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Exploring the Antidiabetic Potential of *Polygonum plebeium R. Br.*: Insights from Rat Models

Mona Motallebi*[1], Durga Madhab Kar[1], Bipin Bihari Panda[2]

1. Department of Pharmacology, Siksha 'O' Anusandhan University, Bhubaneswar
2. Department of Pharmacology, Gayatri College of Pharmacy, Sambalpur

Corresponding author's Address:
School of Pharmaceutical science,
Siksha 'O' Anusandhan University,
Kalinga Nagar, Bhubaneswar- 751003
E-mail: monamotallebi18@gmail.com
Mobile no- 8763099929

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Abstract:

Diabetes mellitus presents a formidable global health challenge, with its prevalence soaring among diverse populations. Traditional herbal remedies have long been explored for their potential in managing this chronic metabolic disorder. In this investigation, we delve into the antidiabetic properties of the hydroalcoholic extract derived from Polygonum plebeium R. Br. shoots, employing various rat models to assess its efficacy.Our study encompasses normoglycemic rats, glucose-loaded rats, and rats induced with hyperglycemia through adrenaline, alloxan, and methylprednisolone administration. Noteworthy findings reveal a significant hypoglycemic effect of the extract at a dosage of 200 mg/kg in normoglycemic rats, observed at the 5-hour mark. Furthermore, it demonstrates remarkable improvements in glucose tolerance compared to the control group subjected to 2 gm/kg p.o. glucose.

Of particular interest is the extract's ability to markedly reduce blood glucose levels in adrenaline-treated rats (0.8 mg/kg, i.p), alloxan-induced hyperglycemic rats, and those with methylprednisolone-induced hyperglycemia. Comparative analysis with Glibenclamide, a standard drug, at a dose of 5 mg/kg p.o., reveals comparable antidiabetic efficacy of the whole plant extract.This study accentuates the significant antidiabetic attributes of Polygonum plebeium R. Br. whole plant extract, advocating its potential as a natural intervention for diabetes management. Further elucidation of its mechanisms and exploration of its bioactive constituents are warranted to solidify its role in clinical applications.

Keywords: Polygonum plebeium R. Br., Normoglycemic, OGTT, alloxan, Methylprednisolone

1. Introduction:

Diabetes mellitus stands as a persistent metabolic irregularity marked by prolonged elevation of blood sugar levels, disrupting the intricate balance of protein, carbohydrate, and lipid metabolism. This condition arises from dysfunctions either in insulin activity, insulin secretion, or both, leading to enduring complications across multiple organs (American Diabetes Association,2009).

The global incidence of diabetes mellitus is on a relentless upward trajectory. By the year 2025, India is projected to surpass all nations in terms of diabetic population, earning the moniker "Diabetic Capital of the world". In 2000, India already led the world in diabetes cases, followed by China and the USA. Projections indicate a doubling of global diabetes prevalence by 2030 compared to 2000 levels, with India bearing the brunt of this surge. By 2030, it is estimated that up to 79.4 million individuals in India alone will be affected by diabetes, while China and the United States will also experience substantial increases, with 42.3 million and 30.3 million affected individuals respectively(Kaveeshwar SA and Cornwall J, 2014).

Within contemporary medical practice, the management of diabetes primarily revolves around the administration of sulfonylureas, biguanides, and insulin. However, these conventional treatments are often associated with adverse side effects, presenting challenges in their long-term utilization (Tripathi KD, Essential of medical Pharmacology, Japee publication, 6th edition).Addressing the escalating challenge of managing diabetes without adverse effects presents a formidable task for the medical community. With a rising preference for natural remedies, there's a growing demand for anti-diabetic products sourced from plants. However, despite traditional claims, only a handful of these botanicals have undergone rigorous scientific scrutiny. It becomes imperative to substantiate the efficacy of plant-based interventions for hyperglycemia while ensuring minimal toxicity.

