BioGecko

Vol 12 Issue 03 2023

ISSN NO: 2230-5807

HAEMATOLOGICAL AND HYPOLIPIDEMIC EFFECTS OF METHANOL EXTRACT OF OLDENANDIA CORYMBOSE (Rubiaceous) SEEDS IN STREPTOZOTOCIN (STZ) DIABETIC IN WISTAR RATS

Niladry Sekhar Ghosh*[1], Anubhav Dubey[2], Karuna Singh [3], Princy Verma[3]

1. Faculty of Pharmaceutical Science, Assam Down town University, Guwahati, Assam, India.
2. Assistant Professor, Department of Pharmacology, Maharana Pratap College of Pharmacy, Kanpur Uttar Pradesh, India.
3. Assistant Professor, Department of Pharmacy, Maharana Pratap College of Pharmaceutical Sciences, Kanpur Uttar Pradesh, India.

Corresponding Author: Niladry Sekhar Ghosh*[1]
Email.-niladry_chem@yahoo.co.in

Abstract

This research used alloxan-induced diabetic rats to examine the hemostatic and hypolipidemic effects of a methanol extract of the seeds of Oldenandiacorymbosa. Thirty male albino rats in good health were randomly split into five groups. Group 1 was the healthy control, Group 2 was the streptozotocin (STZ)-induced diabetic control (at 125 mg/kg body weight), Group 3 was the glibenclamide-treated diabetic control (at 5 mg/kg body weight), and Groups 4 and 5 were the Oldenandiacorymbosa seed methanol extract-treated diabetic control groups (at 50 and 100 mg/kg body weight). streptozotocin (125 mg/kg bodyweight) was injected intraperitoneally to create diabetes in the control, glibenclamide, and treatment groups; diabetes was confirmed using a glucometer. After 28 days of treatment, the rats were slaughtered, and blood samples were taken through a heart puncture for biochemical examination using conventional methods (Randox kits). White blood cells (WBC), haemoglobin (Hb), red blood cells (RBC), and packed cell volume (PCV) were all found to be significantly higher in the extract group compared to the non-treated group (negative control) ($p > 0.05$). High-density lipoprotein (HDL) levels were considerably (p 0.05) raised by the extract's escalating dosages, while total cholesterol (TC), triacylglycerol (TG), and low-density lipoprotein (LDL) levels were significantly (p 0.05) lowered. Based on these results, it is reasonable to propose Oldenandiacorymbosa seed methanol extract as an adjunct to dietary treatment for the correction of certain biochemical and hematological abnormalities associated with diabetes mellitus

Keywords: Streptozotocin, Annona muricata, Diabetes, Hematology, Hypolipidemic**.**

Introduction

Diabetes mellitus causes changes in glucose, lipid, and protein breakdown Insulin resistance is the root cause of diabetes, which leads to hyperglycemia [1-3]. Atherogenic dyslipidemia, marked by an increase in total cholesterol, triglycerides, LDL, VLDL, and HDL particles and a reduction in VLDL, increases the likelihood of death from cardiovascular disease, or CVD, in people with diabetes [3, 4]. Diabetes-related anaemia can arise from hyperglycemia and enhanced nonenzymatic glycosylation of proteins in red blood cell (RBC) membranes [5].The goals of treating diabetes mellitus include glycemic control and lowering cardiovascular risk factors such as hypertension and dyslipidemia [6]. Because of their efficacy, low cost, and lack of side effects, medicinal herbs are often used in traditional treatments for diabetes [2].

Oldenandia is used as an herbal remedy in Nigerian folklore. Oldenandiacorymbosa Linn. is a rubiaceous flowering plant. You may find them often in India. The plant grows upward on slanted stalks. The length of the leaf's ranges from 1 cm to 4 cm, and their width is around 6 mm.

Flowers feature four petals and a tube that is just 1.5–2 mm in diameter. Traditional medicine in Kerala is called "parppatakapullu." This botanical was formerly used in traditional medicine. The plant is effective in dispersing stagnant urine and eliminating urinary warmth and pollutants. Tumours of the larynx, the liver, and lymphosarcoma are all suppressed. Throat pain, ulcers, and skin issues are all aided by this plant. It's a flowering plant that's been used for healthcare for ages. According to studies, this plant may help preserve the liver, kill cancer cells, neutralize free radicals, and even treat malaria. Several kidney diseases may be remedied with this herb. Plant extracts rich in saponins coagulate blood cells and quell inflammation. Saponins cause haemoglobin to clot. Phenolic compounds are quite common in plants. Methods (Randox kits) for avoiding or curing ageing, death, tumours, inflammation, atherosclerosis, coronary artery disease, guarding against dysfunction in endothelial cells, and blocking angiogenesis and proliferation of cells are all included.

