Journal of Pharmaceutical Research International

32(21): 86-90, 2020; Article no.JPRI.50033
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Blood Sugar Lowering Potentials of Aqueous and Ethanol Extracts of the Mixture of Rinds of *Citrullus vulgaris* Schrad (Watermelon) and *Chrysophyllum albidum* G. (Udara) Fruits on Alloxan-Induced Diabetic Wistar Rats

Owo, Gogo James[1*] and Beresford, Simon Jnr[2]

[1]Federal University, Otuoke, Bayelsa State, Nigeria.
[2]University of Saskatchewan, Saskatoon, Canada.

Authors' contributions

This work was carried out in collaboration between both authors. Author OGJ designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author BSJ managed the analyses of the study and the literature searches. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2020/v32i2130755
Editor(s):
(1) Dr. Mohamed Fathy Mohamed Ibrahim, Faculty of Pharmacy, Assiut University, Assiut, Egypt.
Reviewers:
(1) Muruganandan Shanmugam, Harvard University, USA.
(2) Adegbite Adesola Victor, Ladoke Akintola University of Technology, Nigeria.
Complete Peer review History: http://www.sdiarticle4.com/review-history/50033

Original Research Article

Received 12 May 2019
Accepted 18 July 2019
Published 04 September 2020

ABSTRACT

Citrullus vulgaris Schrad, commonly known as "watermelon" and Chrysophyllum albidum G., commonly called ''Udara'' are two important plants known to possess high antioxidant and therapeutic properties especially antidiabetic properties. The present study is aimed at investigating the blood glucose lowering potentials of both the aqueous and ethanolic extracts of the mixture of rinds of *C. vulgaris* Schrad and *C. albidum* in normal and alloxan-induced-diabetic rats. Aqueous and ethanol rinds extracts of the mixture were administered in wistar albino rats of weight range of 150-200g to determine their blood glucose lowering activity. The oral administration of aqueous mixed rinds extracts at dose of 1500 mg/kg body weight (Group 4) for 9 days led to a highly significant blood glucose reduction at $P<0.05$ when compared to the diabetic control (Group 2) and

**Corresponding author: E-mail: gogojames76@gmail.com;*

the ethanol mixed rinds extracts at the same dose (Group 6). There was a significant reduction in blood glucose (P<0.05) by other group dose extracts (Groups 3,5 and 6) compared to diabetic control. Hence, aqueous mixed rinds extracts of Citrullus vulgaris Schrad and *C. albidum* might be recommended as a potential hypoglycemic drug in the treatment of diabetes mellitus.

Keywords: Antihyperglycemic activity; hypoglycaemic; antidiabetic; alloxan; diabetes mellitus; phytochemical; acute toxicity; metformin; aqueous; ethanol; Citrullus vulgaris Schrad; C. albidum.

1. INTRODUCTION

Diabetes mellitus is a common endocrine and metabolic condition found in many parts the world and is characterized by chronic hyperglycemia as a result of insulin deficiency or its resistance [1].

Diabetes mellitus results from the derangements in the metabolism of carbohydrate, lipid and protein [2] Scoppola *et al., [3]* and Unwin *et al. [4]*. The diagnostic features of diabetes mellitus include hyperglycemia, hypoinsulinemia and hyperlipidemia *(*Mallik *et al.,* 2007*).*

Due to the many side effects of synthetic oral hypoglycemic agents such as nausea and vomiting, jaundice, agranulocytosis, anaemias of various aetiology, lactic acidosis, hypersensitivity reactions and skin reactions [5], it is very important to search for effective, low cost and less side affected hypoglycemic agents.

Citrullus vulgaris Schrad, commonly called watermelon, is a crop produced in warm weather, it is rich in citrulline and citrulline is one of the derivatives of amino acid that metabolizes to form arginine, a conditionally essential amino acid for humans by argininosuccinate synthase (ASS) and argininosuccinate lyase [6] in almost all animal cells [7]. The supplementation of arginine in diets decreases blood glucose concentration in diabetic rats [8]. The rind of *Citrullus vulgaris Schrad* is the tough, greenish outer skin of the fruit that is always peeled before consumption, may be applied to feeds, used as fertilizer and may also be used as an edible vegetable [9]. Research has shown that the rinds of watermelon contain alkaloids, tannins, saponins, anthraquinones, cardiac glycosides, flavonoids, phenol, moisture, lipid, protein, fibre, and carbohydrates [10]. The bioactive and phytochemical constituents present in the rind of *Citrullus vulgaris Schrad* have antioxidant and insulin-like properties which may contribute to the reduction of blood glucose and treatment of other ailments.

