ISSN: 2536-7153 SJMLS

Sokoto Journal of Medical Laboratory Science 2022; 7(3): 8 - 16

SJMLS - 7(3) - 001

# Acute and Sub-acute Oral Toxicity of the Methanol Extract of *Adansonia digitata Fruit Pulp.*

*Adebisi, I.M. *[1], Mansur, Y.[1], Fajobi, S.J.[2], Ugwah-Oguejiofor, C.J.[1], Abubakar, K.[1]*
Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University, Sokoto [1], Department of Pharmacy, Specialist Hospital, Sokoto [2].
*Author for Correspondence*:* alaniyab@yahoo.com/+234-803-360-4511/ ORCID *Number: 0000-0003-2140-6897*
https://dx.doi.org/10.4314/sokjmls.v7i3.2

***Abstract***

Most rural and urban-based communities in Africa rely on traditional remedies for their primary healthcare. One probable reason for this is the assumption that they are free of harmful side effects and toxicity, compared to orthodox drugs. However, very few plants have been thoroughly evaluated for their toxic effects. *Adansonia digitata (A. digitata*) also known as (Baobab) is a member of the Malvaceae family. Almost all components of the tree are utilized in traditional African medicine. The present study evaluated the potential toxicity of methanol extract from the fruit pulp of *Adansonia digitata* through acute and sub-acute oral administration in rats. The acute oral toxicity study was done according to Organization of Economic Co-operation and Development (OECD) guidelines no 425 using a limit dose of 2000 mg/kg body weight (BW). Sub-acute oral toxicity using (250, 500, and, 1000 mg/kg BW) was performed by daily administration for 28 days according to the OECD guideline 407. The acute toxicity study revealed no lethal effects and behavioral signs of toxicity at the tested dose indicating that $LD_{50}$ is greater than 2000 mg/kg. In the sub-acute study, no significant difference was observed in the body weight, organ weight, liver, and kidney parameters in all treated groups compared to the control. A non-significant decrease in packed cell volume (PCV) was observed across the groups. Also, a significant increase in the white blood cell count and a decrease in the lymphocyte count occurred in the group treated with 250 mg/kg BW. These results show that methanol extract of *Adansonia digitata* fruit pulp is generally safe on short-term use but can cause changes in haematological parameters on long-term use.

***Keywords***: *Adansonia digitata, Toxicity, Sub-acute, Baobab*

## Introduction

Herbal treatments have become increasingly popular around the world because they are being utilized not only for the basic healthcare of the poor in third-world countries but even in developed nations with sophisticated healthcare systems (Elekwa *et al*., 2017). Natural chemicals have been thoroughly investigated in the search for new drug candidates; they have served as sources of antibiotics, antineoplastic, analgesic, cardioprotective, and other medications for over 5000 years (Anand *et al*., 2019). More than 50% of Food and Drug Administration (FDA)-approved medications are from natural products and their derivatives (Anand *et al*., 2019). Despite the vast array of pharmaceutical drugs in clinical use today, most rural and urban-based communities in Africa still rely on traditional remedies for their primary healthcare. (Nyakudya *et al*., 2020). Many ailments have been treated with medicinal plants, and there are growing calls around the world, particularly in Africa, to promote and incorporate traditional medicine into the conventional health systems (Shobo *et al*., 2019). One probable reason for the heightened interest in medicinal plants is the assumption that they are free of harmful side effects and acute toxicity, compared with orthodox drugs (Nyakudya *et al*.,2020). However, the widespread and irrational use of these plant-derived medications, among other concerns, necessitates the assessment of their toxicity (Shobo *et al*., 2019).

*Adansonia digitata* (*A. digitata*) also known as (Baobab) is a member of the Malvaceae family, widely distributed in the semi-arid and sub-humid regions of Sub-Saharan Africa as well in western Madagascar. It is a multipurpose tree with a long lifespan. Its various parts are commonly used for food and medicinal purposes (Suliman *et al*., 2020). Almost all components of the tree (fruit pulp, seeds, leaves, blossoms, roots, and bark) are utilized in traditional African medicine (Cicolari *et al.,* 2020). Its leaves, fruit pulp, and seeds are all edible portions of the tree and it is one of the primary sources of food and money for the locals (Suliman *et al*., 2020). Dry savannah, dry woods, and human settlements are all common habitats for the Baobab tree and it is an important part of the agricultural landscape in locations where it grows naturally (Braca *et al.,* 2018).

