IJBPAS, May, 2023, 12(5): 2059-2069

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

PHYTOCHEMICAL SCREENING AND EVALUATION OF VARIOUS *ALSTONIA SCHOLARIS* (*L.) R. Br.* LEAVES EXTRACTS ON GLUCOSE HOMEOSTASIS IN NORMAL RATS

MISHRA S, BELADIYA J AND MEHTA A*

Department of Pharmacology, L. M. College of Pharmacy, Gujarat Technological University, Ahmedabad 380009, Gujarat, India

***Corresponding Author: Dr. Anita Mehta: E Mail: dranitalmcp@gmail.com**

Received 10th June 2022; Revised 15th July 2022; Accepted 19th Sept. 2022; Available online 1st May 2023

https://doi.org/10.31032/IJBPAS/2023/12.5.7112

ABSTRACT

Alstonia scholaris (L.) R. Br. is medicinal plant species (Family: Apocynaceae). *A. scholaris* has several drug applications for the treatment of various chronic diseases and it has limited information regarding its traditional use in treating diabetes from a scientific perspective. To determine the phytochemical compositions of three different extracts of *A. scholaris*; chloroform extract (CEAS), ethyl acetate extract (EAEAS), and ethanolic extract (EEAS) of *A. scholaris* leave. In addition, we evaluated the effects of these three extracts on glucose homeostasis in normal rats using the oral glucose tolerance test (OGTT). Male Wistar rats (250-300 g) were randomly divided into twelve groups (n=3/group). Normal saline-treated group, three different doses of all the three extracts (200, 400, 800 mg/kg, p.o.) treated groups, canagliflozin (CANA) 1mg/kg, p.o treated group, and metformin (MET) 200 mg/kg, p.o standard treated group. After 30 minutes of drug administration, all groups were given a glucose solution (2g/kg). At 0, 30, 60, 90, 120, and 150 minutes, blood glucose levels were measured by pricking tail veins with a glucometer. The phytochemical screening of the crude extract revealed the presence of alkaloids, flavonoids, terpenoids, phenols, and saponins. At doses of 400 mg/kg, EAEAS and EEAS significantly reduced blood glucose levels ($p<0.05$) compared to the vehicle control and the standard drugs. However, CEAS did not show any

significant changes compared to vehicle control at any dose. EAEAS and EEAS at 400mg/kg dose have phytochemical constituents that improve the anti-hyperglycemic effect and maintain glucose homeostasis in hyperglycemia.

Keywords: *Alstonia scholaris*, Anti-hyperglycemic, Diabetes, Glucose Homeostasis, Oral Glucose Tolerance Test (OGTT)

INTRODUCTION :

An important part of the physiological function is glucose homeostasis, which is regulated by two hormones, insulin, and glucagon **[1]**. By increasing lipogenesis, and glycogen synthesis, insulin increases glucose disposition in peripheral tissues, while glucagon produces the opposite effect. Diabetes mellitus, or hyperglycemia, is the result of an abnormality in glucose homeostasis that is usually caused by an inability to secrete insulin or by insulin resistance. Furthermore, long-term high blood glucose levels may lead to further macro or microvascular complications. Therefore, improving insulin secretion and resistance is very important for normalizing glucose homeostasis and preventing chronic complications. Numerous research projects are being conducted all over the world, and several pharmacological products contain effective anti-hyperglycemic medications, but few patients achieve the glycemic treatment set by our experts **[2]**. The Oral Glucose Tolerance Test (OGTT) is a test of the body's ability to metabolize glucose that involves the administration of a measured dose of glucose to the fasting stomach and the determination of glucose levels in the blood at measured intervals thereafter and that is used especially to evaluate specific values for normal and disease condition (diabetes mellitus). Currently approved anti-hyperglycemic agents act by enhancing insulin sensitivity, insulin secretion increase, and glucose absorption reduction but available agents have one or more undesirable side effects like hypoglycemia, hematological disorders, obesity, osteoporosis, hepatotoxicity, and lactic acidosis **[3]**. Therefore, it is important to find out an effective medication with fewer side effects for diabetes in which traditional medicinal plants are more preferred. World health organization (WHO) reported that traditional plant medicines are used for the treatment of diabetes with fewer side effects and are cost-effective **[4]**. Many medicinal plants are currently available that also reduce the risk of cardiovascular disease that arises