C. albidum is a widespread humid fruit tree that is broadly distributed in the low land rain forest zones and commonly found in many villages and communities [11]. The roots, seeds, barks and leaves of *C. albidum* have been documented as a traditional medicine for the treatment of diseases. The bark is used for the treatment of yellow fever and malaria, the leaf is used as an emollient and for the treatment of skin eruption, stomachache and diarrhea [12] and the cotyledons from the seeds of *C. albidum* are used as ointments in the treatment of vaginal and skin infections in Western Nigeria. The fruit pulp is used as a very rich source of vitamin C and iron [13], *Adisa [14]; Akubugwo and Ugbogu, [15]*. Some of the phytochemicals that have been reported in *C. albidum* are tannins, flavonoids, terpenoids, proteins, carbohydates and resins [16]. The seed cotyledon of C.*albidum* has been reported to possess hypoglycemic and hypolipidemic effects [17].

2. MATERIALS AND METHODS

Collection of plant sample: The fruits *Citrullus vulgaris Schrad* and C. albidum were purchased in Rumuokoro main market, Obio/Akpor L.G.A, Rivers State, Nigeria in May, 2019. The fruits were identified by Dr. Etukudo Mbosowo Monday, Head of department of biology, Federal University, Otuoke, Bayelsa State, Nigeria. The fruits were washed and the rinds were peeled off with a knife, cut into pieces and shade dried for two weeks. The dried rinds samples were crushed into powder using a mechanical grinder for active solvent extraction.

Chemicals and Reagents: Alloxan monohydrate was purchased from Sigma chemicals (St. Louis, USA). All other chemicals and reagents used were of analytical grade.

Solvent extraction Procedure: The shade dried powdered rinds materials were extracted using ethanol and hot aqueous solvents. The extraction using ethanol was carried out in Soxhlet extractor and hot aqueous extraction in pressurized

extractor at the ratio of 10 g rinds powder with 100 ml of the solvent [14]. The extracts were then concentrated to dryness under reduced pressure and controlled temperature (40-50°C) using rotary evaporator. The obtained concentrated extracts were then stored and used for further analysis by preserving it in refrigerator.

Animal: Male wistar albino rats of weight range 150-200g were obtained from the experimental animal house of the University of Port Harcourt, Rivers State, Nigeria and used all through the period of study. The animals were kept safe in plastic cages at suitable temperatures of 25-27^{0}C and relative humidity of 53% at 12 hr light and dark cycles. The animals were given their normal feeds and water *ad libitum* and then allowed to acclimatize to the new environment for 5days before use.

Acute Toxicity Study: Acute toxicity study was carried out in line with the laid down guidelines 423 (Acute toxic class method) of the Organisation of Economic Cooperation and Development (OECD) as described by Ecobian, D.J [18]. In this study, male wistar albino rats of weight range 150-200g were used for the study. The dried extracts were administered orally to 7 rats, leaving 2 additional rats as control at dose of 50, 100, 300, 450 and 2000 mg/kg. After the oral administration of the extracts to the rats, they were allowed for 48 hr and observed critically. No case of death and change in the behavioural pattern was observed.

Induction of Diabetes mellitus in rats: A 150 mg/kg body weight of freshly prepared solution of alloxan monophosphate was injected into the rats by single intraperitoneal injection. The rats were administered 5% glucose solution for 24 hours to prevent hypoglycaemia. The animals that serve as control were treated with citrate buffer (P^H 4.5).

All the rats developed diabetes mellitus after 3 days and blood glucose level of each rat was estimated. Rats with blood glucose level above 8.0 mmol/L were considered to have diabetes mellitus and used in the study. Blood sample was collected from the tail vein.

