Myanmar Health Science Research Journal, Vol. 35, No. 1-3, 2023

Acute Toxicity and Hypoglycemic Activity of *Dregea volubilis* Benth. Leaves (ခွေးတောက်) on Animal Model

Khine Khine Lwin[*]*, Khin Phyu Phyu, Phyu Phyu Win, Aye win Oo, Nu Nu Win, Myint Myint Khine, San San Myint, Mie Mie Thaw & Shwe Sinn Pyone*

Department of Medical Research

Dregea volubilis Benth. is traditionally used for treatment of Diabetes Mellitus in India and Myanmar traditional medicines. This study was performed to determine phytochemical constituents, acute toxicity in mice and hypoglycemic activity of 70% ethanolic extract of *Dregea volubilus Benth*. leaves in alloxan induced diabetic rats. Phytochemical constituents of the leaves were investigated by using the methods of Harborne (1984) and Physicochemical standards of Unani Formulations (1987). Acute toxicity study of the extract of the leaves in mice was done according to Organization for Economic Co-operation and Development guideline (OECD 423). Hypoglycemic activity was determined in alloxan induced diabetic rats. Hyperglycemia was induced in adult healthy albino rats of both sexes by single intraperitoneal injection of 5% alloxan monohydrate (120 mg/kg). The diabetic albino rats were divided into 5 groups: Group 1 (Diabetic control group) was given distilled water orally, Group 2 to Group 4 were administered orally with 3 different doses (0.5 g/kg, 1g/kg and 2g/kg) body weights of the extracts of the leaves and Group 5 was given standard drug (Metformin, 150 mg/kg) body weight respectively. The test drugs were given to the rats once a day for 3 weeks. Fasting blood glucose levels of the rats were determined by using glucometer at 0 week, 1st week, 2nd week and 3rd week of the treatment. Phytochemical analysis of the leaves showed presence of alkaloids, polyphenol, steroids/terpene, glycosides, flavonoids, amino acid, carbohydrate and saponin. Medium Lethal Dose (LD_{50}) of the extract was more than 5g/kg. At 1st week, 2nd week and 3rd week of the treatment, significant decreases in blood glucose levels were found in the extracts groups ($p<0.05$ - $p<0.001$) and Metformin group ($p<0.001$). After 3 weeks of treatment, percent reductions of hyperglycemia in the extracts (0.5g/kg, 1g/kg and 2 g/kg) receiving groups and metformin group were 37.57%, 67.82%, 71.69 % and 73.77%, respectively. Hypoglycemic effect of the extract (2 g/kg) was comparable to that of Metformin after 3 weeks of treatment. Therefore, the leaves of *Dregea volubilis* Benth. had significant hypoglycemic activity in diabetic rats. The results can provide the scientific information for hypoglycemic effect of traditionally used *Dregea volubilis* leaves.

Keywords: *Dregea volubilus*, hypoglycemic activity, rats

INTRODUCTION

Diabetes mellitus is a chronic disease and it is one of the common metabolic disorders with micro and macro vascular complications that results in significant morbidity and mortality. Diabetes is a major cause of blindness, renal failure, heart attacks, stroke and lower limb amputation. World Health Organization (WHO) reported that

*To whom correspondences should be addressed.
Tel: +09250084728
E-mail: drkkl003@gmail.com
Doi:

the number of people with Diabetes mellitus was 422 million in 2014. Diabetes prevalence has been rising more rapidly in low- and middle-income countries than in high-income countries. WHO estimates that diabetes was the seventh leading cause of death in 2016.[1]

According to results from the International Diabetes Federation Diabetes Atlas, 9th edition, the global diabetes prevalence in 2019 is estimated to be 9.3% (463 million people), rising to 10.2% (578 million) by 2030 and 10.9% (700 million) by 2045.[2]

Treatment of Diabetes Mellitus is challenging problem in medical profession. There is increasing demand by patients to use natural products with antidiabetic activity due to side effects associated with the use of insulin and oral hypoglycemic agents. There are many medicinal plants reported to have hypoglycemic activities.[3]

Plants are used to treat Diabetes Mellitus around the world. Nowadays, herbal medicines are interestingly growing field because the medicines have less or no side effects. The treatment of Diabetes with naturally derived agents has beneficial effect and less side effects as compared to allopathic drugs.

