



Research Article

Acute Toxicity Testing and Phytochemical Screening of Hydromethanolic Leaf Extract of *Maerua angolensis* on Albino Wistar Rats

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ABSTRACT

Maerua angolensis leaves have been used traditionally for the treatment of several ailments which include but not limited to anaemia, jaundice, arthritis, insomnia, liver diseases and neurological disorders. Despite its widespread use and several reported beneficial uses, there is a paucity of data on its toxicity potential. This study was therefore designed to evaluate the phytochemical constituents and acute toxicity potential of hydromethanolic leaf extract of *Maerua angolensis* on albino wistar rats. Phytochemical screening was carried out using a standard procedure for the identification of phytochemicals as described in the literatures. Acute toxicity determination was done in two phases (using Lorke's method). In the first phase, the rats were divided into three groups of three rats each and were administered 10mg/kg, 100mg/kg and 1000mg/kg body weight of the hydromethanolic leaf extract of *Maerua angolensis* respectively. In the second phase, the rats were divided into three groups of one rat each and were administered 1600mg/kg, 2900mg/kg and 5000mg/kg body weight of the hydromethanolic leaf extract of *Maerua angolensis* respectively. Phytochemical screening revealed that the hydromethanolic leaf extract of *Maerua angolensis* contains flavonoids, cardiac glycosides, saponins, tannins and terpenoids. The rats did not show any signs or symptoms of toxicity following the administration of the extract during both phases. Therefore, it could be concluded that *Maerua angolensis* leaves contain essential constituents needed in the treatment and management of various ailments and are also safe for use as the LD₅₀ was >5000mg/kg supporting its folkloric use in disease management.

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INTRODUCTION

Plants have been used for medicinal purposes since ancient times and their importance and vitality have been appreciated by the human population (Fateemah et al., 2018). Traditional medicines have been reported to be safe and relatively non-toxic as a result of their long history of use globally, especially in developing countries (Yuet et al., 2013). However, the unguided traditional use of plants has been implicated in the cause of short- and long-term health complications (Cock, 2015). Scientific studies have shown that the medicinal values and efficiency of these plants are due to the presence of certain phytochemical substances that produce definite physiological responses in the human body (Edeoga et al., 2005).

Screening of these phytochemicals is considered a valuable procedure in the detection of the bioactive constituents present in medicinal plants and subsequently leads to the discovery and development of new and efficient drugs (Yadav et al., 2014). In addition, the screening can also be used to identify toxic compounds present in such plants.

Recent studies have questioned the bioactivities of traditionally used medicinal plants due to reported side effects associated with their usage in both humans and animals (Nath, 2015). Acute toxicity study investigates the safety profile of a plant within a short period. It involves the evaluation of the adverse effects and reactions that occur following exposure of experimental animals to single or multiple doses of test substances within 24 hours by either oro-gastric, dermal or intraperitoneal routes (Saganuwa, 2016). The conventional measure of acute toxicity is the LD50 (median lethal dose) which was first introduced in 1927 by J. W. Trevan to estimate the dose of a test substance that produces 50% death in a given species of

animals (Earnest et al., 2018). Although the major observational endpoint in acute toxicity testing is death, non-lethal acute effects may occur as signs of toxicity depending on the testing chemical (Maheshwari and Shaikh, 2016).

Maerua angolensis belongs to the family “Capparaceae” comprising more than 50 species and are found mostly in the drier areas of tropical Africa as well as in the Middle East and tropical Asia. The English name for *Maerua angolensis* is Bead-bean, bush veld, or bead maerua; Its Fulani name is Leggel Baali (tree of sheep); Its Arabic name is Shegara el zeraf (Giraffe tree); and its Hausa name is Babbajuyi; while its Kanuri name is Apci (Mothanna et al., 2009). Several studies have shown that phytochemical constituents of plants have potential use as drugs, and the pharmacological activity of these substances serves as the basis for their use in modern medicine based on scientific evidence (Ahn, 2017). Therefore, the medicinal values of plants depend on the chemical substances in them that produce certain physiological actions which range from cell toxicity to cell protective effects. The most important of these bioactive substances in medicinal plants include alkaloids, tannins, flavonoids, saponins, cardiac glycosides and phenolic compounds (Krishniah et al., 2009). Methanolic extract of *Maerua angolensis* leaves has been reported to contain carbohydrates, reducing sugars, alkaloids, cardiac glycosides, saponins, flavonoids and tannins while its petroleum ether extract showed the presence of alkaloids, cardiac glycosides and saponins (Ayo et al., 2012).

