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Anti-Hyperglycemic Activities of *Citrullus lanatus* (Cucurbitaceae) Seeds Aqueous Extract in Rats

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Abstract

Background: *Citrullus lanatus* (watermelon) is used in traditional medicine to treat various ailments, including diabetes. However, scientific validation of its anti-hyperglycemic properties is limited. **Objective:** This study aimed to evaluate the phytochemical composition, acute toxicity, and pharmacological effects of the aqueous extract of *C. lanatus seeds* (EACL) on glycemic and lipid parameters in rats. **Methods:** Phytochemical screening, acute toxicity tests in mice, and a 14-day repeated dose study in normoglycemic rats were conducted. The anti-hyperglycemic effect of EACL (2000 mg/kg) was evaluated in three models of glucose-induced hyperglycemia in rats (pre-treatment, post-treatment, and co-administration) and compared to the standard drug glibenclamide. **Results:** Phytochemical analysis revealed the presence of sterols, polyphenols, flavonoids, saponins, quinones, and tannins. EACL was found to be non-toxic (DL50 > 5000 mg/kg). In normoglycemic rats, EACL significantly reduced blood glucose ($p < 0.05$) and total cholesterol (Following administration of doses of 500, 1000, 1500 and 2000 mg/kg body weight, after 14 days, the total cholesterol levels in the rats fell to 0.648 ± 0.02; 0.636 ± 0.03; 0.608 ± 0.04 and 0.588 ± 0.04 g/L, respectively). In hyperglycemic rats, EACL (2000 mg/kg) significantly reduced blood glucose levels in all three models, demonstrating effects comparable to those of glibenclamide. When co-administered with glucose, EACL almost completely prevented the onset of hyperglycemia. **Conclusion:** The aqueous extract of *C. lanatus* seeds possesses significant hypoglycemic and anti-hyperglycemic properties, supporting its traditional use in managing diabetes.

Keywords

Citrullus lanatus, Hyperglycemia, Aqueous Extract, Rats, Antidiabetic

1. Introduction

The use of natural products derived from plant sources for treating various diseases dates back to antiquity [1]. In Africa, nearly 75% of the population has resorted to traditional medicine at least once [2]. Among the most widespread pathologies, diabetes stands out with its increasing prevalence. This non-communicable metabolic disease, characterized by chronic hyperglycemia, results from a defect in insulin secretion, insulin action, or a combination of both [3].

According to the International Diabetes Federation (IDF), approximately 537 million people aged 20 - 79 years were diabetic in 2021, a number projected to reach 783 million by 2045. In Côte d'Ivoire, the prevalence of diabetes is estimated at 9.6% [4]. This alarming increase is attributed to risk factors such as urbanization, lifestyle changes, physical inactivity, obesity, and psychosocial stress [5]. These factors also promote serious complications like stroke, kidney failure, heart disease, blindness, and lower limb amputation.

Faced with this alarming situation, the World Health Organization (WHO) has made the fight against diabetes a major public health priority and encourages the use of traditional medicine for its treatment [6]. While current therapeutic management relies on strict diets, insulin injections, physical activity, and oral antidiabetics, the use of insulin and oral hypoglycemics (such as biguanides and sulfonylureas) can have side effects and remains costly [7]. Therefore, medicinal plants offer an accessible, available, and affordable alternative [8].

Citrullus lanatus (Cucurbitaceae), commonly known as watermelon, is a plant of the African traditional pharmacopoeia used for treating various conditions, including cardiac disorders, constipation, ulcers, and notably, diabetes [9]. It contains several bioactive principles that contribute to its pharmacological properties [9]-[11]. However, its use is often without sufficient scientific evidence [12]. This study was therefore undertaken to investigate the anti-hyperglycemic potential of the aqueous extract of *C. lanatus* seeds.

The general objective of this work is to valorize traditional pharmacopoeia substances for medical use. Specifically, this study aims to:

1) Determine the phytochemical composition of the aqueous extract of *C. lanatus*seeds (EACL).

2) Evaluate the acute oral toxicity of EACL.

3) Determine the pharmacological effects of EACL on glycemic and lipid parameters in rats.