Dregea volubilis Benth. (ခွေးတောက်) (Family-Asclepiadaceae) is a medicinal plant which grows throughout Myanmar. The plant also grows in India and South East Asia. Fresh leaves are used as vegetable. The leaves of *Dregea volubilis* Benth. are traditionally used for the treatment of Diabetes Mellitus,[4, 5] skin infection (Boils and abscess), inflammation of joint, cough and fever.[6, 7] Extract of leaves of *Dregea volubilis* had anti-inflammatory activity,[8] anti-oxidant activity and anti-bacterial activity.[9]

It was reported that ethanol extract of the leaves of *Dregea volubilis* Benth. had hypoglycemic effect in diabetic rats. Active compound, DV 1 from *Dregea volubil*is Benth. leaves had antidiabetic efficacy on diabetic rats.[10, 11] Leaves of *Dregea volubilis* Benth. (ခွေးတောက်) have not been scientifically investigated for its hypoglycemic activity and safety in Myanmar. This study was done to determine the phytochemical constituents, physico-chemical parameters, acute toxicity and hypoglycemic activity of the leaves of *Dregea volubilis* Benth. on alloxan induced Diabetic Mellitus rats.

MATERIALS AND METHODS

Study design

Study design was Laboratory based experimental study.

Place of the study

Place of the Study was in Pharmacology Research Division, Department of Medical Research.

Collection and extraction of leaves

Dregea volubilis Benth. mature leaves were purchased from Thiri Mingalar market in Yangon and was identified by a Botanist from Botany Department, Yangon University.

The leaves were cut into small pieces and air dried in the shade. Air dried leaves were made into powder by using grinding machine. Hundred grams of the dried powder of leaves were put into 5 L conical flask and 1 L of 70% ethanol was added. The flask was put on 60°C water bath for 6 hours for extraction. Then, mit was cooled down to room temperature. The mixture was filtered through filter paper and the filtrate was evaporated by using water bath at 100°C to get dried extract.[12]

Phytochemical analysis and physico-chemical tests of leaves of *Dregea volubilis* Benth.

Phytochemical constituents of the leaves were investigated qualitatively for the presence of alkaloids, steroids, glycosides, flavonoids, phenol etc. by using the methods of Harborne (1984)[13] and Physicochemical standards of Unani Formulations (1987).[14]

For quality control purpose of the leaves, physicochemical properties of the leaves were tested by using the method of WHO (2011).[15]

Physicochemical tests of the leaves involved Swelling index, Foaming index, Water and volatile matter content, Total ash, water soluble ash and acid insoluble ash, extractive values (such as watery extract value, ethanol extract value and petroleum ether extract value) and pH values.

Acute toxicity study

A total of 24 female albino mice (ddy strain) weighing (25 g-30 g) was used for acute toxicity test of 70% ethanol extract of *Dregea volubilis* Benth. leaves. Acute Toxicity test was performed according to OECD guideline 423 (Organization for Eco-nomic Co-operation and Development)[16] by using 3 dose levels of the extract of the leaves (300 mg/kg, 2000 mg/kg and 5000 mg/kg) body weights. Mice were observed for signs of toxicity and mortality after giving the extract daily up to 14 days. Individual body weight of mice was measured and recorded before the test substance was administered and once weekly up to 2 weeks.

Determination of hypoglycemic activity of 70% ethanolic extract of *Dregea volubilis* Benth. leaves on Alloxan induced diabetic rat

Adult healthy albino rats (Wistar strain) of both sexes weighing (180 g-200 g) obtained from Animal Services Division (Department of Medical Research) were used in this experiment. Induction of alloxan diabetes mellitus in rat was done by using the methods of Sikarwar and Patil (2010) and Agrawal and Paridhavi (2007).[17, 18]

All rats were weighed and overnight fasted for 18 hrs before the experiment day. On the experiment day, blood glucose levels (0 hr) of the rats were determined. Diabetes mellitus was induced in rats by single intraperitoneal injection of freshly prepared solution of 5% alloxan monohydrate (Sigma Aldrich) (120 mg/kg) in 0.9% physiological saline solution. They were starved for 3 hours after injection because there was initial hyperglycemia. After 3 hours of alloxan administration, the animals were allowed to take food and water orally. Ten milliliters of 20% glucose solution was given orally to the rats to overcome the early hypoglycemic phase.

The animals were kept under observation and 72 hours after alloxan injection, fasting blood glucose were measured by glucometer. In this study, blood glucose levels of the rats were not increased after 72 hrs. Therefore, fasting blood glucose levels of the rats were determined again at 1 week after alloxan injection. The rats showing stable hyperglycemia (>180 mg/dl) after alloxan injection were selected for the experiment.

