SJIF Impact Factor: 6.711

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 9
Issue: 3
Page N. 135-138
Year: 2025

Original Article www.wjahr.com

EFFECT OF *AVERRHOA BILIMBI* L (OXALIDACEAE) LEAVE EXTRACTS ON THE BLOOD GLUCOSE OF DEXAMETHASONE TREATED MICE

[1]Idio Imoubong Raphael, [1]Mike-Raph Chinecherem Nwachukwu and [1]Mikailu Suleiman*

[1]Department of Pharmacognosy and Phytotherapy, Faculty of Pharmaceutical Sciences, University of Port Harcourt, Choba, Port Harcourt, Rivers State.

Article Received date: 15 January 2025 **Article Revised date:** 05 February 2025 **Article Accepted date:** 25 February 2025

***Corresponding Author: Mikailu Suleiman**

Department of Pharmacognosy and Phytotherapy, Faculty of Pharmaceutical Sciences, University of Port Harcourt, Choba, Port Harcourt, Rivers State.

ABSTRACT

Elevated blood glucose level is a characteristic of a chronic metabolic disorder which may be due to either insufficient insulin production or impaired insulin action. Drugs that elicit hyperglycemia as a side effect has a serious limitation. This study aimed to evaluate the antihypergylcermic potential of *Averrhoa bilimbi L. Oxalidaceae* leaves extracts in dexamethasone treated mice. The leaves of the plant were dried, pulverized and screened for phytochemicals using standard methods. The powdered leaf was successively extracted with n-hexane, dichloromethane, ethyl acetate and methanol. The extracts were concentrated at 40ºC and kept in desicator for studies. Mice were grouped, allowed to acclimatized and then treated with dexamethasone (5 mg/kg) for 7days. Thereafter treatment commenced according to their grouping with doses (200, 400 and 800 mg per kg) for 21 days Fasting Blood Sugar (FBS) levels were monitored across treatment groups on day 0, 7, 14 and 21 using glucometer. Phytochemical analysis of *Averrhoa bilimbi* leaves extracts revealed the presence of Alkaloids, flavonoids, saponins, cardiac glycosides and Absence of Anthraquinones. All extracts significantly reduced the Fasting Blood Glucose levels in treated mice when compared to untreated control. These findings support the use of *A. bilimbi* as a complementary treatment in the use of dexamethasone.

KEYWORDS: *Averrhoa bilimbi*, Dexamethasone, phytochemical constituents, fasting blood glucose.

INTRODUCTION

Dexamethasone is a long-acting synthetic corticosteroid with a wide range of physiologic effects. These include but are not limited to immunosuppression and anti-inflammatory properties mediated primarily by preventing cytokine release via inhibition of cyclo-oxygenase 2. Lately, further research has been reported to better understand its role in supplementing regional anesthetics. Dexamethasone has been studied as an adjuvant in conjunction with several different peripheral nerve blocks including transverse abdominis, brachial plexus, ankle, and paravertebral blocks.[1] Several studies suggest favorable outcomes such as lower pain scores, decreased post-operative opioid usage, and decreased nausea and vomiting.[2] Dexamethasone has found significant use in the treatment of allergic states, dermatologic diseases, adrenal insufficiency, symptomatic neurologic conditions and female infertility. However, side effects usually observed after seven days of usage include hyperglycemia, acne, weight gain, immunosuppression, hypertension, nausea, vomiting, and confusion.[3]

Averrhoa bilimbi, a member of the Oxalidaceae family, is an edible fruit-bearing plant native to Southeast Asia and cultivated in parts of India. It is valued in traditional medicine for its accessibility, affordability, and therapeutic benefits. Traditionally, its fruits have been used to manage inflammatory conditions, including hepatitis, fever, and diarrhea, while its leaves are applied as a paste for itches, swelling, skin eruptions, and poisonous bites. In some rural Indian communities, the fruit has been used in folk medicine to manage obesity and conditions like fever, syphilis, stomach ache, ulcers, hypertension, obesity, and diabetes.[4] The plant showed antibacterial activities against both positive and negative gram stains[5] and showed cytotoxic,[6] antifungal,[7] anti-hyperglycaemic activities too as it abolished the serum insulin level in diabetes mellitus.[8] The presence of plentiful phytoconstituents like alkaloids, glycosides, tannins, steroids and saponins, in different parts of the plant, reflected its potential in the treatment of several diseases.[9] Free radical scavenging properties displayed by fruit extract confirmed its role in the treatment of cardiovascular diseases, inflammatory conditions, aging,

