



Effects of Aqueous Stem Bark Extract of *Stereospermum kunthianum* on Carbon Tetrachloride - Induced Hepatotoxicity in Rats

Mahmoud Suleiman Jada^{1*}, Mohammed Aliyu Sulaiman¹
and Muktar Abdulmalik¹

¹Department of Biochemistry, Modibbo Adama University of Technology, Yola, Adamawa State, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Authors MSJ and MAS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author MA managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJRB/2021/v8i330183

Editor(s):

(1) Dr. V. Spirina Liudmila, Siberian State Medical University, Russia and Tomsk National Research Medical Center, Russia.

Reviewers:

(1) Mariusz Jaremko, King Abdullah University of Science and Technology (KAUST), Saudi Arabia.

(2) Sahar Hassan Orabi, University of Sadat City, Egypt.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/66225>

Original Research Article

Received 05 January 2021

Accepted 11 March 2021

Published 23 April 2021

ABSTRACT

Aim: This study is aimed at evaluating the effects of the aqueous stem bark extract of *Stereospermum kunthianum* on CCl₄-induced hepatotoxicity in rats.

Methodology: Analysis of qualitative phytochemical components and antioxidant activity were carried out. Experimental rats were randomly divided into six groups of five rats each. Group 1: served as the normal control group. Group 2: was administered with CCl₄ only at a dose of 3 ml/kg b.wt by single intraperitoneal administration. Group 3: served as the standard control group. Group 4: was administered with 200 mg/kg b.wt of the aqueous stem bark extract + CCl₄. Group 5: was administered with 400 mg/kg b.wt of the aqueous stem bark extract + CCl₄. Group 6: was administered with 600 mg/kg b.wt of the aqueous stem bark extract+ CCl₄.

Results: The phytochemical analysis showed the presence of flavonoid, phenols, saponins, and terpenoid while tannins and alkaloids were absent. The antioxidant activity showed that the extract significantly (P<0.05) inhibits Ferric Reducing Antioxidant Power (FRAP) and Thiobarbituric Acid

*Corresponding author: E-mail: smjada2007@yahoo.com;

Reactive Substances (TBARS), giving high activity as the concentration of the extract increases. The elevated levels of ALT and AST coupled with Conjugated bilirubin, Total bilirubin, and total protein caused by CCl₄ administration were all reduced significantly (P<0.05) by the extract in dose dependent manner.

Conclusion: These findings demonstrated that stem bark extract of *Stereospermum kunthianum* could be an alternative medication for liver injury.

Keywords: *Stereospermum kunthianum*; hepatotoxicity; phytochemical components and antioxidant activity.

1. INTRODUCTION

Medicinal plant is a plant that is used to maintain health, to be administered for a specific condition, or both, whether in modern medicine or traditional medicine [1]. Medicinal plants, also called medicinal herbs, have been discovered and used in traditional medicine practices since prehistoric times. Medicinal plants contain some organic compounds which provide definite physiological action on the human body and these bioactive substances include *tannins, alkaloids, carbohydrates, terpenoids, steroids* and *flavonoids*. These compounds are synthesized by the primary or rather secondary metabolism of living organisms.

The plant kingdom is a treasure house of potential drugs and in recent years there has been an increasing awareness about the importance of medicinal plants. Recent work revealed the potential of several herbs as sources of drugs. Drugs from the plants are easily available, less expensive, safe, and efficient and rarely have side effects. The plants which have been selected for medicinal use over thousands of years constitute the most obvious choice of examining the current search for therapeutically effective new drugs such as anticancer drugs, antimicrobial drugs, antihepatotoxic compounds [2].

