Trop J Nat Prod Res, March 2024; 8(3):6681-6685 **ISSN 2616-0684 (Print)**
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Effect of *Pterocarpus santalinus* Ethanol Leaf Extract on Haematological, Histopathological and Lipid Profile Indices *in* Wistar Rats

Joseph S. Oyepata[1]*, Joseph T. Opeyemi[2], Adegbuyi T. Adekunle[3], Omoirri A. Moses[3]

[1]*Departmennt of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, Federal University, Oye-Ekiti, Ekiti State, Nigeria*
[2]*Department of Pharmacology, Faculty of Pharmacy, Lead City University, Ibadan, Nigeria*
[3]*Departmennt of Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, Federal University, Oye-Ekiti, Ekiti State, Nigeria.*

ARTICLE INFO

Article history:
Received 10 November 2023
Revised 03 March 2024
Accepted 05 March 2024
Published online 01 April 2024

ABSTRACT

Pterocarpus santalinus (Red Sandalwood) is a medicinal plant used in traditional medicine for many purposes. This study is aimed at evaluating the effect of *Pterocarpus santalinus* leaf extract on haematological, histopathologicaland lipid profile indices in rats. Wistar rats were divided into four groups (1 – 4). Group 1 (control) was given distilled water (10 mL/kg), groups 2 - 4were administered oral doses of *Pterocarpus santalinus* ethanol leaf extract at 100, 200 and 400 mg/kg, respectively once daily for 28 days. The body weights of the rats were monitored on a weekly basis during the experimental period. After the last dose was administered, the rats were sacrificed, and blood samples were collected, used for haematological and lipidprofile analysis. The brain and heart of each rat were harvested and used for histopathological analysis.The extract at 100 mg/kg resulted in a decrease in the RBC, Hg, MCH, MCHC, platelets and WBC. However, there were no changes in the WBC differentials (lymphocytes, neutrophils, basophils, and eosinophils). The levels of total cholesterol and triglycerides were not altered following extract administration, but HDL-cholesterol was slightly elevated while LDL-cholesterol was reduced significantly after extract administration. Histopathological examination of the heart and intestine of the rats showed no significant differences in the histological features of the rats in the treatment groups and those in the control group. These observations suggest that *Pterocarpus santalinus* leaf extract may be relatively safe when used for medicinal purposes.

***Keywords*:** Wistar Rat, *Pterocarpus santalinus*, intestine, Cardiovascular system, Blood.

Introduction

The human heart is located midway between thoracic vertebrae T5 and T8[1]. Pathan *et al*.[2] defined the pericardium as two membrane sacs surrounding and connecting to the heart. The three main arteries connecting to the top of the heart are the vena cava, aorta, and pulmonary artery. The apex of the heart is on the left side of the sternum (8 to 9 cm from the midline), between the fourth and fifth ribs.[3] Atherosclerosis is a condition in which plaque builds up in the walls of the arteries. This accumulation causes blood vessels to become narrow, making blood flow difficult.[4]When a blood clot forms, it blocks blood flow, which can lead to a heart attack or stroke. Appropriate management of heart failure requires not only the treatment recommended by national guidelines, but also the use of non-invasive methods as well as effective medications.[5]

The lower gastrointestinal tract includes most of the small intestine and all of the large intestine[6]. In human anatomy, the intestine is the segment of the gastrointestinal tract extending from the pyloric sphincter of the stomach to the anus and as in other mammals, consists of two segments: the small intestine and the large intestine[7].

