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Effect of *Chysophyllum albidum* Ethanol Leaf Extract on Haematological and Platelet Indices of Apparently Healthy Wistar Rat

Juliet N. Ozioko[1], Obinna V. Ayogu[2], Benjamin O. Ezema[1], Dilibe C. Uramah[3] and Kingsley O. Omeje*[,1]

[1]*Department of Biochemistry, University of Nigeria*
[2]*Department of Zoology and Environmental Biology, University of Nigeria*
[3]*Department of Plant Science and Biotechnology, University of Nigeria*

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Platelet indices, Hematological indices, Phytomedicine, *Chysophyllum albidum*, Enzymes

ABSTRACT

Chysophyllum albidum ethanol leaf extract was studied to ascertain it potentials on hematological indices and hepatocyte of wistar albino rat. Twenty-five rats that weighed 98-168g were separated into five groups. Phytochemicals were quantified using standard methods. Alkaloids, flavonoids, tannins, saponnins and terpernoids were detected. The leaf extract had 0.415 % of alkaloids, 0.102 mg/TAEq of tannins, 0.211 mg/QEq of flavonoids and 0.360 mg/GAEq of phenolics. Phytol, oleic acids, hexadecanoic acids and octadecanoic acids were detected in the leaf extract by Gas Chomatography-Mass Spectroscopy. White blood cells, hemoglobin and platelets were some of the hematological indices increased after the oral administration of the extract. Red cell distribution width (RDW), a platelet index implicated in cardiovascular ailments was lowered after consumption of the leaf extract of *C. albidum.* The liver marker enzymes aspartate transaminase and alanine transaminase showed no significant changes in their serum activity. Similarly, superoxide dismutase and catalase showed no significant increase after the period of study.

INTRODUCTION

Chysophyllum albidum is common tree found in Africa, known for its edible fruits and medicinal values (Amusa *et al*., 2003). It is predominant in rainforests, which can reach 25-37m when matured (Orwa *et al*., 2009). It is known commonly Nigeria as Agbalumo and Udara among the Yorubas and Igbos. It is rich in phytochemicals such as alkaloids, phenols and tannins (Okoli and Okere, 2010), alkaloids and tannins (Ibrahim *et al*., 2017). Imaga and Urua (2013) and Egharevba *et al*. (2015) reported that the plant is rich in phytochemicals.

The plant is used to cure yellow fever, malaria, treatment of infections and and sin eruptions (Idowu *et al*., 2006). Similarly, the stem, seeds and root extracts of *C. albidum* exhibit antimicrobial, anti-inflammatory, anti-diarrheal and anti-haemorrhoidal properties (Okoli and Okere, 2010). These pharmacological activities are elicited by phytochemicals they contain (Omeje *et al*., 2014), it is a remedy for fever due to alkaloids present and the flavonoid is responsible for anti-allergic, anti-microbial and anti-cancer activity (Adisa, 2000). There are several side effects associated with the usage of phytomedicine in the treatment of ailments, such as deleterious effect on blood (Esonu *et al*., 2001), liver and kidney (Stickel *et al*., 2005).

Different parts of *Chysophyllum albidium* plant (leaf, stem-bark and root extracts) have been employed in ethno-medicine as antimicrobial agent (Okoli and Okere, 2010), fertility enhancer (Oigbochie *et al*., 2019) and antimalarial agent (Odediran *et al*., 2020). Though, the choice of preparation method depends on the type of ailment targeted, plant extract could be taken as a tonic (Morton, 1987), boiled or using local gin.

Despite all the medicinal benefits attributed to the different parts of *C. albidum* plant, some individual reports on dizziness and other allergic conditions after ingesting the trado-medicine have appeared. For these reasons it becomes important to evaluate the ethanol *C. albidum* leaf extract on the biochemical indices of Wistar rats.

MATERIALS AND METHODS

C. albidum leaf was harvested from its natural habitat Edem-ani, Nsukka LGA, Enugu State of Nigeria in the month of March, 2019. After fourteen days drying, it was pulverized into fine powder using electric blender. The ground leaf material (773.760 g) was extracted by

* Corresponding author: kingsley.omeje@unn.edu.ng
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macerating in 1.2L of 70% ethanol for 48 h and concentrate, yielding 18.48 g of the extract stored for further use.