One such botanical under investigation is Polygonum plebeium R.Br., colloquially known as small knotweed. Rich in a diverse array of bioactive compounds including tannins, essential oils, flavonoids, unsaturated sterols, triterpenoids, saponins, and alkaloids, this plant holds promise as a potential anti-diabetic agent (Hasan AN *etal*., 2015). It belongs to the family Polygonaceae(Jabeen A*et al.,* 2009;Kirkpatrick JB and Harwood CE, 1983;Kumar S*et al.*, 2008).This plant holds significance under various indigenous names such as "Chemti Sag" and "Dubia Sag", adding to its cultural and traditional importance (Banerjee S*et al.,* 2012), “Anjaban” (Hasan AN *etal*., 2015), and Lalbuti(Kumar S*et al.,* 2008). However, bistort (Jabeen A*et al.,* 2009) and small knotweed are the common English names of this plant. Its morphology is characterized by a triangular shape, with dimensions approximately measuring 1.4 mm in length and 1.0 mm in width, resembling the form of a pyramid(Kantachot C andChantaranothai P, 2011); Thriving in regions with minimal waterlogging, this plant is commonly found in the drier sections of swamps, earning it recognition as a prevalent inhabitant of wetland environments (Chauhan MS andQuamar MF, 2012).

In vitro studies have demonstrated the antioxidant activity of P. plebeium, highlighting its potential as a source of antioxidant compounds (Ho YL*et al.,* 2012). The plant is commonly used for treating pneumonia, bowel complaints, diarrhea (Jabeen A*et al.,* 2009;Banerjee S*et al.,* 2012), dysentery (Dey A and De JN, 2010), eczema, and ring worms(Sreeramulu N*et al.,* 1983). It is found to cure dysentery when crushed with the bark of Butea superba and adventitious roots of Ficusbenghalensis(Dey A and De JN, 2010). A soothing balm crafted

from crushed leaves of P. plebeium finds application in the traditional treatment of skin conditions such as eczema and ringworms (Siddiqui MB*et al.,* 1989). The plant is used as a vegetable and tends to possess vitamin C (Sreeramulu N*et al.,* 1983). In traditional medicine, the roots of P. plebeium are harnessed for their therapeutic properties in addressing bowel complaints. Additionally, the ash and oil derived from this plant are employed in the treatment of eczema, while the powdered herb serves as a remedy for pneumonia (Kantachot C andChantaranothai P, 2011), and the decoction of the plant root is used as a cooling agent (Dey A and De JN, 2010). P. plebeium is revered as a blood purifier and holds a prominent place in traditional medicine in Pakistan, where it is utilized extensively for its efficacy in treating liver disorders such as jaundice and hepatitis (Ahmad S*et al.,* 2014).

Despite its traditional use, there remains a lack of scientific understanding regarding the mechanisms by which P. plebeium operates in the management of hyperglycemia. Thus, this study aims to explore the impact of Polygonum plebeium R. Br. shoot components, including leaves, flowering buds, and stems, on various rat models. These models include normoglycemic rats, glucose-loaded rats, as well as rats induced with hyperglycemia using adrenaline, alloxan, and methylprednisolone.

2. MATERIALS AND METHODS:

2.1.Plant sample collection and preparation of extract:

In December, the shoots of Polygonum plebeium R. Br. were gathered from Bandbahal forest, situated within the roadside market of Bandbahal town in Western Odisha, India. Authentication of the collected plant material was carried out by experts from the Botany Department at Sambalpur University, Odisha, India.

Preparation of Hydroalcoholic extract:

The desiccated shoot of Polygonum plebeium R. Br. underwent a transformation process by first being ground into powder using an electric grinder. Subsequently, 100 grams of the powdered shoot material was immersed in a solution consisting of ethanol and distilled water in a 70:30 ratio, totaling 1000 milliliters. This mixture was allowed to stand at room temperature for duration of 5 days. Following this period, the resulting mixture underwent filtration using Whatman No. 1 filter paper and was subsequently subjected to centrifugation at 3500 revolutions per minute (rpm) for duration of 20 minutes. The supernatant obtained from this process was then dried at a temperature of 37°C, resulting in the formation of a semi-solid mass, which constituted the extract. This extract was then stored at a temperature of 4°C until it was ready for use (Ahangarpour A *et al.,* 2015).