2. Materials and Methods

2.1. Plant Material and Extraction

Citrullus lanatus seeds were purchased from a local market in Abidjan, Côte d'Ivoire, and identified at the National Floristic Center (voucher specimen UCJ004346). The seeds were air-dried and ground into a fine powder. The aqueous extract (EACL) was prepared by macerating 200 g of the powder in 2 L of distilled water under magnetic stirring at 70˚C for 24 hours. The macerate was then filtered and dried

in an oven at 60˚C for 72 hours.

2.2. Phytochemical Screening

A preliminary phytochemical screening of EACL was performed using standard qualitative tests to identify the presence of secondary metabolites, including sterols, polyphenols, flavonoids, saponins, quinones, alkaloids, and tannins [13] [14].

2.3. Acute Toxicity Study

The acute oral toxicity of EACL was evaluated in female Swiss mice (20 - 30 g) according to the OECD Guideline 423 [15]. Mice were administered a single dose of 2000 or 5000 mg/kg body weight (b.w.) and observed for signs of toxicity and mortality for 14 days.

2.4. Pharmacological Studies

2.4.1. Effects on Normoglycemic Rats

Twenty (20) male Wistar rats (100 - 160 g) were divided into five groups (n = 4) and treated orally for 14 days as follows:

- Group 1 (Control): 2 mL distilled water.
- Groups 2 - 5: EACL at doses of 500, 1000, 1500, and 2000 mg/kg b.w., respectively.

Body weight and fasting blood glucose were measured weekly (Day 0, 7, 14). On Day 14, blood was collected for the determination of total cholesterol.

2.4.2. Effects on Hyperglycemic Rats

The study focused on normoglycaemic animals that had received a glucose load, rather than on a model of chronic diabetes. No mechanistic biomarkers were measured.

Sixteen (16) rats were divided into 4 groups of 4 rats each, with an average weight of between 100 and 150 g. Three distinct models were used to evaluate the anti-hyperglycemic effect of EACL (2000 mg/kg) compared to a standard drug, glibenclamide (10 mg/kg), in overnight-fasted rats.

- **Model 1 (Pre-treatment):** The test substances were administered 30 minutes before oral glucose (4 g/kg).
- **Model 2 (Post-treatment):** Oral glucose (4 g/kg) was administered 30 minutes before the test substances.
- **Model 3 (Co-administration):** The test substances were co-administered with glucose (4 g/kg).

In all models, blood glucose was measured at 0, 30, 60, 90, 120, and 150 minutes.

2.4.3. Statistical Analysis

All data were expressed as mean ± standard error of the mean (SEM). Statistical analyses were performed using GraphPad Prism 5.01. Differences between groups were assessed using one-way ANOVA followed by Dunnett's and Turkey-Kramer's multiple comparison tests. A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Phytochemical Composition and Acute Toxicity

The phytochemical screening of EACL revealed the presence of sterols and polyterpenes, polyphenols, flavonoids, saponins, quinones, and catechic and gallic tannins. Screening carried out using Dragendorff's reagent (positive) and Bouchardat's reagent (negative) does not confirm the presence of alkaloids. Further analyses (CCM or spectrophotometry) are essential to reach a definitive conclusion (Table 1). The acute toxicity study showed no mortality or signs of toxicity at doses up to 5000 mg/kg b.w., indicating that the oral LD50 of EACL is greater than 5000 mg/kg.

Table 1. Phytochemicals in the aqueous extract of *Citrullus lanatus* (Cucurbitaceae) seeds.

Compounds sought		Test or reagents	Result
Stérols et polyterpenes		Liebermann	+
Polyphenols		Ferric chloride	+
Flavonoids		Cyanidin	+
Saponins		Vigorous shaking	+
Quinone compounds		Borntraeger	+
Alkaloids		Dragendorff	+
		Bouchardat	−
Tannins	Catechinic	Stiasny	+
	Gallic	Hydrochloric acid	+

(+): Presence of the compound; (−): Absence of the compound.

3.2. Effects in Normoglycemic Rats

Treatment with EACL for 14 days did not lead to a significant change in body weight compared to the control group ($p > 0.05$) (Figure 1).