Qualitative and quantitative phytochemical analysis

Qualitative analysis of the phytochemicals was determined using AOAC (2010) method with little modification. The phytochemicals screened were alkaloids, flavonoids, tannins, saponin, terpenoid and steroids.

The phenolic content was determined using the method described by Nwidu *et al*. (2017). The total flavonoid, alkaloid and tannin content of the leaf extract were determined according to Senguttuvan *et al*. (2014), using quercetin as the reference compound.

Gas chomatography-mass spectroscopy (GC-MS) analysis of the ethanol extract

GC-MS analysis was done using GC system comprising a Gas Chomatograph interfaced to a Mass Spectrometer (Schimadzu GCMS-QP2010).

Experimental animal

Twenty-five (25) adult Wistar albino rats (98-168 g) were used for the study. They were housed Biochemistry Department Animal House, and fed with commercial rat chow. The animals were divided into 5 groups, wach of five rats. They received the extract orally for twenty-eight days as follows: Group I: 2 ml of distilled water/kg body weight per day; Group II: 50 mg/kg b.w. of ethanol extract per day; Group III: 100 mg/kg b.w. of the ethanol extract per day; Group IV: 150 mg/kg b.w. of the ethanol extract per day; Group V: 200 mg/kg b.w. of the ethanol extract per day.

On day 28, blood samples were drawn by cardiac puncture; chloroform was used as a sedative agent. Each container was thoroughly mixed with anticoagulant (3.8% Tri-sodium-citrate) to prevent coagulation of the blood.

Haematological indices

The blood samples were drawn from the animals (control) at the start of experiment and then on the 28th day for determination of hematological parameters such as hemoglobin, white blood cells, haemocrit, red blood cells, platelet concentration, mean cell volume and lymphocyte concentration, platelet indices (red cell distribution width standard deviation, red cell distribution width coefficient of variation, platelet distribution width, mean platelet volume, platelet large cell ratio) by an Automated Hematology Sysmex Analyzer (Coulter Electronics, Bedfordshire, England).

Biochemical components of blood

Superoxide dismutase activity was determined using Martin *et al*. (1987) method. Alanine aminotransferase and aspartate aminotransferase activities were measured as described by Reitman and Frankel (1957). Catalase activity was determined as described by Aebi (1984) by monitoring the ultraviolet absorption of the sample at 240 nm as hydrogen peroxide is decomposed in by catalase.

Statistical analysis

The statistical packaged used was the statistical package for social sciences (SPSS), version 1. Differences were considered significant at $p < 0.05$.

RESULTS AND DISCUSSION

C. albidum was harvested from Edem-ani community, its natural habitat and macerated for 48 h. The extract yield was 18.48 g. Alkaloids, tannins, saponins, terpernoids and flavonoids were detected, while steroids was not detected. The result agreed with the report of Oputah *et al*. (2016), who reported saponins and flavonoids, while tannins, alkaloids, terpenoids, saponins, reducing sugars, steroids and flavonoids were reported by Akinpelu *et al*. (2016) in their study on *C. albidum* stem bark extract. It is evident that the plant parts of *C. albidum* are rich source of phytochemicals, which could be responsible for the reported pharmacological activities. Similarly, Oguntoyinbo *et al*. (2015) reported flavonoids, tannins, terpernoids and cardiac glycoside in the leaf of *C. albidum*.

Table I shows the concentration of alkaloids (0.415%), tannins were (0.102 g/TAEq), total flavonoids (0.211 mg/QEq) and total phenolic (0.360 mg/GAEq). Total phenolic and flavonoid content were high when compared to 68.3 µg GAE/g and total flavonoid of 3.71 mg reported by Asare *et al*. (2015). Also, low total phenol content and total flavonoid content of 0.47mg/gQE were reported by Oguntoyinbo *et al*. (2015). The total flavonoid content of *C. albidum* leaf extract was low, when compared to 1.79 mg/gQE reported for *Euphorbia nerufolia* leaf extract (Pracheta *et al*., 2010). The antimicrobial property may be attributed to the presence of phenolic compounds. This result indicates that the leaf extract could possess antioxidant activity due to the presence of polyphenols. Some pharmacological activities attributed to alkaloids include antimicrobial, cytotoxic, antioxidant, antimutagenic, and hallucinogenic properties (Patel *et al*., 2012). Tannin is important because of its ability to mop up free radicals (Deng *et al*., 2019), that can bind and precipitate or shink proteins (Ashok and Upadhyaya, 2012).