Experimental procedure

Alloxan induced diabetic albino rats (fasting blood glucose level >180 mg/dl) of both sexes were divided into 5 test groups. Each group was consisted of 6 rats. Test drug and drug vehicle (Distilled water) were given orally. Group 1 was untreated diabetic rats (Diabetic control group) and were given 10 ml/kg body weight of distilled water only. Group 2 to Group 4 were diabetic rats and were treated with 3 different doses of 70% ethanolic extract of *Dregea volubilis* Benth. leaves 0.5g/kg b.w, 1g/kg b.w and 2 g/kg b.w, respectively once a day orally for 3 weeks. Group 5 (Standard drug group) was diabetic rats and they were given standard drug, Metformin (150 mg/kg body weight) once a day for 3 weeks.

To determine blood glucose levels of the rats, the rats were overnight fasted for 18 hrs before the experiment. On day 1 of the treatment, fasting blood glucose levels of these rats were measured at 0 hr (before administration of the drug) and 1 hr, 2 hrs, 3 hrs and 4 hrs after administration of the test drug. Then, fasting blood glucose levels of the test group of the rats (before the test drug administration) and the control group were determined at 1st week, 2nd week and 3rd week after the treatment. Blood was taken from the tail vein and blood glucose determinations were done by using

glucometer (GLUCOCARD II GT-1640, ARKRAY, JAPAN).

Data analysis

The results are shown in mean±SD. Unpaired t-test was used to observe the significance of difference between means of the control and experimental groups. Values with $p<0.05$ was considered to be statistically significant.

RESULTS

Extraction of leaves

Yield percentage of 70 % ethanolic extract of *Dregea volubilis* Benth. leaves was 25%.

Phytochemical analysis and physico-chemical test of *Dregea volubilis* Benth. leaves

The results of phytochemical analysis are shown in Table 1.

Table 1. Phytochemical analysis of leaves of *Dregea volubilis* Benth

Phytochemical constituents	70% ethanolic extract	Dried powder
Alkaloid	+	+
Flavonoids	+	+
Glycosides	+	+
Amino acid	+	+
Polyphenol	+	+
Saponin	+	+
Carbohydrates	+	+
Reducing sugar	+	+
Steroids/terpene	+	+
Tannin	+	+
Cyanogenic glycosides	-	-

Present=(+), Absent=(-)

The following results for Physicochemical tests of dried powder of *Dregea volubilis* Benth. leaves were 10ml for Swelling index, >100 for Foaming index, 11.53 % for water and volatile matter content, 12.01% for Total ash, 2.9% for Water soluble ash and 0.88% for Acid insoluble ash. Extractive values such as Watery extract value, Ethanol extract value and Petroleum ether extract value were found to be 43.15%, 12.14% and 1.39%, respectively. pH 1% solution (w/v) and pH 10% solution (w/v) were 5.84 and 6.46.

Acute toxicity study

It was found that 70% ethanolic extract of *Dregea volubilis* Benth. leaves showed no toxic effect and mortality in the mice up to the maximum dose level of 5 g/kg b.w during the observation period of 14 days. So, Medium Lethal Dose (LD_{50}) of the extract was more than 5 g/kg b.w.

Determination of hypoglycemic activity of 70% ethanolic extract of *Dregea volubilis* Benth. leaves on Alloxan induced diabetic rat

The results of determination of hypo-glycemic activity of 70 % ethanolic extract of the leaves are shown in Table 2.

Mean baseline blood glucose levels of the control group and the extract (0.5 g/kg b.w, 1 g/kg b.w and 2 g/kg b.w) receiving groups and metformin group were 73±12.28 mg/dl, 77.67±15.41 mg/dl, 79.33±3.88 mg/dl, 66.17±8.18 mg/dl and 88.5±8.1 mg/dl, respectively.

Mean blood glucose levels of the control group, the extract (0.5 g/kg b.w, 1 g/kg b.w and 2 g/kg b.w) receiving groups and metformin group at 1 week after injection of alloxan were 250.17±59.1 mg/dl, 305.83 ±46.91 mg/dl, 262.83±48.22 mg/dl, 287.83 ±78.19 mg/dl and 309.33±58.77 mg/dl, respectively.

In all these groups, there were significant increases in blood glucose levels at 1 week after the injection of alloxan when compared with baseline levels ($p<0.001$). On the first day of treatment, there were no significant decreases in blood glucose levels of the extracts receiving group and metformin group when compared with those of the diabetic control group.