as a facial moisturizer and in the management of cancer.[10], [11] Compounds namely 2,3-bis(2,6,10-trimethylundeca-1,5,9-trienyl) oxirane, squalene, 3-(6,10,14-trimethylpentadecan-2-yl) furan-2 (5H)-one, phytol, 3,4-dihydroxyhexanedioic acid were isolated from the methanolic extract of the leaves.[12].[13] Isolated 3 new compounds along with 12 known compounds namely Beta (β)-amyrenone, β-amyrin, phytol, β-sitosterol, stigmastanol, aurantiamide benzoate, trans-cinnamic acid, 4-hydroxycinnamic acid, phloretic acid, (S)-dehydrovomifoliol, (6S,7aR)- loliolide and carambolaflavone from ethyl acetate extract of leave. Consequently, the purpose of this study was to investigate the effect of A. bilimbi on the blood glucose of mice receiving dexamethasone treatment.

MATERIALS AND METHODS

Plant Material

The leaves of *Averrhoa bilimbi* was collected from a private compound at Rumuolumeni, Port Harcourt, Rivers State. The sample was identified and authenticated with voucher specimen number UPH00651 deposited in the herbarium in the Department of Pharmacognosy and Phytotherapy, University of Port-Harcourt. The sample was washed and air-dried under room temperature for 3-4 days. The dried sample was ground to fine powder using a blender and stored in air-tight container until further use.

3.5. Extraction process

1000g of the powdered leaves of *Averrhoa bilimbi* was successively macerated with n-hexane, dichloromthane, ethyl acetate and methanol for 72 hours each. Each extract was filtered and evaporated to dryness using rotary evaporator en vacou. The extracts were weight and kept in a dessicator fur further analysis.

Phytochemical screening

Phytochemical screening was carried out on the dried powdered sample obtained according standard procedures.[14], [15]

EXPERIMENTAL ANIMAL

Healthy albino mice with weight range of about 20-30g were selected for this experiment. They were obtained from the animal house of the Department of Pharmacology, Faculty of Basic Medical Sciences, University of Port Harcourt. The rats were fed and properly housed in a cleaned, labelled uniform cages and allowed to acclimatize for two weeks before commencement of the experiment.

Dexamethasone and extracts treatment

The test animals were divided into Nine groups, each containing 5 rats. The test animals, were fasted overnight of food and water. The fasting blood glucose levels of the animals were determined by using glucometer and strips (accucheck). The test animals from group 1-9, except those in control were made hyperglycemic by a single intraperitoneal injection of dexamethasone using 5mg/kg/day for 21 days. After seven (7) of treatment with dexamethasone the animals were divided into groups as follows:

Group 1 – Albino mice without treatment (normal control)

Group 2 – Dexamethasone treatment only (negative control)

Group 3, Group 4, Group 5, – Dexamethasone and *A. bilimbi* n-hexane extract at doses of 200mg,400mg and 800mg respectively

Group 6, Group 7, Group 8– Dexamethasone and *A. bilimbi* dichloromethane extract at doses of 200mg, 400mg and 800mg respectively.

Group 9, Group 10, Group 11– Dexamethasone and *A. bilimbi* ethylacetate extract at doses of 200mg,400mg and 800mg respectively.

Group 12, Group 13, Group 14– Dexamethasone and *A. bilimbi* methanol extract at doses of 200mg,400mg and 800mg respectively.

Blood Sugar Test

The test animals were fasted overnight of food and water. The fasting blood glucose levels of the animals were determined through Viva check Glucometer and strips using blood withdrawn from the tail vein of the test animal The FBS was checked for Day 0 before induction, Day 7, Day 14 and Day 21 and recorded.

Statistical Analysis

Data obtained from the study were expressed as mean -/+ standard deviation and were analysed for statistical significance at $p < 0.05$ using one-way Analysis of Variance (ANOVA). The percentage reduction in blood glucose level were calculated.

RESULTS

Table 1: Result of phytochemical screening carried out on the leaves of *Averrhoa bilimbi*.