due to hyperlipidemia in diabetics **[5]**. Many diabetic patients have consumed extracts, whole plants, and herbal formulations along with hypoglycemic drugs to accomplish the anti-diabetic effect and prevent its complications **[6]**. Hence, in light of these shreds of evidence, the development of plant sources and drugs are considered potential sources for the treatments. *Alstonia. scholaris* R.Br. (Apocynaceae) is the medicinal plant described in Ayurveda with its therapeutic importance. It is also known as saptaparna in which "Sapta" means seven and "Parna" means leaves. In Ayurveda, *A. scholaris* is used in Jwara, Shwas, Kushtha, Gulma, Vranaetc **[7]**. It is widely distributed and used in India, Thailand, Philipines, Africa, China, Australia **[8]**, etc. It has various pharmacological activities also as antibacterial, anti-anxiety, antiulcer, anti-microbial, antioxidant, anti-diarrheal, and is also used in wound healing **[9]**, etc. Traditionally the plant is used in whooping cough, chronic bronchitis, asthma, and other respiratory tract infections **[10]**. On the other hand, some phytoconstituents such as alkaloids, steroids, reducing sugars, and flavonoids showed anti-diabetic activity **[11]**. Since the major phytochemical constituent of *A. scholaris* may cause anti-hyperglycemic activity. Anti-hyperlipidemic and anti-hyperglycemic activity of *A. scholaris* leaves have been reported on rats **[12]**. There is not enough data on the investigation of different extracts of *A. scholaris* and their anti-hyperglycemic activity. Therefore, to further identify the beneficial glucose-lowering effect of petroleum ether, ethyl acetate, chloroform, and ethanolic extract of *A. scholaris* leaves was investigated and maintaining glucose homeostasis in normal rats.

MATERIALS AND METHODS:

The chemicals and solvents used in the experiments were the entire analytical grade. Metformin (Apollo, Knoll Pharmaceuticals Ltd.), canagliflozin (INVOKANA, Johnson & Johnson's), and Streptozotocin were procured from (ANJ biomedical, USA).

Plant material collection and authentication

The *Alstonia scholaris* (Leaves) specimens were collected in September from Krishna Nagar, Nava Naroda, Ahmedabad, and Gujarat. It was authenticated by the Department of Botanyat Gujarat University.

Extraction method

The *A. scholaris* leaves were thoroughly cleaned in distilled water and shade dried

for seven days at room temperature. 1kg of powdered form of *A. scholaris* leaves was extracted by soxhlet extraction. The powdered *A. scholaris* leaves were packed in a soxhlet apparatus and extracted using petroleum ether, chloroform, ethyl acetate, and ethanol solvents followed by successive methods **[13]** for 48 hours **(Figure 1)**. Extracts were then concentrated in a rotary evaporator and vacuum oven used for complete dryness. The concentrated extracts were subjected to phytochemical screening and Oral Glucose Tolerance Test.

Phytochemical screening

The preliminary phytochemical screening of bioactive compounds, including carbohydrates, alkaloids, flavonoids, steroids, phenols, tannins, saponins, terpenoids, glycosides, and proteins were carried out using standard protocols **[14]**.