Table 2. Effect of 70% ethanolic extract of *Dregea volubilis* Benth. leaves on blood glucose levels of alloxan induced diabetic rats on first day of treatment (n=6)

Groups	Baseline	Mean blood glucose level (mg/dl) (mean±SD) after treatment				
		0 hr	1 hr	2 hrs	3 hrs	4 hrs
Diabetic control (Distilled water)	73±12.28	250.17±59.1	316.83±102.53	356.17±127.54	346.5±129.76	342±141.49
Leaves extract (0.5g /kg)	77.67±15.41	305.83±46.91	320.67±51.02	296.5±54.32	282.1764.34	299.33±39.86
Leaves extract (1 g/kg)	79.33 ±3.88	262.83± 48.22	264.17± 81.86	241.67±90.5	216.83±75.14	207.5±75.14
Leaves extract (2 g/kg)	66.17±8.18	287.8 3±78.19	352.33±37.92	334.33± 44.89	334.5±46.43	332.83±50.62
Metformin (150 mg/kg)	88.5 ±8.1	309.33 ±58.77	385.67±73.97	346.33±67	258±91.34	213±86.59

Sample size for each group (n=6).
The statistical comparison was made between the control and each test group.

After treatment with the extract and metformin to respective groups for 3 weeks, the following results were found. The diabetic rats in Group 2 treated with the extract (0.5g/kg b.w) showed significant decreases in blood glucose levels when compared with those of the diabetic control group at 1 week ($p<0.01$), 2 weeks ($p<0.001$) and 3 weeks ($p<0.05$) after treatment.

The diabetic rats in Group 3 treated with the extract (1g/kg b.w) showed significant decreases in blood glucose levels when compared with those of the diabetic control group at 2 weeks and 3 weeks after treatment ($p<0.001$).

The diabetic rats in Group 4 treated with the extract (2g/kg b.w) and the rats in Group 5 treated with Metformin (150 mg/kg b.w) showed significant decreases in blood glucose levels when compared with those of the diabetic control group at 1 week, 2 weeks and 3 weeks after treatment ($p<0.001$). The results are shown in Table 3.

Table 3. Effect of 70% ethanolic extract of *Dregea volubilis* Benth. Leaves on blood glucose levels of alloxan induced diabetic rats at 1st week, 2nd week and 3rd week of treatment

No.	Group	Baseline	Mean blood glucose level (mg/dl) (mean ± S.D) after treatment			
			0 week	1st week	2nd week	3rd week
1	Diabetic control (Distilled water)	73±12.28	250.17±59.1	328.83±61.52	411.83±58.48	343.83±107.34
2	Leaves extract (0.5g /kg)	77.67±15.41	305.83±46.91	173±61.69**	207.17±89.74***	214.67±76.08*
3	Leaves extract (1 g/kg)	79.33±3.88	262.83±48.22	207±137.51NS	134.33±76.1***	110.67±49.97***
4	Leaves extract (2 g/kg)	66.17±8.18	287.83±78.19	165.67±27.88***	137±7.21***	97.33±16.13***
5	Metformin (150mg/kg)	88.5±8.1	309.33±58.77	89.17±16.31***	112.33±26.52***	90.17±16.58***

Sample size for each group (n=6).
The statistical comparison was made between the control and each test group.
*=$p<0.05$, **=$p<0.01$, ***=$p<0.001$, NS (not significant)=$p>0.05$

Table 4. Mean percent reductions of hyperglycemia with 70% ethanolic extract of *Dregea volubilis* Benth. leaves on alloxan induced diabetic rats after treatment

Group	Mean percent reductions of hyperglycemia after treatment		
	1st week	2nd week	3rd week
Leaves extract (0.5g/kg)	47.39	49.7	37.57
Leaves extract (1 g/kg)	37.05	67.38	67.82
Leaves extract (2 g/kg)	49.62	66.73	71.69
Metformin (150mg/kg)	72.88	72.72	73.77

Percent reductions of hyperglycemia with 70% ethanolic extract *Dregea volubilis* Benth. leaves on alloxan induced diabetic rat

The results of percent reductions of hyperglycemia are shown in Table 4. It was found that mean percent reductions of hyperglycemia in Metformin receiving group were more than the extract of the leaves receiving groups at 1 week and 2 weeks after the treatment. But, after 3 weeks of treatment, percent reductions of hyperglycemia of the extract (2 g/kg b.w) was comparable to that of Metformin.