Figure 1 shows Gas Chomatography-Mass Spectrometry analysis (GC-MS) (Shibula and Velavan, 2015) of the ethanol extract of *C. albidum* which shows eight peaks. The corresponding compounds identified are

shown in Table II. n-Hexadecanoic acid is an important biocidal agent. It has hypo-cholesterolemic and antioxidant properties (Komansilan *et al*., 2012). Phytol has been reported to significantly reduce the parasitic load of human schistosomiasis (Moraes *et al*., 2014). GC-MS was employed in studying the bioactive components of Physalis minima leaves (Karpagasundari and Kulothungan, 2014).

Table I. Quantitative phytochemical composition of ethanolic leaf extract *C. albidum*.

Phytochemicals	Composition
Alkaloid content	0.415 %
Tannin	0.102 mg/TAEq
Total Flavonoid content	0.211 mg/QEq
Total phenolic content	0.360 mg/GAEq

Table II. Compounds identified by GC-MS from ethanol extract of *C. albidum*.

S. No.	Name of compound	Conc. (Area %)	Retent. time (s)	Mol. formular
1	Pentadecanoic acid	1.72	19.32	$C_{17}H_{34}O_2$
2	n-hexadecanoic acid	19.86	19.97	$C_{16}H_{32}O_2$
3	11, 14, 17 eicosatrienoic acid	1.33	21.79	$C_{21}H_{36}O_2$
4	Trans-phytol	2.92	22.08	$C_{20}H_{40}O$
5	Oleic acid	56.40	22.77	$C_{18}H_{34}O_2$
6	Octadecanoic acid	9.42	23.15	$C_{18}H_{36}O_2$
7	Hexadecanoic acid	1.70	25.16	$C_{19}H_{38}O_4$
8	9-Octadecenal	6.65	27.44	$C_{18}H_{34}O$

Table III shows that the oral administration of the extract had no significant impact on the red blood cell count, while the white blood cell increased significantly when compared with the control. At 200 mg/kg bwt of the extract, the hemoglobin concentration increased significantly when compared to the control. Also, PCV and MCHC reduced significantly when compared to the control. The values of lymphocytes and neutrophil did not show any significant change when compared with the control. This suggests that, the leaf extract of *C. albidum* contain some important pharmacological agents responsible for impairment in the production of blood cells (PCV and MCHC) (Adebayo *et al*., 2011). The changes observed in some of the indices are an indication that some of the phytochemicals present have impact on blood indices synthesis and morphology. Tannin and alkaloids have been reported to cause changes in blood parameters (Deng *et al*., 2019). Similarly, the mechanism of antimicrobial property of *C. albidum* leaf extract could by increasing the concentration of the white blood cells, thereby mobilizing them to the site of infection. Omeje *et al*. (2014) had reported the alteration of blood indices by the leaf extract of *C. olitorus*. The significant increase in the values of platelet at all doses suggests that *C. albidum* may be of great importance to an individual who is to under cesarean section in order to help boost platelet aggregation, thereby leading to wound healing.

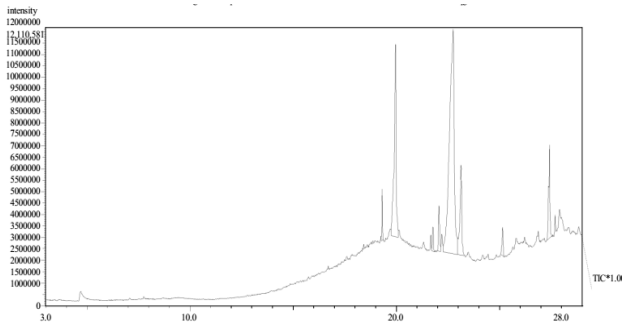

Fig. 1. GC-MS spectra of the leaf extract of *C. albidum*.