S/No	Phytoconstituents	Remark
1	Alkaloid	+
2	Flavonoids	+
3	Anthraquinones	-
4	Saponins	+
5	Triterpenoids	+
6	Steroids	+
7	Cardiac glycosides	+

KEYS: (+) = present, (-) = absent

Table 2: Percentage yield of the various extracts of Averrhoa bilimbi leaves.

S/No	Extract	Wt. of dried extract (g)	Yield (%w/w)
1	n-hexane	37.67	3.77
2	Dichloromethane	46.59	4.66
3	Ethylacetate	78.8	7.88
4	Methanol	162.90	16.29

Weight of powdered material: 1kg

Table 3: Effect of dexamethasone and *Averrhoa bilimbi* extracts on the blood glucose of mice.

Treatment Group	Day 0-FBS (Mmol/L)	Day 7–FBS (Mmol/L)	Day 14-FBS (Mmol/L)	Day 21-FBS (Mmol/L)
1	3.08 ± 0.7	3.14 ± 0.1	3.12 ± 0.1	3.30 ± 0.1
2	3.40 ± 0.4	4.72 ± 0.4	5.80 ± 0.4	5.88 ± 0.5
3	3.08 ± 0.4	5.08 ± 0.5	2.76 ± 0.5	2.88 ± 0.5
4	3.20 ± 0.5	5.18 ± 0.5	3.18 ± 0.6	3.33 ± 0.3
5	3.40 ± 0.3	5.16 ± 0.6	3.50 ± 0.3	3.32 ± 0.2
6	2.44 ± 0.1	4.98 ± 0.5	2.38 ± 0.6	3.00 ± 0.4
7	2.62 ± 0.3	5.20 ± 0.3	3.22 ± 0.2	3.18 ± 0.2
8	2.82 ± 0.4	4.92 ± 0.4	2.88 ± 0.2	3.14 ± 0.1
9	3.16±0.2	5.28±0.2	2.64±0.4	2.88±0.2
10	3.24±0.4	4.84±0.6	2.82±0.8	3.30±0.2
11	3.08±0.5	5.90±0.4	3.72±0.4	3.50±0.2
12	3.18±0.3	5.90±0.2	3.45±0.3	3.30±0.2
13	2.48±0.4	5.46±0.7	4.22±0.8	3.86±0.6
14	3.22±0.4	5.42±0.4	3.82±0.7	3.72±0.6

Values represented as Mean ± Standard deviation (SD), N=5

Tabe 4: Percentage reduction of blood glucose level of mice treated with dexamethasone and A. bilimbi on Day 14 and Day 21.

TREATMENT Groups	DAY 14 (%)	DAY 21 (%)
3	52.4	51.0
4	45.2	43.4
5	39.7	43.5
6	60.0	49.0
7	44.5	45.9
8	50.3	46.6
9	54.5	51.0
10	51.4	43.9
11	35.9	40.5
12	40.5	43.9
13	27.2	34.3
14	34.1	36.7

DISCUSSION

Drug side effect is a considerable factor in the choice of medications. Despite the Significant use of dexamethasone in inhibition of multiple inflammatory cytokines and effectiveness in both children and adult for the prevention postoperative nausea and vomiting, croup and pain,[16] its inducement of hyperglycemia after 7 days is a concern that deserves attention. Plant and plant products exhibit multiple pharmacological activities due to their multi-constituent nature. Side effect of pure compounds are believed to be ameliorated with plants that are rich in antioxidants that are not contraindicated with such drugs such drugs. In this study, it was observed that blood glues of the mice were elevated after day seven of treatment with dexamethasone. As the treatment continue with the introduction of *A. bilimbi* on day 8 to day 21. The blood glucose of the mice in the various groups showed significant reduction to normal range when compared with group 2 mice that were given only dexamethasone throughout the study in table 2. One striking observation in the study is that all the extracts showed significant reduction of blood glucose at every concentration which suggests that a concentration lower than 200mg/kg that was experimented could also exhibit reduction in blood glucose level. The phytoconstituents detected in the leave powder was in agreement with previous report. [17] The percentage yield of the extract in table 1, showed increase with an increase in the polarity of the solvent of extraction making the most polar solvent (methanol) among them to have the highest yield of 16.29%.