***Corresponding author. E mail: oyepata.joseph@fuoye.edu.ng
Tel: +2348038248352

Citation: Oyepata JS, Opeyemi JT, Adekunle AT, Moses OA. Effect of *Pterocarpus santalinus* Ethanol Leaf Extract on Haematological, Histopathological and Lipid Profile Indices *in* Wistar Rats. Trop J Nat Prod Res. 2024; 8(3):6681-6685. https://doi.org/10.26538/tjnpr/v8i3.30

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria

Pterocarpus santalinus commonly calledred Sandalwoodis a small to medium-sized tree belonging to the Fabaceae family. It is widely distributed in many parts of the world, especially in India, Sri Lanka, Saudi Arabia, Taiwan and China.[8] The leaves are trifoliate and alternate, and are approximately 3-9 cm long. The flowers are in long clusters, and the fruit is a 6-9 cm long pod with one or two seeds. *Pterocarpus santalinus* is a flavonoid- and phenolic-rich medicinal plant that has many medicinal uses.[9,10]In herbal medicine, *Pterocarpus santalinus* is used as an antibacterial, antibiotic and diaphoretic agent.[11,12]The aim of this study was to evaluate the sub-acute toxicity of ethanol leaf extract of Pterostilbenein Wistar rats.

Materials and Method

Plant collection

Fresh *Pterocarpus santalinus* leaves were collected in December, 2021 from Karu village and neighboring communities in Nasarawa State, Nigeria. The plant material was identified and authenticated in the Department of Botany, Bingham University, Nasarawa State, Nigeria. Herbarium specimen with the voucher number BU1183 was deposited.

Drying and extraction of plant material

Pterocarpus santalinus leaves were dried in the shade for two weeks. The dried plant material was cut into small pieces and crushed using a mechanical grinder. The powdered plant material (200 g) was extracted with 70% ethanol (1 L) by maceration at room temperature. The extract was filtered and the filtrate was concentrated*in vacuo*at 40°C using a rotary evaporator. The concentrated extract was stored at -4°C until needed.

Animals

Male and female Wistar rats were obtained from Bingham University Animal House. They were fed with rodent pellets (Grand Cereals

Limited) and allowed access to drinking water *ad libitum*. Ethical approval with reference number BU/2021/1130 wasobtained from Bingham University Faculty of Health Sciences Animal Ethics Committee. The rats were acclimatized to the laboratory conditions, they were handled and cared for in accordance to the public health guidelines in the Guide for the Care and Use of experimental animals.

Study design
The Organization for Economic Development (OECD) guideline no. 425 for analysis of Chemicals was employed for this study (OECD 2008). Twenty-four (24) rats of either sexes (weighing between 190 and 289g) were chosen at random and grouped into four groups (1 -4) of six rats each.Group 1 rats were used as the control animals and received normal saline (10 mL/kg). Groups 2, 3, and 4 were administered *Pterocarpus santalinus* extract at doses of 100, 200, and 400 mg/kg, respectively. The extract was administered orally, once daily for 28 days. The weights of the rats were recorded at the start of the experiment (D0) and thereafter once weekly.

Assessment of food and water consumption
The daily food and water intake was estimated from the difference between daily food and water intake and the balance after 24 hours.

Haematological analysis
On the 29thday of the experiment, mice were sacrificed by diethyl ether anaesthesia. Blood samples were collected by cardiac puncture. The blood samples were collected into EDTA sample tubes and used for the following hematological analysis; white blood cell count (WBC), WBC differentials (neutrophils, eosinophils, basophils, lymphocytes, and mononuclear cells), red blood cell count (RBC), haemoglobin concentration (HGB), mean cell volume (MCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC),and platelets count. Haematological analysis was done using an automatic hematology machine (Cell-Dyn, Abbott, USA).

Lipid profile analysis
The blood samples were also analysed for the following lipid parameters; high density lipoprotein (HDL), low density lipoprotein (LDL), total cholesterol (TC), and triglycerides (TG).

Histopathological analysis
The heart and intestine of each animal were surgically removed, weighed, and stored in 10% formaldehyde for histopathological analysis. Sections of the organs were made and stained with hematoxylin and eosin (H&E) according to standard procedures.
.
Statistical analysis
Data were reported as mean ± standard deviation (SD). Data were entered into a Microsoft Excel spreadsheet and subjected to one-way analysis of variance (ANOVA) using SAS (Citation2011, version 9.3). Differences between means were determined using Tukeypost hoc test. P value < 0.05 was regarded as significant.