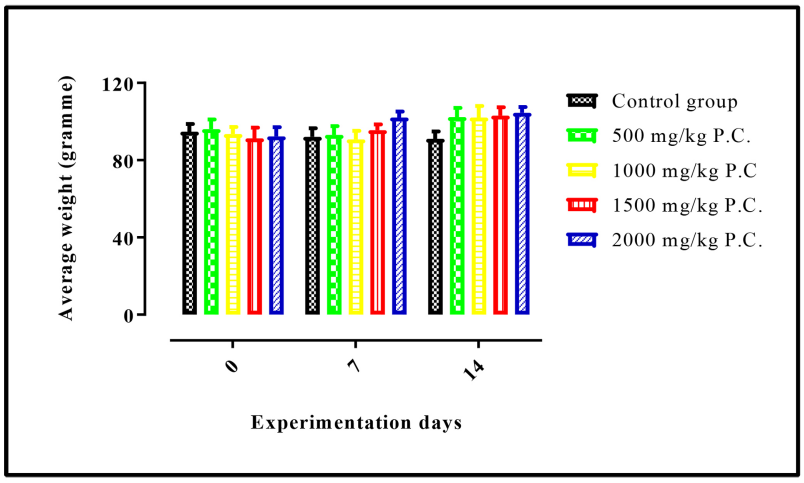

Figure 1. Changes in body weight in normal rats during 14 days of treatment with an aqueous extract of *Citrullus lanatus* seeds. n = 5; $p > 0.05$.

However, there was a dose-dependent and statistically significant decrease in fasting blood glucose levels, with the greatest reduction of 45.9% observed at the highest dose of 2000 mg/kg by Day 14 (Figure 2).

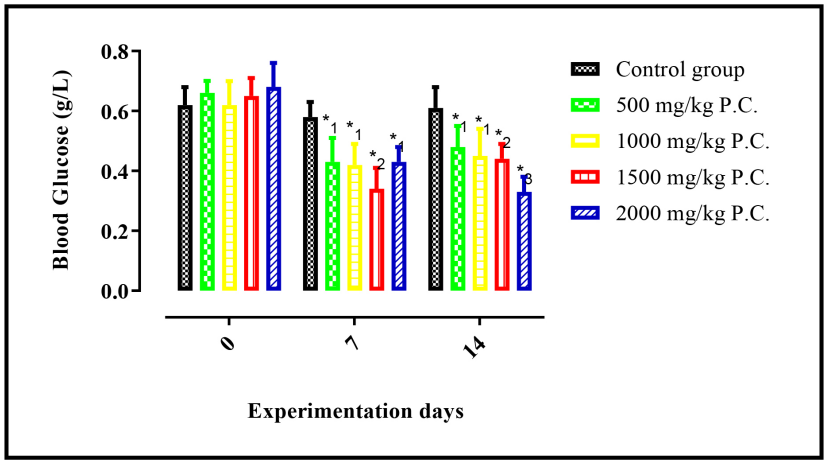

Figure 2. Evolution of fasting blood glucose in normoglycemic rats treated with EACL for 14 days. Values are mean ± SEM (n = 5). *p < 0.05, **p < 0.01, ***p < 0.001 vs control at same time point. (Data presented as mean ± SEM).

Furthermore, EACL significantly reduced total cholesterol. Following administration of doses of 500, 1000, 1500 and 2000 mg/kg body weight, after 14 days, the total cholesterol levels in the rats fell to 0.648 ± 0.02; 0.636 ± 0.03; 0.608 ± 0.04 and 0.588 ± 0.04 g/L, respectively (Figure 3).

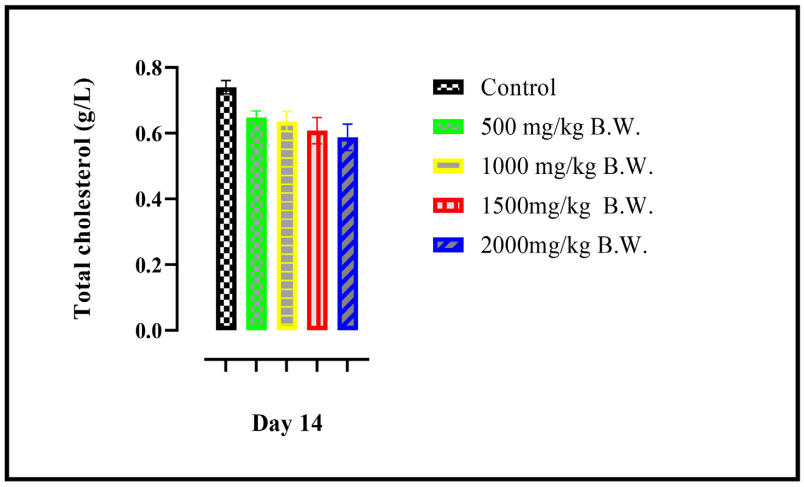

Figure 3. Changes in total cholesterol concentration in normal rats treated for 14 days with an aqueous extract of *Citrullus lanatus* seeds. n = 5; *: p < 0.05; **: p < 0.01; ***: p < 0.001 Statistically significant compared with the control.