Figure-1 Oldenandiacorymbosa seeds

The insulin-producing beta cells of the pancreas in mammals are especially vulnerable to the toxicity of streptozotocin (STZ), a naturally occurring substance that is generated from the bacterium Streptomyces chromogens. In the realm of medicine, it is used as a chemotherapeutic agent for the treatment of certain tumours that affect the islets of Langerhans. Additionally, it is utilized in the field of medical research for the purpose of producing an animal model for type 1 diabetes. In addition to that, it is an antibiotic that is successful against Gram-negative bacteria. STZ suppresses the production of DNA in mammalian cells and microorganisms by alkylating DNA and cross-linking its strands. It also has an effect on all phases of the mammalian cell cycle. In humans, STZ has the potential to have teratogenic effects, as well as mutagenic and carcinogenic effects.

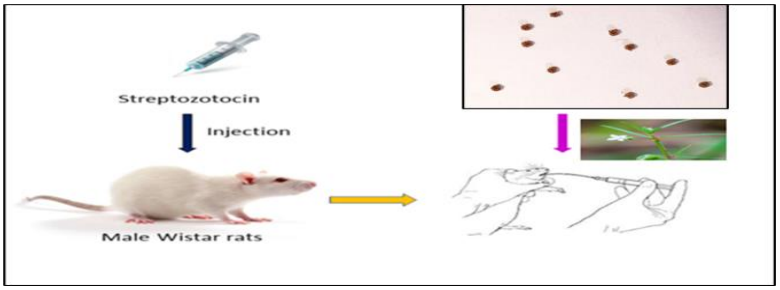

Figure-2 Streptozotocin induced diabetes and oral seed plant treatment

When comparing the extracted group to the non-treated group (negative control), we found that every measure of white blood cell count, haemoglobin count, red blood cell count, and volume of packed cells was significantly greater in the extract group (p compared to 0.05). Total cholesterol (TC), triacylglycerols (TG), and low-density lipoprotein (LDL) were all substantially (p 0.05)

lower in the dose-dependent extract group compared with the untreated diabetes group. The results reveal that Oldenandiacorymbosa seed methanol extract is safe and effective and may be recommended as an adjunct to dietary therapy for the treatment of certain biochemical and hematological abnormalities related to diabetes mellitus. Oldenandiacorymbosa seed methanol had hematological and hypolipidemic effects in induced diabetic rats. The research examined the effects of the extract on lipid parameters (HDL, TCHOL, TAG, and LDL) in induced diabetic rats and hematological parameters (PVC, RBC, and WBC). Diabetes is characterized by biochemical and hematological alterations, making this research crucial. Diabetes consequences are inevitable due to biochemical and hematological marker dysregulation, making this study relevant [11-13].

Materials and Methods

Elements and Minerals

Well-hydrated streptozotocin Type -1 diabetes was caused by Sigma-Aldrich Chemicals. Analytical-grade chemicals and reagents were used for every other step

Plant Materials/Extraction

The Seeds of Oldenandia corymbose obtained from a local farm at Kanpur. The plant identification and authentication were carried out at the Department of Botany, Christ Church College Kanpur. After approval of an Oldenandia corymbose seedling We harvested, cleaned, and oven-dried the seeds. We weighed out 250 grammes and powdered it. For three days, the powered form was immersed in an 80:20 butanol: distilled water mixture with periodic rocking. Whatman For this filtering, we utilized an excellent No. 1 paper filter. After filtering the liquid, it was dried using a rotary evaporator at 400 °C and reduced pressure.

Experimental animals

Thirty male Wistar rats weighing between 100 and 120g were used in the study, all of which came from the Maharana Pratap College of Pharmacy in Kanpur. At the Maharana Pratap College of Pharmacy in Kanpur, the animals were weighed upon arrival and allowed to adjust for 14 days. Animals were provided with food and water and given 12 hours of sunlight each day under tropical conditions for the duration of the 28-day trial. All rats were housed in 25°C metal cages with frequent access to sunlight and humidity levels of 30–50%. Free pellets along with flowing water were provided to the rats throughout the study, as approved by the Maharana Pratap College of Pharmacy's Departmental Committee on Animal Use Rules in Kanpur.