Results and Discussion

Effect of Pterocarpus santalinus ethanol leaf extract on haematological parameters
Pterocarpus santalinus ethanol leaf extractat 100 mg/kg dose in rats caused a significant($p<0.05$) decrease in white blood cells, red blood cells, haemoglobin, platelets, mean corpuscular haemoglobin(MCH) and concentration (MCHC) compared to the control group. However, the decrease in white blood cell count was not associated with any change in the differentials (basophils, neutrophils, eosinophils, and lymphocytes) (Table 1).
The decrease in RBC and haemoglobin concentration at 100 mg/kg, suggest that at lower doses, *Pterocarpus santalinus* ethanol leaf extractmay limit the oxygen carrying capacity of the blood, resulting in anaemia. In *in vivo* systems, haematological markers can be used to evaluate the toxicity of plant extracts.[13,14] They can also be used to explain how chemical molecules or plant extracts affect the blood. Anaemia is a disease in which the blood does not have enough haemoglobin, the iron-rich protein that carries oxygen in the red blood cells and supplies oxygen to other parts of the body.Previous studies have shown that *Pterocarpus santalinus* extractreduced red blood cell (RBC) and packed cell volume (PCV) in rats[15,16]. This suggests that *Pterocarpussantalinus* may affect the osmoregulation system of the blood cells and/or cause oxidative damage to cell membranes. The inhibitory effect of the extract on the haematopoietic system, and the breakdown of blood cells may have played a role in the decrease in the RBC and haemoglobin concentration by the extract.[17,18] A study have shown that mice fed with *Pterocarpus santalinus*leaf extract had lower levels of red blood cells, PCV, haemoglobin, and lymphocytes compared to control mice.[19] The main function of the white blood cells is to fight infection, protect the body from foreign organisms through phagocytosis and participate in other biological and physical processes.[19-22]In this study, no changes in the white blood cell differentials (neutrophils, basophils and eosinophils) was observed following treatment with*Pterocarpus santalinus* ethanol leaf extract. This suggests that the extract have no effect on humoralimmunity. Platelets are small cells that play an important role in the body as components of the coagulation complex. As shown in Table 1, the ethanol leaf extract of *Pterocarpus santalinus* at 100 mg/kg dose caused a significant reduction in platelets count. This finding suggests that the extract may have a direct or indirect effect on coagulation process.

Effect of Pterocarpus santalinus ethanol leaf extract on the body weight
Pterocarpus santalinus ethanol leaf extract at 400 mg/kg caused a significant ($p<0.05$) increase in body weight of the rats from the first week up to the fourth week when compared to the control group.At 200 mg/kg, the extract caused an increase in body weight of the rats at the second and third week, whereas, the body weight of the rats were not significantly affected at the first and fourth week (Table 2).

Effect of Pterocarpus santalinus ethanol leaf extract on relative organ to body weight
At 400 mg/kg, the ethanol leaf extractof*Pterocarpus santalinus* resulted in a significant increase in heart size compared to the control group ($p<0.05$). The relative organ to body weight ratio was 0.73 ± 0.24*at 400 mg/kg dose compared to 0.42 ± 0.44 for the control group, whereas at lower doses of 100 and 200 mg/kg, there was no significant difference in the relative organ to body weight ratio between the extract treated group and the control group (Table 3).

Effect of Pterocarpus santalinus ethanol leaf extract on lipid profile
The extract did not cause any significant changes in total cholesterol, and triglyceride levels, but the HDL levels were significantly increased at 100 mg/kg and 400 mg/kg doses of the extract, while the LDL levels significantly decreased at all the treatment doses (Table 4).
LDL cholesterol is often considered bad cholesterol because it causes atherosclerosis. HDL acts as a garbage collector, carrying LDL (bad) cholesterol from the arteries to the liver, where it is broken down and excreted. However, HDL cholesterol cannot remove all LDL cholesterol from the arteries. Only one-fourth to one-third of LDL cholesterol is carried by HDL.[23] Triglycerides are a type of fat that stores extra energy. High triglyceride levels, along with high LDL cholesterol or low HDL (good) cholesterol, are associated with fatty deposits in the arteries and increase the risk of heart attack and stroke. Epidemiological and clinical studies have clearly demonstrated an association between low HDL cholesterol levels and increased CVD risk.[24]