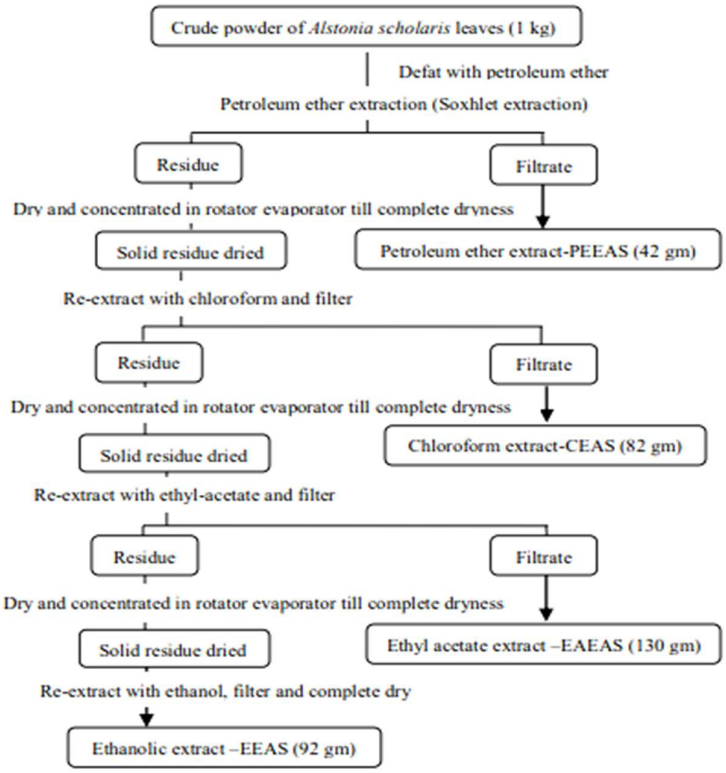

Figure 1: Flow chart of extraction process

In-vitro Oral glucose tolerance test (OGTT)

Experimental animals

Wistar albino rats (200–250 g) of either sex were procured from Zydus research center (ZRC), Ahmedabad, India for the experiment. The protocol (LMCP/P'Cology/19/10) of the experiment was accepted by the institutional animal ethical committee (IAEC), and these experiments were regulated as per the guidance of the

Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Animal Welfare Division, and New Delhi, India. Rats were supplied water ad libitum and a standard pellet diet according to their weight of rats. They were kept at a constant temperature of 22 ± 1 °C, relative humidity of 55 ± 5%, and 12/12 h light/dark cycle.

Experimental design

Male Wistar rats were divided into twelve groups containing three animals in each group as Group I: Vehicle control (VC) treated with 0.9% saline (p.o.)**;** Group II: CEAS 200 mg/kg (p.o.)**;** Group III: CEAS 400 mg/kg (p.o.)**;** Group IV: CEAS 800 mg/kg (p.o.)**;** Group V: EAEAS 200 mg/kg (p.o.)**;** Group VI: EAEAS 400 mg/kg (p.o.)**;** Group VII: EAEAS 800 mg/kg (p.o.)**;** VIII: EEAS 200 mg/kg (p.o.)**;** Group IX: EEAS 400 mg/kg (p.o.)**;** Group X: EEAS 800 mg/kg (p.o.)**;** Group XI: Standard drug Metformin (MET) 200 mg/kg (p.o.)**;** Group XII: Standard drug Canagliflozin (CANA) 1mg/kg (p.o.). The three test doses 200mg/kg, 400mg/kg, and 800mg/kg were selected with the reference of acute toxicity studies **[15]**. All these extracts were dissolved in sodium carboxymethycellulose (CMC).

Study Protocol

OGTT was performed according to the standard method **[16]**. Rats were starved for 16 hours before being tested for OGTT. The baseline glucose level was measured using a glucometer (OneTouch Select plus Simple, Lifescan medical devices India Pvt Ltd). The different extracts (Group II, III, IV, V, VI, VII, VIII, IX, and X), and standard drugs (Group XI, and XII) were then orally administered to the respective groups. After one hour of drug administration, the rats were orally fed with glucose of 2g/kg, b.wt. At 30, 60, 90, 120, and 150 minutes, the serum glucose level of blood from tail veins was assessed with a glucometer.

Statistical analysis

All the data of fasting blood glucose levels were expressed as the Mean ± SEM (Standard error of the mean). Statistical analysis was performed by student unpaired t-test comparison using Graphpad Prism 8.01 software (Graphpad, San Diego, CA). $P < 0.05$ was considered statistically significant.