Diabetic Induction

After the animals had adjusted to their new environment, they were allowed to fast after getting a shot of 120 milligrams per litre of the alloxan monohydrate solution by means of the intra-peritoneal (IP) route to induce diabetes. If the blood glucose level in the induced rats was more than 150 mg/dl after three days, those rats were considered diabetic and included in the study.

Experimental Animal Techniques

A total of five groups of six rats were used: group 1 was the "typical command," group 2 was the power source, a "negative control," group 3 was known as the "positive/glipalamide" group, group 4 was the "OCSME extract" group, and group 5 was the "OCSME extract" group.

Groups		**Treatment**
Group 1	Normal control	Feed + H_2O ad libitum

Group 2	Negative control	Streptozotocin + Feed + H_2O ad libitum
Group 3	Positive control	Streptozotocin + Standard drug (Glibenclamide) + Feed + H_2O
Group 4	Oldenandiacorymbosa	Streptozotocin + 50mg/kg extract + Feed + H_2O ad libitum
Group 5	Oldenandiacorymbosa	Streptozotocin + 100mg/kg extract + Feed + H_2O ad libitum

Offerings and specimen gathering

Blood samples were collected in an EDTA vial after the experiment by puncturing the heart when the patient was under anaesthetic. Blood samples were collected from every one of the rats (9 ml for each treatment) and analyzed biochemically.

Determination of Biochemical Parameters

The enzymatic colorimetric Chod-Pap test [14], Tietze [15], and Grove [16] were used to assess total cholesterol, triglycerides, and HDL.After the LDL fraction was precipitated by polyvinyl sulphate (PVS) in polyethene-glycol monomethyl ether, all cholesterol was subtracted from the cholesterol content of the supernatant in order to determine the amount of low-density lipoprotein (LDL) [17].

Hematological Parameter Determination

According to Chhabra [18], a Mind Ray Auto Blood Disorders Analyzer (BC-5200, USA) was used for examining hematopoietic parameters. We measured WBC, RBC, Hb, and PCV.

Statistical Analysis

One-Way ANOVA was utilized for statistical analysis in SPSS version 22.0. In this case, the statistics were shown as Mean SD. If p0.05, then Tukey's Post Hoc test was accepted.3.0

Results

Table1: Weight of Diabetic rats treated with methanol extract of (0ldenandia corymbosa) seed. Our study found that the body weight of rats administered either 50 or 100 milligrams per kilogram of OCSME extracts increased significantly between weeks 1 and 3, in contrast to week 0.

Groups	Treatment	week 0 (g)	week 1 (g)	week 2 (g)	Week 2 (g/dl)
1	Normal Control (Feed + H_2O ad libitium)	112.13 ± 0.230	105.14 ± 1.20*	114.24 ± 2.20*	135.4 ± 2.705*
2	Negative Control (Streptozotocin + Feed + H_2O ad libitium)	119.42 ± 4.404	121.27 ± 2.170*	127.63 ± 2.430*	131.8 ± 6.720*
3	Positive Control (Streptozotocin + Standard drug, Glibenclamide + Feed + H_2O ad libitium)	109.20 ± 1.610	113.45 ± 3.601*	123.04 ± 1.366*	127.7 ± 2.370*
4	0ldenandia corymbosa 50mg/kg extract (Streptozotocin + Feed + H_2O ad libitium)	100.14 ± 3.064	118.34 ± 2.500*	124.57 ± 0.740*	129.4 ± 0.620*

5	0ldenandia corymbosa 100mg/kg extract (Streptozotocin + Feed + H_2O ad libitium)	105.25 ± 5.301	125.34 ± 1.405*	131.41 ± 0.401*	133.5 ± 0.670*

The table is expressed as mean ± SEM* n=5, p<0.05 significant difference compared to week 0.OCSME: 0ldenandia corymbose seed methanol extract

Table2: Effect of Hematological indices of Streptozotocin -induced diabetic albino rats treated with methanol extract of (0ldenandia corymbosa) seed

Diabetic animals had lower TWBC, HB, RBC, and PCV (P<0.05). 0ldenandia Corymbosa extracts enhance these parameters in diabetic mice (P< 0.05).