Table 1: Effect of *Pterocarpus santalinus* ethanol leaf extract on haematological parameters in Wistar rats

	Control	PSE Treatment (mg/kg)		
Hematological parameters	**DW(10 mL/kg)**	**100**	**200**	**400**
WBC ($\times10^9$/L)	8.22± 0.77	6.74± 1.31*	7.72± 0.72	7.28± 1.82
RBC ($\times10^{12}$/L)	8.31± 0.44	6.64± 0.36*	8.12 ± 0.57	7.70 ± 0.55
HGB (g/dL)	15.85± 0.56	11.49 ± 0.56*	14.38 ± 0.97	14.67 ± 0.19
HCT (%)	60.25± 2.03	56.61 ± 3.75	34.62 ± 3.17	53.41 ± 1.82
MCV (fL)	66.63 ± 0.43	60.30 ± 1.49	57.07 ± 0.91	69.62 ± 1.71
MCH (pg)	19.10 ± 0.12	17.80 ± 1.00*	18.63 ± 0.31	18.90 ± 0.21
MCHC (g/dL)	35.70 ± 0.03	27.41 ± 1.22*	32.76 ± 0.42	34.44 ± 0.75
PLT ($\times10^9$/L)	683.84 ± 40.55	471.20 ± 23.02*	652.41 ± 11.20	667.34 ± 59.32
LYM (%)	92.12 ± 4.46	89.22 ± 4.13	89.86 ± 6.18	86.14 ± 1.20
NEU ($\times10^9$/L)	12.34 ± 3.66	11.97 ± 3.55	13.24 ± 5.68	11.16 ± 5.33
EOS ($\times10^9$/L)	2.57 ± 0.85	2.42 ± 0.68	1.99 ± 0.149	1.91 ± 0.24

*Significantly different from the control (DW) at p<0.05. DW = distilled water,PSE = *Pterocarpussantalinusiethanol*leaf extract,WBC = white blood cells, MCHC = mean corpuscular hemoglobin concentration, PLT = platelet, RBC = red blood cells, HGB = haemoglobin, HCT = hematocrit, EOS = eosinophils, MCV = mean corpuscular volume, MCH = mean corpuscular hemoglobin, LYM = lymphocyte, NEU = neutrophils,z

Table 2: Effect of 28 days oral administration of *Pterocarpus santalinus* ethanol leaf extract on body weight of Wistar rats

Treatment	**Body Weight (g)**			
	Week 1	**Week 2**	**Week 3**	**Week 4**
DW (10 mL/kg)	185.31 ± 6.71	166.10 ± 4.31	189.11 ± 5.55	195.72 ± 4.12
PSE (100 mg/kg)	197.33 ± 30.10	196.65 ± 15.18	197.28 ± 3.12	198.22 ± 5.17
PSE (200 mg/kg)	201.23 ± 19.51	212.11 ± 12.35*	211.23 ± 11.53*	212.10 ± 17.44
PSE (400 mg/kg)	215.68 ± 11.39*	220.11 ± 8.21*	225.47 ± 6.71*	233.14 ± 1.23*

*Significantly different from the control (DW) at p<0.05. DW = distilled water,PSE = *Pterocarpus santalinus ethanol* leaf extract

Table 3: Effect of 28 days oral administration of *Pterocarpus santalinus*ethanol leaf extract on relative organ to body weight ratio in rats

Treatment	**Relative organ to body weight ratio**	
	intestine	**heart**
DW (10 mL/kg)	0.42 ± 0.14	0.42 ± 0.44
PSE (100 mg/kg)	0.45 ± 0.11	0.41 ± 0.13
PSE (200 mg/kg)	0.49 ± 0.19	0.44 ± 0.17
PSE (400 mg/kg)	0.75 ± 0.04*	0.73 ± 0.24*