3.3. Anti-Hyperglycemic Effects of *Citrullus lanatus* Aqueous Seed Extract

The anti-hyperglycemic activity of EACL (2000 mg/kg) was evaluated in three dis-

tinct experimental models of glucose-induced hyperglycemia in rats, and compared to the standard drug glibenclamide (10 mg/kg) (Figures 4-6).

3.3.1. Pre-Treatment Model (EACL Administered before Glucose)

In the pre-treatment model, EACL and glibenclamide significantly reduced blood glucose levels at T30 (0.73 ± 0.04 g/L and 0.68 ± 0.03 g/L, respectively, $p < 0.01$) compared to the positive control group (0.94 ± 0.02 g/L). Following glucose administration at T30, both treatments significantly attenuated the hyperglycemic peak at T60 compared to the positive control (1.19 ± 0.5 g/L for EACL vs. 1.45 ± 0.5 g/L for positive control, $p < 0.01$). Blood glucose levels continued to decline progressively, reaching 0.82 ± 0.4 g/L for EACL and 0.62 ± 0.3 g/L for glibenclamide by T150 (Figure 4).

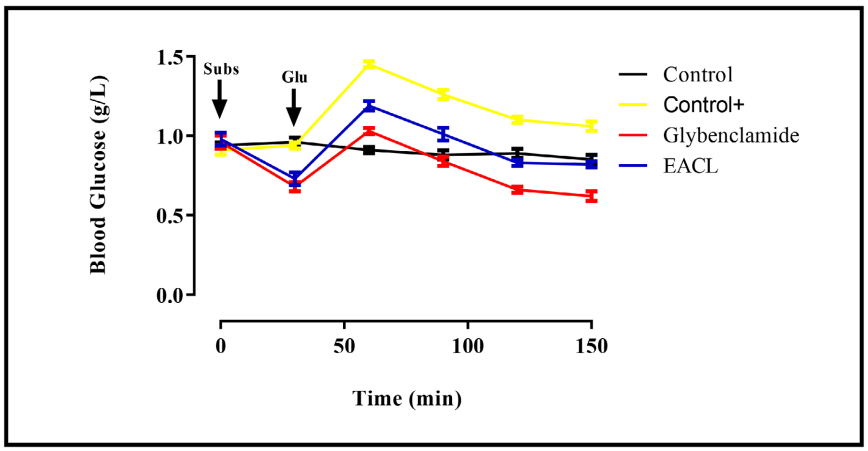

Figure 4. Effect of EACL and glibenclamide on blood glucose levels in hyperglycaemic rats, administered prior to glucose over a period of 150 minutes.

3.3.2. Post-Treatment Model (EACL Administered after Glucose)

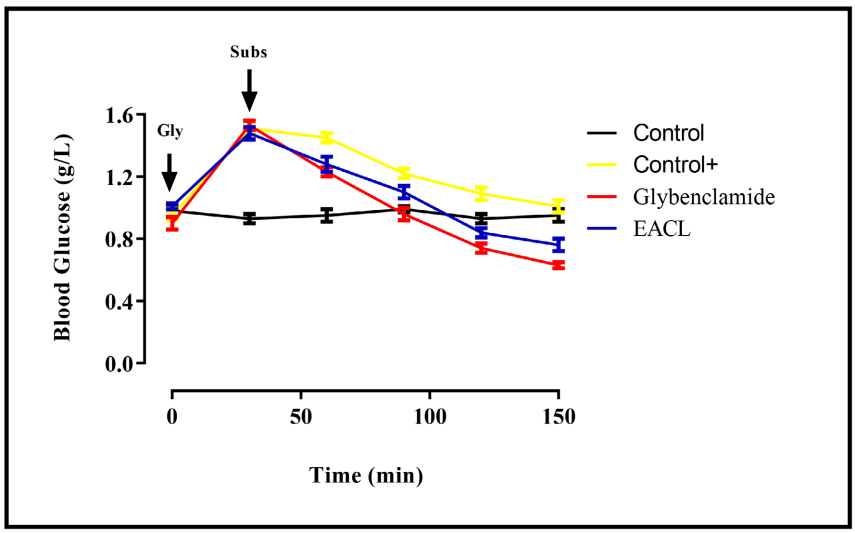

Figure 5. Effect of EACL and glibenclamide on blood glucose levels in hyperglycaemic rats following glucose administration over a 150-minute period.