Various parts of *A. digitata* have traditionally been employed in the management of dysentery, diarrhoea, dehydration, ulcer, urinary difficulties, fever, skin problems, anaemia, and malaria in various countries. In pharmacological studies, it has been proven to be an analgesic, antilipidemic, hypoglycemic, antimicrobial, anti-obesity, cardioprotective, and hepatoprotective agent (Suliman *et al*., 2020). According to Ebaid and his Colleagues, Baobab leaf extract has powerful antioxidant and anti-inflammatory properties that could help to forestall inflammation-induced cancer (Ebaid *et al*., 2019). Baobab leaves have also been used as an antipyretic or febrifuge in traditional medicine (Braca *et al.,* 2018). Previous studies have determined that methanolic extracts of several portions of the tree exhibited a substantial free radical scavenging activity that was linked to their phytochemical contents; suggesting that the extracts could be used to make antioxidant medications for the treatment of a variety of illnesses (Ebaid *et al*., 2019).

The Baobab fruit pulp has been shown in biological research to have antidiabetic and anticancer properties (Braca *et al.,* 2018). Additionally, several parts of the tree have been reported to have immunostimulant, insect-repellent, and pesticide qualities (Ebaid *et al*., 2019).

The fruit pulp of *A. digitata* is a rich source of aromatic compounds, minerals, organic acids especially ascorbic acid, amino acids including; alanine, arginine, glycine, lysine, methionine, proline, serine, and valine, vitamins including; B1, B2, B3, beta carotene and vitamin C, triterpenoids including; beta-sitosterol, beta-amyrin, alpha-amyrin and ursolic acid (Suliman *et al*., 2020). When compared to vegetables and other fruits, the fresh fruit pulp of indigenous Baobab trees contains a significant level of vitamin C (Evang *et al*., 2020). The Baobab fruit pulp has been reported to contain more vitamin C than other fruits as well as calcium, iron, and magnesium (Braca *et al.,* 2018). Also, its leaf extract contains ten times the antioxidative power of vitamin C (Ebaid *et al*., 2019). A study showed that baobab pulp is a nutritious, natural, and economical source of vitamin C, with beneficial effects on the iron status of Nigerian school children (Evang *et al*., 2020). The Baobab fruit pulp is also high in polyphenolic chemicals, which may help to protect against oxidative stress (Braca *et al.,* 2018).

Its leaves include a diverse range of reducing sugars, flavonoids, terpenoids, saponins, tannins, alkaloids, anthraquinones, steroids, resins, phenols, and cardiac-active glycosides, according to a recent phytochemical investigation (Ebaid *et al*., 2019). In a phytochemical analysis of a Nigerian Baobab fruit pulp, hydroxycinnamic acid glycosides, iridoid glycosides, and phenylethanoid glycosides were isolated (Braca *et al.,* 2018).

Despite the numerous pharmacologic and economic benefits of *A. digitata*, its toxicity profile is largely unexplored. Thus, we report the acute and sub-acute toxicity profile of the dried methanolic extract of *A. digitata* in this study.

## Materials and Methods

### Study Location

The study was conducted at the Department of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University, Sokoto, Nigeria.

***Plant Collection, Identification, and Authentication***

The fruit pulp of *A. digitata* was purchased from Sokoto central market, Sokoto State. It was identified and authenticated at the Herbarium unit, Department of Pharmacognosy and Ethnopharmacy, Faculty of Pharmaceutical Science, Usmanu Danfodiyo University with the specimen voucher number PCG/UDUS/Bomb/0001.

***Plant Extraction Procedure***

The fruit pulp was ground into powder using a mortar and pestle. The seeds were separated from the pulp using a mesh. The fineness of the powdered pulp was achieved by sieving through a clean white muslin cloth allowing the fiber to be completely removed. The powder was extracted through maceration for three days using 80% methanol, and the extract was then dried over a water bath at 45°C.

***Experimental Animals***

Thirty (30) female albino rats weighing between 100 to 120g were purchased from the Faculty of Pharmaceutical Sciences, Ahmadu Bello University Zaria. The animals were housed in well-ventilated cages in the animal house of the Department of Pharmacology, Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University Sokoto. The rats were allowed to acclimatize for two weeks before the experiment and had access to food and clean water. Principles of laboratory animal care and ethical guidelines for the investigation of experimental pain in conscious animals were observed during the study. Before the commencement of the study, the animals were examined physically and found to be in a very good state of health. Ethical approval was obtained from the institutional ethics committee for the use of laboratory animals with approval number (PTAC/Ad/(Me)OT/45-22).