*Significantly different from the control (DW) at p<0.05. DW = distilled water, PSE = *Pterocarpus santalinusi ethanol* leaf extract

The protective effect of HDL cholesterol on cardiovascular system has been shown to be voluntary in many ways. HDL displays its anti-atherosclerotic activity by preventing LDL oxidation. According to recent research, HDL improves cholesterol transport by promoting the removal of excess cholesterol from the cell, thus preventing the formation of oxidatively modified LDL.[25] the ability of *Pterocarpus santalinus* ethanol leaf extract to increase HDL levels and decrease LDL levels in rats, indicate that the plant has a potential to lower serum cholesterol levels in hyperlipidaemic conditions.

Effect of Pterocarpus santalinus ethanol *leaf extract on the histology of rat intestine and heart*

Histopathological studies of the brain showed normal histopathological features at all doses and moderate vacuolation at the 100 mg/kg dose of the extract. At all doses, histopathological analysis of the heart showed mild myocardial necrosis, while the control group (10 mL/kg) had normal characteristics. Normal long rod cells, striated muscle, and blood vessels were seen (Figures 1 and 2).

In the present study, the brain and heart of ratsadministered ethanol extract of *Pterocarpus santalinus* leaves for 28 days had almost normal histological features. No lesions (pathological abnormalities) were observed in these organs.Our findings are in agreement with previous studies on the biochemical and haematological responses of Wistar rats to *Pterocarpus santalinus*.[26,27] Additionally, studies have shown that fresh and dried leaves of *Pterocarpu ssantalinus* contain alkaloids, flavonoids, glycosides, saponins, tannins, phenolics and triterpenoids.[28,29]The antioxidant activity of some of the secondary metabolites such as saponins, tannins, phenols and triterpenoids present in the plant may be responsible for their ability to reduce necrotic tissue in the organs (brain and heart) investigated. Additionally, *Pterocarpus santalinus* extract has been shown to promote wound healing through three different mechanisms: contraction, tissue matrix deposition, and epithelialization. Open wound healing by contraction; Cell-matrix contact causes tissue to migrate to the wound site. Matrix deposition is the process of deposition of collagen, proteoglycans and binding of proteins to form a new extracellular matrix.[30,31] The process in which epithelial cells or remaining skin appendages (such as hair follicles and sebaceous glands) in the wound lose contact inhibition and migrate into the wound is called epithelialization. As migration progresses, the number of underlying cells increases and more epithelial cells are produced.[32]

The authors hereby recommend further studies on the characterization and subcellular studies of active components in the extracts of *Pterocarpus santalinus* leaves.

.

Table 4: Effect of *Pterocarpus santalinus* ethanol leaf extract on lipid profile in Wistar rats

	Control	PSE Treatment (mg/kg)		
Lipid profile	**DW(10 mL/kg)**	**100**	**200**	**400**
TC (mmol/L)	45.00 ± 8.11	48.80 ± 3.16	45.43 ± 3.43	50.17 ± 8.23
HDL (mmol/L)	36.20 ± 3.28	53.00 ± 3.12*	40.20 ± 1.88	56.75 ± 4.11*
LDL (mmol/L)	7.90 ± 2.51	6.20 ± 1.81*	6.51 ± 4.35*	6.50 ± 2.18*
TG (mmol/L	57.40 ± 2.11	55.40 ± 3.42	60.60 ± 10.19	58.00 ± 3.11

*significantly different from the control(DW) at p<0.05.DW = distilled water, PSE = *Pterocarpus santalinus ethanol*leaf extract, HDL = high density lipoprotein, LDL = low density lipoprotein, TC = total cholesterol, TG = triglycerides.