Groups	Treatment	RBC (g/dl)	TWBC (g/dl)	Hb (g/dl)	PCV (g/dl)
1	Normal Control (Feed + H_2O ad libitium)	165.13 ± 0.30	75.14 ± 1.20	12.24 ± 2.20	53.24 ± 2.05
2	Negative Control (Streptozotocin + Feed + H_2O ad libitium)	131.32 ± 1.40	43.20 ± 2.10	8.13 ± 2.00	31.16 ± 1.20
3	Positive Control (Streptozotocin + Standard drug, Glibenclamide + Feed + H_2O ad libitium)	160.20 ± 1.10*	73.05 ± 3.01*	11.04 ± 1.30*	53.07 ± 2.30*
4	0ldenandia corymbosa 50 mg/kg extract (Streptozotocin + Feed + H_2O ad libitium)	170.14 ± 3.04*	78.04 ± 2.00*	14.17 ± 0.40*	55.04 ± 0.20*
5	0ldenandia corymbosa 100mg/kg extract (Streptozotocin + Feed + H_2O ad libitium)	173.25 ± 5.01*	82.34 ± 1.05*	15.01 ± 0.01*	58.24 ± 0.10*

Table data are presented as mean SEM*, with a significance level of p 0.05 indicating a significant difference from the untreated diabetics in group 2. Mean standard deviation (n = 5) values are provided. *p0.05 against the null hypothesis.

Table 3: The treatment of Streptozotocin induced diabetic albino rats with a methanol extract of (0ldenandia corymbosa) seed had an effect on their lipid profiles.

Treatment	TCHOL (mg/dl)	TG (mg/dl)	LDL-C (mg/dl)	HDL-C (mg/dl)
Normal Control (Feed + H_2O ad libitium)	75.12 ± 1.230	72.14 ± 4.420	15.24 ± 10.20	83.04 ± 2.105
Negative Control (Streptozotocin + Feed + H_2O ad libitium)	91.02 ± 1.450	163.20 ± 3.170	78.13 ± 2.300	31.16 ± 1.720
Positive Control (Streptozotocin + Standard drug, Glibenclamide + Feed + H_2O ad libitium)	66.21 ± 1.140	90.25 ± 30.31*	13.04 ± 1.430*	73.27± 2.430*
0ldenandia corymbosa 50mg/kg extract (Alloxan + Feed + H_2O ad	70.17 ± 3.724	101.4 ± 2.030*	24.17 ± 0.440*	65.84 ± 6.720*

libitium)				
0ldenandia corymbosa 100mg/kg extract (Streptozotocin + Feed + H_2O ad libitium)	57.25 ± 2.051	92.34 ± 1.405*	10.41 ± 10.01*	68.24 ± 5.310*

Notethat there is a statistically significant distinction in groups 1 and 2 (untreated diabetics) (p 0.05) in the table.

DISCUSSION

There is a statistically significant distinction between group 2 (untreated diabetic) with group 1 (treated diabetic) (p0.05; see table for information). Abbreviation: Total Cholesterol, Triacyl Glyceride, High Density Lipoprotein, Low Density Lipoprotein, 0ldenandia Corymbosa Seed Methanol Extract, and Additional Lipoproteins are

A frequent side effect of diabetes mellitus is hyperlipidemia, which results from changes in lipid metabolism. A higher risk of coronary artery disease has been linked to alterations in lipid profiles in patients with diabetes[23-24]. Hypertriglyceridemia, decreased HDL, increased LDL, and hypercholesterolemia were all seen in diabetic rats induced with alloxan compared to control rats. In addition, Alaebo et al.[4]observed an increase in blood cholesterol, TAG, LDL-c, VLDL-c, and HDL cholesterol levels but a reduction in HDL lipid in alloxan-induced diabetic rats. Researchers hypothesized that elevated triglyceride and cholesterol levels were caused by the improved mobilization of free fatty acids from peripheral reserves due to insulin insufficiency or sensitivity. MEAM improved HDL levels and decreased triglyceride, cholesterol, and LDL levels in diabetic rats. Possibly owing to the presence of a phenolic component in OCSME, which helps to normalize the lipid profile, OCSME is able to alleviate abnormalities in lipid metabolism in diabetic rats.