RESULT:

Physiochemical assessment

The physicochemical assessment of raw crude drugs is essential to identify their purity. It revealed the presence of foreign organic matter, total ash, acid insoluble

ash, water-soluble extractives, and alcohol extractive of plant drugs, within the Ayurvedic pharmacopeia limits **[17] (Table 1)**.

Percentage yield

The yield values of all four extracts of *A. scholaris* leaves are expressed in %yield (w/w) **(Table 2)**. Yields of extracts were achieved by the soxhlet extraction method.

Phytochemical screening

Phytochemical screening of PEEAS, CEAS, EAEAS, and EEAS was performed according to the standard method. The results of the preliminary phytochemical screening are presented in tabular form **(Table 3)**. Phytochemical constituents were predominant in EAEAS and EEAS, including alkaloids, flavonoids, steroids, and carbohydrates. However, PEEAS does not contain any constituents other than fixed oils and fats. Thus, only three extracts (CEAS, EAEAS, and EEAS) were analyzed for glucose homeostasis via OGTT in normal Wistar rats.

Effect on oral glucose tolerance test (OGTT)

The OGTT results after single oral administration of CEAS, EAEAS, and EEAS at a dose of 200, 400, 800 mg/kg, p.o were represented as mean±SEM depicted in **(Table 4)**. Blood glucose level was represented in mg/dl. EAEAS and EEAS at a dose of 400 mg/kg had produced the maximum anti-hyperglycemic effect. EAEAS showed a significant ($p<0.05$) reduction in the blood glucose level (BGL) at 30, and 60 min. EEAS showed a significant ($p<0.05$) BGL reduction at 30, 60, and 90 min as compared to vehicle control. The standard drugs (Canagliflozin and metformin) prevent a drastic rise in BGL after 60 min of glucose administration. On the other hand, CEAS did not show any significant changes at any doses compared to vehicle control. The fasting blood glucose level of the vehicle control group reached a peak at 30 min and subsequently fell to the normal level. As compared to vehicle control, all the treatment groups showed similar anti-hyperglycemic effects at 120 min deferring significantly.

Table 1: Physicochemical assessment of *A. scholaris* leaves

S. No.	Physicochemical parameter	Obtained Value % (w/w)	API limit
1	Foreign matter	0.62	NMT 2%
2	Total ash	6.85	NMT 11%
3	Acid -insoluble ash	2.2	NMT 3%
4	Water soluble extractive	18.5	NLT 12%
5	Alcohol soluble extractive	11.25	NLT 4%

(NMT-Not more than, NLT –Not less than)

Table 2: The percentage yield of different extracts of *A. scholaris* (leaves)

S. No.	Extracts	Colour	Physical nature	%Yield (w/w)
1.	PEEAS	Dark Green/Sticky mass	Waxy greasy semisolid	4.2±0.33%
2.	CEAS	Dark Green/ Solid mass	Solid	8.2±0.54%
3.	EAEAS	Green/ Thick solid mass	Solid	13±0.36%
4.	EEAS	Dark green/ Thick solid	Solid	9.3±0.71%

PEEAS Petroleum ether extract of *A. scholaris* ; CEAS Chloroform extract of *A. scholaris* ; EAEAS Ethyl acetate extract of *A. scholaris* ; EEAS Ethanol extract of *A. scholaris* . All the values of % yield (w/w) were expressed in terms of mean±standard deviation

Table 3: Qualitative chemical analysis of phytoconstituents of the various extracts of *A. scholaris* leaves

Plant constituents	PEEAS	CEAS	EAEAS	EEAS
Alkaloid	-	-	+	+
Flavonoid	-	-	+	+
Tannins	-	-	-	+
Phenolic compound	-	+	-	+
Saponins	-	-	-	+
Terpenoids	-	+	-	+
Carbohydrate	-	-	+	+
Steroid	-	+	+	+
Fixed oil and fat	+	-	-	-