Maerua angolensis leaves have a long history of use traditionally in the management of various ailments (SEPASAL, 2012). The leaves are used medicinally, either alone or in combination with other drug plants, to treat a

range of human ailments including stomach aches, asthenia, anorexia, headaches, and rheumatism (Yusuf *et al.*, 2017). *Maerua angolensis* extract inhibits vincristine-induced peripheral neuropathy in mice suggesting that it may exert an analgesic effect in cancer patients with neuropathic pain and an antinociceptive effect in abdominal constrictions (Iliya *et al.*, 2016). The stem bark extract of *Maerua angolensis* also protects the generation of free radicals and oxidative products of pentylenetetrazole-induced oxidative stress and seizures in rats (Charles *et al.*, 2018). *Maerua angolensis* is a potential source of antibiotics with a broad spectrum of activity as demonstrated by the antimicrobial activity of the leaf extract against pathogenic microorganisms (Amina *et al.*, 2017). The powdered leaves are laid over hard pus-filled abscesses to mature them and

the leaf sap is dropped on fresh wounds as an antiseptic dressing (Latham, 2007). In Nigeria, the fruits are used by youths as a love charm, mixed with tozali (galena, or so-called antimony) and rubbed on the eyelids to render themselves irresistible to girls (Adamu *et al.*, 2007) and the plant was reported to be used in the treatment of arthritis by the Hausas of North-western Nigeria (Magaji *et al.*, 2009; Mohammed *et al.*, 2008).

Unfortunately, little or no attention has been paid in the literature to the examine the phytochemical constituents and toxicity potential of this plant despite its widespread use. Hence, this study was aimed at evaluating the acute toxicity and phytochemical constituents of the hydromethanolic leaf extract of *Maerua angolensis* on albino wistar rats.



Figure 1: *Maerua angolensis* leaves in its natural habitat (Adapted from Burkill, 1985).

METHODOLOGY

Plant Collection and Identification

Leaves of the plant were obtained from Yola, Adamawa State Northeastern Nigeria and authenticated by a botanist in the Department of Biological Sciences, University of Maiduguri. The leaves were air-dried at room temperature to preserve the heat-labile compounds.

Experimental Animals

A total of twelve (12) male and female albino wistar rats weighing 180-200g were obtained and kept in separate well-aerated laboratory cages in the animal house, College of Medical Sciences, University of Maiduguri. The animals were allowed to acclimatize to the laboratory environment for a period of two weeks before the commencement of the experiment. They were allowed access to feed

and water ad libitum throughout the period of the experiment.

Preparation of Extract

The extract was prepared using the method employed by Erica *et al.* (2016). 1000g of the grounded leaves of *Maerua angolensis* was dissolved in five litres of methanol and allowed to stand for 48 hours. The resulting

suspension was filtered and the residue was extracted further. The filtrate was concentrated using a rotary evaporator with the aid of a vacuum pump. The concentrate was evaporated further to dryness in a vacuum oven at 50°C and the powder obtained (56.5g) was stored in a refrigerator until use.

The percentage yield was calculated in terms of air-dried weight of the plant material as:

$$\text{Percentage yield} = \frac{\text{Weight of Extract obtained (g)}}{\text{Weight of Initial sample (g)}} \times 100$$

Phytochemical Screening of Hydromethanolic leaf extract of *Maerua angolensis*

Phytochemical screening was carried out using the standard procedure for the identification of phytochemical constituents as described by Harborne, (1973); Trease and Evans, (1983) and Sofowora, (1993). The extract solution was prepared by dissolving 10g of extract in distilled water to make up a 100 ml solution. The extract solution was then used for phytochemical screening. Tests were done for confirmation of alkaloids, flavonoids, cardiac glycosides, anthraquinones, terpenoids, tannins, starch, phlobotannin and carbohydrates.