2.2.Animals:

The study involved 114 healthy male Albino wistar rats with weights ranging between 150 to 200 grams. These rats were housed in the animal facility of Gayatri College of Pharmacy, Sambalpur, dedicated to experimental research. The rats were carefully maintained under controlled environmental conditions, including a temperature of 23 ± 2°C, humidity maintained at 50 ± 5%, and a standard 12-hour light-dark cycle. Prior to the commencement of the study, all animals underwent a seven-day acclimatization period to adapt to their surroundings. The rats were then randomly allocated into experimental and control groups and individually housed in clean polypropylene cages furnished with sterile paddy husk bedding. They were provided with unrestricted access to standard pellets as their basal diet

and were allowed ad libitum access to water throughout the duration of the study(Ahangarpour A *et al.,* 2013).

To mitigate any potential non-specific stressors, the animals underwent a 48-hour acclimatization period to laboratory conditions prior to the commencement of the experimental protocol. All research procedures were ethically approved by the Institutional Animal Ethical Committee (IAEC) of Gayatri College of Pharmacy, Sambalpur, with registration number 1339/PO/Re/S/10/CPCSEA, adhering to the guidelines set forth by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), as per the regulations established by the Government of India.

2.3.Experimental Assessment:

2.3.1. Hypoglycemic activity screening in normal rats

In the hypoglycemic activity screening conducted on normal rats weighing between 150 to 200 grams, the animals were fasted overnight prior to the experiment. They were then divided into three groups, each consisting of six rats.

Control Group: This group received a gavage of 0.2 mL of normal saline daily for duration of 21 days.

Test Drug Group: Rats in this group were administered 0.2 mL of Polygonum plebeium R. Br. hydroalcoholic extract at a dose of 200 mg/kg via oral gavage for 21 days.

Standard Drug Group: Animals in this group received Glibenclamide orally at a dose of 5 mg/kg for the same duration (Karimi G *et al.,* 2010).

These experimental conditions were established to evaluate the hypoglycemic effects of the test drug compared to both a control group receiving saline and a standard drug group receiving Glibenclamide.

Blood samples were obtained from the tail of each rat for subsequent analysis. Initially, blood samples were collected prior to treatment (designated as 0 hours) and then at 1, 3, 5, and 7 hours following the administration of the respective drugs to the treated animals. The concentration of blood glucose was determined using a Glucometer (one touch select) to monitor changes over the specified time intervals (Mandlik RV *et al.,* 2008).

2.3.2. Oral Glucose tolerance test in normal rats (OGTT)

During the Oral Glucose Tolerance Test (OGTT), fasted rats were orally administered glucose at a dose of 2 grams per kilogram of body weight. This administration occurred 2 hours after the initial drug administration. Blood samples were subsequently collected from the tail vein at intervals of 30 minutes, 60 minutes, 90 minutes, and 120 minutes following the glucose treatment(Jain S *et al.,* 2010).

The experimental groups were as follows:

Normal Group: Rats in this group received a solvent solution (0.2 mL normal saline).

Glucose Loaded Group: Rats in this group were administered both glucose and solvent.

Test Drug Group: Rats in this group were given glucose along with the test drug at a dosage of 200 mg/kg.

Standard Drug Group: Rats in this group received glucose in conjunction with the standard drug Glibenclamide at a dose of 5 mg/kg orally.

These experimental groups were established to assess the effects of the test drug and standard drug on glucose tolerance compared to a control group receiving only solvent or glucose.

2.3.3. Adrenaline induced hyperglycemic rats

The experimental design consisted of dividing the animals into four groups, each comprising six rats:
Group I: Normal Control - Rats in this group received a solvent solution at a dosage of 2 ml/kg body weight.
Group II: Hyperglycemic Control - Rats in this group were administered adrenaline at a dosage of 0.8 mg/kg body weight, inducing hyperglycemia, after 1 hour of drug treatment.
Group III: Test Drug Group - Rats in this group received adrenaline at a dosage of 0.8 mg/kg body weight, followed by the administration of extracts from Polygonum Plebeium R. Br. at a dosage of 200 mg/kg body weight.
Group IV: Standard Drug Group - Rats in this group received adrenaline at a dosage of 0.8 mg/kg body weight, followed by oral administration of Glibenclamide at a dosage of 5 mg/kg (Naik S R and Filho J M B, 1991).