***Acute oral Toxicity study***

The acute oral toxicity study was done using the "Up and Down method" in healthy adult female albino rats according to OECD guidelines no 425 (OECD, 2008). A limit dose of 2000 mg/kg was used for the study. Five female rats were used for the study. Oral administration of the drug was done using a gastric feeding tube. Each animal was observed after dosing for the first 5 minutes for signs of regurgitation and then kept in a metallic cage. Each was then observed every 15 minutes in the first 4 hours after dosing, then every 30 minutes for 6 hours, and then daily for 48 hours for the short-term outcome according to the specifications of the OECD. The animals were monitored for a total of 14 days for the long-term possible lethal outcome.

***Sub-acute Toxicity Study***

Sub-acute oral toxicity study was performed according to the Organization of Economic Co-operation and Development (OECD) guideline 407 for testing of chemicals (OECD, 2008). The animals were divided into four experimental groups (n=6 animals per group). Three different doses (250 mg/kg, 500 mg/kg, and, 1000 mg/kg) were administered orally for 28 consecutive days. The control group received only the vehicle (distilled water). During treatment, weekly body weight, possible signs of toxicity, and mortality were observed and monitored.

***Sample Collection***

All surviving animals were fasted overnight and anesthetized at the end of the study. Blood samples were collected through cardiac puncture into EDTA-containing sample bottles for the determination of haematological parameters while plain bottles were used for collection of blood samples meant for the determination of clinical blood chemistry. The rats were euthanized after blood collection and the internal organs (heart, liver, spleen, kidney, pancreas, testes/ovaries, and lungs) were harvested and weighed to determine the relative organ weights. The organs were also observed for any gross lesions.

***Haematological analysis***

Haematological parameters were determined in blood samples using a Mythic 22 CT C2 Diagnostic Analyzer (Orphée, SA, Switzerland). The parameters determined include total white blood cell count (WBC), differentiated neutrophils (NEU), monocytes (MON), lymphocytes (LYM), eosinophils (EOS), and basophils (BAS), the percentage of total blood volume occupied by red blood cells (packed red blood cell volume, PCV), Platelet count (PLT) and reticulocyte count.

***Biochemical analysis***

Serum biochemical parameters measured include: alanine amino-transaminase (ALT) aspartate aminotransaminase (AST), Alkaline phosphatase (ALP), total protein, bilirubin, glucose, Chromium, urea, sodium, potassium, and chloride. They were analyzed in a BS-200 Chemistry Analyzer (Shenzhen Mindray Biomedical Electronics, Shenzhen, China).

**Data Analysis**

The result generated was analyzed using Graph Pad Prism software version 8.0. One-way analysis of variance (ANOVA) was used to compare the test and control, followed by Dunnet's post hoc test. Results were expressed as mean plus or minus standard error of the mean (SEM). A p-value of $<0.05$ was considered significant.

***Results***

***Acute oral toxicity***

The methanol extract of *Adansonia digitata* orally administered at a dose of 2000 mg/kg in the female rats did not induce any death or toxic symptoms in treated rats. All animals displayed normal behavior throughout the study and survived until the end of the 14-day experiment period. During the entire observation period, they did not present any significant clinical alteration. The $LD_{50}$ of the methanol extract of *Adansonia digitata* is, therefore greater than 2000 mg/kg.

***Sub-acute oral Toxicity***

The methanol extract of *Adansonia digitata* at doses of 250, 500, and 1000 mg/kg administered to the rats daily for 28 days did not induce any death or toxic symptoms in the animals, who behaved normally throughout the study and survived until the end of the experiment (28 days). Also, no significant clinical changes were observed for the duration of the experiment.

***Effect on Body Weight and Organ Weight.***

The body weights of the experimental animals were taken weekly. There was an increase in the body weights of all the animals but there was no significant difference in the weight gain across the groups (Figures 1 and 2). Also, no significant difference was observed in the organ weights of all the animals across the groups as shown in Table 1.