Determination of Median Lethal Dose (LD₅₀)

The LD₅₀ was determined by a procedure described by Lorke (1983) using 12 rats. In the first phase, nine (9) rats were divided into 3 groups of 3 rats each and were treated with the hydromethanolic leaf extract of *Maerua angolensis* at doses of 10mg/kg, 100mg/kg and 1000mg/kg body weight orally. They were observed for 2 weeks for signs of toxicity and mortality. In the second phase, three (3) rats were divided into three (3) groups of one (1) rat each and were treated with the extract at doses of 1600mg/kg, 2900mg/kg, and 5000mg/kg body weight orally and were observed for 24hours for signs of toxicity or mortality. From the results of the two phases, the LD₅₀ was determined.

RESULTS

Table 1: Showing results for phytochemical screening of hydromethanolic leaf extract of *Maerua angolensis*

Phytochemical constituents	Results
Alkaloids	-
Flavonoids	+
Cardiac glycosides	+
Anthraquinones	-
Terpenoids	+
Saponins	+
Tannins	+
Soluble starch	-
Phlobatanin	-
Carbohydrates	+

+ = present

- = absent

Table 2: Showing results of median lethal dose determination of hydromethanolic extract of *Maerua angolensis* leaves on albino wistar rats

Phase	Dose (mg/kg)	No of animals	No of death	% Mortality
1 st Phase				
Group 1	10	3	0	0
Group 2	100	3	0	0
Group 3	1000	3	0	0
2 nd Phase				
Group 1	1600	1	0	0
Group 2	2900	1	0	0
Group 3	5000	1	0	0

LD₅₀ > 5000mg/kg body weight

DISCUSSION

Phytochemical screening of the hydromethanolic leaf extract of *Maerua angolensis* revealed the presence of flavonoids, cardiac glycosides, tannins, terpenoids, saponins, and carbohydrates. Anthraquinones, Alkaloids, soluble starch, and phlobatanin were absent. This is in agreement with previous studies reported by Ayo *et al.* (2012) that were conducted in Zaria, Kaduna state of Nigeria, and that of Amina *et al.* (2017) conducted in Katsina State of Nigeria; although, in addition, the present study revealed the presence of terpenoids and absence of alkaloids. The methanolic stem bark extract of *Maerua angolensis* also revealed the presence of saponins, steroids, tannins, flavonoids, alkaloids, glycosides, terpenoids, carbohydrates and proteins (Adamu *et al.*, 2007; Mohammed *et al.*, 2008; Magaji *et al.*, 2009). These differences might be attributed to variations in the nature of soil of the two geographical regions or the part of the plant used during the screening or might be due to the differences in the extraction methods used. Tannins are reported to possess antioxidant and anti-microbial potencies (Majid, 2013). Flavonoids are significantly recognized for their antioxidant, anti-carcinogenic, anti-microbial and anti-tumour properties (Okwu,

2001). Polyphenols and flavonoids scavenge free radicals such as peroxide, hydroperoxide or lipid peroxy and thus inhibit oxidative mechanisms that lead to degenerative diseases (Lee *et al.*, 2014). They are therefore necessary for preventing haemolytic diseases such as anaemia (Upadhyay and Dixit, 2015). Epidemiological studies revealed that flavonoid prevents the oxidation of low-density lipoproteins, and lowers blood cholesterol level and triglycerides, thereby reducing the risk of atherosclerosis (Subramani and Casmir, 2002). Terpenoids are naturally occurring hydrocarbons produced by a wide variety of plants and animals. Important therapeutic uses of terpenoids include antioxidant, antimicrobial, antifungal, antiviral, anti-inflammatory, antiparasitic, hyperglycemic, immunomodulatory and skin permeation enhancer (Priyarka and Pathik, 2013). Saponins have been reported to have beneficial effects on blood cholesterol levels (Oyewole and Akingbala, 2011). Saponin glycosides are amphipathic glycosides that act as surfactants i.e., they possess detergent properties (Bissinger *et al.*, 2014).