Blood glucose levels were then measured at intervals of 1, 3, 5, and 7 hours following the administration of the respective drugs to evaluate their effects on hyperglycemia.

2.3.4. Antidiabetic activity in alloxan induced hyperglycemic rats
The animals were divided into four groups, each consisting of six individuals.

In Group 1, which served as the normal control, no specific treatment was administered. Diabetes was induced in the remaining animals by intraperitoneal injection of alloxan monohydrate at a dosage of 150 mg/kg body weight. After 72 hours, fasting blood glucose levels were measured to confirm the establishment of diabetes. Rats with blood glucose levels exceeding 250 mg/dl were considered diabetic and included in the study(Antia B S and Okokon J E, 2005).

Following confirmation of diabetes induction, the rats were equally distributed into the following groups:

Group II: Diabetic Control (received alloxan treatment only)

Group III: Test Drug Group (received alloxan treatment along with Hydroalcoholic extract of Polygonum plebeium R. Br. at a dosage of 200 mg/kg body weight)

Group IV: Standard Drug Group (received alloxan treatment along with Glibenclamide at a dosage of 5 mg/kg)

The drugs were administered orally once daily for a period of 15 days using a gastric catheter. This regimen aimed to assess the effects of the test drug and standard drug on diabetic conditions over the specified duration.

2.3.5. Antidiabetic activity screening in Methylprednisolone induced hyperglycemia

The animals were segregated into four groups, with each group comprising six rats. Group 1 was designated as the normal control, while diabetes was induced in the remaining animals by intraperitoneal injection of Methylprednisolone (MPL) at a dosage of 50 mg/kg body weight. To confirm the establishment of diabetes, fasting blood glucose levels were measured 72 hours after MPL injection, with rats exhibiting blood glucose levels exceeding 250 mg/dl considered diabetic and eligible for the study (Fang J*et al.*, 2013).

Following the confirmation of diabetes induction, the animals were equally distributed into the following groups:
Group II: Diabetic Control (received MPL treatment only)

Group III: Test Drug Group (received MPL treatment along with Hydroalcoholic extract of Polygonum plebeium R. Br. at a dosage of 200 mg/kg body weight)
Group IV: Standard Drug Group (received MPL treatment along with Glibenclamide at a dosage of 5 mg/kg)

The drugs were orally administered consecutively for 15 days on a once-daily basis using a gavage, aiming to evaluate the effects of the test drug and standard drug on diabetic conditions over the specified duration.

RESULT

Table-1: Effect of hydro-alcoholic extracts of shoot of *Polygonum Plebeium R. Br.*on normoglycemic rats.

Group	Treatment (Dose mg/kg)	Initial Glucose (mg/dl)	Final Glucose Level (mg/dl)			
			1hr	3 hr	5hr	7 hr
I	Control (solvent 5ml/kg)	91.15 ±4.54	85.52 ±4.23	87.13 ±4.54	84.58 ±4.70	867.02 ±4.44
II	Extract of Polygonum Plebeium R. Br.*(*200mg/kg)	92.32 ±4.21	84.86 ±4.06	78.52 ±3.76	72.59 ±4.06*	74.51 ±4.10*
III	Glibenclamide (5mg/kg)	91.07 ±4.22	71.63 ±4.38*	66.59 ±4.74*	61.58 ±4.19*	67.65 ±4.32*

Values presented are as mean± SEM (Standard error of mean), n= 6, *= significant treated with Group II and group III compared with Group I.Statistical analysis by Students t-test.p value <0. 01.

Table-2: Effect of hydro-alcoholic extracts of shoot of *Polygonum Plebeium R. Br.* on glucose loaded rats.