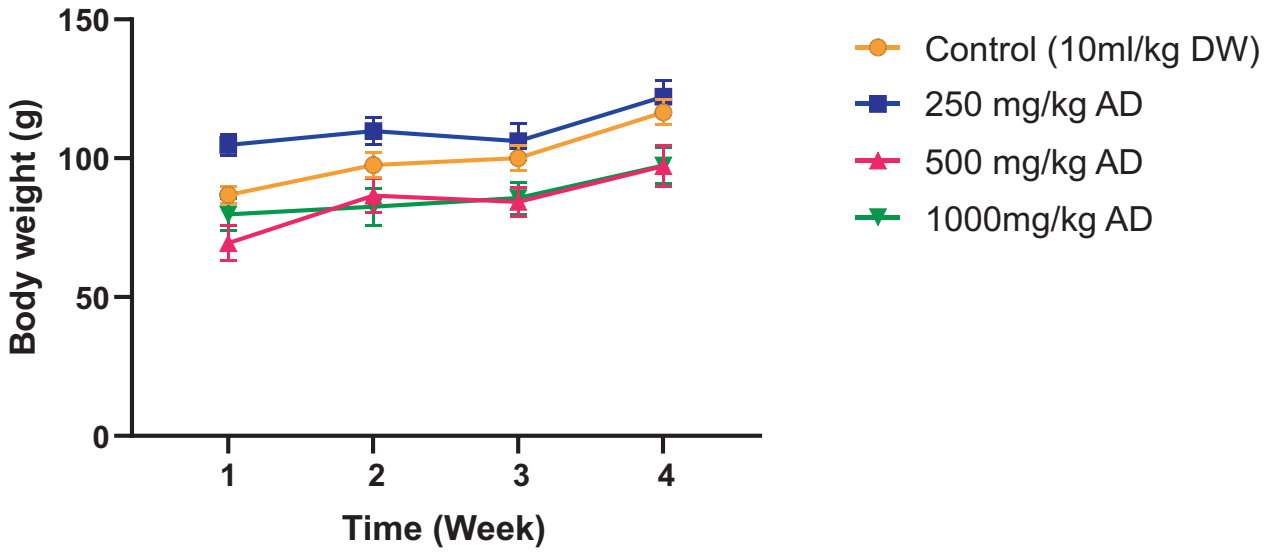


**Figure 1: Body weight of rats treated with repeated doses of methanol extract of *Adansonia digitata*. Values are presented as mean± SEM, n=6. AD= *Adansonia digitata,* DW= Distilled water.**

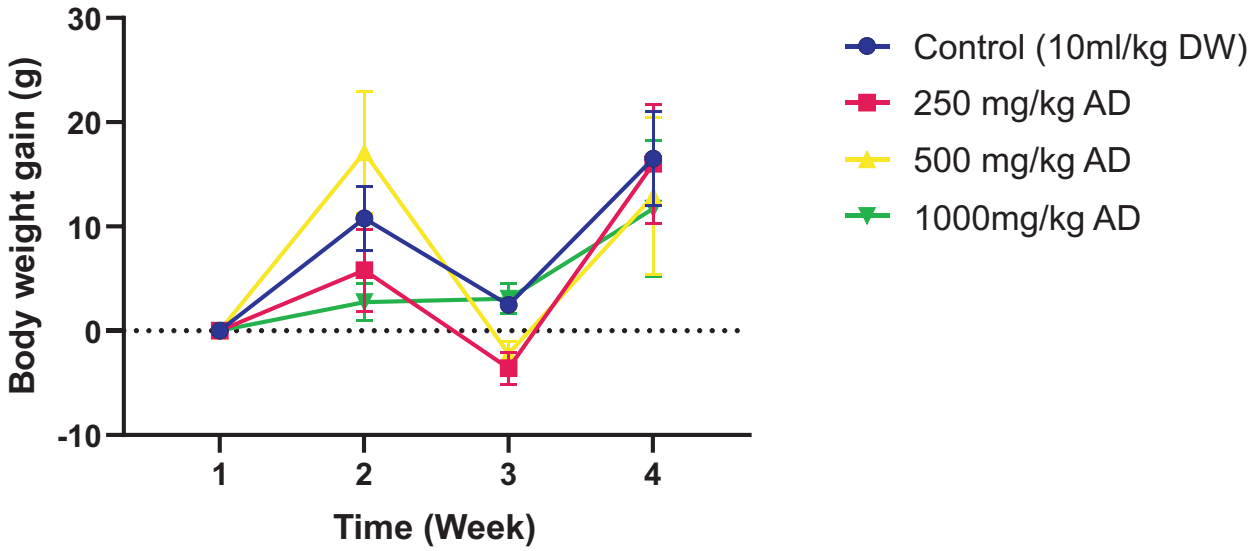


**Figure 2: Body weight gain of rats treated with repeated doses of methanol extract of *Adansonia digitata.* Values are presented as mean±sem, n=6. AD= *Adansonia digitata,* DW= Distilled water**