Table IV shows the effect of leaf extract on platelet indices. There was significant decrease of RDW-CV and PDW when compared to control group. A dose dependent decrease of the RDW-CV concentration was observed. The concentrations of MPV and P-LCR and RDW-SD increased significantly when compared with the control group. This is in accordance with the findings of Ofem *et al*. (2012) where doses of plant extract caused decrease in MPV, P–LCR and PDW of albino rats. This suggests the ethanol extract of *C. albidum* does not contain bioactive compound that affects the tested parameters. One of the indicators of cardiovascular mortality is increased red cell distribution width (RDW) (Söderholm, *et al*., 2015). This suggests the consumption of *C. albidum* leaf extract may not be predisposing a consumer to any cardiovascular illness. According to Tonelli *et al*. (2008), increased RDW is implicated in long-term mortality of patients suffering from coronary artery disease. Hence, the decrease observed, shows that the ethanol extract of *C. albidum* leaf may not cause or induce cardiovascular diseases by platelet index increase. Similarly, iron deficiency anemia has been linked with increased RDW (Khan *et al*., 2014). The non-significant increase in RDW shows that the extract may not have deleterious effect or inhibit red blood cell synthesis. Presence of tannin in plant extract has been implicated in the alteration of platelet indices (Muriithi *et al*., 2015).

Aspartate aminotransferase (AST) and alanine

Table III. Effect of *C. albidum* leaf extract effect on haematological indices of albino rats.

Hematological parameter	Control	50 mg/kg bwt	100 mg/kg bwt	150 mg/kg bwt	200 mg/kg bwt
White blood cell ($\times10^9$/L)	5.28±1.29	5.35±0.14	7.41±1.62	7.21±0.22	9.05±0.13
Red blood cell ($\times10^{12}$/L)	5.11±1.77	5.20±1.31	6.45±0.31	5.34±0.40	6.09±0.62
Hemoglob. (g/dl)	6.72±0.43	6.53±0.83	8.64±0.92	6.07±0.11	8.35±1.03
HCT (%)	32.17±0.38	23.91±1.65	31.60±0.52	24.31±1.46	33.24±0.29
PCV(fl)	66.24±2.46	45.72±2.52	48.14±3.87	49.74±2.38	44.04±4.23
MCHC(pg)	22.75±0.18	21.92±0.59	19.20±0.53	19.73±1.26	19.60±0.22
Platelet ($\times10^9$/L)	131.73±63.34	147.72±11.07	129.66±21.40	301.80±0.74	344.46±4.23
Lymphocyte (%)	68.29±0.56	69.85±0.62	66.39±2.81	74.27±3.70	70.04±0.28
Neutrophils (%)	25.42±1.37	24.72±0.56	30.44±0.41	33.63±1.64	23.89±3.22

Table IV. Effect of oral administration of ethanol extract of *C. albidum* on platelet indices of wistar rat

Platelet indices	Control	50 mg/kg bwt	100 mg/kg bwt	150 mg/kg bwt	200 mg/kg bwt
RDW-CV (%)	20.73±1.92	16.22±1.50	14.38±0.80	13.85±0.62	13.42±0.00
PDW (fL)	9.94±0.41	5.42±0.46	3.76±0.63	5.11±1.28	7.93±2.06
MPV (fL)	-9.27±0.77	5.29±0.31	-6.83±0.40	-9.61±.0.43	-8.63±0.10
P-LCR (%)	4.65±0.43	9.42±0.38	5.61±0.92	7.52±0.10	7.16±0.53
RDW-SD (fL)	27.59±0.28	27.65±0.90	25.40±0.65	22.65±0.00	19.34±0.44

RDW.CV, red cell distribution width coefficient of variation; PDW, platelet distribution width; MPV, mean platelet volume; P-LCR, platelet large cellratio; RDW-SD, red cell distribution standard deviation.

Table V. Effect of oral administration of ethanol extract of *C. albidum* on representative liver function and oxidative stress related enzymes in wistar rats.

Biochemical indices	Control	50 mg/kg bwt	100 mg/kg bwt	150 mg/kg bwt	200 mg/kg bwt
Alanine transaminase (IU/L)	116.05±0.43	113.92±0.30	109.20±0.42	132.09±0.18	193.22±0.12
Aspartate transaminase (IU/L)	184.76±0.26	184.45±0.18	139.28±0.30	170.58±0.07	186.41±0.25
Catalase (IU/L)	194.50±0.49	207.53±0.32	171.06±0.61	193.41±0.70	176.39±0.10
Superoxidismutase (IU/L)	202.70±0.90	200.65±0.25	186.14±1.30	185.29±0.05	213.12±0.29