Group	Treatment (mg/kg)	Initial glucose level (mg/dl)	Final glucose level (mg/dl)			
			30 min	60 min	90 min	120 min
Group 1	Solvent	87.6±5.61	84.8±5.4	80.3±4.3	82.0±4.5	81.4±4.3
Group 2	Glucose (2 gm/kg)	86.5±5.73	199.50±7.6*	160.33±7.3*	140.66±7.5*	109.16±6.5*
Group 3	Glucose +Extract of Polygonum Plebeium R. Br.(200mg/kg)	83.5±5.54	189.81±8.5	149.96±7.4	125.03±6.5*	97.95±5.3*
Group 4	Glucose+ Glibenclamide (5mg/kg)	85.7±4.74	125.61±6.9*	100.2±7.3*	100.70±6.5*	87.81 ±5.4*

Values presented are as mean± SEM (Standard error of mean), n= 6, *= significant group IIcompared with Group I and groupIII,IV compared with Group II.Statistical analysis by Students t-test.p value <0. 01.

Table-3: Effect of hydro-alcoholic extracts of shoot of *Polygonum Plebeium R. Br.* on adrenaline induced hyperglycaemic rats.

Groups	**Treatment (Dose mg/kg)**	**Initial glucose (mg/dl)**	**Final glucose (mg/dl)**			
			1hr	**3hr**	**5 hr**	**7 hr**
I	Normal control (Solvent 5ml/kg)	90.0 ±5.11	85.50 ±5.56	80.93 ±5.84	79.93 ±5.61	80.46 ±5.24
II	Hyperglycaemic control (Adrenaline)	87.33 ±6.94	173.81 ±8.10*	215.03 ±8.31*	189.66 ±8.42*	142.61 ±7.15*
III	Adrenaline + Extract of Polygonum Plebeium R. Br.(200mg/kg)	85.20 ±5.86	182.18 ±8.42	194.73 ±7.22	150.18 ±6.55*	122.62 ±6.24*
IV	Adrenaline + Glibenclamide(5mg/kg)	79.26 ±5.27	74.11 ±8.48	166.88 ±8.36*	147.71 ±6.74*	121.43 ±5.04*

Values presented are as mean± SEM (Standard error of mean), n= 6, *= significant group II compared with Group I and groupIII,IV compared with Group II.Statistical analysis by Students t-test.p value <0. 01.

Table 4: Effect of hydro-alcoholic extracts of shoot of *Polygonum plebeium R. Br.*on blood glucose concentration on Alloxan induced acute hyperglycaemic albino rats.

Group (n)	Dose (mg/kg body wt)	Blood glucose level (mg/dl) (mean ± SEM)				
		Initial	1h	3h	5h	7h
Normal Control (saline)	2 ml saline/kg body weight	91.45 ± 3.37	87.35 ± 3.77	84.97 ± 3.43	81.62 ± 3.30	78.34 ± 3.21
Hyperglycemic control	Alloxan 150mg/kg body weight	93.50 ± 3.26	274.15 ± 6.37	271.01 ± 5.78	267.81 ± 5.89	272.19 ± 6.03
Hydro alcoholic extract	200 mg/kg b. wt.	92.31 ± 3.10	247.32 ± 5.83	245.41 ± 5.54	233.24 ± 5.17*	210.84 ± 5.61*
Standard drug (Glibenclamide)	0.5 mg/kg b. wt.	90.42 ± 3.33	192.57 ± 3.31	180.81 ± 3.42	168.50 ± 4.46*	157.62 ± 4.27*
Values presented are as mean± SEM (Standard error of mean), n= 6, *= significant group II compared with Group I and groupIII,IV compared with Group II.Statistical analysis by Students t-test.p value <0. 05.						

Table-5: Effect of hydro-alcoholic extracts of leaves of*Polygonum plebeium R. Br.* on blood glucose level on Alloxan induced chronic hyperglycaemic albino rats.