In the post-treatment model, glucose loading significantly increased blood glucose in the positive control group, reaching a peak of 1.51 ± 0.80 g/L at T30 ($p < 0.001$). Administration of EACL (2000 mg/kg) at T30 induced a significant reduction in blood glucose at T60 (1.28 ± 0.6 g/L, $p < 0.01$), with levels continuing to decline to 0.76 ± 0.4 g/L by T150. This effect was comparable to glibenclamide, which reduced blood glucose from 1.53 ± 0.5 g/L at T30 to 0.63 ± 0.3 g/L at T150 (Figure 5).

3.3.3. Co-Administration Model (EACL Combined with Glucose)

When EACL was co-administered with glucose (4 g/kg), it significantly attenuated the hyperglycemic peak at T30 compared to the positive control group (0.8 ± 0.3 g/L vs. 1.28 ± 0.4 g/L, $p < 0.001$), representing a 37.5% reduction. This effect was superior to that of the glibenclamide + glucose mixture, which showed a 22.6% reduction at the same time point. Blood glucose levels then continued to decline progressively, reaching 0.75 ± 0.4 g/L for EACL and 0.54 ± 0.3 g/L for glibenclamide by T150 (Figure 6).

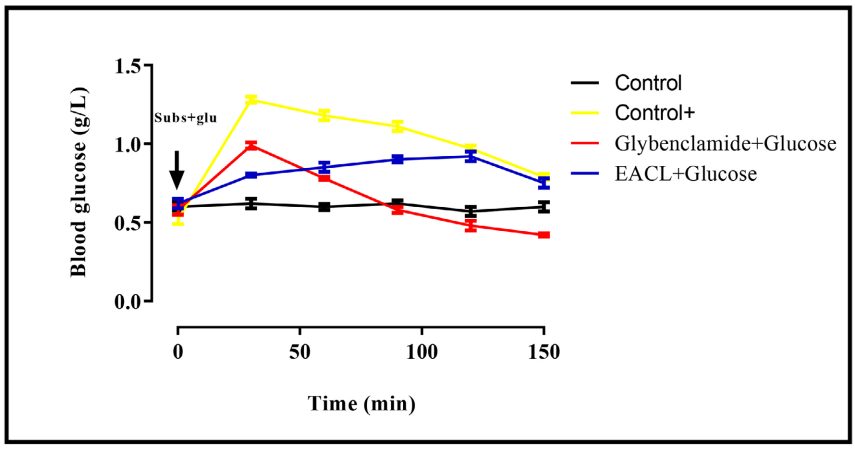

Figure 6. Effect of the combinations (EACL + glucose) and (glibenclamide + glucose) on blood glucose levels in rats over a 150-minute period.

Overall, these results demonstrate that EACL possesses potent anti-hyperglycemic activity in all three models, with effects comparable to the reference drug glibenclamide. Notably, co-administration of EACL with glucose almost completely prevented the establishment of postprandial hyperglycemia.

4. Discussion

The present study investigated the anti-hyperglycemic potential of *Citrullus lanatus* seeds, a plant used in traditional medicine. The preliminary phytochemical analysis revealed the presence of several bioactive compounds, including flavonoids, saponins, and polyphenols. These compounds have been widely described for their antidiabetic properties and their ability to improve lipid metabolism [16].

The acute toxicity study confirmed the safety of the aqueous extract, with an LD50 > 5000 mg/kg, consistent with the traditional use of the plant.

The significant hypoglycemic effect observed in normoglycemic rats after 14 days of treatment with EACL suggests a potential for chronic glucose management. This effect could be attributed to the presence of bioactive compounds that may improve insulin sensitivity or inhibit intestinal glucose absorption [17]. The beneficial effects on the lipid profile, including a reduction in total cholesterol are crucial in managing diabetes-related dyslipidemia. These findings are consistent with previous reports on the hypolipidemic effects of plant extracts and are likely linked to the antioxidant properties of the bioactive constituents [18] [19].

