Journal of Advances in Medical and Pharmaceutical Sciences

Volume 26, Issue 12, Page 43-49, 2024; Article no.JAMPS.127071
ISSN: 2394-1111

Hepatotoxicological Evaluation of *Parsonsia straminea* (R.Br) F. Muel Stem Bark Crude Extract in Mice

Ozakieoniso James Kemelayefa [a*], Bonsome Bokolo [b] and Amarachi Favour Morka [a]

[a] Department of Pharmacology and Toxicology, Faculty of Pharmacy, Niger Delta University, Wilberforce Island, Nigeria.
[b] Department of Pharmacology and Therapeutics, Faculty of Basic Clinical Science, Niger Delta University, Wilberforce Island, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: https://doi.org/10.9734/jamps/2024/v26i12730

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/127071

Original Research Article

Received: 16/09/2024
Accepted: 18/11/2024
Published: 25/11/2024

ABSTRACT

Background: Toxicity is defined as the degree to which a substance can harm humans or animals. In reality, every entity that makes substances is undoubtedly labelled poisonous except it is quantified to make safety certain for therapeutic purposes. Herbal medicines are generally considered to be safe and efficacious among people of various ethnic backgrounds globally. The plant *Parsonsia straminea* has been traditionally claimed to be used in arthritis and seizures, although it is not widely explored. *P. straminea* a plant used medicinally cannot be said to be free from toxicity owing to fact on its use.

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

Cite as: *Kemelayefa, Ozakieoniso James, Bonsome Bokolo, and Amarachi Favour Morka. 2024. "Hepatotoxicological Evaluation of Parsonsia Straminea (R.Br) F. Muel Stem Bark Crude Extract in Mice". Journal of Advances in Medical and Pharmaceutical Sciences 26 (12):43-49. https://doi.org/10.9734/jamps/2024/v26i12730.*

Aim of the Study: The aim of the study is to assess the potential hepatotoxicity of *P. straminea* stem bark extract in mice
Methodology: For the study, about thirty rodents (mice) were set into six groups with five (5) mice in each group. The study groups (GPs) include 1=0.2 ml/kg of distilled water as control; 2 to 6=50,100, 200, 400 and 800 mg/kg of *P. straminea* extract. The harvested tissues were sent for histopathological examination.
Results: This study has proven that the extract relatively impacted no significant toxicity on the liver enzymes such as alanine aminotransferase (ALT), alkaline phosphatase (ALP), albumin (ALB) aspartate aminotransferase (AST) and total protein (TP).
Conclusion: The study findings have shown that the ethanolic stem bark of *P. straminea* possesses relatively no remarkable toxicity impact on the liver as revealed in the liver enzymes and the histology assessment.

Keywords: Toxicity; liver; P. straminea; liver enzymes; histology.

