipetted in various concentrations (0µg/ml, 10µg/ml, 20µg/ml, 30µg/ml, 40µg/ml, and 50µg/ml) and diluted with distilled water to form 1 ml.

After pipetting 0.02 ml of plasma and 0.1 ml of supernatants into the designated test tubes, 4 ml of TCA solution was added. The mixture was then centrifuged using a Bosch centrifuge (Model R-8C-DX) at 4000 rpm for 10 minutes following this, 0.2 ml of the supernatant of the sample and a standard pipette were added in triplicate, together with 0.9 ml of phosphate buffer and 2 ml of DTNB solution. The absorbance was read at 412 nm against a blank containing the reagents and distilled water. The GSH content in the samples was calculated as g GSH/g sample, and the results were obtained from the conventional curve.

Statistical analysis

Data were presented as mean ± standard error of the mean (SEM) of triplicates. Statistical significance was determined by t test compare between non control and control group and One-Way Analysis of Variance (ANOVA) followed by Dennett's test multiple comparisons be - control and treated rats in all groups.

3. Results

Fasting Blood Glucose Changes in diabetic rats

Animals in all groups were tested for fasting blood glucose at 1, 2, 3, and 4 weeks of the study, as indicated in Table 3.1. During the study, a progressive reduction in fasting blood glucose was observed in all PL treatment groups. At the end of the trial, the blood glucose levels of the Metformin 100 mg/kg p.o. increase and *Polyalthia longifolia* seeds methanolic extract 50, 100, and 200 mg/kg p.o. reduced significantly on 28th day.

Table 3.1: Effect of *Polyalthia longifolia* seeds on blood glucose level in Streptozotocin induced diabetes in rat in week 1, 2, 3, 4.

Glucose level (mg/dl)	Week1	Week2	Week3	Week 4
Vehicle group	96 ± 2.13	117 ± 2.44	129 ± 6	202 ± 13.87
STZ group (Control group)	127.33 ± 10.40 #	123.33 ±4.22	142.33 ± 9.83	182 ± 12.22
Standard (Metformin) group [100 mg/kg] p.o.	125.66 ± 6.16	99.66 ± 1.34 ***	128.5 ± 5.91	165.66 ± 17.21
PL Low Dose group [50 mg/kg] p.o.	114 ± 2.96	116 ± 2.403	161.33 ± 8.26	158.33 ± 12.09

PL Medium Dose group [100 mg/kg] p.o.	142 ± 15.67	123.33 ± 6.37	183 ± 7.31	169.33 ± 8.55
PL High Dose group [200 mg/kg] p.o.	133 ± 0.69	115.33 ± 2.91	231 ± 20.00 ***	159.33 ± 7.67

Each Value represents Mean ± SEM, n = 6, # p< 0.001 as compared to vehicle group, * p< 0.001 as compared with STZ Control group.

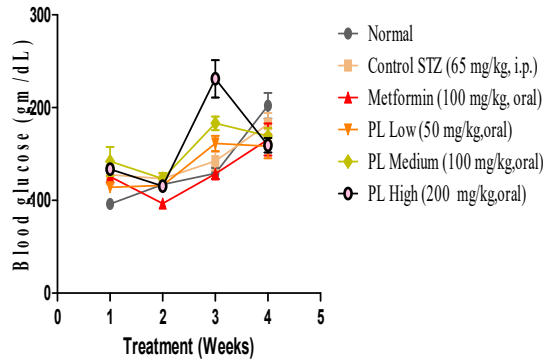


Figure 3.1: Change in Fasting Blood Glucose level in normal and diabetic rats

Effect of MEPLS on superoxide dismutase (SOD) activity

The activity of Superoxide Dismutase (SOD) was activity of 5.513 IU/mg, which was 59.65% lower than the control. The most significant reduction of SOD activity was shown by the medium-dose *PL* at 2.896 IU/mg, which was a 78.8% reduction from the control. The high-dose *PL* showed an SOD activity of 5.113 IU/mg, which was a 62.6% reduction from the control. The findings show that both *PL* and Metformin significantly reduced SOD activity with the highest reduction in the medium-dose *PL* group.