**Table 1: Organ weights of rats treated with repeated doses of methanol extract of *Adansonia digitata***

| Organ | Dose of *Adansonia digitata* (mg/kg Body weight) | | | |
|---|---|---|---|---|
| | **0 (Control)** | **250** | **500** | **1000** |
| Heart | 0.47±0.04 | 0.50±0.13 | 0.5±0.03 | 0.46±0.04 |
| Kidney | 0.50±0.13 | 0.54±0.06 | 0.54±0.05 | 0.51±0.04 |
| Liver | 5.11±1.36 | 5.29±0.38 | 5.30±0.41 | 5.31±0.40 |
| Spleen | 0.76±0.22 | 0.74±0.10 | 0.74±0.10 | 0.98±0.11 |
| Pancreas | 0.96±0.20 | 0.98±0.32 | 0.83±0.27 | 1.20±0.19 |
| Lungs | 0.99±0.05 | 0.90±0.29 | 0.87±0.23 | 1.17±0.10 |
| Testes | 0.38±0.08 | 0.31±0.05 | 0.30±0.06 | 0.29±0.04 |
| Ovaries | 0.02±0.01 | 0.13±0.01 | 0.06±0.04 | 0.10±0.05 |

Values are presented as Mean± SEM, n=6.

### *Effect on Haematological analyses*

The haematological parameters were estimated and there was a significant increase in the white blood cell count and a significant decrease in lymphocyte count in the group treated with 250 mg/kg extract. All the other parameters did not show any significant difference across the groups (Table 2).

**Table 2: Effect of repeated doses of *Adansonia digitata* on haematological parameters**

| Parameter | Dose of *Adansonia digitata* (mg/kg Body weight) | | | |
|---|---|---|---|---|
| | 0 (Control) | 250 | 500 | 1000 |
| WBC ($X10^3$/mm3) | 7.3±1.86 | 13.84±4.84* | 6.58±0.00 | 7.38±0.81 |
| PCV (L/L) | 39.40±1.17 | 37.41±1.47 | 34.42±2.78 | 36.01±1.50 |
| Lymphocytes ($x10^9$/L) | 82.81±3.22 | 57.23±14.20* | 82.8±2.33 | 79.23±2.48 |
| Monocytes ($x10^9$/L) | 2.80±1.02 | 1.60±1.12 | 2.81±1.63 | 2.84±1.63 |
| Basophils | 0 | 0 | 0 | 0.2±0.02 |
| Eosinophils | 0 | 0 | 0.2±0.2 | 1.6±1.36 |
| Platelet ($x10^9$/L) | 103.34±20.50 | 126.40±37.20 | 87.25±43.36 | 68.45±23.99 |
| RTC (%) | 1.42±0.40 | 1.64±0.45 | 1.06±0.37 | 1.64±0.24 |
| Neutrophils ($x10^9$/L) | 16.41±3.12 | 37.60±16.48 | 14.2±2.31 | 17.62±2.06 |

Values are presented as Mean± SEM, n=6. *= significant at $p < 0.05$. N = 6

WBC= White blood cell, PCV=Packed cell volume, RTC= Reticulocyte

***Effect on Biochemical analyses***

The biochemical estimation of the blood was conducted to assess the effect of the extract on the liver and kidney. No significant difference was observed in all the measured parameters (Table 3).

**Table 3: Effect of repeated doses of *Adansonia digitata* on biochemical parameters**

| Parameter | Dose of *Adansonia digitata* (mg/kg Body weight) | | | |
|---|---|---|---|---|
| | 0 (Control) | 250 | 500 | 1000 |
| ALT (IU/L) | 141.20±15.12 | 180.21±36.65 | 154.80±12.67 | 106.21±21.13 |
| AST (IU/L) | 2.48±0.36 | 2.50±0.22 | 2.60±0.18 | 2.76±0.21 |
| TP (g/L) | 0.14±0.40 | 0.14±0.03 | 0.10±0.01 | 0.13±0.03 |
| ALP (IU/L) | 794.30±161.89 | 952.60±12.93 | 927.42±79.03 | 894.21±164.84 |
| Total protein | 0.136±0.04 | 0.142±0.03 | 0.094±0.03 | 0.134±0.03 |
| Bilirubin (mol/L) | 1.65±0.17 | 1.11±0.06 | 1.12±0.25 | 1.7±0.29 |
| Glucose (mmol/L) | 4.72±0.88 | 2.78±1.18 | 2.04±0.86 | 3.82±0.18 |
| Chromium (mmol/L) | 0.86±0.11 | 0.76±0.10 | 0.86±0.14 | 0.92±0.11 |
| Urea (mmol/L) | 4.04±0.27 | 3.76±0.29 | 4.68±0.14 | 3.74±0.68 |
| Potassium (mmol/L) | 4.46±0.26 | 2.72±0.20 | 4.75±0.21 | 4.46±0.14 |
| Chlorine (mmol/L) | 102±0.84 | 99.80±1.60 | 101.01±0.95 | 101.80±0.92 |
| Sodium (mmol/L) | 140.20±0.84 | 138.40±0.51 | 138.45±0.75 | 1421.40±0.51 |