+ = Present; - = absent

Table 4: Effects of CEAS, EAEAS, and EEAS on oral glucose tolerance test in normal rats

Treatment Groups	Blood glucose level (mg/dl)					
	Initial	30 min	60 min	90 min	120 min	150 min
Vehicle Control	77.67±4.81	155.34±2.72	145.34±1.76	128.34±1.45	114.67±1.23	99.67±3.71
CEAS (200mg/kg)	78.66 ±1.76	150.67±1.45	136± 2.64	129.34±3.52	116.67±1.2	92±2.31
CEAS (400mg/kg)	74.34±3.38	152±2.64	136.34±1.76	125±1.52	114.34±1.21	91.67±2.96
CEAS (800mg/kg)	77.67±4.91	150±1.15	141±2.08	128±2.08	114±2.8	99±5.68
EAEAS(200mg/kg)	80.67±1.45	149.33±2.84	136±1.15	123±0.57	111±0.57	89.34±3.48
EAEAS (400mg/kg)	74.77±3.25	145.33±2.18*	130.34±1.45**	121.67±2.6	112.67±1.76	90.34±2.72
EAEAS (800mg/kg)	79±3.78	149.34±4.05	138.34±2.02	126.23±1.61	114.67±1.76	100.56±0.98
EEAS (200mg/kg)	80±4.58	150.67±2.34	135.34±1.76	124.34±1.26	108.67±1.2	91±2.51
EEAS (400mg/kg)	77.67±3.17	140±2.51**	127±3.21**	116±1.52**	104.67±3.75	89.34±2.18
EEAS (800mg/kg)	77±3.05	148.43±3.36	135.34±0.88	126.67±0.88	115.34±0.88	99.34±3.17
CANA (1mg/kg)	75.67±2.34	131±0.57***	123±2.51***	108.67±3.28***	99±4.51**	84.34±3.84
MET (200mg/kg)	79.67±5.23	139±2.08**	130±2.52**	115.67±1.2**	101.67±2.34*	90.67±4.67

The values are expressed in Mean ± SEM, n=3 in each group. *P<0.05, **p<0.01 and ***p<0.001 significant difference as compared with vehicle control followed by student unpaired t-test comparison

DISCUSSION

Glucose homeostasis is the foundation of energy supply and balance action between insulin and glycogen hormones to maintain blood glucose levels **[18]**. The pancreas maintains blood glucose levels within the range of 4-6mM **[19]**. Despite its important mechanism of action its vital role and the threshold between physiological requirements that turn to the metabolic disorder remain unknown **[20]**. Diabetes mellitus is a metabolic disorder in which patients suffer from persistent hyperglycemia for the long term. Therefore, the development and investigation of new substances with new strategies always highlights the research. In the traditional system, Ayurveda describes the trustworthy and reliable medicinal system

