



Influence of *Chrysophyllum albidum* Seed Endosperm Extract on Hematologic, Hepatic, Nephrotic and Histologic Alterations in Monosodium Glutamate-Compromised Rats

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Abstract

To minimize its waste burden, underutilized *Chrysophyllum albidum* (*C. albidum*) seed could be exploited as a plant-based pharmafood together with widely used but potentially toxic food flavouring, monosodium glutamate (MSG). This study was designed to ascertain the influence of *C. albidum* seed endosperm extract (CASEE), on the hematologic, hepatic, nephrotic and histologic alterations in MSG-compromised rats. Adult male albino rats (120-160 g) were randomly allotted to six groups of 10 rats each. Group 1 rats received normal saline (1 ml), Group 2 received CASEE (200 mg/kg), Group 3 received MSG (8000 mg/kg), while groups 4, 5 and 6 rats in addition respectively received 200, 400 and 600 mg/kg of CASEE. Exposure was orally and daily for 14 days. Results revealed significant ($P < 0.05$) alterations in the hematologic, hepatic, nephrotic and histologic parameters in MSG-treated rats compared to others. CASEE (200 mg/kg)-fed rats had comparable effect as the control and caused significant ($P < 0.05$) but selective dose dependent reduction in MSG effect. This study demonstrated that CASEE (200 mg/kg) improved but MSG (800 mg/kg) compromised the rats' hematologic, hepatic, nephrotic and histologic integrity. CASEE reduced the MSG effect in the rats *via* probable concerted mechanism leading to beneficial response on the rats' hematology, liver and kidney functions and histology. The dietary and pharmacologic prospects of the results in rats warrant further studies to elucidate the structure of the responsible bioactive compound(s) and confirm the suggested probable mechanism (s) of action.

Keywords: Histology, African star apple, *Chrysophyllum albidum*, Hematology, Monosodium glutamate Nephrotoxic, Hepatotoxic

Introduction

Animal health status is fundamental to, and assessed through, hematology or the haematopoietic system (Olugunagba *et al.*, 2017) and through bio-functional and histologic integrity of high metabolic organs as the liver and kidney (Jimoh *et al.*, 2015). Alteration in hematological balance results to diseased states including anemia and reduced immunity (Achi *et al.*, 2021). Liver and kidneys work in synergy to maintain homeostasis, ensure the proper production and excretion of metabolic wastes and facilitate the re-absorption of required metabolites (Imo *et al.*, 2021). Monosodium glutamate, MSG, is a sodium salt of L-glutamic acid (Airaodion *et al.*, 2019). It is a popular flavour enhancer known to cause diarrhea with potential and reported adversity on the liver, kidney, hematology and histology of experimental animals (Airaodion *et al.*, 2019; Kianifard *et al.*, 2019). Ongoing studies seek natural products to counter its possible adverse effect. *Telfairia occidentalis* leaf extract (Owoeye *et al.*, 2018), vitamin C (Adebayo *et al.*, 2019) and other natural

products (Hajihassani *et al.*, 2020) mitigated MSG-induced effect in animal study models suggesting that plant-based exogenous agents could mitigate MSG effects in animals. Complementary and alternative medicine researches recently focused on functional foods and their bioactive compounds to ameliorate MSG effect (Ibrahim *et al.*, 2020). Plant-based natural products with dietary and therapeutic potentials abound (Jimoh *et al.*, 2015; Musa *et al.*, 2019; Ezeigwe *et al.*, 2020). Exploiting neglected and underutilized sources as *Chrysophyllum albidum* (*C. albidum*) seed endosperm could in addition minimize the attendant waste burden on the environment. *C. albidum* belongs to the *Sapotaceae* family (Jimoh *et al.*, 2015). It is common in Nigeria where it is known as *Agbalumo* in South-west and *Udara* in South-east (Ibrahim *et al.*, 2020). Pharmacological and ethno medicinal uses of its edible fruit pulp (mesocarp) and other parts were attributed to the numerous phyto-constituents (Ogunleye *et al.*, 2020). These include uses as anti-ulcerative (Salami *et al.*, 2020), antioxidant, antihyperglycemic anti-

diabetes, anti-plasmodial, anti-microbial (Ogunleye *et al.*, 2020; Adekanmi and Olowofoyeku, 2020), pharmafood (Adekanmi and Olowofoyeku, 2020) and anti-diarrheal (Dandare *et al.*, 2017) agents.