Values are presented as Mean± SEM, n=6. ALT=Alanine aminotransaminase, AST=Aspartate aminotransaminase, ALP=Alkaline phosphatase, TP=Total protein

**Discussion**

Considering the numerous potentials of *Adansonia digitata* as an alternative medicine effective for a wide range of diseases and its nutritional value, it is only pertinent that a safety profile of the plant is established as a guide for the management of its applications and usage in herbal medicine. This should serve to prevent exposing human subjects to potential toxicity-related health risks. Herbal products made from medicinal plants are falsely believed to be safe with no adverse health effects; however, there has recently been growing concern about their safety (Mensah *et al*., 2019). Furthermore, medicinal herbs are usually self-prescribed by the consumers and there is a lack of control and review in terms of dose, manner, and frequency of administration. Therefore, evaluating the toxicological effects of many medicinal plant extract intended to be used in animals or humans is a crucial part of its assessment for potential toxic effects. Hence, this study focused on assessing the toxicity of an herbal plant, *Adansonia digitata* which has extensively been used in West Africa for its ethnomedicinal properties.

The preliminary step in the screening of pharmacological activity is the evaluation of toxic features of the plant extract or isolated compounds. In animal research, acute toxicity provides information that can be utilized to classify, label, and calculate the dose of a novel chemical. In the current study, the acute dosing of methanol extract of *Adansonia digitata* i.e. 2000 mg/kg body weight is found to be safe as no mortality or any significant clinical changes occurred, therefore an acute $LD_{50}$ of *Adansonia digitata* in rats was determined to be greater than 2000 mg/kg body weight.

Evaluation of repeated dosing toxicological studies is important because a frequent (*e.g* daily) use of a substance in the course of disease treatment may lead to drug accumulation which may impair the functioning of some target organs. Therefore, sub-acute toxicity testing is essential in assessing the impact of the substance on the target organ and repeat-dose toxicity studies are actually the backbone of the pre-clinical drug development program (Faqi, 2013). The design of our 28 days repeated toxicity study was based on $LD_{50}$ dose and three different doses (250, 500, and 1000 mg/kg) representing low, medium, and high doses, respectively, were examined.

Throughout 28 days of observation, rats in this present study showed no mortality nor were signs of behavioral changes or abnormalities detected. Also, no significant difference was observed in the body weights and organ weights of the animals in the control and treated groups. Bodyweight and organ weights are some of the parameters used for evaluating the health status of experimental animals which could reflect toxicity (Raza *et al*., 2002). Weekly body weights recorded in this study showed no significant changes ($p>0.05$) between the control and all treated groups. Organ weight is also an important index of physiological and pathological status. The relative organ weight is fundamental to evaluate whether the organs were injured or not. Organ relative weight is used to evaluate organ injury (Kyolo *et al*., 2019). Throughout the study, regardless of the dose used (250, 500, or 1000 mg/kg), *Adansonia digitata* extract did not appear to affect the organ weight of the rats. This indicates that the administration of extract has a negligible level of toxicity on the growth of the animals.

A review of the haematological results in this study showed a significant increase in WBC and a significant decrease in lymphocyte counts between rats placed on 250 mg/kg extract and the controls. A non-significant decrease was also observed in the PCV between the control and all the treated groups. Analysis of blood parameters is important in the evaluation of risks associated with test compounds under investigation as the changes in the haematological system have a greater indicative value for human toxicity, when the data are converted from animal studies (Olson *et al*., 2000). Evaluation of the haematological parameters can be used to determine the extent of deleterious effects of foreign compounds including plant extracts, on the blood constituents in animal studies. (Agbaje *et al*., 2009). *Adansonia digitata* has been shown to contain alkaloids, saponins, flavonoids, tannins and phenols (De Caluwé *et al*., 2009). These phytochemicals may have suppressed the growth and differentiation factors in the bone marrow. Another probable reason for the observed decrease in PCV may be haemolysis or failure of erythropoietin production leading to anaemia.