aminotransferase (ALT) are some enzymes considered as indicators of the health of the liver (Trampuz *et al*., 2003). Table V shows effect of varying concentrations (50, 100, 150 and 200mg/kg) of extract of *C. albidum*. Increase in serum ALT is common in hepatic necrosis (Duncan *et al*., 2006). At concentrations of 150 and 200 mg/kg body weight, there was significant increase in the serum ALT. The observed increase suggests the low concentration of free radicals in the biological system, which could be attributed to the ability of some bio active agents to mop up these free radicals or maintaining the integrity of the hepatocytes to produce adequate enzymes needed to play the antioxidant role. Omeje *et al*. (2016) reported hepatoprotective potential of ethanol extract of *C. olitorus***.** AST increase in serum signifies liver damage (Dasofunjo *et al*., 2013). The oral administration of the extract showed a similar result to *Buchholzia coriacea* extract on *Plasmodium berghei* infected mice as reported by Enechi *et al*. (2016)**.** Therefore, the significant decrease obtained suggests the extract has the ability to protect the integrity of the animal liver.

Superoxide dismutase (SOD) is an enzyme responsible for scavenging free radicals for physiological defense strategies in living organisms (Stephanine *et al*., 2020). Varying concentration of *C. albidum* ethanol extract has shown a significant decrease when compared to control group. The results show a dose dependent decrease in the activity of SOD except for 200 mg/kg group. This is suggestive that high concentration of free radical was generated in vivo, hence the decreasing

concentration of the enzyme responsible its mop up. This report is in line with the study by Owolabi *et al*. (2008). Similarly, Nwobodo *et al*. (2018) reported decreased SOD in their work on *Azadirachta indica*. Catalase is one of the antioxidant enzymes that plays essential role in the antioxidant protection biological systems (Ighodaro and Akinloye, 2018). Among the concentrations studied, there was no significant difference when compared to the control. Suggesting that, the rate of generation of free radical was in equilibrium with the rate of its clearance. This could be attributed to the presence of polyphenolic compounds in the ethanol extract. Sani *et al*. (2012) reported increased concentration of catalase and superoxide dismutase in their work on thee medicinal plants. There is synergistic relation between catalase and superoxide dismutase, since they are the first line of body defense against oxidative stress (Ighodaro and Akinloye, 2018).

CONCLUSION

In conclusion, the oral administration of *C. albidum* leaf extract did not cause significant alteration in the hematological and platelet indices (RDW, PDW, MPV and P–LCR) at the doses studied after 28 day consumption. One of the indicators of cardiovascular mortality is increased red cell distribution width (RDW), which was reduced by the ethanol extract. This suggests that the consumption of *C. albidum* leaf extract may not be predisposing a consumer to any cardiovascular illness. This suggests therefore, there is no harmful effect associated with the consumption of *C. albidum*, however, having established the preservatory property of the *C. albidum* extract on healthy models, further studies could be carried out on diseased conditions to ascertain if the extract is curative.

Statement of conflict of interest

The authors have declared no conflict of interest.

REFERENCES

Adebayo, A.H., Abolaji, A.O., Kela, R., Ayepola, O.O., Olorunfemi, T.B. and Taiwo, O.S., 2011. Antioxidant activities of the leaves of *C. albidum* G. *Pak. J. Pharma. Sci*., **24**: 545-551. https://doi.org/10.1055/s-0031-1282414

Adisa, S.A., 2000. *Vitamin C, protein and mineral contents of African apple* (*Chysophyllum Albidum*) In: *Proceedings of the l8th annual conference of NIST* (Eds. S.A. Garba, I.F. Ijagbone, A.O. Iyagba, A.O. lyamu, A.S. Kilani and N. Ufaruna). pp. 141-146.

Aebi, H., 1984. *Catalase in vitro: Methods of enzymatic analysis.* Published by Academic Press, New York. pp. 671-684.

Akinpelu, D.A., Odewade, J.O., Aiyegor, O.A., Ashafa, A.O.T., Akinpelu, O.F. and Agunbiade, M.O., 2016. Biocidal effects of stem bark extract of Chysophyllum albidium G. Don on vancomycin-resistant Staphylococcus aureus. *BMC Complem. Altern. Med*., **16**: 105-last page. https://doi.org/10.1186/s12906-016-1080-6

Amusa, N.A., Ashaye, O.A. and Oladapo, M.O., 2003. Biodeterioration of african star apple (*Chysophyllum albidum)* in storage and the effect on its food value. *Afri. J. Biotech*., **2**: 56-59. https://doi.org/10.5897/AJB2003.000-1011

AOAC, 2010. *Official methods of analysis of association of official analytical chemists*. 18th Edition, Washington, DC.