Stereospermum kunthianum is a small woody tree of about 5 to 15 m high and 25 cm in diameter. It is found in the Sudano-Guinea savannah regions of Africa and Asia. It has thin, grey-black bark, smooth or flaking in patches, the trunk is rarely straight, with twisted branches with abundant, fragrant, precocious, pink or purplish flowers, making the tree a spectacular sight. The plant also referred to as pink jacaranda, in English, is known locally as "Sansami" among the Hausa of Northern Nigeria; "Ayada" among the Yoruba of Southwest Nigeria, and "Alakiriti" among the Igbo of Southeast Nigeria [3]. The

plant parts are used to treat various ailments [3]. The pods are chewed with salt to treat coughs and are used in the treatment of ulcers, leprosy, skin eruptions and venereal diseases, while the stem bark decoction or infusion is used to cure bronchitis, pneumonia, cough, rheumatic arthritis and dysentery [3]. The roots and leaves have been found useful in treating venereal diseases, respiratory ailments, gastritis [3]. Analgesic and anti-inflammatory activities of stem bark [4], as well as the anthelmintic activity of ethanol leave extract has been reported [5]. Other pharmacologic activities such as, antibacterial, antidiarrhoeal and antiplasmodial activity of lipophilic root bark extract have also been reported [6,7]. Parts of the plant often used for ethno medicinal purposes are leaf, stem bark and root bark.

Hepatotoxicity refers to liver dysfunction or liver damage that is associated with an overload of drugs or xenobiotics [8]. The chemicals that cause liver injury are called hepatotoxicants. Hepatotoxicants are exogenous compounds of clinical relevance and may include overdoses of certain medicinal drugs, industrial chemicals, natural chemicals like microcystins, herbal remedies and dietary supplements [9,10]. Hepatotoxicity may result not only from direct toxicity of the primary compounds but also from reactive metabolites or from an immunologically-mediated response affecting hepatocytes, biliary epithelial cells and/or liver vasculature [11,12]. Hepatotoxicity related symptoms may include a jaundice or icterus appearance causing yellowing of the skin, eyes and mucous membranes due to high level of bilirubin in the extracellular fluid, pruritus, severe abdominal pain, nausea or vomiting, weakness, severe fatigue, continuous bleeding, skin rashes, generalized itching, swelling of the feet and/or legs, abnormal and rapid weight gain in a short period [13]. The rate of hepatotoxicity is so alarming, certain medicinal agents, when taken in overdoses or sometimes even when introduced within therapeutic ranges, may injure the organs [14]. Moreover, the

available drugs for the management of hepatotoxicity have been associated with number of side effects coupled with high cost. These make it difficult for the less privileged to obtain. For this reason, there is need for an alternative therapy in the field of hepatotoxicity management using available and easily accessible effective medicinal plants, therefore, this work was designed to determine the effects of aqueous stem bark extract of *Stereospermum kunthianum* on carbon tetrachloride - induced hepatotoxicity in rats.

2. MATERIALS AND METHODS

2.1 Plant Material

The fresh Stem bark of *Stereospermum kunthianum* was collected in Yolde-Pate in Yola south LGA, Adamawa state. The Plant was identified and authenticated at the department of Plant Science, Modibbo Adama University of Technology, Yola Adamawa state.

2.2 Experimental Animals

Adult albino rats of both sexes weighing between 90-100 g were purchased from National Veterinary Research Institute VOM, Plateau State, Nigeria. The animals were allowed to acclimatize for a period of 2 weeks under ambient environmental conditions in a well aerated cages in Biochemistry laboratory, Biochemistry department, Modibbo Adama University of Technology, Yola Adamawa State. They were allowed free access to grower's mash (Vital feeds Grand Cereal plc, Bukuru, Jos, Plateau State) and water ad libitum.