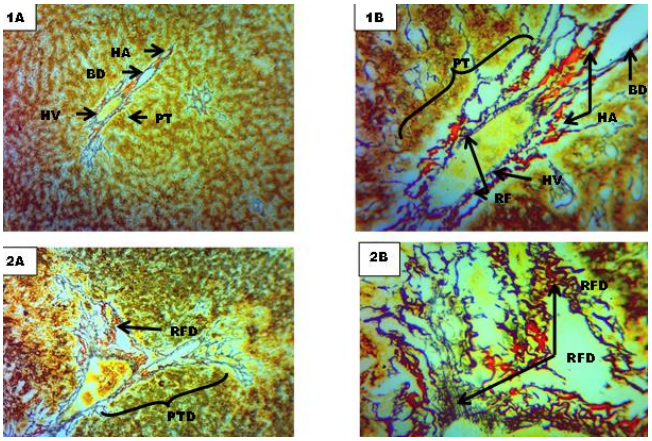

Figure 1: Histological section of the intestine (Hematoxylin and Eosin. H&E ×100).**(1A):** Control group, Shows normal neurons (N). **(1B):** 100 mg/kg PSE**(2A):** 200 mg/kg PSE**(2B):** 400 mg/kg PSE. PSE =*Pterocarpus santalinus* ethanol leaf extract.

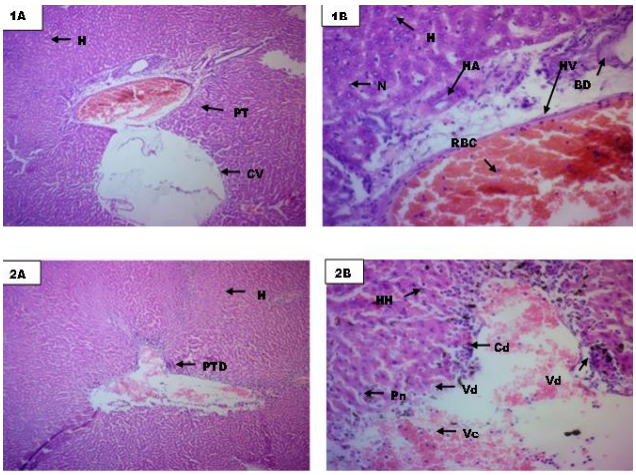

Figure 2: Histological section of the heart (Hematoxylin and Eosin. H & E ×100).**(1A):** Control group, Shows normal myocardium (M). **(1B):** 100 mg/kg PSE, no pathological feature of the myocardium (MN). **(2A):** 200 mg/kgPSE,no necrosis of myocardium (M). **(2B):** 400 mg/kgPSE, slight necrosis of myocardium (MN). PSE = *Pterocarpus santalinus*ethanol leaf extract.

Conclusion

The findings from this study show that *Pterocarpus santalinus* otherwise called red sandalwood does not have significant toxic effects when taken in low to moderate doses and is therefore relatively safe for use for medicinal purposes. However, more research is needed to determine its effect on vital organs of the body.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