Asare, I.K., Okyere, A.A., Duah-Bissiw, D., Ofosu, D.O. and Darfour, B., 2015. Nutritional and phytochemical constituents of the african star apple (*chysophyllum albidum* g. Don). *Annls Fd. Sci. Tech*., pp. 138-146.

Ashok, P.K. and Upadhyaya, K., 2012. Tannins are astringent. *J. Pharmacog. Phytochem*., **1**: 45-50.

Dasofunjo, K., Nwodo, O.F.C., Yakubu, O.E., Ejoba, R., Ukpanukpong, R.U., Ipav, S.S., Ugwu, M.N., Okafor, A.I, Girgi, S.L., 2013. Hepatoprotective effect of *Piliostigma thonningii* leaves on male Wistar albino rats. *Asian J. Pl. Sci. Res*., **3**: 13-17.

Deng, L., Qi, Y., Liu, Z., Xi, Y. and Xue, W., 2019. Effect of tannic acid on blood components and functions. *Coll. Surf. B: Biointer*., **184**: 110505. https://doi.org/10.1016/j.colsurfb.2019.110505

Duncan, G.E., Moy, S.S., Lieberman, J.A. and Koller, B.H., 2006. Typical and atypical antipsychotic drug effects on locomotor hyperactivity and deficits in sensorimotor gating in a genetic model of NMDA receptor hypofunction. *Pharmacol. Biochem. Behav*., **10**: 481-491. https://doi.org/10.1016/j.pbb.2006.09.017

Egharevba, H.O., Ibrahim, J.A., Nduaguba, G.A. and Kunle, O.F., 2015. Phytochemical, proximate pharmacognosy analyses and thin layer chomatography of Chysophyllum albidum seed. *Ew. J. Herb. Chem. Pharmacol. Res*., **1**: 6-12, 40.

Enechi, O.C., Okpe, C.C., Ibe, G.N., Omeje, K.O. and Ugwu Okechukwu, P.C., 2016. Effect of *Buchholzia coriacea* methanol extract on haematological indices and liver function parameters in *Plasmodium berghei*-infected mice. *Glob. Vet.,* **16**: 57-66.

Esonu, B.O., Emenalom, O.O., Udedibe, A.B.I., Okoli, I.C., Herbert, U. and Ekpor, C.F., 2001.

Performance and blood chemistry of weaner pigs fed raw *Mucuna* bean (Velvet bean) meal. *Trop. Anim. Prod. Invest*., **4**: 49-54

Ibrahim, H.O., Osilesi, O., Adebawo, O.O., Onajobi, F.D. and Karigidi, K.O., 2017. Nutrients compositions and phytochemical contents ofedible parts of chysophyllum albidum fruit. *J. Nutr. Fd. Sci*., **7**: 579.

Idowu, T.O., Iwalewa, E.O., Aderogba, M.A., Akinpelu, B.A. and Ogundaini, A.O., 2006. Biochemical andbehavioural effects of eleagnine from *Chysophyllum albidum*. *J. biol. Sci*., **6**: 1029-1034.

Ighodaro, O.M. and Akinloye, O.A., 2018. First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in theentire antioxidant defence grid. *Alex. J. Med*., **54**: 287–293. https://doi.org/10.1016/j.ajme.2017.09.001

Imaga, N.O.A. and Urua, E.E., 2013. Chemical and antioxidant evaluation of star apple fruit (*Chysophyllum albidum*) crude extracts. *Planta Med. Congress Abstract,* pp. 79-83. https://doi.org/10.1055/s-0033-1336525

Karpagasundari, C. and Kulothungan, S. 2014. Analysis of bioactive compounds in Physalis minima leaves using GC MS, HPLC, UV-VIS and FTIR techniques. *J. Pharmacog. Phytochem.,* **3**: 196-201.

Khan, H., Khan, K., Raziq, F. and Naseem, A., 2014. Iron deficiency anemia; red cell distribution width (RDW) and red cell indices in the prediction of among healthy women in third trimester of pregnancy. *Prof. med. J*., **21**: 100-105.