2.3 Preparation of Extract

The collected plant sample was rinsed in clean water and shade dried under ambient temperature for two weeks. The dried plant sample was then grinded into powder using a mortar and pestle; the powder obtained was used to prepare the extract. Exactly 100 g of the powdered Stem bark was weighed into sterilized conical flask and 500 ml of distilled water was poured into the flask. The contents of the flask were shaken and the top was covered with aluminium foil and kept at ambient temperature for 48 h (2 days) after which the extracts were obtained by filtering using a clean cloth with fine pore. The extract was then concentrated in crucibles using water bath set at a temperature

of 45°C. The weight of the concentrated extracts was taken and then stored in an airtight sample bottles in a refrigerator until required for analysis.

2.4 Experimental Design

The method of Parvez, et al. [15] with slight modification was used for both grouping and administration.

Group1: Normal control, Animals were fed with normal diet and water throughout the experimental period.

Group 2: Negative/disease control. Animals were induced with hepatotoxicity using CCl₄ and left untreated throughout the experimental period.

Group 3: Positive/standard control. Animals were induced with hepatotoxicity and treated with Silymarin 0.12 ml.

Group 4: Experimental group, Animals were induced with hepatotoxicity and treated with 200mg/kg/bwt of *Stereospermum kunthianum* aqueous stembark extract.

Group 5; Experimental group. Animals were induced with hepatotoxicity and treated with 400 mg/kg/bwt of *Stereospermum kunthianum* aqueous stem bark extract.

Group 6; Experimental group. Animals were induced with hepatotoxicity and treated with 600 mg/kg/bwt of *Stereospermum kunthianum* aqueous stem bark extract

2.5 Phytochemical Screening

The methods of Trease and Evans [16] was used to detect the following phytochemicals in the extract: alkaloids, saponins, tannins, flavonoids, terpenoids, phenols

2.5.1 Test for phenols

Exactly 3 ml of ferric chloride was added to 3 ml of extract. A deep bluish color indicates the Presence of phenols.

2.5.2 Test for flavonoids

Exactly 1 ml of 10% lead acetate solution, 1 ml of aqueous extract was added. Formation of a yellow precipitate indicated the presence of flavonoids.

2.5.3 Test for terpenoids

Exactly 2 ml of chloroform was used to dissolve the 2 ml of the organic extract and allowed to dry. Another 2 ml of conc. sulfuric acid was added and heated for about 2 min. A greenish coloration was developed and that shows the presence of terpenoids.

2.5.4 Test for tannins

Exactly 2 ml of the aqueous extract combined with 2 ml of de-ionized water and two drops of FeCl₃ was added. The formation of a green precipitate indicated the presence of tannins.

2.5.5 Test for saponins

Exactly 5 ml of aqueous extract plus 5 ml of distilled water was put into a test tube. It was thoroughly shake and warmed for some time. The formation of stable foam was considered as indication for the presence of saponins.

2.5.6 Alkaloids test

Exactly 3 ml of 1% HCl was added in to the 3 ml of aqueous extract, placed on a steam bath and stirred for some time. Mayer's and Wagner's reagents was added. Turbidity of the resulting precipitate will indicate the presence of alkaloids.

2.6 Antioxidant Activity Assay

2.6.1 Ferric reducing antioxidant power (FRAP) assay

The antioxidant capacity of *Stereospermum kunthianum* was estimated spectrophotometrically using the method of Benzie and Strain [17]. The method is based on the reduction of Fe³⁺-TPTZ complex (colorless complex) to Fe²⁺-tripirydyltriazine (blue colored complex) formed by the action of electron donating antioxidants at low pH. The reaction was monitored by measuring the change in absorbance at 593 nm. Freshly prepared working FRAP reagent was pipetted using 1-5 ml variable micropipette (3.995 ml) and mixed with 5 µl of *Stereospermum kunthianum* stem aqueous extract and mixed thoroughly.