References

1. Pathan, MM, Khan MA,Moregaonkar SD, Somkuwar AP and Gaikwad, NZ. Amelioration of paracetamol induced nephrotoxicity by Maytenusemarginata in male wistar rats. Int. J. Pharm. Pharm. Sci. 2013, 5: 471-474.
2. Kang SG, Lee GB, Vinayagam R, Do GS, Oh SY, Yang SJ, Kwon JB, Singh M. Anti-Inflammatory, antioxidative, and nitric oxide-scavenging activities of a quercetinnanosuspension with polyethylene glycol in LPS-Induced RAW 264.7 Macro Mol. 2022; 27(21):7432.
3. von Bartheld CS, Bahney J, Herculano-Houzel S. "The search for true numbers of neurons and glial cells in the human brain: A review of 150 years of cell counting". J. Comp. Neurol. 2016; 524 (18): 3865–3895.
4. Charkiewicz ED, Backstrand JR. Lead Toxicity and Pollution in Poland Int J Environ Res Public Health. 2020, 17 (12), p. 4385
5. Eid A, Zawia N. Consequences of lead exposure, and its emerging role as an epigenetic modifier in the aging brain. ToxicolLett. 2016, 15 (296), pp. 173-183
6. UgboguOC Okezie E, Agi GO, Ibe C,Ekweogu CN, Ude VN. A review on the traditional uses, phytochemistry, and pharmacological activities of clove basil (Ocimumgratissimum L.). Heliyon, 7 (11) (2021), p. e08404
7. Oyem JC, Chris-Ozoko LE, Enaohwo MT, Otabor FO, Okudayo VA, Udi OA.Antioxidative properties of Ocimumgratissimum alters Lead acetate induced oxidative damage in lymphoid tissues and hematological parameters of adult Wistar rats. Toxicol. Rep, 8 (2021), pp. 215-222
8. Zubairu SA, Festus OA, Simeon JO, Irabor I, Tosin JO. Effect of Anacardiumoccidentale Fruit Juice Extract on Haematological Parameters and Spleen of Paracetamol Induced Injury in Albino Rats.Global SciJou. 2021. Volume 9, Issue 7. Page 1640-1654.
9. Emily M. Toxicity. In: Cutler J, (2007). editor. In: Encyclopedia of Earth. Cleveland, Washington D.C.
10. Arumugam G, Swamy MK, Sinniah UR. Plectranthusamboinicus (Lour.)Spreng: Botanical, phytochemical, pharmacological and nutritional significance. Molecules. 2016; 21(4):369.
11. Anachuna KK, Moke EG, Oyem JC, Omogbiya AI, Daubry TME, Ebuwa EI. Ethanolic Extract of OcimumGratissimum (Scent Leaf) Leaves Improves Haematological Parameters in Restrain-Stressed Rats. J ApplSci Environ Manage 2021, 25 (9), pp. 1605-1611
12. Dutta K, Kli M, Najam A, Kumar R. and Kumar A. Ameliorative effect of seed extract of Pterocarpussantalinus