More importantly, EACL demonstrated potent anti-hyperglycemic effects in all three models of acute hyperglycemia. The effectiveness of the extract when administered before glucose suggests a preventive role, possibly by delaying carbohydrate digestion and absorption [20]. When administered after glucose, its ability to rapidly reduce the glycemic peak indicates a potential for postprandial glucose control, possibly by increasing peripheral glucose uptake [21]. Most significantly, the co-administration of EACL with glucose nearly prevented hyperglycemia, highlighting its strong potential to modulate glucose absorption and metabolism from the very start of a meal.

The results demonstrate that the anti-hyperglycemic efficacy of EACL is comparable to that of glibenclamide, a standard sulfonylurea. This supports the traditional use of *Citrullus lanatus* in the management of diabetes and suggests that its effect may be mediated by multiple mechanisms, including promotion of insulin secretion, increased peripheral glucose utilization, and inhibition of α-glucosidase activity.

5. Conclusions

This study demonstrates that the aqueous extract of *Citrullus lanatus* seeds (EACL) is non-toxic and possesses significant hypoglycemic and anti-hyperglycemic properties, effectively modulating both glycemic and lipid parameters in rats. These promising results, comparable to those of a conventional antidiabetic drug, confirm the anti-hyperglycaemic effect of *Citrullus lanatus* (Cucurbitaceae) seeds and their potential use in the management of diabetes.

These findings pave the way for further research. Future studies should focus on the subacute toxicity profile, evaluate its efficacy in a chronic diabetic model (e.g., alloxan or streptozotocin-induced diabetes), and explore the formulation of a functional dietary supplement to aid in diabetes management.

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Author Contributions

All authors contributed equally to the study. They made substantial contributions to the design of the study, the collection of the data, as well as the preparation and analysis of the data. They also drafted the manuscript and gave final approval for its submission to the journal for consideration of publication.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Newman, D.J. and Cragg, G.M. (2007) Natural Products as Sources of New Drugs over the Last 25 Years. *Journal of Natural Products*, **70**, 461-477. https://doi.org/10.1021/np068054v

[2] Pousset, J. (2004) Plantes Médicinales d'Afrique: Comment les Reconnaître et les Utiliser. Le Monde des Plantes, 484. https://www.tela-botanica.org/2004/12/article291/

[3] Kolling, M., Winkley, K. and von Deden, M. (2010) "For Someone Who's Rich, It's Not a Problem". Insights from Tanzania on Diabetes Health-Seeking and Medical Pluralism among Dar Es Salaam's Urban Poor. *Globalization and Health*, **6**, 1-9. https://doi.org/10.1186/1744-8603-6-8

[4] Kroa, E., Doh, S.K., Soko, Y.N., Yohou, K.S., Koulaï, O.J.D., Gbogbo, M., *et al.* (2016) Effet de l'extrait aqueux de l'écorce de tige de *Anthocleista djalonensis* A. Chev (Gentianaceae) sur la glycémie des lapins. *International Journal of Biological and Chemical Sciences*, **10**, 552-558. https://doi.org/10.4314/ijbcs.v10i2.9

[5] Whiting, D.R., Guariguata, L., Weil, C. and Shaw, J. (2011) IDF Diabetes Atlas: Global Estimates of the Prevalence of Diabetes for 2011 and 2030. *Diabetes Research and Clinical Practice*, **94**, 311-321. https://doi.org/10.1016/j.diabres.2011.10.029

[6] Efui, H.G., Karou, D.S., Gnoula, C., Agbodeka, K., Anani, K., Tchacondo, T., *et al.* (2015) Étude Ethnobotanique des Plantes Utilisées dans le Traitement du Diabète au Togo. *The Pan African Medical Journal*, **20**, Article No. 437.

[7] Bailey, J. (2008) Premier pas dans l'Analyse de Données Qualitatives. *Pratique Familiale*, **25**, 127-131.

[8] Onsiyor, E.J., Akaffou, N.A., Zahoui, O.S. and Traore, F. (2019) Effets antidiabétiques de l'extrait aqueux de *Ageratum conyzoïdes* (Astéraceae) chez les rats rendus diabétiques par pancréatectomie partielle et évaluation de leurs paramètres hématologiques. *International Journal of Biological and Chemical Sciences*, **13**, 1621-1628. https://doi.org/10.4314/ijbcs.v13i3.33

[9] Ismael, R.N., Mustafa, Y.F. and Al-Qazaz, H.K. (2022) *Citrullus lanatus*, a Potential Source of Medicinal Products: A Review. *Journal of Medicinal and Chemical Sciences*, **5**, 607-618.