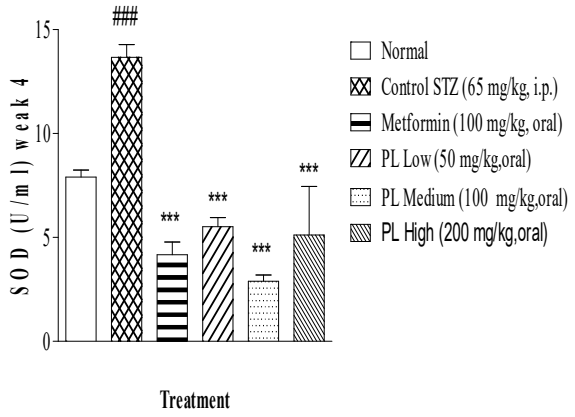
Sr. no.	Compound	SOD Activity IU/mg
1	Vehicle group	7.91 ± 0.336
2	STZ group (Control group)	13.663 ± 0.619 ###
3	Standard (Metformin) group [100 mg/kg] p.o.	4.174 ± 0.604 ***
4	*PL* Low Dose group [50 mg/kg] p.o.	5.513 ± 0.438 ***
5	*PL* Medium Dose group [100 mg/kg] p.o.	2.896 ± 0.297 ***
6	*PL* High Dose group [200 mg/kg] p.o.	5.113 ± 0.958 ***

Each Value represents Mean ± SEM, n = 6, # p< 0.001 as compared to vehicle treated group, *p< 0.001 as compared with metformin.

Figure 3.2: SOD level in normal and diabetic rats

Evaluation of Malondialdehyde (MDA) activity in pancreas

The experiment determined Malondialdehyde (MDA) activity in various experimental groups. The Normal group's MDA activity was 6.23. Comparatively, the control group (STZ) showed a significantly higher MDA measured in various experimental groups. The Normal group exhibited an SOD activity of 7.91 IU/mg. In contrast, the control group showed a highly elevated SOD activity of 13.663 IU/mg, which is a 72.8% increase in SOD compared with the Normal group. The SOD activity of the standard treatment group (Metformin) was 4.174 IU/mg, which decreased by 69.44% relative to the control group. In the *PL*-treated groups, the lowest-dose *PL* group had SOD activity of 9.848, which was an increase of 58.1% in MDA levels over the Normal group. The Metformin standard treatment group had MDA activity of 8.358, indicating a 15.1% decrease in MDA levels from the control group. In the *PL*-treated groups, the low-dose *PL* group indicated MDA activity of 5.252, with a 46.7% decrease in MDA levels from the control. The medium-dose *PL* group exhibited the greatest decline of MDA activity at 2.656, which is a 73% decline relative to the control. The high-dose *PL* group exhibited an MDA activity of 6.486, which suggests a 34.1% decline relative to the control. These findings suggest that both Metformin and *PL* treatment significantly reduced MDA levels, but the greatest decline was in the medium-dose *PL* group.



Sr. no.	Compound	MDA Activity
1	Vehicle group	6.23 ± 1.05
2	STZ group (Control group)	9.848 ± 1.27
3	Standard (Metformin) group [100 mg/kg] p.o.	8.358 ± 0.78
4	*PL* Low Dose group [50 mg/kg] p.o.	5.252 ± 0.45 **
5	*PL* Medium Dose group [100 mg/kg] p.o.	2.656 ± 0.54 ***
6	*PL* High Dose group [200 mg/kg] p.o.	6.486 ± 0.91 *

Each Value represents Mean ± SEM, n = 6, # p< 0.001 as compared to vehicle treated group, *p< 0.001 as compared with metformin.

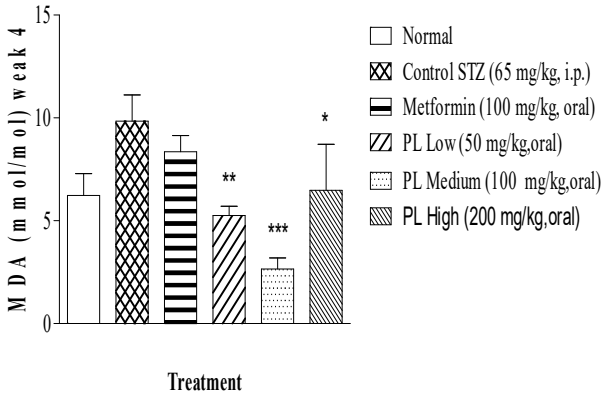


Figure 3.3: MDA level in normal and diabetic rats

Effect of MEPLS on Catalase (CAT) activity in the pancreas

In this experiment, Catalase activity was assessed in different experimental groups. The Catalase activity of the vehicle control group were 12.795, respectively. However, the control group (STZ) showed a notable decrease, Catalase activity of 6.627, which was 48.2% lower than that of the normal group.