Komansilan, A., Abadi, A.L., Yanuwiadi, B. and Kaligis, D.A., 2012. Isolation and identification of biolarvicide from Soursop (Annona muricata Linn) seeds to mosquito (Aedes aegypti) larvae. *Int. J. Eng. Technol*.**, 12**: 28–32.

Martin, J.P., Dailey, M. and Sugarman, E. 1987. Negative and positive assays of superoxide dismutase based on hematoxylin autoxidation. *Arch. biochem. Biophys.,* **255**: 329-336.

Moraes, Jd., de Oliveira, R.N., Costa, J.P., Junior, A.L.G., De Sousa, D.P., Freitas, R.M., Allegretti, S.M. and Pinto, P.L.S., 2014. Phytol, a diterpene alcohol from chlorophyll, as a drug against neglected tropical disease schistosomiasis mansoni. *PLoS Neglect. Trop. Dis*., **8**: e2617. https://doi.org/10.1371/journal.pntd.0002617

Morton, J., 1987. *Fruits of warm climate*. Star Apple. Johnson pub. Miami, pp. 408-410.

Muriithi, N.J., Maina, G.S., Maina, M.B., Kiambi, M.J., Kelvin, J.K., Umar, A., Mwonjoria, K.J., Njoroge, W.A., Ngugi, M.P., Njagi, N.M.E., 2015. Determination of hematological effects of methanolic leaf extract of *Vernonia lasiopus* in normal mice. *J. Blood Lymph,* **5**: 3-9.

Nwidu, L.L. Elmorsy, E., Thornton, J., Wijamunige, B., Wijesekara, A., Tarbox, R., Warren A. and Carter, W.G., 2017. Anti-cholinesterase activity and antioxidant properties of extracts and fractions of *Carpolobia lutea*. *Pharm. Biol*., **55**: 1875-1883. https://doi.org/10.1080/13880209.2017.1339283

Nwobodo, E.I., Nwosu, D.C., Ogbodo, S.O., Ugwuene, F.O., Ihim, A.C., Ani, O.N., Nnodim, J.K. and Ani, O., 2018. Effects of *Azadirachta indica* leaf aqeous extract on the antioxidant enzymes in paracetamol-induced hepatotoxicity in Wistar rats. *Int. J. Biol. Chem. Sci*., **12**: 1-10. https://doi.org/10.4314/ijbcs.v12i1.1

Odediran, S.A., Awosode, K.E., Adegoke, T.A., Odebunmi, K.A., Oladunjoye, B.B. and Obasanya, A.A. 2020. Combinations of *Chysophyllum albidum* and *Citrus aurantifolia* as antimalarial agents and their effects on orthodox antimalarial drugs in mice. *Annls. Complement. Altern. Med*., **2**: 1007.

Ofem, O.E., Ani, E.J. and Eno, A.E., 2012. Effect of aqueous leaves extract of *O. gratissimum* on hematological parametres in rats. *Int. J. appl. Basic med. Res*., **2**: 38-43. https://doi.org/10.4103/2229-516X.96807

Oguntoyinbo, O.O., Abdus-Salaam, R.B., Bello, W.A. and Ifesan, B.O.T., 2015. Evaluation of the phytochemical, antioxidant and antimicrobial properties of extracts from *Chysophyllum albidum* (African star Apple) leaf. *J. Fd. Techn. Res*., **2**: 1-10. https://doi.org/10.18488/journal.58/2015.2.1/58.1.1.10

Oigbochie, E.V., Omage, K. and Odiase, E.D., 2019. Aqueous root extract of *C. albidum* caused dose and duration dependent increase in some reproductive hormone and spermatogenic arrest in the testes of male Wistar rats. *Clin. Phytosci*., **5**: 1-8. https://doi.org/10.1186/s40816-018-0095-6

Okoli, B.J., Okere, O.S., 2010. Antimicrobial activity of the phytochemical constituents of *Chysophyllum albidum* (African star apple) plantation. *J. Res. Nat. Dev*., **8**: 1-8.