on coragen induced haematological alterations and serum biochemical changes in rats, JTEHS. 2004, 6(10): 194 – 202.
13. Olamilosoye KP, Akomolafe RO, Akinsomisoye OS, Adefisayo MA, Alabi QK.The aqueous extract of Ocimumgratissimum leaves ameliorates acetic acid-induced colitis via improving antioxidant status and hematological parameters in male Wistar rats. Egypt. J. Basic Appl. Sci. 2019, 5 (3), pp. 220-227.
14. Okechukwu N, Elizabeth F, Godwin U. Effects of aqueous extract of Ocimumgratissimum leaves and vitamin C on lead acetate-induced changes in the Thymus of adult Wistar rats effects of aqueous extract of Ocimumgratissimum leaves and vitamin C on lead acetate-induced changes in the Thymus of adult Wistar rats. IJBCCR, 26 (1) (2019), pp. 1-9
15. Asagba SO, Ichipi-Ifukor PC, Ichipi-Ifukor RN, J. Oyem JC. Palm oil fractions alter acute cadmium mediated haematotoxicity. Galician Med J, 26 (3) (2019), p. E201933
16. Duke, James. Handbook of Legumes of World Economic Importance.Springer Science & Business Media.2012. p. 49.
17. Balaban H, Balaban M,Nazıroğlu K, Demirci İS.The protective role of selenium on scopolamine-induced memory impairment, oxidative stress, and apoptosis in aged rats: the involvement of TRPM2 and TRPV1 channels. Mol. Neurobiol., 54 (2017), pp. 2852-2868, 10.1007/S12035-016-9835-0
18. Joseph OS., Jude EO and Joseph OT.Hepatoprotective activity of extract of HomaliumLetestui stem against carbon tetrachloride-induced liver injury. Adv. Herb. Med.2018;Vol 4(4), Page 1-11.
19. Widodo N, Puspitarini S, Widyananda MH, Alamsyah A, Wicaksono ST, Masruri M, Jatmiko YD. Anticancer activity of Caesalpiniasappan by downregulating mitochondrial genes in A549 lung cancer cell line. F1000Res. 2022; 11:169.
20. Ilesanmi OB, Ikpesu T. Neuromodulatory activity of trèvo on cyanide-induced neurotoxicity viz neurochemical, antioxidants, cytochrome C oxidase and p53. AdvTrad Med. 2020;21(2):297-304. https://doi.org/10.1007/s13596-020-00450-w.
21. Krishnamoorthy P, Stella J, Mohamed AJ, Anand M. Radical scavenging and antibacterial evaluation of Pterocarpussantalinus leaf in-vitro study. Int J Pharm Sci Res. 2011;2:1204–8.
22. Abdi Z, Eskandary H, Nematollahi-Mahani SN. Effects of Two Types of Human Cells on Outgrowth of Human Glioma in Rats.Turk Neurosurg. 2018;28(1):19-28. [PubMed ID: 27943226]. https://doi.org/107/1019-5149.JTN.18697-16.1.
23. Joseph OS , Builders M , Joseph O T , Famojuro TI, Ogira JO, Moses FD, Musa TL. Effect of the Demographic of Covid-19 on Different Countries; Using the USA for Comparism.IJMRA. Volume 04 Issue , 2021; 02. Page 193-203.
24. Joseph SO, Opeyemi JT. Effect of Clinical Study of Moringaoleifera on Body mass index, Low density lipoprotein and Triglyceride level in Patients on Tenofovir/lamivudine/efavirenz Combination Therapy. Adv. Herb. Med. 2021, Vol. 6.Issue 1.Page. 14-27 .
25. Mishra A, Srivastava R, Strivastava SP, Gautam S, Tamrakar AK, Maurya R. and Strivastava AK.Antidiabetic activity of heart wood of PterocarpusmarsupiumRoxb.and analysis of phytoconstituents. Indian J. Exp. Biol., 2013; 51(5): 363 – 374.
26. Sheikhbahaei F, Khazaei M, Nematollahi-Mahani SN. Teucriumpolium Extract Enhances the Anti-Angiogenesis Effect of Tranilast on Human Umbilical Vein Endothelial Cells. Adv Pharm Bull. 2018;8(1):131-9. [PubMed ID: 29670848]. [PubMed Central ID: PMC5896388].
27. Okokon JE., Joseph OS.andUmoh EE.. Nephroprotective activity of Homaliumletestui stem extract against paracetamol induced kidney injury. J ExpIntegr Med2016. Volume 6 (1): 38-43. DOI: 10.5455/jeim.250216.or.147.
28. Falodun A, Siraj R, Choudhary MI. GC-MS Insecticidal Leaf essential oil of *P. staudtii* Hutch and Dalz (Icacinaceae). Trop J. Pharm Res. 2009; 82:139-143.
29. Okolie NP, Falodun A, Oluseyi D. Evaluation of the antioxidant activity of root extract of pepper fruit (*Dennetiatripetala*), and its potential for the inhibition of Lipid peroxidation. Afr J. TradCompl and Altern Med. 2014; 11(3):221-227. Doi: 10.4314/ajtcam. v11i3.31
30. Simonyan KV, Chavushyan VA. Protective effects of hydroponic Teucriumpolium on hippocampal neurodegeneration in ovariectomized rats. BMC Complement Altern Med. 2016;16(1):415. [PubMed ID: 27776515]. [PubMed Central ID: PMC5078961]. https://doi.org/10.1186/s12906-016-1407-3.
31. Joseph OS, Builders M, Emem EU and Joseph OT. Effect of ethanol leaf extract of cassia angustifolia extract on liver of wister rats. GSJ.2021; 8(9).1112-11120.
32. Cheng-Chung WJ, Huang H.C, Chen WJ, Huang CN, Peng CH, and Lin CL. Epigallocatechingallate attenuates amyloid β-induced inflammation and neurotoxicity in EOC 13.31 microglia. Eur. J. Pharmacol. 2016;770, 16–24. doi: 10.1016/j.ejphar.2015.11.048