The Metformin standard treatment group showed Catalase activity of 4.643, which was 29.94% lower Catalase activity when compared to the control group. Of the groups treated with *PL*, the lowest dose of *PL* had Catalase activity of 1.242, showing a decrease of 81.27% when compared to the control. The medium-dose *PL* group had Catalase activity of 2.565, with a 61.29% decrease compared to the control group. The high-dose *PL* group had Catalase activity of 7.505, which was 13.23% greater than the control. These results show that *PL* and metformin treatments significantly altered Catalase activity. While there was a significant decrease in Catalase activity for the low-dose and medium-dose *PL* groups, the high-dose *PL* group demonstrated the recovery effect by showing higher Catalase activity compared to the control group.

Sr. no.	Compound	Catalase Activity
1	Vehicle group	12.795 ± 1.48
2	STZ group (Control group)	6.627 ± 0.91 ##
3	Standard (Metformin) group [100 mg/kg] p.o.	4.643 ± 0.77
4	*PL* Low Dose group [50 mg/kg] p.o.	1.242 ± 0.07 ***
5	*PL* Medium Dose group [100 mg/kg] p.o.	2.565 ± 0.28 ***
6	*PL* High Dose group [200 mg/kg] p.o.	7.505 ± 0.42

Each Value represents Mean ± SEM, n = 6, # p< 0.001 as compared to vehicle treated group, *p< 0.001 as compared with metformin.

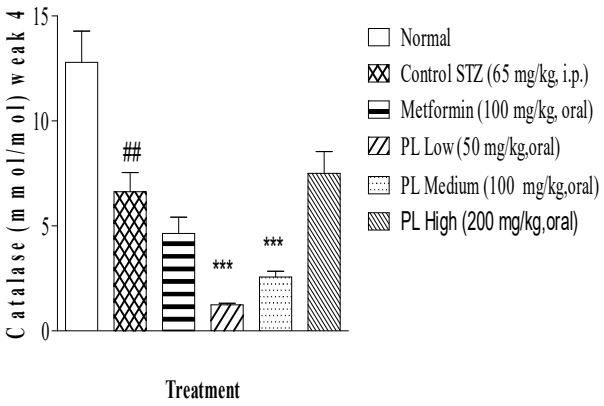


Figure 3.4: Catalase level in normal and diabetic rats

Effect of MEPLS on reduced glutathione (GSH) concentrations

The research quantified the GSH activity in the various experimental groups. The control normal group measured GSH activity of 1.614. Compared to the control normal group, the control (STZ) group, however, reported a drastic reduction in the form of GSH activity of 0.916 (a fall of 43.24%).

The GSH activity of the control treatment group (Metformin) was 0.814, which was reduced by 11.14% from the control, respectively. The low-dose PL treatment group among the *PL* treatment groups showed GSH activity of 0.557, which was reduced by 39.19% from the control, respectively. The *PL* treatment at the medium dose also had a similar trend with the GSH of 0.548 decreasing by 40.17%, respectively, relative to the control. In an unexpected twist, the high-dose *PL* responded more favorably with the best GSH activity of 0.947, showing an increase of 3.39% over the control, respectively. These results show that STZ lowered GSH activity significantly in comparison to the normal group. Although Metformin improved these parameters, *PL* treatment at low and medium doses resulted in further decreases in comparison to the control. The high-dose *PL* group, however, showed a slight improvement compared to the control group, indicating a possible dose-dependent effect of *PL* treatment.

Sr. no.	Compound	GSH Activity ± SEM
1	Vehicle group	1.614 ± 0.31
2	STZ group (Control group)	0.916 ± 0.16
3	Standard (Metformin) group [100 mg/kg] p.o.	0.814 ± 0.23
4	*PL* Low Dose group [50 mg/kg] p.o.	0.557 ± 0.14
5	*PL* Medium Dose group [100 mg/kg] p.o.	0.548 ± 0.14
6	*PL* High Dose group [200 mg/kg] p.o.	0.947 ± 0.15

Each Value represents Mean ± SEM, n = 6, # p< 0.001 as compared to vehicle treated group, *p< 0.001 as compared with metformin.