to use crude drugs as a powerful disease healing property. It is observed that screening of natural products has medicinal benefits from the actions of secondary metabolites that are present in the extracts **[21]**. In this regard, phytochemical screening and OGTT have been shown potential hypoglycemic effects. Phytochemical screening of four different extractions (with solvent petroleum ether, chloroform, ethyl acetate, and ethanol) of leaves of *A. scholaris* was carried out. Evaluation of the anti-diabetic activity of *A. scholaris* was carried out in streptozotocin-induced diabetic rats **[22]**. The determination of qualitative phytochemicals by various chemical tests that consider the presence of alkaloid, flavonoid, terpenoid, phenol, and steroid are major chemical constituents present in CEAS (phenolic, terpenoid, and steroid) EAEAS (alkaloids, flavonoids, and steroids) and EEAS (alkaloids, flavonoids, and steroid) of *A. scholaris* leave. Some of these classes of compounds have been implicated in the anti-diabetic activity of the plants. They also reported alkaloids, flavonoids, and phenolics as bioactive constituents for diabetic treatment **[11]**. Fortunately, *A. scholaris* contains all these bioactive constituents in reasonable quantities. Therefore, phytochemical constituents of *A. scholaris* leaves may improve the anti-hyperglycemic potential to manage type two diabetes **[12]**. OGTT is used as a diagnostic test for type two diabetes **[23]**. It is also extremely used for gestational diabetes. In our present work, we demonstrate the hypoglycemic effect by using OGTT which is an important preliminary test in preclinical study. OGTT is the indication of both insulin secretion and insulin resistance in glucose intolerance. It is the real-time in vivo whole-body test that can be used to identify the best treatment to prevent and possibly delay to development of diabetes mellitus. The non-toxic dose of *A. scholaris* was up to 200mg/kg **[24]** when it was administered orally while 100mg/kg showed toxicity with exhibited damage to the major organ of the body when it was administered by the intraperitoneal route. We selected three test doses with the reference of acute toxicity studies is 200mg/kg, 400mg/kg, and 800mg/kg of four different extracts PEEAS, CEAS, EAEAS, and EEAS. EAEAS and EEAS showed hypoglycemic effects following single-dose administration at 400mg/kg body weight in normal rats. EAEAS at 30 min and 60 min while EEAS at 30 min, 60 min, and 90 min showed a significant

reduction in blood glucose level after glucose administration in normal rats. Both are favorably competing against standard drugs though 150 min the test lasted. It prevents glucose-induced hyperglycemia better than other extracts. However, these suggest that both EEAS and EAEAS produce anti-hyperglycemic effects. In the future, long-term protocols and fractionation of highly effective extract may be helpful for the treatment of diabetes mellitus.

CONCLUSION

The ethyl-acetate and ethanol extracts of *A. scholaris* leaves at a dose of 400 mg/kg showed an anti-hyperglycemic effect in the normal rats, which was comparable to metformin and canagliflozin. These results are suggesting that ethyl-acetate and ethanol extract may show beneficial activity in the diabetic condition.

ACKNOWLEDGMENT

The author would like to acknowledge L.M. College of pharmacy for its munificent support and excellent facility.

CONFLICT OF INTEREST

There is no conflict of interest revealed by the author regarding this research.

REFERENCES

[1] Röder PV, Wu B, Liu Y, Han W. Pancreatic regulation of glucose homeostasis. Experimental & molecular medicine. 2016 Mar;48(3):e219-e219.

[2] Liang Y, Arakawa K, Ueta K, Matsushita Y, Kuriyama C, Martin T, Du F, Liu Y, Xu J, Conway B, Conway J. Effect of canagliflozin on renal threshold for glucose, glycemia, and body weight in normal and diabetic animal models. PloS one. 2012 Feb 15;7(2):e30555.

[3] Nisha M, Vinod BN, Sunil C. Evaluation of Boerhavia erecta L. for potential antidiabetic and antihyperlipidemic activities in streptozotocin-induced diabetic Wistar rats. Future Journal of Pharmaceutical Sciences. 2018 Dec 1;4(2):150-5.

[4] Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TP. Indian herbs and herbal drugs used for the treatment of diabetes. Journal of clinical biochemistry and nutrition. 2007;40(3):163-73.

[5] Abubakar US, Abdullahi S, Ayuba V, Kaigama S, Halidu US, Ayuba MK. Medicinal plants used for the management of diabetes mellitus in Zaria, Kaduna state, Nigeria. Journal of Pharmacy & Pharmacognosy Research. 2017;5(3):156-164.

[6] Gawali VB, Vyawahare NS. Anti-

Hyperglycemic effect of Polyherbal Formulation in Glucose Loaded and Epinephrine Induced Hyperglycemic Wistar rats. Research Journal of Pharmacy and Technology. 2022 Jan 25;15(1):365-369.

[7] Khatale VL, More DB. A Review on Saptaparna (Alstonia Scholaris R. Br). International Ayurvedic Medical Journal. 2016;4(03):334-337.