2.6.2 Thiobarbituric acid reactive substances (TBARS) assay

TBA method was used for evaluating the extent of lipid peroxidation. At low pH (2-3), and high temperature (100°C), melondialdehyde (MDA)

binds TBA to form a red complex that can be measured spectrometrically at 532 nm. A volume of 2 ml of 20% trichloroacetic acid (TCA) and 2 ml of 0.67% TBA solutions was added to 2 ml of the mixtures containing 4 mg of the sample in 4 ml of 99.5% ethanol (final concentration 0.02%). This mixture was kept at 1000 C for 10 min and after cooling to room temperature. It was centrifuged at 3000 rpm for 20 min. The antioxidant activity was based on the absorbance of the supernatant at 532 nm on the final day of the assay [18]. The percentage of antioxidant activity was calculated by the following formulae for all the methods.

$$\text{Percentage of antioxidant activity} = 100 \times \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}}$$

2.7 Induction of Hepatotoxicity

The liver damage was induced by the administration of Carbon tetrachloride (Sigma chemicals Co., St. Louis USA). Rats were injected intraperitoneally with a single dose of CCl₄ (5 m/kg body weight).

2.8 Biochemical Markers for Hepatotoxicity Assays

2.8.1 Determination of serum alanine aminotransferase (ALT)

Principle: ALT was measured as described by Reitman and Frankel [19], by monitoring the concentration of pyruvate hydrazone formed with 2, 4-dinitrophenylhydrazine. The colour intensity is measured against the blank at 540 nm.

Method: The blank and sample test tubes was setup in duplicates. 0.1 ml of serum was pipetted into the sample tubes. To these, 0.5 ml of buffer solution containing phosphate buffer. L-alanine and oxaloacetate was added. The mixtures were thoroughly mixed and incubated for exactly 30 minutes at 37°C and pH 7.4. Then 0.5 ml of reagent containing 2,4-dinitrophenylhydrazine will later be added to both tubes. The tubes were mixed thoroughly and incubated for exactly 20 mintues at 25°C. Then five millilitres of sodium hydroxide solution was added to each tube and mixed. The absorbance was read against the blank after 5 minutes at 540 nm.

2.8.2 Determination of serum aspartate amino transferase (AST)

Principle: AST is measured as described by Reitman and Frankel [19], by monitoring the concentration of oxaloacetate hydrazone formed

with 2,4- dinitrophenylhydrazine. The colour intensity being measured at 546 nm.

Method: The blank and sample test tubes was setup in duplicates. 0.1 ml of serum was pipette into the sample tubes. To these, 0.5 ml of buffer solution containing phosphate buffer. L-alanine and oxaloacetate was added. The mixtures were thoroughly mixed and incubated for exactly 30 minutes at 37°C and pH 7.4. Then 0.5 ml of reagent containing 2,4-dinitrophenylhydrazine was later be added to both tubes. The tubes were mixed thoroughly and incubated for exactly 20 minutes at 25°C. Then 5.0 ml of sodium hydroxide solution was added to each tube and mixed. The absorbance was read against the blank after 5 minutes at 546 nm.

2.8.3 Determination of serum bilirubin (Van Den Bergh's reaction)

Principle: Serum bilirubin react with diazo reagent to form pink to reddish-purple coloured compound (azobilirubin), which is measured spectrophotometrically. The reaction is accelerated by alcohol.

Method: in a test tube containing 0.1 ml of serum and 3.9 ml of 50% methanol, 1.0 ml of the diazo reagent was added and mixed well. The reaction mixture was allowed to stand for 30 minutes at 25°C. The absorbance was measured at 540 nm against a reaction blank, consisting of 4.0 ml of 50% methanol and 1.0 ml of the diazo reagent.

2.8.4 Determination of serum total protein (Biuret Reaction)

Principle: At alkaline pH 7.0, Copper (II) binds with nitrogen present in peptides of proteins, which is photometrically measured.

Method: Three test tubes, blank, standard and sample was labeled and to the sample, 0.02 ml of serum was added, to the standard test tube, 0.02 ml of protein standard was added, and 0.02 ml of water to the blank test tube. One millilitre of the protein reagent was added to the test tubes each. This was mixed well and allow to stand for 25 minutes at room temperature (20⁰-25⁰C). The absorbance was read at 540 nm.