DISCUSSION

It was reported that acute oral toxicity studies of ethanol extract of *Dregea volubilis* Benth. leaves in albino mice showed that the extract was not toxic upto the dose of 2g/kg b.w in albino mice.[19] In this study, acute toxicity study of 70% ethanolic extract of *Dregea volubilis* Benth. leaves showed that the extract had no toxic effect and lethality in mice up to maximum dose of 5 g/kg b.w. Therefore, LD_{50} of the extract was more than 5g/kg b.w.

Alloxan is a cyclic urea compound which induces permanent diabetes mellitus Administration of alloxan cause rapid destruction of β islet cells of pancreas and cause cell death. Alloxan produces free radical damage to β islet cells and causes cell death. It is used as a diabetogenic drug in experimental animals. Oral hypoglycemic agents can be screened by this method.[20]

In this study, the blood glucose levels were markedly increased in alloxan induced diabetic rats. The rats treated with the extract of *Dregea volubilis* Benth. leaves (0.5 g/kg b.w, 1 g/kg b.w and 2 g/kg b.w) showed significant reduction in blood glucose levels at 1 week, 2 weeks and 3 weeks after treatment when compared with diabetic control groups.

It was reported that ethanol extract of *Dregea volubilis* Benth. leaves administered orally to Streptozotocin induced diabetic rats was found to lower the fasting blood glucose levels significantly in the diabetic rats. The active compound, DV-1 isolated from ethanol extract of *Dregea volubilis* Benth. leaves also caused significant eduction in fasting blood glucose levels in the Streptozotocin induced diabetic rats [10, 11] Natarajan & Arul Gnana Dhas reported that the active compound, DV-1 from ethanol extract of *Dregea volubilis* Benth. leaves was Palmitic acid.[10]

Venkatesan, Anton Smith & Viswanath stated that the active compound, DV-1 from ethanol extract of *Dregea volubilis* Benth. leaves was found to be phenolic compound.[11] Moreover, ethanol extract of *Dregea volubilis* Benth. leaves was reported to have anti-diabetic effect in alloxan induced diabetic rats.[21]

In this study, mean percent reductions of hyperglycemia in the extracts (0.5g/kg b.w, 1g/kg b.w and 2 g/kg b.w) and metformin (150 mg/kg) receiving groups of the rats after 3 weeks of treatment were 37.57%, 67.82%, 71.69% and 73.77%, respectively.
In comparison between the hypoglycemic effects of the extract and Metformin, hypoglycemic effect of the extract was found to be lower than that of Metformin at 1st week and 2nd week of the treatment. But, hypoglycemic effect of the extract (2g/kg) was comparable to Metformin after 3 weeks of treatment.

The previous researchers reported that several medicinal plants have been scientifically investigated as potent anti-diabetics and include flavonoids, alkaloids, glycosides, polyphenol, saponins, triterpenoid and steroids In this study, the presence of phytochemical constituents such as flavonoids, alkaloids, glycosides, polyphenol, terpene and steroids obtained in the extract may be responsible for hypoglycemic activity.[22, 23]

Conclusion

Seventy percent ethanolic extract of *Dregea volubilis* Benth. leaves had significant hypoglycemic activity in alloxan induced diabetic rats. The results can provide the scientific information for hypoglycemic effect of traditionally used *Dregea volubilis* leaves.

ACKNOWLEDEMENT

Authors are thankful to Director General, Dr Zaw Than Tun (Department of Medical Research) for allowing us to perform this research.

REFERENCES

1 World Health Organization, Geneva. Diabetes [Internet] (8 June 2020*)* Available from: https:// www.who.int/news-room/ fact-sheets/detail/diabetes

2. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, *et.al.* Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th ed. *Diabetes Research and Clinical Practice* 2019; 157: 107843. [Internet] Available from: https:// www. diabetesresearchclinicalpractice. com/ article/ S0168-8227(19)31230-6/ fulltext.

3. Mya Bwin & Sein Gwan. Plants with Reputed hypoglycemic action. In: *Burmese Indigenous Medicinal Plants*. Rangoon, Burma Medical Research Institute, 1967; Special report series; (4).

4. *Dregea volubilis* From Wikipedia, the free encyclopedia [Internet] Available from: https://en.wikipedia.org/ wiki/ *Dregea volubilis*

5. Department of Medical Research. Pyilonchanthar hsay (TMF-27). In: *Myanmar Traditional Medicine Formulary* 1989; 199.

6. Department of Traditional Medicine, Ministry of Health, Myanmar. In:*Collection of Commonly Used Herbal Plants.* 2003; Jan: 95-98.