Group (n)	Dose (mg/kg body wt)	Serum Glucose Level (mg/dl) on different Days of treatment			
		Initial	5th Day	10th Day	15th Day
Normal Control (saline)	2 ml saline/kg body weight	91.56 ± 3.47	90.51 ± 3.59	91.31 ± 3.92	89.80 ± 3.30
Hyperglycemic control	Alloxan 150mg/kg body weight	93.82± 3.28	273.20 ± 5.22	276.11 ± 5.45	267.1 ± 4.71
Hydro alcoholic extract	200 mg/kg b. wt.	92.42 ± 3.41	265.2 ± 5.48	223.8 ± 5.72*	191.6 ± 5.77*
Standard drug (Glibenclamide)	5 mg/kg b. wt.	91.43 ± 3.20	232.01 ± 5.69	146.71 ± 4.53*	112.81 ± 4.39*
Values presented are as mean± SEM (Standard error of mean), n= 6, *= significant group II compared with Group I and groupIII,IV compared with Group II.Statistical analysis by Students t-test.p value <0. 05.					

Table-6: Effect of hydro-alcoholic extracts of shoot of *Polygonum Plebeium R. Br.* on Methylprednisolone induced hyperglycaemic rats.

Group (n)	Dose(mg/kg body wt)	Serum Glucose Level (mg/dl) on different Days of treatment			
		Initial	1st Day (24hrs)	5th Day	10th Day
Normal Control (saline)	2 ml saline/kg body weight	91.46 ± 3.39	90.51 ± 3.15	91.25 ± 3.18	90.01 ± 3.28
Hyperglycemic control	Methylprednisolone 50mg/kg body weight	93.52 ± 3.26	122.20 ± 5.10	147.23 ± 5.29	249.2 ± 5.02

Hydro alcoholic extract (Test Drug)	MPL 50mg/kg + Polygonum Plebeium R. Br.200 mg/kg b. wt.	92.32 ± 3.12	112.2 ± 5.36	100.8 ± 5.16*	140.5 ± 5.66*
Standard drug (Glibenclamide)	MPL+ Glibenclamide (5 mg/kg b. wt.)	90.43 ± 3.28	102.01 ± 5.62	98.71 ± 4.50*	90.81 ± 4.38*
Values presented are as mean± SEM (Standard error of mean), n= 6, *= significant group II compared with Group I and groupIII,IV compared with Group II.Statistical analysis by Students t-test.p value <0. 05.					

DISCUSSION

The extract derived from Polygonum plebeium R. Br. showcases notable radical scavenging properties, underscoring its role as an effective antioxidant agent. This plant species is abundantly found in western Odisha, making it readily accessible for medicinal purposes. The utilization of its leaves holds potential in treating various ailments. Moreover, the comprehensive extract of Polygonum plebeium R. Br. suggests its potential in safeguarding vital tissues, particularly the liver, thereby exhibiting anti-fibrotic properties beneficial for liver diseases (Rehman *et al.*, 2018).

The current investigation aimed to evaluate the impact of Polygonum plebeium R. Br. on various rat models, including normoglycemic rats, adrenaline-induced hyperglycemia, glucose-loaded rats, and rats induced with diabetes using alloxan and methylprednisolone. A dosage of 200 mg/kg body weight was administered orally for the studies.

In normoglycemic rats, the administered drug notably decreased blood glucose levels, demonstrating significant glucose-lowering activity. This effect was particularly pronounced after 5 hours of administration, persisting up to the 7-hour time point. These findings highlight the potential of Polygonum plebeium R. Br. as a promising candidate for mitigating hyperglycemia in normoglycemic conditions, showcasing its efficacy even after a single dose administration (Table-1). In normoglycemic glucose-loaded rats, Polygonum plebeium R. Br. demonstrated a significant reduction in blood glucose levels when administered 2 hours prior to the administration of glucose. This suggests that the plant extract possesses the ability to attenuate the rise in blood glucose induced by glucose loading, indicating its potential as a preventive or therapeutic agent for managing postprandial hyperglycemia (Table-2).