The median lethal dose (LD50) of hydromethanolic leaf extract of *Maerua angolensis* using Lorke’s method did not reveal any signs and symptoms of toxicity or mortality after oral administration of the

extract following observation in the first phase and the second phase even at the highest dose of 5000mg/kg body weight (Table 2). Therefore, this result gives the impression that the lethal doses for the extract must be higher than 5000 mg/kg body weight, which is the highest reference dose (Nanthini *et al.*, 2014). In this regard, the extract may be considered safe at the tested levels of 5000 mg/kg body weight and below as consistent with a previous study of acute toxicity (Nanthini *et al.*, 2014; Olaniyan *et al.*, 2015; Porwal *et al.*, 2017). Since the LD50 test of hydromethanolic leaf extract of *Maerua angolensis* could not reveal dreadful outcomes from all doses subjected, then it can be postulated that the compounds in the extract probably do not express any deleterious effects in rats.

REFERENCES

- Adamu, A., Abdurrahman, E. M., Ibrahim, H., Abubakar, M. S., Magaji, M. G. and Yaro, A. H. (2007). Effects of Aqueous-Methanolic Stem-Bark Extract of *Maerua Angolensis* DC on Acute and Sub-Acute Inflammations. *Nigerian Journal of Pharmacological Sciences*. 6(2): 1-6
- Ahn, K. (2017). The Worldwide Trend of Using Botanical Drugs and Strategies for Developing Global Drugs. *BMB Reports Journal*. 50 (3): 111-116.
- Amina, S. Y., Ibrahim, S., Yusuf, H. and Ibrahim, L. K. (2017). Phytochemical Screening and Antibacterial Activity of *Acalypha Wilkesiana* and *Maerua Angolensis*. *Journal of Pharmaceutical, Chemical and Biological Sciences*. 5(2): 103-107
- Ayo, R. G., Audu, O. T., Amupitan, J. O. and Uwaiya, E. (2012). Phytochemical Screening and Antimicrobial Activity of Three Plants Used in Traditional

CONCLUSION

Because the hydromethanolic leaf extract of *Maerua angolensis* contains some essential phytochemical constituents needed in the management of various ailments coupled with its non-toxic potential, the extract is therefore considered to be relatively safe for use.

RECOMMENDATIONS

Because our findings are essentially preliminary and could benefit from further investigations, the following recommendations are made;

1. Quantitative phytochemical screening be carried out on the hydromethanolic leaf extract of *Maerua angolensis*
2. A sub-acute and chronic toxicity evaluation experiment be conducted for histopathological examination of cells and to determine long-term effects of the hydro methanolic leaf extract of *Maerua angolensis*.
3. Further toxicity study should be considered using different animal models.

Medicine in Northern Nigeria. *Journal of Medicinal Plants Research*. 7 (5): 191-197.

Bissinger, R. (2014). Effects of Saponin on Erythrocyte Surface. *International Journal of Haematology*. 100 (1): 51-59.

Burkhard. M. J., Brown, D. E., McGrath, J. P., Meador, V. P., Mayle, D. A., and Keaton, M. J. (2001). Evaluation of the Erythroid Regenerative Response in two Different Models of Experimentally-Induced Iron Deficiency Anaemia. *Veterinary and Clinical Pathology*. 30:76-85.

Charles, K.B., Robert, P.B., Augustine, T., Felix, A. A., Donathus, W. A., Jonathan, J. and Eric, W. (2018). *Maerua Angolensis* Stem Bark Extract Protects against Pentylentetrazole-Induced Oxidative Stress and Seizures in Rats. *Evidence Based Complementary and Alternative Medicine Journal*. Hindawi: 14.