1. INTRODUCTION

Every substance applicable as food or medicine needs to be assessed for its safety in both the human and non-human population in order to be accepted as medicine or food.
Thus, this study tends to provide more information about the safety of *Parsonsia straminea* (R.Br.) F. Muell on the hepatic system that can project short- and long-term use either topically or orally (WHO, 2017). Toxicity is defined as the degree to which a substance can harm humans or animals. It refers to the quality, relative degree, or specific degree to which a substance is highly averse to physiological events. Every consumable including edible substances are potential poison depending on the dose and range of exposure (Aleksunes and Eaton, 2019). It has been considered and accepted by the majority of traditional medicine users that plants with medicinal values are safer, though they may be characterized with little toxic potential that must be identified in other further guide users and enhance the alternative medicine practice, especially in the developing nations (Boukandou et al., 2015). This claimed toxicity related to medicinal plants may differ from species to species and from geographical locations, as they greatly play a phytoconstituent role that defines the toxicity profile of individual plants (Ferreira-Machado et al., 2004). However safe a plant based traditional medicine, maybe the quantification as dose for the right disease state should be prioritized to improve positive treatment outcome and avoid product induced toxicity and mortality (Tamokou and Kuete, 2014). The plant *P. straminea* has little or no ethno pharmacological records (Kemelayefa et al., 2022). The plant was accidently identified by means of local use for seizure control in the Wilberforce Island of Bayelsa State, Nigeria. Thus, this study is aimed at the screening for *P. straminea* stem-bark hydro-ethanol extract possible toxicological impact on the hepatic tissues. *P. straminea,* also known as silk pod or “monkey rope”, known to be a woody vine of the dog-bane family of *Apocynace*, "*P. straminea*" as described from the publication of Australian Plant Name Index (APNI, 2009). It occurs in the states of New South Wales and Queensland in Australia. *Parsonsia species* of woody climbing vines in eastern Australia: Family *Apocynaceae.* It has been recorded in some parts of the world to be relatively toxic with unknown toxins; some literature is pointing that the possible toxicity claim could be linked to the presence of cardiac glycosides in the *Apocynaceae* family. Other species of *Parsonsia* like the *euclyptophylla* also referred to “gargaloo” and “monkey vine” are given as feed to cattle and sheep without any toxicity record observed (Everist 1981, Everist 1985). The claim that *P. straminea is* responsible for the death of sheep and cattle (McBarron 1978) is inconsistent with other literature (Everist 1981, Everist 1985) as well our previous phytochemical work *P.straminea* that is yet to be published. However, some other claims of toxicity signs recorded in ruminant animals include interstitial-oedema and hemorrhage of the heart and lung congestion without scientific evidence of the cause in all acclaimed cases. The main constituents responsible for the toxicity of *P. straminea* are pyrrolizidine alkaloids (PAs) particularly lycopsamine and its N-oxide (Smith and Culvenor 1981). These alkaloids are present primarily as N-oxides in the plant, accounting for up to 99% of the total PAs in the pods (Edgar et al., 2011). PAs are known to be hepatotoxic, causing liver damage (Hunter et al., 1997). This study evaluated the single and repetitive (14 days) treatment through the oral route to determine toxicity potential of *P. straminea* in the liver using mice as the subject of interest.

2. METHODS

2.1 Plant Identification, Authentication and Crude Drug Preparation

The plant *P. straminea* was, identified by Dr. Gideon Alade and authenticated by Prof. Kola Ajibesin of the Department of Pharmacognosy and Herbal Medicine, Faculty of Pharmacy, Niger Delta University followed by Herbarium deposition number NDUP/21/001. *P.straminea* stem-bark was harvested from the Wilberforce Island rainforest. In preparation for the extraction, the stem bark of *P.straminea* was washed with clean water and air dried under 16^{o}c temperature in a clean and dust free room, afterwards it was reduced to smaller pieces and grinded. Weight of 200g of the stem bark was taken for maceration in hydro-ethanol of 1000 ml. The maceration stands for 72 hrs with daily manual shaking. After 72 hrs maceration, filtered and concentrated at 45^{o} C using rotary evaporator and water bath to make dry extract.

2.2 Experimental Animal

In this study, the animal subject of interest was male mice and was obtained from the animal house of the Department of Pharmacology and Toxicology, Niger Delta University, Nigeria, with all handling conditions strictly adhered to (NIOSH) (1998).

2.3 Study Design

The study was designed as a sub-acute study that lasted for 21 days. About 30 mice were randomly allocated into six groups (n=5). Group one (1) treated with 0.2 mg/kg of distilled water daily as normal control. Group (2) was treated with 50 mg/kg of *P. straminea* daily; group three (3) was treated with 100 mg/kg *P. straminea* daily; group four (4) 200 mg/kg daily of *P. straminea*; group five (5) treated with 400 mg/kg daily of *P. straminea*; and group six (6) was treated with 800 mg/kg daily of *P. straminea*. The animals were sacrificed 18 hours later. At the sacrifice, the blood was collected from the individual animal for liver enzyme assay. The blood was separated using a blood centrifuge to obtain the serum. The serum was contained in their respective labeled container with regards to their groups. The serum samples that was obtained were sent to the laboratory for liver enzyme assay. The liver was excised and rinsed with normal saline before it was placed into a 10% formal saline solution in labeled containers according to their groups.

2.3.1 Determination of liver function biomarkers

Determination of alanine aminotransferase (ALT) activities: The method adopted to quantify the enzyme alanine aminotransferase (ALT) in the mice serum in this research was described by Reitman and his colleague Frankel (Reitman 1957) using Randox kits.