[8] Zhao YL, Gou ZP, Shang JH, Li WY, Kuang Y, Li MY, Luo XD. Anti-microbial effects in vitro and in vivo of Alstonia scholaris. Natural Products and Bioprospecting. 2021 Feb;11(1):127-135.

[9] Khyade MS, Kasote DM, Vaikos NP. Alstonia scholaris (L.) R. Br. and Alstonia macrophylla Wall. ex G. Don: A comparative review on traditional uses, phytochemistry and pharmacology. Journal of ethnopharmacology. 2014 Apr 11;153(1):1-8.

[10] Misra CS, Pratyush K, Dev L, James J, Veettil AK, Thankamani V. A comparative study on phytochemical screening and antibacterial activity of roots of Alstonia scholaris with the roots, leaves and stem bark. International Journal of Research in Phytochemistry and pharmacology. 2011 Apr 30;1(2):77-82.

[11] Tran N, Pham B, Le L. Bioactive compounds in anti-diabetic plants: From herbal medicine to modern drug discovery. Biology. 2020 Sep; 9(9):252.

[12] Arulmozhi S, Mazumder PM, Lohidasan S, Thakurdesai P. Antidiabetic and antihyperlipidemic activity of leaves of Alstonia scholaris Linn. R. Br. European journal of integrative medicine. 2010 Apr 1;2(1):23-32.

[13] Feng W, Li M, Hao Z, Zhang J. Analytical methods of isolation and identification. InPhytochemicals in human health, IntechOpen, London: 2019 Jul 15, p.45-52.

[14] Senguttuvan J, Paulsamy S, Karthika K. Phytochemical analysis and evaluation of leaf and root parts of the medicinal herb, Hypochaeris radicata L. for in vitro antioxidant activities. Asian Pacific journal of tropical biomedicine. 2014 May 1;4:S359-67.

[15] Baliga MS, Jagetia GC, Ulloor JN, Baliga MP, Venkatesh P, Reddy R, Rao KM, Baliga BS, Devi S, Raju SK, Veeresh V. The evaluation of the acute toxicity and long term safety of hydroalcoholic extract of Sapthaparna (Alstonia scholaris) in mice and rats. Toxicology letters. 2004 Jul 15;151(2):317-26.

[16] Chaimum-aom N, Chomko S, Talubmook C. Toxicology and oral glucose tolerance test (OGTT) of Thai medicinal plant used for diabetes controls, Phyllanthus acidus L.(Euphorbiaceae). Pharmacognosy Journal, 2017;9(1).

[17] World Health Organization. Quality control methods for herbal materials. Geneva: WHO Press, Malta, 2011, 20.

[18] Acharya KD, Parakoyi AE, Tetel MJ. Endocrine Disruption and the Gut Microbiome. InEndocrine Disruption and Human Health, Academic Press, Wellesley: 2022 Jan 1, p. 355-376.

[19] Ahmed A, Khalique N. Molecular Basis of Blood Glucose Regulation. In Blood Glucose Levels, IntechOpen, London: 2019 Nov 15, p.11-32.

[20] Yager JY. Glucose and perinatal brain injury. Questions and controversies. Neurology. 2012 Mar 2:143-162.

[21] Sahu MK, Singh VK, Rao SP. Development and Evaluation of Antidiabetic Potential of Polyherbal Formulation in Streptozotocin Induced Animal Model. Int J cell Sci & mol boil. 2018;5(2):29-37.

[22] Bandawane D, Juvekar A, Juvekar M. Antidiabetic and antihyperlipidemic effect of Alstonia scholaris Linn bark in streptozotocin induced diabetic rats. Indian Journal of Pharmaceutical Education and Research. 2011 Apr 1;45(2):114-20.

[23] Darden CM, Farrow AE, Rajan SK, Lakhani M, Lawrence MC, Naziruddin B. Predicting the function of islets after transplantation. InTransplantation, Bioengineering, and Regeneration of the Endocrine Pancreas,Vol.1, Academic Press, Dallas: 2020 Jan 1, p.547-561.