Erythrocytes have been proven to be crucial in supplying oxygen to tissues throughout the body through the circulatory system [19]. The deformability of red blood cells is decreased among individuals with diabetes mellitus, which is marked by hypoglycemia [20]. In order to maintain constant flow rates through microscopic capillaries, normal red blood cells can withstand deformation without rupturing. Reactive oxygen species generation is associated with diabetes mellitus and contributes to this impairment. TWBC, HB, RBC, and PCV levels were all significantly decreased in diabetic animals; therefore, this result is in line with what was seen. The observed reductions in WBC, Hb, RBC, and PCV following administration of alloxan may be explained by aberrant haemoglobin production, poor blood osmoregulation, and greater plasma osmolarity [22]. When the extract was administered, the number of red blood cells and similar measures shot far up. This supports the idea that OCSME extract could increase production of erythropoietin, a hormone that tells stem cells from the bone marrow to produce red blood cells [21].

CONCLUSION

Ingesting OCSME extracts, namely at dosages between 50 and 100 mg/kg of body weight, has been demonstrated to induce hypolipidemic effects. Reversal of diabetes's effects on many biochemical and hematological parameters was linked to the ability to decrease blood cholesterol, which may be connected to an elevated level of phytonutrients. The researchers' high concentration of phytonutrients might explain this result. Therefore, it is feasible to claim that OCSME extracts safely and effectively normalize all hematological anomalies that are linked with diabetes mellitus. Therefore, they may be provided as an auxiliary component of nutritional diabetic care.

ACKNOWLEDGEMENTS

We appreciate the help from the faculty and staff of Maharana Pratap College of Pharmacy in Kanpur, which is Uttar Pradesh, led by Prof. Dr. Vikram Sahu. The technical personnel at the School of Pharmacy deserve our appreciation.

DECLARATIONS

Conflict of Interest:

The authors declare no potential conflicts of interest.

Ethical approval:

The Ethics Committee at the College of Maharana Pratap Pharmacy has reviewed all of the experiments and given its permission.

REFERENCES

1. Dubey A, Dash SL, Kumari M, Patel S, Singh S, Agarwal S, A Comprehensive Review on Recent Progress in Invivo and Invitro Models for Hyperlipidemia Studies. Pakistan Heart Journal, 2023:56(01),286-297. http://www.pkheartjournal.com.
2. KumariM,A Comprehensive Review on Stem Cells a better way for Treatment: Diabetes. Asian Journal of Pharmaceutical Research and Development. 2021; 9(1): 190-197.
3. Kumar, R., Saha, P., Kumar, Y., Sahana, S., Dubey, A., & Prakash, O. (2020). A Review on Diabetes Mellitus: Type1 & Type2. *World Journal of Pharmacy and Pharmaceutical Sciences, 9*(10), 838-850.
4. Dubey Anubhav, Tiwari Mamta, Kumar Vikas, Srivastava, Kshama, Singh, Akanksha. Investigation of Anti-Hyperlipidemic Activity of Vinpocetine in Wistar Rat.International Journal of Pharmaceutical Research 2020; 12(02):1879-1882. DOI:https://doi.org/10.31838/ijpr/2020.12.02.250.
5. Akshay Tiwari, Shalini Singh, Anubhav Dubey and Yatendra Singh. “A preliminary study on anti-hyperlipidemic activity of cinnamon oil in wistar rat”, 2021. International Journal of Current Research, 13, (03), 16741-16745.
6. Abinash Kumar Sahu, Amiya Ranjan Padhan, Nishigandha Sa, Anjan Kumar Padhan The Pharmaceutical College, Tingipal. International Research Journal of Pharmaceutical and Biosciences Phytochemical Evalution and In-vitro Anthelmintic Activity of OldenlandiacorymbosaPri -ISSN: 2394 - 5826 http://www.irjpbs.com e-ISSN: 2394 – 5834; 2020
7. Delse P. Sebastian, Satheesh George, Jishna K. P. and Binu Thomas. Research Article effect of different plant growth regulators and elicitors on secondary metabolite production in oldenlandiacorymbosa l. (rubiaceae) Volume 4, Issue 12 535-542, 2017.
8. Dr. Rajagopal m.v. hanima sana Yousef Professor and Head, Department of Pharmacognosy and Phytochemistry Academy of Pharmaceutical sciences, Pariyaram Medical College, Kannur, Kerala, india therapeutic utility of “oldenlandiacorymbosalinn.” journal of international academic research for multidisciplinary Impact Factor 4.483, ISSN: 2320-5083, Volume 5, Issue 12, January 2018 178 www.jiarm.com ,
9. Dr.p.l.rajagopalm.v.hanima, sana yousef therapeutic utility of “oldenlandiacorymbosalinn.” journal of international academic research for multidisciplinary impact factor 4.483, issn: 2320-5083, volume 5, issue 12, january 2018.
10. Alaebo, P. O., Onyeabo, C., Oriaku, C. E., Njoku, G. C., Iloanusi, D. U., &Ekwunoh, P. O. (2022). Hepato-protective Effect and Lipid Profile of Honey on Alloxan-induced Diabetic Rats. Asian Journal of Research in Biochemistry, 10(1), 16–24.