Total serum proteins (in g/dl) = $\frac{A_{sample}}{A_{control}} \times \text{conc. of standard}$

2.9 Statistical Analysis

One way Analysis of Variance (ANOVA) was used, results were expressed as mean ± SEM.

P<0.05 was considered statistically significant. The statistical significance of the difference was evaluated using Statistical Package for Social Sciences (SPSS) Version 24.0.

3. RESULTS

Table 1 gives the result of phytochemical analysis of aqueous stem bark of extract of *Stereospermum kunthianum*. Flavonoids, phenols, saponins, and terpenoids were found to be present, while alkaloids and tannins were absent.

Table 2 shows the percentage inhibition of FRAP of the Aqueous stem bark extract of *Stereospermum kunthianum*. The ferric reducing antioxidant power assay of the extract showed an increase in chelating activity with increase in concentration. Significantly higher (p<0.05) inhibition was observed at 100 mg/ml while the inhibition was observed at the lowest concentration (20 mg/ml) of both the plant extract and ascorbic acid. The ferric reducing antioxidant power of the aqueous extract of *Stereospermum kunthianum* was significantly (p<0.05) higher compared to that of ascorbic acid at the same concentrations.

The percentage inhibition of thiobarbituric acid reacting substances of the aqueous stem bark extract of *Stereospermum kunthianum* is shown in Table 3. The result showed that the extract is capable of inhibiting lipid peroxidation in the dose dependent manner. The aqueous stem bark extract of *Stereospermum kunthianum* was also found to have a significantly (P<0.05) TBARS inhibitory activity than the standard (Ascorbic acid).

The effects of aqueous extract of *Stereospermum kunthianum* on hepatic function marker enzymes carbon tetrachloride induced hepatotoxicity in rats on liver enzymes (AST, ALT) and non-enzymatic biomarkers (Total and conjugated bilirubin and total protein) in serum of treated animals are given in Table 4. The extract showed positive effect and ameliorated most of the biological derangements observed in the induced, untreated animals.

4. DISCUSSION

The analysis of qualitative phytochemical components of the stem bark of *Stereospermum kunthianum* revealed the presence of Flavonoids, phenols, saponins, and terpenoids while alkaloids and tannins were found to be absent.

This observation might suggest that the extract could possess hepatoprotective potentials because a study by Divya et al. [20] revealed that natural products rich in triterpenes, flavonoids or polyphenols, have been established as powerful hepatoprotective agents in experimental liver-injury cell and animal models. Saponins prevent hyperlipidemia and liver injury induced by lipid peroxidation [21]. The ameliorative effect of the aqueous extract of stem bark of *Stereospermum kunthianum* observed on the hepatic function marker enzymes could be attributed to the presence of saponins.

The antioxidant potentials of the extract observed may also be attributed to the presence of these phytochemical components especially flavonoids because they have been reported to act as natural antioxidants and have an effect on many diseases. They have been shown to exert antimicrobial, antiviral, antiulcerogenic, cytotoxic, antineoplastic, mutagenic, anti-inflammatory, antioxidant, antihepatotoxic, antihypertensive, hypolipidemic and antiplatelet activities [22].

Oxidants and free radicals are harmful to the body's health when their overload cannot steadily be destroyed and consequently generate an occurrence called oxidative stress [23]. Oxidative stress, including the decrease of antioxidant

capacity, plays an important role in the pathogenesis of liver fibrosis via different pathways. Hepatic fibrosis is usually initiated by hepatocyte damage, leading to the recruitment of inflammatory cells and platelets with the subsequent release of cytokines, chemokines, and growth factors [24]. These factors probably affect the inflammatory and repairing phase of liver fibrosis by activating hematopoietic stem cells [24]. The radical scavenging activity of the aqueous stem bark extract of *Stereospermum kunthianum* revealed that the FRAP and TBARS activity of the aqueous extract of *Stereospermum kunthianum* exhibited significantly higher ($p < 0.05$) antioxidant activity compared to ascorbic acid. This observation further suggests that the extract could possess hepatocurative activity. The work of Vijay and Vimukta [25] also revealed that antioxidants play a vital role in treating liver diseases.