The application of blood serum or plasma enzymes as markers to measure organ or cell damage; enzyme induction, activation, or inhibition is becoming very common in toxicology studies. A number of blood measurements/tests could be used to assess the level of tissue damage, potential target organs, and reduced organ functions. A wide range of evaluation information might be obtained by combining these tests, indicating their physiological and metabolic processes. The liver and the kidney are target organs in toxic chemicals due to their essential functions in bodily detoxification and excretory processes. Thus, they are considered highly useful in toxicity studies because of their sensitivity to harmful compounds and their potential to predict toxicity. Therefore, it could safely be claimed that the liver and the kidneys could serve as the primary target organs in investigations related to sub-acute oral toxicity of herbal extract, therefore, estimation of some kidney and liver toxicities is of paramount importance (Abdulhamid *et al.,* 2019).

There were no significant differences ($p>0.05$) in the levels of AST, ALT, ALP, bilirubin, and total protein between the control and treated groups. Similarly, the kidney parameters measured, namely: serum urea, and electrolytes were also not significantly different across the groups, suggesting that sub-acute administration of *Adansonia digitata* did not cause any damage to the liver and kidney. The decrease in serum glucose observed in this study is consistent with the reports of Gwarzo, (2013) and Muhammad *et al*. (2016) both of whom reported that the fruit pulp of *Adansonia digitata* possesses hypoglycemic properties.

**Conclusion**

The oral $LD_{50}$ of methanol extract of *Adansonia digitata* has been shown to be greater than 2000 mg/kg and is generally considered safe. *Adansonia digitata* caused a non-significant decrease in serum glucose, hence may be hypoglycaemic. Prolonged administration revealed that it may cause elevation of white blood cells and reduced packed cell volume. It had no observed toxicity on the liver and kidney.

**Recommendation**

A more comprehensive toxicity study involving other organs and for a longer period (*e.g* 90 days) is recommended in order to further ascertain the toxicity of this plant.

**Conflict of Interest**

The authors declare no conflict of interest.

**References**

Abdulhamid, A., Ismail, A.M., Sani, I., Sulaiman, A. and Kabir, A. (2019). Acute and sub-chronic toxicity evaluation of crude methanolic leaves extract of Acacia nilotica (Linn.). *Research Journal of Medicinal Plant; **13**(**3**)*:109-118.

Agbaje, E.O., Adeneye, A.A. and Daramola, A.O. (2009). Biochemical and toxicological studies of aqueous extract of Syzigium aromaticum (L.) Merr. & Perry (Myrtaceae) in rodents. *African Journal of Traditional, Complementary and Alternative Medicines; **6**(**3**)*: :241-254.

Anand, U., Jacobo-Herrera, N., Altemimi, A., and Lakhssassi, N. (2019). A comprehensive review on medicinal plants as antimicrobial therapeutics: potential avenues of biocompatible drug discovery. *Metabolites*; ***9*(11)**:258.

Braca, A., Sinisgalli, C., De Leo, M., Muscatello, B., Cioni, P.L., Milella, L., Ostuni, A., Giani, S. and Sanogo, R. (2018). Phytochemical profile, antioxidant and antidiabetic activities of Adansonia digitata L. (Baobab) from Mali, as a source of health-promoting compounds. *Molecules; **23*(12)**:3104.

Cicolari, S., Dacrema, M., Tsetegho Sokeng, A.J., Xiao, J., Atchan Nwakiban, A.P., Di Giovanni, C., Santarcangelo, C., Magni, P. and Daglia, M. (2020). Hydromethanolic Extracts from Adansonia digitata L. Edible Parts Positively Modulate Pathophysiological Mechanisms Related to the Metabolic Syndrome. *Molecules; **25*(12)**:2858.

De Caluwé, E., Halamová, K. and Van Damme, P. (2009). Baobab (Adansonia digitata L.): a review of traditional uses, phytochemistry and pharmacology. *Afrika Focus*;***23*(1)**: 11-51.

Ebaid, H., Bashandy, S.A., Alhazza, I.M., Hassan, I., and Al-Tamimi, J. (2019). Efficacy of a methanolic extract of Adansonia digitata leaf in alleviating hyperglycemia, hyperlipidemia, and oxidative stress of diabetic rats. *BioMed*

*Research International*:2835152. doi: 10.1155/2019/2835152.

Elekwa, I., Ugbogu, A.E., Okereke, S.C. and Okezie, E. (2017). A review of selected medicinal plants with potential health benefits in South-Eastern Nigeria. *International Journal of Pharmaceutical and Chemical Sciences;* ***6*****(4)**:162-171.