The serum obtained from each animal in all the groups was used in the determination of ALT level. For the determination of ALT in each sample, about 0.2 mL of serum was dispensed into a 5 mL capacity test tube in which 1 mL of ALT buffered substrate (Randox) was added. This mixture was incubated for 30 minutes at 37^{o}C. Afterwards, (2, 4-dinitrophenylhydrazine) a colouring agent was introduced to the mixture. This mixture was allowed to stand at room temperature (37^{o}C) for 30 minutes, and subsequently, 10 mL of 0.4N of Sodium Hydroxide was then added and allowed for 5 minutes without disturbance. The above steps were followed by replacing the serum with water (0.2 mL) as a blank. The absorbance wavelength of all mixtures in all groups were set up at 500 nm against the blank. The enzyme activities were extrapolated from the standard curve and expressed as unit/ml.

Determination of aspartate aminotransferase (AST) activity: The method adopted in the quantification of the enzyme aspartate aminotransferase (AST) in this study as described by Reitman and his colleague Frankel Reitman, (1957) was employed with modifications. The procedure is similar to that of the ALT as described above, except for the replacement of the enzyme, ALT substrate buffer with AST substrate buffer (Randox) and the incubation period was set at 60 minutes in room temperature (37^{o}C).

Determination of alkaline phosphatase (ALP) activity: Determination of ALP level was done using Reitman (1957) method similar to the ALT, and AST procedures as described above.

Determination of albumin (ALB): The level of ALB was quantified in the samples using the (Doumas et al., 1971) described method with slight modification.

Determination of total protein (TP): The level of TP was quantified in the samples using the Tietz, (1976) described method with minor modification.

2.3.2 Histological examinations

The liver tissues that were excised from the animals in this study, were taken to the histology laboratory for histological processing and the photomicrograph of each liver sample in all groups were viewed with light microscope and proper interpretation for each liver's photomicrograph was given by the histopathologist (Alturkistani et al., 2015).

2.4 Statistical Analysis

The data generated from the laboratory were analyzed using Graph Pad Prism 10.2, Two-way ANOVA and multiple comparison (Dunnett's) test was used. The analyzed data were presented as Mean ± Standard Error of Mean (SEM) format in either graph or table form with $P<0.05$ considered as significant.

3. RESULTS

3.1 Biochemical Evaluations

This study evaluated the toxicological potential of *P. straminea* stem bark crude extract, which revealed that the extract relatively impacted no significant toxicity on the liver enzymes such as alanine aminotransaminase (ALT), alkaline phosphatase (ALP), albumin (ALB), aspartate aminotransferase (AST), and total protein as shown in Table 1.

3.2 Histological Evaluations

The histological evaluation of *P.straminea* stem bark crude extract showed no remarkable toxicity impact on the cellular structure of the liver tissues in the various study groups as it is in Figs. 2 to 6.

Table 1. Sub-acute biochemical (Liver) parameters evaluation

Parameters	VEH	50 mg/kgPSE	100 mg/kgPSE	200 mg/kgPSE	400 mg/kgPSE	800 mg/kgPSE
ALT (U/L)	15.0±0.4	15.6±0.0	15.2±0.8	14.8±1.7	15.6±1.0	14.0±0.5
ALP (U/L)	21.0±0.3	20.3±0.2	21.5±1.5	20.9±0.5	19.0±1.2.0	18.0±3.0
ALB(g/dL)	3.2±0.4	3.6±0.2	2.8±0.3	3.0±0.2	3.1±0.2	3.1±0.2
AST (U/L)	67.1±5.8	65.7±1.2	70.8±0.8	68.7±1.7	68.7±0.4	72.6±2.9
TP (g/dL)	26.6±0.8	24.6±0.8	27.2±0.8	27.5±3.7	25.5±3.1	27.0±3.4

VEH=Vehicle/control, PSE= P.Straminea Stem Bark Extract. TP (g/dl) = total protein; ALT U/L) = alanine aminotransferase; ALP (U/L) = alkaline phosphatase; ALB (mg/dl) = albumin; AST (U/L) = aspartate amino transferase; (P>0.05)