Aspartate aminotransferase (AST) is predominantly found in mitochondria of hepatocytes. ALT is more specific to liver, and this is a better parameter for detecting liver injury. Serum total protein and bilirubin are also associated with liver cell damage. The ALT and AST activity and serum bilirubin level are largely used as the most common biochemical markers to evaluate liver injury [26].

Table 1. Qualitative phytochemical composition of aqueous stem bark extract of *Stereospermum kunthianum*

Phytochemicals	Aqueous stem bark extract
Saponins	+
Terpenoid	+
Flavonoids	+
Phenols	+
Tannins	-
Alkaloids	-

Key: + = Present; - = Absent

Table 2. Percentage inhibition of ferric reducing antioxidant power of stem bark extract of *Stereospermum kunthianum*

Concentration (mg/ml)	<i>S. kunthianum</i> extract (% inhibition)	Ascorbic acid (% inhibition)
20	44.10±0.13	45.49±1.07
40	60.01±0.18	58.24±0.36
60	75.08±0.12 ^a	65.86±0.00
80	87.97±0.12 ^a	74.31±0.66
100	89.91±0.12 ^a	78.35±0.04

All values are presented as mean ± SEM for 3 determinants. Superscript 'a' denotes significantly ($P < 0.05$) higher compared to ascorbic acid

Table 3. Percentage inhibition of thiobarbituric acid aqueous stem bark extract of *Stereospermum kunthianum*

Concentration (mg/ml)	<i>S. kunthianum</i> extract (% inhibition)	Ascorbic acid (% inhibition)
20	32.1 ±0.0013	33.5 ±0.0018
40	39.4 ±0.0101 ^a	34.0 ±0.0008
60	47.2 ±0.0006 ^a	42.1 ±0.0002
80	57.1 ±0.2112 ^a	49.3 ±0.0043
100	66.2 ±0.2321 ^a	60.4 ±0.0052

All values are presented as mean ± SEM for 3 determinants
Superscript 'a' denotes significantly (P<0.05) higher compared to ascorbic acid

Table 4. Effects of aqueous stem bark extract of *Stereospermum kunthianum* on biochemical markers of hepatotoxicity in rats

Groups	AST (IU/L)	ALT (IU/L)	Total bilirubin (mg/dl)	Conjugated bilirubin (mg/dl)	Total protein (g/dl)
Normal	192.33±14.10 ^b	47.70±1.67 ^b	12.33±0.77 ^b	4.27±0.26 ^b	56.00±0.58 ^b
Negative	351.00±1.15 ^a	76.01±3.21 ^a	24.93±0.12 ^a	8.30±0.06 ^a	70.00±2.08 ^a
Standard	189.33±2.73 ^b	48.34±4.70 ^{ab}	14.77±0.33 ^{ab}	5.63±0.09 ^{ab}	58.00±0.58 ^{ab}
<i>S.konthianum</i> (200 mg)	327.67±4.41 ^{ab}	67.00±1.00 ^{ab}	20.43±1.07 ^{ab}	6.80±0.36 ^{ab}	59.67±0.88 ^{ab}
<i>S.konthianum</i> (400 mg)	231.67±4.08 ^{ab}	50.00±5.29 ^{ab}	18.67±1.08 ^{ab}	6.87±1.02 ^{ab}	58.67±2.85 ^{ab}
<i>S.kontinum</i> (600 mg)	200.00±2.10 ^{ab}	47.11±2.08 ^{bc}	16.60±0.49 ^{ab}	5.13±0.03 ^{abc}	57.67±1.86 ^{abc}