In adrenaline-induced hyperglycemic rats, the administration of Polygonum plebeium R. Br. extract at a dosage of 200 mg/kg resulted in a significant reduction in blood glucose levels compared to the control group treated with solvent after 5 hours of administration. Adrenaline induces hyperglycemia primarily by triggering the release of glucocorticoids, which disrupt glucose metabolism in the liver. Additionally, adrenaline inhibits insulin release from the pancreas, further contributing to elevated blood glucose levels. The observed reduction in blood glucose levels following treatment with the plant extract suggests its potential in counteracting the hyperglycemic effects induced by adrenaline, possibly through mechanisms involving modulation of glucocorticoid release and insulin secretion (Table-3).

Table 4 displays the effect of a single dose of hydro-alcoholic extracts of leaves on blood glucose levels of alloxan-induced acute hyperglycemic rats. The results indicate a significant reduction ($P < 0.05$) in blood glucose levels at the 5th and 7th hours following treatment with

the hydro-alcoholic extract. This suggests a potential therapeutic effect of the extract in mitigating hyperglycemia induced by alloxan, highlighting its efficacy in managing acute hyperglycemia.
Table 5 illustrates the effect of continuous treatment (15 days) of the extract on blood glucose levels of alloxan-induced hyperglycemic rats. The results indicate a reduction in blood glucose levels on the 10th and 15th day after treatment, with statistical significance ($P < 0.05$) observed. This reduction in blood glucose levels in alloxan-induced diabetic rats post-treatment highlights the potential therapeutic efficacy of the extract in managing diabetes.

Alloxan exerts its pathological effects through two distinct mechanisms. Firstly, it selectively inhibits glucose-induced insulin secretion by targeting the enzyme glucokinase, a key regulator of glucose sensing in beta cells. Secondly, alloxan induces a state of insulin-dependent diabetes through its ability to induce the formation of reactive oxygen species (ROS). These dual effects are attributed to the specific chemical properties of alloxan.

Methylprednisolone (MPL), a corticosteroid which is used in avariety of disease condition for acute and chronic treatment. It increases glucose levels in both non-diabetic and diabetic patients(Hector Eloy TamezPerez*et al.*,2012).Table 6 shows that the effect of continuoususe of Polygonum plebeium R. Br. extract shows a significant drop in blood glucose levels of methylprednisolone induced hyperglycemic rats with statistical significance ($P<0.05$). This reduction in the blood glucose levels in methylprednisolone induced diabetic rats' post-treatment shows the potential therapeutic activity of the extract in managing diabetes in various patients taking steroids.

Plants possessing antidiabetic properties exert their effects on blood glucose levels through various pathways. Some of these plants contain insulin-like substances, while others stimulate beta cells to produce and release insulin. Additionally, certain plants facilitate the regeneration of pancreatic cells, thereby increasing beta-cell mass in the pancreas.

The observed hypoglycemic activity of the extract in both normal and diabetic rats, following single and multiple doses, may be attributed to the release of insulin and activation of existing pancreatic cells in animals with diabetes. These mechanisms collectively contribute to the beneficial effects of the extract in managing blood glucose levels.

CONCLUSION

The findings of this study suggest that extracts derived from Polygonum plebeium R. Br. hold promise as potential sources of oral hypoglycemic agents. The plant exhibits compelling potential for further investigation into the mechanisms underlying its hypoglycemic activity.

In summary, our research indicates that the administration of hydroalcoholic extract from the shoots of Polygonum plebeium R. Br. significantly enhances systemic insulin sensitivity and improves glucose homeostasis in normoglycemic rats. These results underscore the extract's overall antihyperglycemic activity and its positive effects on impaired glucose tolerance, thereby highlighting its clinical relevance in the management of diabetes. Based on our pharmacological investigations, it is evident that further experimentation is warranted to isolate and characterize the potential hypoglycemic compounds present in the plant extract. Our study provides preliminary insights into the hypoglycemic compounds present in the reported plant fractions, paving the way for future research aimed at elucidating the precise mechanisms of action underlying the therapeutic effects of Polygonum plebeium R. Br.

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