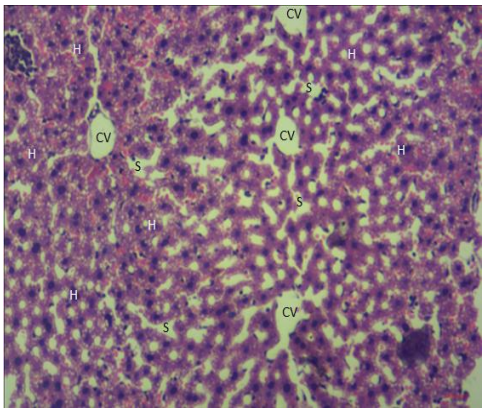

Fig. 1. VEH. Control of toxicity study group of histology showing normal liver architectural integrity. Patent central vein (CV), intact hepatocytes (H), Sinusoids (s) containing Kupffer cells & capillaries. Photomicrographs of Liver, Mag X 400 H & E

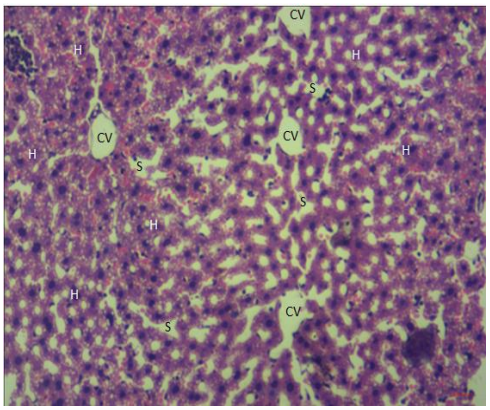

Fig. 2. 50 mg/kg PS. Extract toxicity study group of histology showing normal liver architectural integrity. Patent central vein (CV), intact hepatocytes (H), Sinusoids (s) containing Kupffer cells & capillaries. Photomicrographs of Liver, Mag X 400 H & E

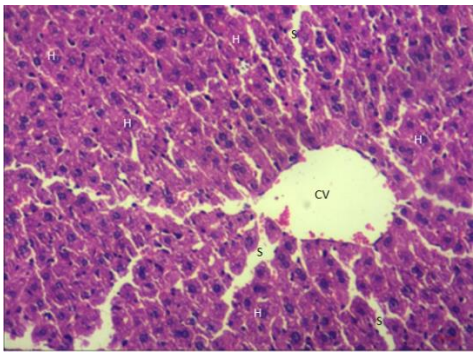

Fig. 3. 100 mg/kg PS. Extract toxicity study group of histology showing normal liver architectural integrity. Patent central vein (CV), intact hepatocytes (H), Sinusoids (s) containing Kupffer cells & capillaries. Photomicrographs of Liver, Mag X 400 H & E

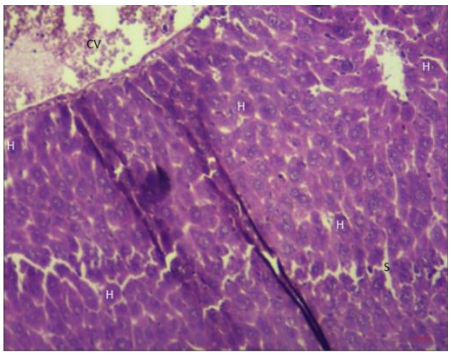

Fig. 4. 200 mg/kg PS. Extract toxicity study group of histology showing normal liver architectural integrity. Patent central vein (CV), intact hepatocytes (H), Sinusoids (s) containing Kupffer cells & capillaries. Photomicrographs of Liver, Mag X 400 H & E

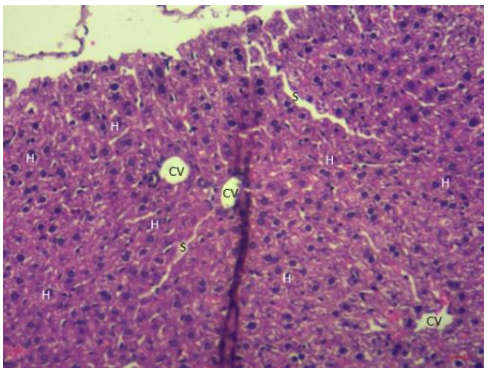

Fig. 5. 400 mg/kg PS. Extract toxicity study group of histology showing normal liver architectural integrity. Patent central vein (CV), intact hepatocytes (H), Sinusoids (s) containing Kupffer cells & capillaries. Photomicrographs of Liver, Mag X 400 H & E