- Cock, J.E (2015). The Safe Usage of Herbal Medicine. *Pharmacognosy*. 5(1):2-50.
- Damodara, K. M. (2013). Ethanolic Extract of *Nardostachys Jatamansi* Potentiates Haematopoietic System in Albino Wistar Rats. *Universal Journal of Health Science*., 3(1): 25-29.
- Earnest, O. A., Chibueze, P. I. and Emmanuel, E. I. (2018). Advances in Acute Toxicity Testing: Strengths, Weaknesses and Regulatory Acceptance. *Interdisciplinary Toxicology*. 11(1):5-12.
- Edeoga et al., (2005). Phytochemical Constituents of some Nigerian Medicinal Plants. *African Journal of Biotechnology*. 4(7).
- El-Nawawy, A., Barakat, S., Elwalily, T., Abdel, M., Deghady, A. and Hussein, M. (2002). Evaluation of Anaemia in Severe Under Nutrition in Protein Energy Malnutrition. *East Mediterranean Health Journal*. (2-3): 281-9.
- Erica, C. L., Cristopher, D. P., Prem, P. R., Teatulohi, K. M., Pius, P., Michael, R. F. and Louis, R. B. (2016). Traditional Preparations and Methanol Extracts of Medicinal Plants from Papua New Guinea Exhibit Similar Cytochrome P450 Inhibition. *Evidence Based Complementary Alternative Medicine Journal*. Doi: 10/155/2016/7869710 PMID:27642356
- Fateemah, J. K., Zahra, L. and Hossein, A. K (2018). Medicinal Plants: Past History and Future Perspectives. *Journal of Herbal Medicine Pharmacology*. 7(1): 1-7.
- Gbolahan, D. (2001). Lesson Note on Medical Importance of Trace Elements. Centre for Natural Health Studies.
- Iliya, H. A., Boakye-gyasi, E., Adongo, W. D., Ampadu, F. A. and Woode, E. (2016). Antinociceptive Activity of Various Solvent Extracts of *Maerua Angolensis* DC Stem Bark in Rodents. *Phytopharmacology Journal*. 13: 1 - 8.
- Krishniah, D., Devi, T., Bono, A. and Sarbatly, R. (2009). Essential Oil Composition of *Ocimum Bacilucum L.*, *O. Graticimum L* and *O. Suave*. *Journal of Medicine and Plant Research*. 3(2): 67-72.
- Latham, P. (2007). Plants Visited by Bees and Other Useful Plants of Southern Tanzania. 3rd Edition. Tanzania. 216.
- Lee, G. J., Cho, I. A., Kang, K. R., Kim, D. K., Sohn, H. M., You, J. W., Oli, J. S., Seo, Y. S., Yu, S. J. and Kim, C. S. (2014). Biological Effects of Herbal Plant-Derived Phytoestrogen in Primary Rat Chondrocytes. *Bio-Pharmacological Bulletin*. 38: 1199-1207
- Magaji, M. G., Yaro, A. H., Adamu, A., Yau, J., Malami, S., Abubakar, Y. and Hussaini, I. M. (2009). Some Neuropharmacological Studies on Hydroalcoholic Extract of *Maerua Angolensis* in Mice and Chicks. *International Journal of Pure and Applied Science*. 3: 14-21.
- Maheshwari, G. G. and Shaikh, N. K. (2016). An Overview of Toxicity Testing Method. *International Journal of Pharmaceutical Technology*. 8(2): 3834-3849.
- Majid, A., Malik, M. R., Junaid, A. S., Kamran, K., Muhammad, A. A., Imran, Z., Zakir, U., Muhammad, I. and Qamar, Z. (2013). Invitro Antibacterial Activity of *Camellia Sinensis* Leaf Extract to Some Selective Pathogenic Bacterial Stains. *International Journal of Biosciences*. 3(9): 69-75
- Mohammed, A., Tanko, Y., Okasha, M. A., Sadiq, Y. and Isa, A. I. (2008). Effects of Aqueous-Methanolic Stem-Bark of *Maerua Angolensis* Extract on Blood Glucose Levels of Streptozocin-Induced Diabetic Wistar Rats. *Research Journal of Pharmacology*. 1 (4): 75-78.
- Mothanna, R. A., Lindequist, U., Gruenert, R. and Bedmerski, P. J. (2009). Studies of the Invitro Anticancer, Antimicrobial and Antioxidant Potentials of Selected Yemeni Medicinal Plants from the Island Soqotra. *BMC Complementary and Alternative Medicine Journal*. 9(1): 7.
- Nanthini, K., Kadarkarai, K. and Venkatachalam, K. (2014). Acute and Subacute Toxicity Study of Siddha Drug Mandoora Chooranam. *International Journal of Pharmaceutical and Biological Achives*. 5(2): 86-91.