Evang, E.C., Habte, T. Y., Owino, W.O. and Krawinkel, M.B. (2021). Can the supplementary consumption of baobab (Adansonia digitata L.) fruit pulp improve the hemoglobin levels and iron status of schoolchildren in Kenya? Findings of a randomized controlled intervention trial. *European Journal of Nutrition;* ***60*****(5)**:2617-2629.

Faqi, A.S. (2013). A Comprehensive Guide to Toxicology in Preclinical Drug Development. London, UK: Academic Press, Elsevier. *International Journal of Toxicology;* ***32****:*6.

Gwarzo, M.Y. (2013). Hypoglycemic Activity of Methanolic Fruit Pulp Extract of" Adansonia digitata" on Blood Glucose Levels of Alloxan Induced Diabetic Rats. *International Journal of Animal and Veterinary Advances;* ***5*****(3)**:108-113.

Khwaja, A. (2012). KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clinical Practice;* ***120*****(4):**179-184.

Kyolo, S.K., Odda, J., Lubega, A. and Bbosa, G.S. (2019). Blood Chemistry and Major Body Organ Induced-Toxicity by Locally-Made Traditional OMGKRP Karuho Poison in Wistar Albino Rats. *Neuroscience and Medicine;* ***10*****(03)**:272.

Lala, V., Goyal, A. and Minter, D.A. (2021). Liver function tests. In *StatPearls [Internet]*. StatPearls Publishing. *Advances in Bioscience and Biotechnology;* ***12(6)***.

Mensah, M.L., Komlaga, G., Forkuo, A.D., Firempong, C., Anning, A.K. and Dickson, R.A., (2019). Toxicity and safety implications of herbal medicines used in Africa. *Herbal Medicine*; ***63****:1992*.

Muhammad, I.U., Jarumi, I.K., Alhassan, A.J., Wudil, A.M. and Dangambo, M.A. (2016). Acute toxicity and hypoglycemic activity of aqueous fruit pulp extract of Adansonia digitata L. (Afpead) on alloxan induced diabetic rats. *Journal of Advances in Medical and Pharmaceutical Sciences;* ***6*****(3)**:1-6.

Nyakudya, T.T., Tshabalala, T., Dangarembizi, R., Erlwanger, K.H. and Ndhlala, A.R. (2020). The potential therapeutic value of medicinal plants in the management of metabolic disorders. *Molecules;* ***25*****(11)**:2669.

OECD (2008). *Test No. 407: Repeated Dose 28-day Oral Toxicity Study in Rodents*, OECD Guidelines for the Testing of Chemicals, Section 4, OECD Publishing, Paris, https://doi.org/10.1787/9789264070684-en.

Olson, H., Betton, G., Robinson, D., Thomas, K., Monro, A., Kolaja, G., Lilly, P., Sanders, J., Sipes, G., Bracken, W. and Dorato, M. (2000). Concordance of the toxicity of pharmaceuticals in humans and in animals. *Regulatory Toxicology and Pharmacology;* ***32*****(1)**:56-67.

Raza, M., Al-Shabanah, O.A., El-Hadiyah, T.M., and Al-Majed, A.A. (2002). Effect of prolonged vigabatrin treatment on hematological and biochemical parameters in plasma, liver and kidney of Swiss albino mice. *Scientia Pharmaceutica;* ***70*****(2)**:135-145.

Shobo, A.A., Daniyan, M.O., Olayiwola, G., Idowu, T.O., Ogundaini, A.O. and Adesanya, S.A. (2019). Toxicity evaluation of the extract and fraction of Chrysophyllum albidum seed cotyledons in rats. *SOJ Pharmacy & Pharmaceutical Sciences;* ***6****:*1-12.

Suliman, H.M., Osman, B., Abdoon, I.H., Saad, A.M. and Khalid, H. (2020). Ameliorative activity of Adansonia digitata fruit on high sugar/high fat diet-simulated Metabolic Syndrome model in male Wistar rats. *Biomedicine & Pharmacotherapy; 125:*109968.

**Citation**: Adebisi, I.M., Mansur, Y., Fajobi, S.J., Ugwah-Oguejiofor, C.J., Abubakar, K. Acute and Sub-acute Oral Toxicity of the Methanol Extract of Adansonia digitata Fruit Pulp. ***Sokoto Journal of Medical Laboratory Science*****; 7(3): 8 - 16.** https://dx.doi.org/10.4314/sokjmls.v7i3.2