https://doi.org/10.9734/ajrb/2022/v10i130212

11. Kumari Mamta, Research Paper on Recent trends on treatment and management of type 2 diabetes mellitus Academia Journal of Scientific Research 5(12): 760-767, December 2017.doi: 10.15413/ajsr.2017.0635 ISSN 2315-7712

12. Souza DO, Dos Santos Sales V, de Souza Rodrigues CK, de Oliveira LR, Santiago Lemos IC, et al. Phytochemical Analysis and Central Effects of Annona Muricata Linnaeus: Possible Involvement of the Gabaergic and Monoaminergic Systems. *Iran Journal of Pharmaceutical Research.* 2018 Fall;17(4):1306-1317. PMID: 30568689; PMCID: PMC6269576.

13. Allain CC, Poon LS, Chan LS, Richmond CSG, FuPC. Enzymatic determination of total serum cholesterol. *Clinical Chemistry*. 20, 1974: 470-475.

14. Tietz NW. Clinical guide to laboratory test. 2ndedition. Philadephia, USA: W.B. *SaundersCompany;* 1990. p. 554-556.

15. Grove TH. Effect of reagent pH on determining high-density lipoprotein cholesterol by precipitation with sodium phosphotungstate-magnesium. *Clinical Chemistry* 25, 1979:260-264.

16. Bergmenyer HU. Methods of enzymatic analysis. 3rdedition. New York: Academic Press; 1985. 154-160

17. Chhabra G. Automated haematology analyzers: recent trends and applications. *Journal of Laboratory Physics*. 10(1), 2018: 015 – 016.

18. Waggiallah H, Alzohairy M. "The effect of oxidative stress on human red cells glutathione peroxidase, glutathione reductase level, and prevalence of anaemia among diabetics," *Northern American Journal of Medical Science*, 3(7), 2011: 344– 347.

19. Dubey, A., Yadav, P., Peeyush, , Verma, P., & Kumar, R. (2022). Investigation of Proapoptotic Potential of Ipomoea cornea Leaf Extract on Breast Cancer Cell Line. *Journal of Drug Delivery and Therapeutics*, *12*(1), 51-55. https://doi.org/10.22270/jddt.v12i1.5172
20. Dubey, Anubhav, Niladry Sekhar Ghosh, Nidhee Agnihotri and Amit Kumar et al. “Herbs Derived Bioactive Compounds and their Potential for the Treatment of Neurological Disorders.” Clin SchizophrRelat Psychoses 16 (2022). Doi: 10.3371/CSRP.DANG.081922.
21. KHUSHNUMA RASHEED, DAKSHINA GUPTA, DR. ABHINAV PRASOON MISHRA, ANUBHAV DUBEY. (2021). Evaluation of hypoglycemic potential of β Escin. Annals of the Romanian Society for Cell Biology, 25(6), 13965–13975. Retrieved from https://www.annalsofrscb.ro/index.php/journal/article/view/8259.
22. Gaurava Srivastav, Dakshina Gupta, Anubhav Dubey, & Neeraj Kumar. (2022). Investigation of Anti- Pyretic Activity of Cinnamon Oil in Wistar Rat. Journal for Research in Applied Sciences and Biotechnology, 1(3), 51–56. https://doi.org/10.55544/jrasb.1.3.7

23. SHAFQAT ZAIDI, R. K. MEHRA, Dr. SACHIN TYAGI, ROSHAN KUMAR ANUBHAV DUBEY.(2021). Effect of Kalahari Cactus Extract on Appetitte, Body Weight And Lipid Profile In Cafeteria Diet Induced Obesity In Experimental Animal. *Annals of the Romanian Society for Cell Biology*, *25*(6), 13976-13987.

24. Dubey A, Pandey M, Yadav S, Tripathi D, Kumari M, Purohit D, Hypolipidemic and haematological effects of ethanolic extract of Tecoma stans linn(bignoniaceae) seeds in alloxan-induced diabetic albino rats.Korean Journal of Physiology and Pharmacology, 2023:27(1),85-90. DOI:10.25463/kjpp.27.1.2023.8.