Omeje, K., Omeje, H., Odiba, A., Anunobi, O. and Ukegbu, C., 2016. Liver enzymes and lipid activities in response to Corchorus olitorius leaf extract. *Int. J. Curr. Res. Biosci. Pl. Biol*., **3**: 45-49. https://doi.org/10.20546/ijcrbp.2016.306.007

Omeje, K.O., Odo, C.E., Ejembi, D.O., Ossai, N.I.,

Eneje, V.O., Chukwuka, R.S. and Omeje, H.C., 2014. The effects of ethanol extract of *Corchorus olitorus* leaves on haematological indices of Wistar albino rat. *Acad. J. Fd. Res*., **2**: 7-9. https://doi.org/10.13005/OJPS01.0102.02

Oputah, S.I., Mordi, R.C., Ajanaku, K.O., Olugbuyiro, J.A.O., Olorunshola, S.J. and Azuh, D.E., 2016. Phytochemical and antibacterial properties of ethanolic seed extracts of *Chysophyllum albidum* (African Star Apple). *Orient. J. Physi. Sci*., **1**: 05-09.

Orwa, C., Mutua, A., Kindt, R., Jamnadass, R. and Anthony, S., 2009. *Agroforestry database: A tree reference and selection guide version 4.0.* World Agroforestry Centre, Kenya.

Owolabi, M.A., Jaja, S.I., Oyekanmi, O.O. and Olatunji, J., 2008. Evaluation of the antioxidant activity and lipid peroxidation of the leaves of *Vernonia amygdalina*. *J. Compl. Integr. Med*., **5**: 1-9. https://doi.org/10.2202/1553-3840.1152

Patel, K., Gadewar, M., Tripathi, R., Prasad, S.K. and Patel, D.K., 2012. A review on medicinal importance, pharmacological activity and bioanalytical aspects of beta-carboline alkaloid "Harmine". *Asian Pac. J. trop. Biomed*., **2**: 660-664. https://doi.org/10.1016/S2221-1691(12)60116-6

Pracheta, V.S., Ritu, P. and Sadhana, S., 2010. *In vitro* free radical scavenging and antioxidant potential of ethanolic extract of euphorbia neriifolialinn. *Int. J. Pharm. Pharmaceut. Sci*., **3**: 238-242.

Reitman, S. and Frankel, S.A., 1957. Colorimetric method for determination of serum glutamic-oxaloacaetic and glutamic-pyruvic transaminases. *Am. J. clin. Pathol*., **28**: 56-62. https://doi.org/10.1093/ajcp/28.1.56

Sani, M.F., Kouhsari, S.M. and Moradabadi, L., 2012. Effects of thee medicinal plants extracts in experimental diabetes: antioxidant enzymes activities and plasma lipids profiles in comparison with metformin. *Iran. J. Pharma. Res*., **11**: 897-903.

Senguttuvan, J., Paulsamy, S. and Karthika, K., 2014. Phytochemical analysis and evaluation of leaf and root parts of the medicinal herb, *H. radicata* L. for *in vitro* antioxidant activities. *Asian Pac. J. trop. Biomed*., **4**: S359-S369. https://doi.org/10.12980/APJTB.4.2014C1030

Shibula, K. and Velavan, S., 2015. Determination of phytocomponents in methanolic extract of Annona muricata leaf using GC-MS technique. *Int. J. Pharmacogn. Phytochem. Res*., **7**: 1251-1255.

Söderholm, M., Borné, Y., Hedblad, B., Persson, M. and Engström, G., 2015. Red cell distribution width in relation to incidence of stroke and carotid atherosclerosis: A population-based cohort study. *PLoS One*, **10**: e0124957. https://doi.org/10.1371/journal.pone.0124957

Stephenie, S., Chang, Y.P., Gnanasekaran, A., Esa, N.M. and Charles, G., 2020. An insight on superoxide dismutase from plants for mammalian health enhancement. *J. Funct. Fds*., **68**: 103917. https://doi.org/10.1016/j.jff.2020.103917

Stickel, F., Patsenker, E. and Schppan, D., 2005. Herbal hepatotoxicity. *J. Hepatol*., **43**: 901–910. https://doi.org/10.1016/j.jhep.2005.08.002

Tonelli, M., Sacks, F., Arnold, M., Moye, L., Davis, B. and Pfeffer, M., 2008. Relation between red blood cell distribution width and cardiovascular event rate in people with coronary disease. *Circulation,* **117**: 163–168. https://doi.org/10.1161/CIRCULATIONAHA.107.727545

Trampuz, A., Jereb, M.J., Muzlovi, C.I. and Prabhu, R.M., 2003. Clinical review of severe malaria. *Crit. Care*, **7**: 315-323. https://doi.org/10.1186/cc2183