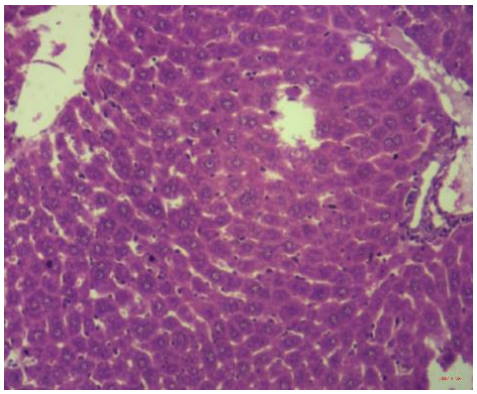

Fig. 6. 800 mg/kg PS. Extract toxicity study group of histology showing normal liver architectural integrity. Photomicrographs of Liver, Mag X 400 H & E

4. DISCUSSION

The metabolic enzymes and proteins of interest in this study are -ALT, -AST, ALP and ALB of the organ liver which play a pivotal role in metabolism especially in the hepatic system. If the liver enzymes are elevated, it could indicate liver injury or damage. The implication of elevated liver enzyme level depends on the treatment doses and the clinical presentations. For instance, a moderate increase in the level of the liver enzymes may be an early sign of liver injury, while a marked or remarkable increase could indicate acute or chronic liver disease. On the other hand, decreased liver enzymes level may suggest impaired liver function and could be due to a number of factors including pharmacologically treatment agents including extracts, genetic variations, among others (Iluz Freundlich et al., 2020).

From the result recorded in Table 1, the biochemical evaluation indicates no toxicity potential of the stem bark extract of *P. straminea* in the sub-acute treatment duration of the study. This finding suggests that *P. straminea* may not alter the metabolic role of the liver or cause any liver damage, which could lead to elevated levels of liver enzymes in the tissues (Kemelayefa et al., 2022). Also, the lack of hepatotoxicity may

indicate that *P. straminea* extract does not relatively consist of any toxic constituents that are harmful to the liver. This is supported by the finding that the plant has antioxidant and antimicrobial properties, which suggest that it contains beneficial compounds such as flavonoids and saponins which have strong antioxidants and antimicrobial properties (Ikomi et al., 2017, Ogbonna et al., 2013). Another reason could be due to species-specific differences, soil, and environmental factors. The absence of hepatotoxicity in mice may be due to species-specific differences in the metabolism or sensitivity of the cytochrome enzymes in the liver (Perlman, 2016). Based on the non-hepatotoxicity findings, it can be said that these doses may not be high enough to cause hepatotoxicity in mice. The lack of hepatotoxicity with these doses used in this study, suggests that *P. straminea* may be relatively safe for use as a traditional remedy. Histopathological examination of the liver tissue from the control group and the treated group showed no remarkable changes in the tissue architecture in any of the groups. The results obtained shows little or no deleterious effect on the liver and liver enzyme because of the vital phytochemical constituents of the stem bark of *P. straminea* (Kemelayefa et al., 2024) that presents bio protective potential which proves right in the normal architectural integrity of the liver assessment even in the relatively long period of exposure (sub-acute). The results obtained in this study have proven contrary to the claim that *P. straminnea* is toxic except for other species (McBarron, 1978). However, the toxic claim was made on goats and sheep and not rodents like mice (McBarron, 1978).

5. CONCLUSION

The study findings have shown that the crude extract of *P. straminea* stem bark possesses relatively no remarkable toxicity impact on the liver as revealed in the liver enzymes and the histology assessment. However, this should be an opening for further research.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The study was approved with reference number, NDU/PHARM/AEC/044a in the Department of Pharmacology and Toxicology, Niger Delta University, Wilberforce Island, Nigeria.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Authors declare that no generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Aleksunes L.M., & Eaton D.L. (2019). Principles of toxicology. Klaassen C.D. (Ed.), [publicationyear2] Casarett & Doull's Toxicology: The Basic Science of Poisons, 9th edition. McGraw-Hill Education.

Alturkistani, H. A., Tashkandi, F. M., & Mohammedsaleh, Z. M. (2015). Histological Stains: A Literature Review and Case Study. *Global journal of health science*, 8(3), 72–79.

Boukandou, M.M., Mewono, L., & Aboughe, A.S. (2015). Toxicity studies of medicinal plants used in sub-Saharan Africa. *Journal of ethnopharmacology*, 174, 618–627

Doumas, B.T., Watson, W.A., & Biggs, H.G. (1971). Albumin Standards and the Measurement of Serum Albumin with Bromcresol Green. *Journal of Clinica Chimica Acta*, 31, 87-96.