Experimental design: In the present study, the experimental rats have subjected to 12 hours fasting and divided into 7 groups of 4 rats each. With exception of the wistar rats in Group 1, all other rats were diabetic. The rats received either standard hypoglycemic drug metformin (MET), classified doses of aqueous mixed rinds extracts (ARE) of the *Citrullus vulgaris Schrad* and C. albidum or classified doses of ethanol mixed rinds extracts (ERE) of *Citrullus vulgaris Schrad* and C. albidum as follows:

Group 1 - Normal control (Normal saline)
Group 2 - Diabetic control (Normal saline + Alloxan 10 ml/kg body weight)
Group 3- ARE 250 mg/kg body weight
Group 4- ARE 1500 mg/kg body weight
Group 5- ERE 250 mg/kg body weight
Group 6- ERE 1500 mg/kg body weight
Group 7- Metformin (MET) 15 mg/kg body weight

Rats were made diabetic by a single intraperitoneal injection of alloxan at a dose of 10 ml/kg body weight and with normal saline and diet for 9 days. The extracts were dissolved in 0.5% DMSO and 1 mg/kg body weight was administered through oral route using an intragastric tube at classified doses (250, 1500 mg/kg body weight). The blood samples were collected after 9 days of treatment and the fasting blood glucose level of each rat was measured using an automatic one touch glucometer. The glucose levels were estimated on 3rd, 6th and 9th day respectively.

Statistical analysis: All groups (Groups 3,4,5,6 and 7) were statistically compared with the diabetic control group (Group 2). The results obtained from the comparisons were analysed using Analysis Of Variance (ANOVA) from standard statistical package SPSS 21.0 at a significance level of $p < 0.05$. Scheffe's test was used to reveal the sources of the difference between the treated groups and diabetic control. Each result is a mean of triplicate analysis.

3. RESULTS AND DISCUSSION

The blood glucose levels of the normal and diabetic rats for days 3, 6 and 9 are presented in Table 1. Oral administration of the aqueous and ethanol mixed rinds extracts reduced blood glucose level in a dose-dependent manner in agreement to the report given by [19] The aqueous mixed rinds extracts of *Citrullus vulgaris Schrad* and C. albidum revealed significant reduction in blood glucose levels at a dose of 1500 mg/Kg body weight higher than the ethanol mixed rinds extracts at the same concentration. Aqueous and ethanol rinds extracts at a high dose of 1500 mg/kg showed significant blood glucose lowering effects when compared with diabetic control (Group 2).

Table 1. Hypoglycemic activity of aqueous and ethanol extracts of *C. vulgaris Schrad* and *C. albidum*

	Blood glucose level in mmol/L (days)		
Groups	**3rd**	**6th**	**9th**
1	4.16 ± 0.11	4.05 ± 0.32	4.48 ± 0.64
2	8.76 ± 0.17	9.87 ± 0.61	8.48 ± 0.56
3	8.15 ± 0.34	9.34 ± 0.63	8.26 ± 0.55
4	5.75 ± 1.02	6.31 ± 0.88	6.53 ± 0.58
5	7.72 ± 0.21	9.11 ± 0.81	9.18 ± 0.77
6	7.43 ± 0.21	8.87 ± 0.83	8.17 ± 1.16
7	5.03 ± 0.55	5.51 ± 0.86	7.05 ± 0.42

** Data presented in Mean±SE*

Alloxan induced diabetes in the rats by causing the destruction of the β cells of the pancreas, thereby slowing or inhibiting the secretion of insulin. Alloxan produces free radicals which may damage the pancreas and this may be one of the reasons for diabetes in the rats. Administration of 15 mg/kg of metformin (Group 7) by oral route led to a highly significant hypoglycemic activity at $P<0.05$ compared with Groups 3 and 5, less significant when compared with Group 6 and not significant when compared with Group 4. This, however, implies that the aqueous extract at a dose of 1500 mg/kg (Group 4) has the highest hypoglycemic activity compared to all other groups. This may be that the aqueous mixed rinds extracts had significantly abundant bioactive compounds like alkaloids, flavonoids, saponins, tannins, phenols and cardiac glycosides than the ethanol mixed rinds extracts and may be recommended as a hypoglycemic agent. Also, the hypoglycemic activity of the aqueous and ethanol mixed rinds extracts of *Citrullus vulgaris Schrad* and C. albidum may be as a result of their ability to stimulate the β-cells of the pancreas to produce insulin [6].