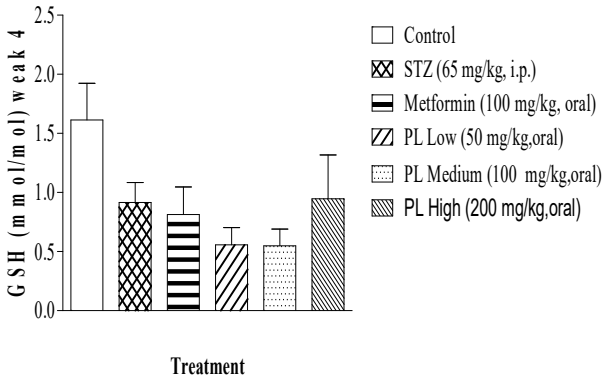


Figure 3.5: GSH level in normal and diabetic rats

4. Discussion and Conclusion

Discussion

Hyperglycemia enhances the production of free radicals through glucose auto-oxidation and this drains the activity of the antioxidant defense mechanism and thus facilitation de novo free radical formation [26]. The study evaluated the antidiabetic and antioxidant effect of *Polyalthia longifolia* seed extract in Streptozotocin (STZ)-induced diabetic rats. Results showed that *PL* extract had a dose-dependent effect on controlling fasting blood glucose levels and enhancing oxidative stress markers. The state of diabetes produces oxidative stress as a consequence of the formation of oxidative species from various triggered chains of pathologic occurrences produced by excess glucose that cumulatively form diabetic complications. The STZ group showed a decreased fasting blood glucose level, and Metformin and *PL* extract significantly reduced these levels. The greatest reduction was seen in the medium dose *PL* group, followed by Metformin and high-dose *PL* [27, 28].

Oxidative stress is one of the key causes of β-cell dysfunction in diabetes. Therefore, assessment of antioxidant enzyme activities such as of Superoxide Dismutase (SOD), CAT, and Malondialdehyde (MDA) gives important information regarding protective effects of treatments. The STZ group also demonstrated a marked elevation of Superoxide Dismutase (SOD) activity, i.e., 72.8% greater than that of the normal group. *PL* and metformin treatment lowered SOD levels remarkably, with the *PL* medium-dose group experiencing the greatest reduction. *Polyalthia longifolia* is highly antioxidant in action through the reduction of oxidative stress [29]. This decrease in SOD could indicate normalization of oxidative status and not suppression of antioxidant defense, as elevated SOD activity tends to be an overcompensation for increased oxidative burden.

The STZ group had a 48.2% decrease in Catalase (CAT) activity, with Metformin reducing it by 29.94%. The medium-dose and low-dose *PL* groups had marked decreases, whereas the high-dose *PL* group had a 13.23% increase in CAT activity, indicating a potential recovery effect at higher doses [30].

Malondialdehyde (MDA): The MDA level was markedly higher in the STZ group (9.848 IU/mg), indicating higher lipid peroxidation. Metformin reduced MDA level by 15.1%, whereas the low-dose, medium-dose, and high-dose *PL* groups reduced by 46.7%, 73%, and 34.1%, respectively. These findings suggest that *Polyalthia longifolia* has dose-dependent reduction in lipid peroxidation and oxidative damage [31].

Decreased GSH was considerably lowered in the STZ group, with Metformin reversing activity by 11.14%. The low-dose and medium-dose *PL* groups depleted further GSH, whereas the high-dose *PL* group had a slight increase in GSH, indicating potential antioxidant recovery at high doses [32]. This observation indicates that whereas low doses might not activate GSH synthesis pathways, higher doses would potentially activate the up regulation of glutathione reductase or associated enzymes, which support cellular redox homeostasis.

The antioxidant and hypoglycemic activity demonstrated in the current study is a result of phytoconstituents present in *P. longifolia* such as flavonoids, diterpenoids, and alkaloids, which have been established to possess free-radical scavenging and insulin-mimetic activities. Greater potency of the medium dose in inhibiting the SOD and MDA activities and the revivifying activity of the high dose on CAT and GSH mirrors the dose dependence of bioactivity of the extract.

Significantly, efficacy for glucose reduction overcomes improvement by antioxidants, suggesting a two-fold mode of action involving oxidative damage protection along with glycemic control. Notably, the multifaceted mechanism of the extract acting on both glycemic control and oxidative stress inhibition makes it a potential lead for integrative diabetic treatment aside from traditional approaches.

Conclusion

The results of the present study reveal the antidiabetic and antioxidant potential of *Polyalthia longifolia* seed extract in STZ-induced diabetic rats. The extract decreased fasting blood glucose significantly and showed appreciable antioxidant activity by regulating the indicators of oxidative stress, i.e., SOD, MDA, CAT, and GSH. Medium-dose *PL* was found to improve the markers of oxidative stress maximally, and high-dose *PL* exhibited a mild restitution effect. These findings suggest that *Polyalthia longifolia* seeds might be a candidate natural remedy for diabetes therapy, and future studies should be done in clinical trials.

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