- Nasima, A., Raghieb, A., Abdul, W. M., Mostafa, C. G. M., Sakhi, C. and Hai, M. A. (2003). Relationship Between Zinc and Anaemia in Chronic Haemodialysis Patients. *Journal of Teachers Association. RMC.* 16 (1): 1019-8555.
- Nath, K. A. (2015). Evaluation of Glomerular Hyperfiltration and Albuminuria in Sickle Cell Disease Adolescents. *Nature Reviews Nephrology.* 11:161-171.
- Ogbe, R. J., Adoga, G. I. and Abu, A. H. (2010). Antianemic Potentials of Some Plant Extracts on Phenylhydrazine-Induced Anaemia in Rabbits. *Journal of Medicinal Plants Research.* 4(8): 680-684.
- Okwu, D.E. (2001). Evaluation of the Chemical Composition of Indigenous Spices and Flavouring Agents. *Global Journal of Pure and Applied Sciences.* 7(3): 455-459.
- Olaniyan, J. M., Hadiza, L. M., Hussaini, A. M., Musa, B. B. and Abubakar, S. A. (2015). *Journal of Acute Diseases.* 5(1).
- Ondiek, J. O., Abdulrazaq, S. A. and Njoka, E. N. (2010). Effects of Supplementing Chloris Gayana Hay and Maerua Angolensis with Graded Levels Maize Germ Meal on Voluntary Feed Intake, Diet Digestion, Nitrogen Balance and Average Daily Gains of Growing Small East African Goats. *Animal Nutrition and Feed Technology Journal.* 10: 147-155.
- Oyewole, O. I. and Akingbala, P. I. (2011). Phytochemical Analysis and Hypolipidemic Properties of *Jatropha Tanjorensis* Leaf Extract. *European Journal of Medicinal Plants.* 1(4):180-185.
- Porwal, M., Najam, A. K. and Kmal, K. M. (2017). Evaluation of Acute and Subacute Oral Toxicity Induced by Ethanolic Extract of *Marsdenia tenacissima* leaves in Experimental Rats. *Scientia Pharmaceutica.* 85, 29.
- Priyarka, P. B. and Pathiks, B. (2013). Terpenes: Chemistry, Biological Role and Therapeutic Applications. Natural Product. Pp 2665-2691
- Saganuwa, S. A. (2016). Toxicity Study of Drugs and Chemicals in Animals: An Overview. *British Journal of Veterinary Medicine.* 1311-1477.
- SEPASAL (2012). *Maerua Angolensis*. Survey of Economic Plants for Arid and Semi Arid Lands; Database. Royal Botanic Gardens, Kew, Richmond, U. K.
- Subramani, S. and Casmir, C. A. (2002). Flavonoids and Antioxidant Activity of Georgia Grown *Vidalia* Onions. *Journal of Agricultural and Food Chemistry.* 50(19): 5338-5342.
- Upadhyay, S. O. and Dixit, M. (2015). Role of Polyphenols and Other Phytochemicals on Molecular Signalling. *Oxidative Medicine and Cellular Longevity Journal.* 504253
- Yadav, D., Tiwari, A., Mishara, M., Subramanain, S. S., Usha, S.B., Sunil, M., Bisen, P.S. (2014). Antihyperglycaemic and Antihyperlipidaemic Potential of a Polyherbal Preparation 'Diabegon' in Metabolic Syndrome Subject with type 2 Diabetes. *African Journal of Complementary and Alternative Medicine.* 11(2):249-256.
- Yuet, P. K., Darh, I., Chen., Sreeeramana, S. and Sasidharam, S. (2013). Acute and Subchronic Toxicity Study of *Euohorbia Hirta* L Methanolic Extract in Rats. *Biomedical Research International Journal.* Article ID 182064.
- Yusuf, A. S., Sada, I., Hassan, Y. and Kane, I. L. (2017). Phytochemical Screening and Antibacterial Activity of *Acalypha wilkesiana* and *Maerua angolensis*. *Pharmaceutical, Chemical Biological Sciences Journal.* 5 (2): 103-107
- Whitney, E. N. and Rolfes, S. R. (2001). *Understanding Nutrition: 9th Edition* Wadsworth/Thomson Learning, Belmonty. USA. 355-457. *Bukina Faso. International Journal of Pharmacology,* 6(6): 880-887.