[10] Adelani-Akande, T.A., Ajiba, L.C., Dahunsi, S.O. and Oluyori, A.P. (2015) Antibacterial Activity of Watermelon (*Citrullus lanatus*) Seed against Selected Microorganisms. *African Journal of Biotechnology*, **14**, 1224-1229. https://doi.org/10.5897/ajb2014.14101

[11] Poduri, A., Rateri, D.L., Saha, S.K., Saha, S. and Daugherty, A. (2013) *Citrullus lanatus* "Sentinel" (Watermelon) Extract Reduces Atherosclerosis in LDL Receptor-Deficient Mice. *The Journal of Nutritional Biochemistry*, **24**, 882-886.

https://doi.org/10.1016/j.jnutbio.2012.05.011

[12] Fleurentin, J. (2012) L'ethnopharmacologie au service de la thérapeutique: Sources et méthodes. *Hegel*, **2**, 12-18. https://doi.org/10.4267/2042/47400

[13] Lazureski, G.V., Terenteva, I.V. and Chamchurin, A.A. (2007) Praticheskii Raboti po Khimii Soedinienii. Vischaya Chkola, 334 p.

[14] Abo, K.J.C. (2013) From Plant to Molecule: Toxicity, Pharmacological Effects and Mechanism of Action of *Justicia secunda* (Acanthaceae), an Antihypertensive Plant, on the Cardiovascular System of Mammals. State Doctoral Thesis in Natural Sciences, Félix Houphouët-Boigny University, No. 752/2013, 351 p.

[15] OECD (2001) Guideline for the Testing of Chemicals No. 423: Acute Oral Toxicity—Acute Toxic Class Method.

[16] Okoroh, P.N., Onuigbo, M.C., Godwin-Nwakwasi, E.U., Chukwuka, O.C. and Ekanem, E.I. (2021) Trace Mineral, Qualitative Phytochemical Composition and Antidiabetic Effect of Ethanol Extract of *Citrullus lanatus* Seeds on Diabetic Rats. *Asian Journal of Biotechnology and Bioresource Technology*, **7**, 77-86. https://doi.org/10.9734/ajb2t/2021/v7i430111

[17] Anthony, G.S., Moore, A.G.S. and Okoduwa, S.I.R. (2026) Modulation of PDX1 Gene Expression and Glycemic Control by *Citrullus lanatus* in Experimental Type 2 Diabetes. *Scientific Reports*, **16**, Article No. 3793.

[18] Ogbeifun, H.E., Peters, D.E. and Monanu, M. (2020) Effect of Aqueous Extract of *Citrullus lanatus* (Watermelon) Seeds on Alloxan Induced—Diabetic Wistar Rats. *Asian Journal of Research in Biochemistry*, **6**, 30-44. https://doi.org/10.9734/ajrb/2020/v6i230115

[19] Upe Babaiwa, U., Erharuyi, O., Falodun, A. and Akerele, J.O. (2017) Phytochemical and Antioxidant Properties of *Citrullus lanatus* Seed Extracts. *Nigerian Journal of Pharmaceutical Sciences*, **16**, 55-60. https://www.researchgate.net/publication/366714617_Phytochemical_and_antioxidant_properties_of_Citrullus_lanatus_seed_extracts

[20] Bnouham, M., Ziyyat, A., Mekhfi, H., Tahri, A. and Legssyer, A. (2019) Medicinal Plants with Potential Antidiabetic Activity—A Review of Ten Years of Herbal Medicine Research (1990-2000). *International Journal of Diabetes and Metabolism*, **14**, 1-25. https://doi.org/10.1159/000497588

[21] Yasodha, K.J., Jayaveera, K.N., Ravindra, R., Rupesh, K. and Raghavendra, D. (2008) Anti-Diabetic Activity of Aqueous Extract of *Talinum cuneifolium* Linn. in Rats. *Pharmacologyonline*, **2**, 198-206. https://www.researchgate.net/publication/288412423_Anti-diabetic_activity_of_aqueous_extract_of_Talinum_cuneifolium_Linn_in_rats