Edgar RC, Haas BJ, Clemente JC, Quince C, Knight R. UCHIME improves sensitivity and speed of chimera detection. Bioinformatics. 2011 Aug 15;27(16):2194-200. DOI: 10.1093/bioinformatics/btr381. Epub 2011 Jun 23. PMID: 21700674; PMCID: PMC3150044.

Everist, S.L. (1981)' Poisonous Plants of Australia. Revised edition, Angus & Robertson, Sydney. p.87

Everist, S.L. (1985). Use of Fodder trees and Shrubs. Revised edition, Queensland Department of Primary Industries, sydBrisbane. p.51.

Ferreira-Machado, S.C., Rodrigues, M. P., Nunes, A. P. M., Dantas, F. J. S., De Mattos, J. C. P., & Silva, C. R. (2004). Genotoxic potentiality of aqueous extract prepared from *Chrysobalanus icaco* L. leaves. *Toxicological Letters.* 3, 481–487.

Hunter, J. T. (1997). Severe blistering caused by *Parsonsia straminea* (R.Br.). Muell, F. (Apocynaceae) at Girraween. National

Park. *The Australian Naturalist*, 35(1-3), 28-29

Ikomi, O. E., Ilaboya, M. O., Olaniyan, A.O., & Ilaboya, J. O. (2017). Antioxidant and antimicrobial activities of *Parsonsia straminea* leaf aqueous extract. International *Research Journal of Pure and Applied Chemistry*, 10(9), 29-34.

Iluz-Freundlich, D., Zhang, M., Uhanova, J., & Minuk, G. Y. (2020). The relative expression of hepatocellular and cholestatic liver enzymes in adult patients with liver disease. *Annals of hepatology*, 19(2), 204–208.

Kemelayefa, J., Kagbo, H., & Georgewill, U. (2022). Acute and Sub-Acute Evaluations of *Parsonsia straminea* Stem Bark Ethanol Extract Impact on Some Behavioral Parameters in Mice. *Journal of Advances in Medical and Pharmaceutical Sciences*, 24(3), 28–39.

McBarron, E. J. (1978) Poisonous plants of western New South Wales. Department of Agriculture, New South Wales.

National Institute for Occupational Safety and Health (NIOSH) (1998) Criteria for Recommended Standard Occupational Noise Exposure. United States Department of Health and Human Services, National Institute for Occupational Safety and Health Publication, Cincinnati, Ohio, 98-126.

Ogbonna, A.O., Adedeji, A.T., Okomi, O.E., Iyare, M.O., Uzochukwu, S.C., Ogah, A.I., & Kolawole, 0.0. (2013). In• vitro cytotoxicity of some Nigerian medicinal plants on human prostate cancer cells (PC3). *American Journal of Experimental and Clinical Research*, 2(2), 89-94.

Kemelayefa Ozakieoniso James, Bonsome Bokolo, Precious Awipi (2024). Anti-Oxidant Assessment of *Parsonsia Straminea* Hydro-Ethanol Stem Bark Extract. Journal of advances in medical and pharmaceutical sciences. Volume 26. 12 (in press).

Perlman R. L. (2016). Mouse models of human disease: An evolutionary perspective. *Evolution, medicine, and public health* (1), 170–176.

Reitman, N., Frankel, E. N., & Pearce, D.E. (1957). A reagent for measuring the combined action of mammalian liver homogenates and metabolites on halogenated p-nitroanilines. *The Biochemical Journal*, 68(1), 286-292.

Smith, L.W., & Culvenor, C.C. (1981). Plant sources of hepatotoxic pyrrolizidine alkaloids. (1981) *Journal of Natural Product*, 44: 129-152.

Tamokou, J.D., & Kuete, V. (2014). "—toxic plants used in African traditional medicine," in *Toxicological survey of African Medicinal Plants*. 7 135–180.

Tietz, N. (1976) Fundamentals of Clinical Chemistry. W.B. Saunders, Philadelphia

World Health Organisation (WHO) (2017). Safety of herbal medicine: guidelines on quality, safety and efficacy. Accessed from http://.www.who.int/medicines/areas/traditional/guidelines/areas/safety/en/

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/127071