7. Rajadurai M, Vidhya VG, Ramya M & Anusha Bhaskar. Ethno-medicinal Plants Used by the Traditional Healers of Pachamalai Hills, Tamil nadu, India. *Ethno Medicine* 2009; 3(1): 39-41.

8. Divya TS, Latha PG , Usha K , Anuja GI, Suja SR, Shyamal S, *et al* .Anti-inflammatory, analgesic and anti-lipid peroxidative properties of *Wattakaka volubilis* (Linn. f.) Stapf. *Natural Product Radiance* 2009; 8(2); 137-141.

9. Purushoth Prabhu T, Maheswaran VS, SelvakumaribS, Suriyapadminimoka, Ragadeepthi S & Guduvalli Dileep. An anti-oxidant and Anti-bacterial activity of *Dregea volubilis* leaves extract. *Der Pharmacia Lettre* 2012; 4(2): 525-529. [Internet] Available from: http://scholarsresearchlibrary.com/archive. html

10. Natarajan V & Arul Gnana Dhas AS. Effect of active fraction isolated from the leaf extract of *Dregea volubilis* [Linn.] Benth. on plasma glucose concentration and lipid profile in streptozotocin-induced diabetic rats. *Springer plus* 2013; 21(2): 394. [Internet] Available from: https:// pubmed. ncbi. nlm. nih.gov/ 24010048/

11. Venkatesan N, Anton Smith A & Viswanath BA. Isolation and characterization of anti-diabetic compounds from ethanolic extracts of *Dregea volubil*s [Benth.] and *Leptadenia* reticulata [W&A]. *Natural Product Chemistry & Research* 2014; 2(5): 204. [Internet] Available from: https:// www. iomcworld. com/ proceedings/ isolation-
and- characterization-of- antidiabetic-compounds-from-ethanolic- extracts-of-dregea-volubils-benth- and - leptadenia-reticulata-wa-25275.html.

12. Handa SS, Khanuja SPS, Longo G & Rakesh DD. General Methods of Extraction of Medicinal Plants. In: *Extraction Technologies for Medicinal and Aromatic Plants.* (ICS, UNIDO) International Centre for Science and High Technology, 2008; 22.

13. Harborne JB. Phytochemical method. In: *A Guide to Modern Techniques of Plant analysis*, Chapman and Hall; 2nd ed. 1984; 9-192.
14. Government of India New Delhi. *Physicochemical standards of Unani Formulations* Part 2. Central Council for Research in Unani Medicine, Ministry of Health and Family Welfare, 1987.
15. World Health Organization, Geneva. Quality Control Methods for Medicinal Plant Materials, 2011.
16. OECD guideline for testing chemicals. Acute oral toxicity- Acute toxic class method. 2001; 423: 1-14.
17. Sikarwar MS & Patil MB. Antidiabetic activity of *Crateva nurvala* stem bark extracts in alloxan-induced diabetic rats. *Journal of Pharmacy & Bioallied Science* 2010; 2(1): 18-21.
18. Agrawal SS & Paridhavi M. Screening Method for Antidiabetic drugs. In: *Herbal Drug Technology*. Universities Press (India), 2007; 512-513.
19. Natarajan V & Vishwanath BA. Toxicity Study of Various Leaf Extracts of *Dregea volubilis* [Benth] (DV) and *Leptadenia reticulata* [W&A] (LR). *Global Veterinaria* 2016; 17(1): 45-51.
20. Ighodaro OM, Adeosun AM & Akinloye OA. Alloxan-induced diabetes, a common model for evaluating the glycemic-control potential of therapeutic compounds and plants extracts in experimental studies. *Medicina* 2017; 53(6): 365-374.
21. Devarakonda Shivani, Srivani A & Krishna Mohan G. A review on *Wattakaka volubilis* (L.f.) Stapf. *Journal of Pharmacognosy and Phytochemistry* 2023; 12(2): 199-203.
22. Bharti SK, Krishnan S, Kumar A & Kumar A. Antidiabetic phytoconstituents and their mode of action on metabolic pathways. *Therapeutic Advances in Endocrinology and Metabolism* 2018; 9(3): 81-100.
23. Gaikwad SB, Mohan GK & Rani MS. Phytochemicals for Diabetes Management. *Pharmaceutical Crops* 2014; 5 (Suppl 1: M2): 11-28.