4. CONCLUSION

This study reveals that the mixed rinds of *Citrullus vulgaris Schrad* and Chrysophyllum albidum G. have high anti-diabetic activity probably due to the presence of some highly concentrated potential antioxidant and antidiabetic bioactive compounds such as flavonoids, phenols, terpenoids, tannins and steroids. The aqueous mixed rinds extract at a dose of 1500 mg/kg (Group 4) had the highest hypoglycemic activity compared to all other groups. It is therefore recommended that further studies on the isolation and characterization of the bioactive compounds may also lead to the interesting research process.

The habit of peeling off and discarding the rinds of the two plants during consumption should be avoided.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard animal ethics committee approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Kim SH, Hyun SH, Choung SY. Anti-diabetic effect of cinnamon extract on blood glucose in db/db mice. J Ethnopharmacol. 2006;104:119-123.
2. Damjanov I, McCue PA. Histopathology. A colour Atlas and Textbook, Williams and Wilkins. A Waverly company, Baltimore, USA; 1996.
3. Scoppola A, Montecchi FR, Mezinger G, Lala A. Urinary mevalonate excretion rate in type 2 diabetes. Role of metabolic control. Atherosclerosis. 2001;156:357-361.
4. Unwin N, Sobngwi E, Alberti KGMM. Type 2 diabetes: The challenge of preventing a global epidemic. Diabetes Int. 11:4-8.
5. Bailey CJ. New pharmacological approach to glycemic control. Diabetes Rev. 1999;7:94-113.
6. Haslam DW, James WP. Obesity. Lancet. 2005;366:1197–1209.

7. Wu G, Morris SM Jr. Arginine metabolism: Nitric oxide and beyond. Biochem. J. 1998;336(Pt. 1): 1–17
8. Kohli R, Meininger CJ, Haynes TE, Yan W, Self JT, Wu G. Dietary L-arginine supplementation enhances endothelial nitric oxide synthesis in streptozotocin-induced diabetic rats. J. Nutr. 2004;134:600–608. Google Scholar
9. Pons L. Exploring important medicinal uses for watermelon rinds. United States Department of Agriculture. Agricultural Research Service; 2003. Available:http://www.ars.usda.gov/is/pr/2003/030221/html.2003
10. Erukainure OL, Oke OV, Daramola AO, Adenekan SO, Umanhonlen EE. Improvement of the biochemical properties of watermelon rinds subjected to Saccharomyces cerevisae solid media fermentation. Pak J Nutr. 2010;9(8):806-9.
11. Madubuike FN, Ogbonnaya O. The Potential Use of White Star Apple seed (Chrysophyllum albidum) and Physic Nut (Jatropha Curcas) as Feed Ingredients for Rats. J. Fac. Agric. Vet. Med. 2003;1:97-105.
12. Adisa SA. Vitamin C, Protein and Mineral content of African Apple (*Chrysophillum albidum*) in proceedings of the 18th Annual Conference of NIST.(eds) Garba SA, Ijagbone IF Iyagba AO, Iyamu AO, Kiliani AS, Ufaruna N. 2000;141-146
13. Hassig A, Liang WX, Schwabl H, Stampfli K. Flavonoids and tannins: plant based antioxidants with vitamin character. Med Hypotheses. 1999;52:479–81.
14. Harbone JB. Methods of Extraction and Isolation. In: Phytochemical Methods, Chapman and Hall, London. 1998;60-66.
15. Akubugwo IE, Ugbogu AE. Physicochemical studies on oils from five selected Nigerian plant seeds. Pak. J. Nutr. 2007;6:75-78.
16. Akaneme FI. Identification and preliminary phytochemical analysis of herbs that can arrest threatened miscarriage in Orba and Nsukka towns of Enugu State. Afr. J. Biotechnol. 2008;7:6-11.
17. Olorunnisola DS, Amao IS, Ehigie DO, Ajayi ZAF. Anti-Hyperglycernie and Hypolipidemic Effect of Ethanolic Extract of Chrysophyllum albidum Seed Cotyledon in Alloxan Induced-Diabetic Rats. Res. J. Appl. Sci. 2008;3:123-127.
18. Ecobian DJ. The basis of toxicity testing, 2nd Ed, CRC Press, New York. 1997;43-88.
19. Ahn J, Choi W, Kim S, et al. Food Sci Biotechnol. 2011;20:251. DOI: 10.1007/310068-011-0034-5

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/50033