Values are presented as Mean ± SEM; (n=5).
Superscript 'a' denotes significantly (P<0.05) higher compared to normal control
Superscript 'b' denotes significantly (P<0.05) lower compared to negative control
Superscript 'c' denotes significantly (P<0.05) lower compared to positive control

Administration of CCl₄ caused a significant elevation of enzymes level such as AST, ALT and bilirubin levels has been attributed to the damage to structural integrity of liver, because they are cytoplasmic in location and released into circulation after cellular damages indicating development of hepatotoxicity [26]. The administrations of aqueous stem bark extract of *Stereospermum kunthianum* in this study have shown a significant (P<0.05) decreased in serum marker enzymes AST and ALT level and bilirubin level compared to negative control. This is in agreement with the commonly accepted view that serum levels of AST and ALT return to normal with the healing of hepatic parenchyma and the regeneration of hepatocytes [27].

5. CONCLUSION

The present study have demonstrated that carbon tetrachloride - induced hepatotoxicity in rats resulted in a significant elevation in serum ALT and AST levels and non-enzymatic biomarkers of liver injury. Following the administration of aqueous stem bark extract of *Stereospermum kunthianum*, it was observed that the serum marker enzymes AST and ALT levels and bilirubin level significantly (P<0.05) decreased compared to negative control. This may be attributed to the presence of the phytochemicals detected in the extract, which ameliorated the observed derangements probably via antioxidative mechanism. These findings demonstrated that the stem bark extract of *Stereospermum kunthianum* could be an alternative medication for liver injury.

ACKNOWLEDGEMENTS

Authors sincerely appreciate the Department of Biochemistry, Modibbo Adama University Yola, especially the technologists for the support given towards the actualization of this work.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- Ahn K. The worldwide trend of using botanical drugs and strategies for developing global drugs. *BMB Reports*. 2017;50(3):111–116.
- Wong CKT, Huang TY, YW Lin Y. Tannins and human health: A review. *Critical Reviews in Food Science and Nutrition*. 1998;38:421–464.
- Gill LS. *Ethnomedicinal uses of plants in Nigeria*. University of Benin Press, Nigeria. 1992;223.
- Ching FP, Omogbai EKI, Ozulua R. Okpo SO. Analgesic activity of aqueous Extract of *Stereospermum Kunthianum* (Cham, Sandrine Petit) stem bark. *Acta Poloniae Pharmaceutica-Drug Resistance*. 2009; 66(1):83-88.
- Monglo D, Njongmeta LM, Musonggong G, Ngassoum M, Nukeinine EN. Evaluation of antihelmintic potential of ethanolic plant extract from Northern Cameroon against eggs and infective larvae of *Haemonchus contortus*. *Journal of Biological Science*. 2006;6(2):426-433.
- Aliyu MS, Hauwa UA, Tijjani MB, Aliyu AB, Ya'u B. Phytochemical and Antibacterial properties of leaf extract of *Stereospermum kunthianum* (*Bignoniaceae*). *Nigerian Journal of Basic and Applied Science*. 2009;17(2):235-239.
- Ching FP, Otokiti IO. Egert-omoneukanrin B. Dimethoxyflavone isolated from the stem bark of *Stereospermum kunthianum* possesses antidiarrhoeal activity in rodents. *African Journal of Traditional Complement and Alternative Medicine*. 2013;10(4):47-51.
- Navarro VJ, Senior JR. *Active plant ingredients used for medicinal purposes*. United States Department of Agriculture. 2006;18
- Willett KL, Roth RA, Walker L. Workshop overview: Hepatotoxicity assessment for botanical dietary supplements. *Toxicological Science*. 2004;79:4-9.
- Papay JI, Clines D, Rafi R, Yuen N, Britt SD. Drug-induced liver injury following positive drug rechallenge. *Regulatory Toxicology and Pharmacology*. 2009;54: 84-90.
- Saukkonen JJ, Cohn DL, Jasmer RM, Schenker S, Jereb JA, et al. An Official ATS Statement: Hepatotoxicity of antituberculosis therapy. *American Journal of Respiratory and Critical Care Medicine*. 2006;174:935-952.
- Deng X, Luyendyk JP, Ganey PE, Roth RA. Inflammatory stress and idiosyncratic hepatotoxicity: Hints from animal models. *Pharmacology Review*. 2009;61:262-282.
- Chang CY, Schaino TD. Review article: Drug hepatotoxicity. *Aliment Pharmacology and therapeutics*. 2007;25:1135-1151.