CONCLUSION

The findings revealed that the extracts of A. bilimbi have antiherpglycemic effect on the heyperglycemic side effect of dexamethasone that was observed after 7 days of treatment. This therefore suggests that any of the n-hexane, dichloromethane, ethylacetate and methanol extract could be administered concomitant with dexamethasone for a long-time dose.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

1. Patrick Ifesinachi Emelife, Matthew R. Eng, Bethany L. Menard, Andrew S. Myers, Elyse M. Cornett, Richard D. Urman, Alan D. Kaye, Adjunct medications for peripheral and neuraxial anesthesia, Best Practice & Research Clinical Anaesthesiology, 2018; 32(2): 83-99, ISSN 1521-6896
2. N.H. Waldron, C.A. Jones, T.J. Gan, T.K. Allen, A.S. Habib, Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis, British Journal of Anaesthesia, 2013; 110(2): 191-200, ISSN 0007-0912, https://doi.org/10.1093/bja/aes431.
3. Rebecca S. Usadi, Kathryn S. Merriam, On-label and off-label drug use in the treatment of female infertility, Fertility and Sterility, 2015; 103(3): 583-594, ISSN 0015-0282,
4. Anandhalakshmi, J., Bakyalakshmi, G., & Hemamalini, V. In vitro antibacterial potential of synthesized silver nanoparticles from leaves of Averrhoa bilimbi L. World Journal of Pharmaceutical Research, 2018; 7(7): 323-335.
5. Karon, B. S., et al. Cytotoxic potential of Averrhoa bilimbi against selected cancer cell lines. *International Journal of Cancer Research*, 2011; *9*(2): 1–6.
6. Das, P. S., Ahmed, R., & Singh, K. Antimicrobial and anti-inflammatory activities of Averrhoa bilimbi Linn fruit extracts. *Journal of Natural Products Research*, 2011; *5*(3): 1–6.
7. Nazmul MH, Salmah I, Syahid A, Mahmood AA. In vitro screening of antifungal activity of plants in Malaysia. Biomed Res., 2011; 22(1): 28-30.
8. Patel, D. K., Prasad, S. K., Kumar, R., & Hemalatha, S. An overview on antidiabetic medicinal plants having insulin mimetic property. Asian Pacific Journal of Tropical Biomedicine, 2012; 2(4): 320-330.
9. Chowdhury, A., & Kabir, M. Phytochemical screening and antioxidant potential of Averrhoa bilimbi Linn extracts. *International Journal of Pharmaceutical Sciences and Research*, 2012; *4*(5): 1–8.
10. Suluvoy JK, Berlin Grace VM. Phytochemical profile and free radical nitric oxide (NO) scavenging activity of Averrhoa bilimbi L. fruit extract. 3Biotech. 2017 May; 7(1): 85. doi: 10.1007/s13205-017-0678-9. Epub 2017 May 12. PMID: 28500407; PMCID: PMC5429310.
11. Pirante, A. P., Garcia, C. G., Caliwliw, C. M., & Mangapot, J. J. The feasibility of bilimbi (Averrhoa bilimbi) fruit and oregano (Origanum vulgare) leaf extract as a potential facial moisturizer. Philippine Journal of Natural Sciences, 2019; 3(1).
12. Gunawan, S. & Paano, A. Isolation of novel bioactive compounds from Averrhoa bilimbi leaves. *Natural Product Communications*, 2013; *8*(2): 1–10.
13. Auw L, Subehan, Sukrasno, Kadota S, Tezuka Y. Constituents of Indonesian medicinal plant Averrhoa bilimbi and their cytochrome P450 3A4 and 2D6 inhibitory activities. Nat Prod Commun., 2015; 10(1): 1934578X1501000116.
14. Harborne JB. Phytochemical methods: a guide to modern techniques of plant analysis. Chapman and Hall, 1998.
15. Houghton PJ, Raman, A. Laboratory Handbook for Fractionation of Natural Extracts. Chapman and Hall, London, 1998.
16. Erica L. Sivak, Denise M. Hall-Burton, 13 - Anesthetic Adjuncts, Editor(s): Peter J. Davis, Franklyn P. Cladis, Smith's Anesthesia for Infants and Children (Ninth Edition), Elsevier, 2017; 258-264.e4, ISBN 9780323341257
17. Uddin, N., & Shahriar, M. Preliminary phytochemical screening and evaluation of biological properties of Averrhoa bilimbi. *Journal of Medicinal Plants Research*, 2013; *7*(18): 1–7.