14. Aashish M, Kruse A, Kobilá T. Crystal structure of the opioid receptor bound to a morphinan antagonist. *Nature*. 2012;485: 321-326.
15. Parvez MK, AIDosari MS, Arbab AH, et al. Hepatoprotective effect of *Solanum surattense* leaf extract against chemically induced oxidative and apoptotic injury in rats. *BMC Complementary and Alternative Medicine*. 2019;19:154. Available:<https://doi.org/10.1186/s12906-019-2553-1>
16. Trease GE, Evans WC. *Textbook of Pharmacognosy*. 12th edition balliere, Tindall London. 1989;45-50.
17. Benzie IFF, Strain JJ. The ferric reducing ability of plasma (FRAP) as a measure of antioxidant power: The FRAP Assay, *Analytical Biochemistry*. 1996;239:70–76.
18. Sawarkar HA, Khadabadi SS, Wandhare MD. The antioxidant activity of the leaves of *barleria grandiflora* dalz. (Acanthaceae), *Ethnobotanical Leaflets*. 2006;13(4):443-49.
19. Reitman A, Frankel G. Determination of alanine aminotransferase ALT/GPT in clinical samples. *Clinical Chemistry*. 1975; 3:32–28.
20. Divya S, William CC, Ghanshyam U. Drug-induced liver toxicity and prevention by herbal antioxidants: An Overview. 2016;26
21. Nyamai DW, Arika W, Ogola PE, Njagi ENM, Ngugi MP. Medicinally Important Phytochemicals: An Untapped Research Avenue. *Journal of Pharmacology and Phytochemistry*. 2016;1(1):17-20.
22. Mona SM, Wadah JA, Osman Elrashied, AE Zuheir O, Bashier O, Hassan S, Khalid A. Secondary metabolites as anti-inflammatory agents. *The Journal of Phyto Pharmacology*. 2014;3(4):275-285.
23. Sima G, Sima R, Maryam J, Hossein KH, Soheila N. A Review on Antioxidants and Their Health Effects. *Journal of Nutrition and Food Security*. 2018;3(2):106-112.
24. Khan RA, Khan MR, Sahreen S. CCl₄-induced hepatotoxicity: Protective effect of rutin on p53, CYP2E1 and the antioxidative status in rat. *BMC Complement Alternative Medicine*. 2012;8:172-178.
25. Vijay P, Vimukta S. The role of natural antioxidants in oxidative stress induced diabetes mellitus. *Research Journal on Pharmaceutical Sciences*. 2014;3(4):1-6.
26. Simon RP, Patel HV, Kiran K. Hepatoprotective Activity of Some Plants Extract against Paracetamol Induced Hepatotoxicity in Rats. *Journal of Herbal Medicine and Toxicology* 2010;4(2):101-106.
27. Shi-Yu Lin, Dan X, XiaXia Du, ChongLin R, Lu Xu, ShaoJun Ren, et al. Protective effects of salidroside against carbon tetrachloride (ccl₄)-induced liver injury by initiating mitochondria to resist oxidative stress in mice. *International Journal of Molecular Science*. 2019;220(3187): 2-14.

© 2021 Jada et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:
<http://www.sdiarticle4.com/review-history/66225>