The *C. albidum* fruit contains flattened seeds (constituting a strong seed endocarp that covers the soft seed endosperm). Unlike the fruit pulp, the soft seed endosperm is not utilized but discarded alongside the endocarp as waste (Olugunagba *et al.*, 2017)) which constitutes environmental challenge. Oputa *et al.* (2016) reported rich phytochemical content and antibacterial potency of ethanol extract of *C. albidum* seed. Olugunagba *et al.* (2017) characterized the physicochemical, microbial and toxicological properties of *C. albidum* seed endosperm and concluded that it is suitable for use as excipient in pharmaceutical formulations. Jimoh *et al.* (2015) reported that *C. albidum* seed meal did not cause any adverse effect on the liver and kidney histology of experimental fish. Adebayo *et al.* (2011) demonstrated the hepatoprotective effect of *C. albidum* leaf extract against carbon tetrachloride (CCl₄) induced liver damage in Wistar rats. Ibrahim *et al.* (2020) reported that supplementation of fruit-skin of *C. albidum* protected the liver and kidney in diabetic rats' model. These spiked up quest to ascertain possible utilization of *C. albidum* seed endosperm in animals' diets and drugs which could in addition minimize its waste burden on the environment. Egbuonu *et al.* (2020) reported dietary benefits and antioxidant potential of *C. albidum* seed endosperm extract. Other reports abound of non-toxic dietary (Jimoh *et al.*, 2015) and therapeutic (Salami *et al.*, 2020) potentials of *C. albidum* seed. The *C. albidum* seed endosperm extract, CASEE, may interact with MSG with unknown influence on the hematologic, liver and kidney functions necessitating further studies on possible effects on the hematology and some major organs (liver and kidney) functions *prior* to its use in animals. This study aimed to ascertain the influence of *C. albidum* seed endosperm extract, CASEE, on the hematologic, hepatic, nephrotic and histologic alterations in MSG-compromised male albino rats. Hematologic function was monitored through bio-indicators including hemoglobin (HB), red blood cell (RBC), white blood cell (WBC) and packed cell volume (PCV) (Nwuke *et al.*, 2020, Alaabo *et al.*, 2022). Optimal liver function was assessed through the specific marker alanine aminotransferase enzyme (ALT) and the less specific marker aspartate aminotransferase enzyme (AST) (Imo *et al.*, 2021). Kidney function was evaluated through urea and creatinine levels (Ibrahim *et al.*, 2020, Imo *et al.*, 2021). Histological assessment of organs was important in determining agent related effect in experimental animal model (Kianifard *et al.*, 2019; Jubaidi *et al.*, 2019).

Material and Methods

Geographical Location of Study

The study was conducted at Michael Okpara University of Agriculture Umudike, close to Umuahia Abia State in South East Nigeria.

Sample collection, preparation and extraction

Fresh fruits of *C. albidum* were collected from a local farm near *Afor Ogbe* market, Ahiazu, Mbaize Local Government Area of Imo state, Nigeria. The fruits were identified by Professor M.C. Dike of the College of Natural Resources and Environmental Management, Michael Okpara University of Agriculture, Umudike, Abia state, Nigeria. The endosperms, obtained after crushing the seed endocarp with a local pestle and mortar, were subsequently cleaned, oven dried at 40°C and ground into powder using Arthur Thomas Laboratory Mill (Crypto model, USA,). Five hundred grams (500g) of the ground *C. albidum* seed endosperm was soaked in 900ml of 70% ethanol for five (5) days with intermittent shaking to facilitate the extraction process and thereafter filtered using a Whatman No. 1 (125mm) filter paper. The filtrate was concentrated at 40°C in a Laboratory oven to obtain a dried extract (referred to as *Chrysophyllum albidum* seed endosperm extract, CASEE) that was refrigerated until used.

Ethical adherence

The study adhered strictly to the ethical guidelines on animal use as stipulated by the National Research Council, NRC, USA (2011).

Experimental Animals

Sixty adult male albino rats (120-160g) obtained from the animal house unit of the Department of Biochemistry, University of Nigeria, Nsukka, Enugu State, Nigeria were used. All animals were allowed free access to food and water and were housed in aluminum cages maintained under standard laboratory conditions with light and dark cycles of 12h each and room temperature of 25°C.

Experimental Design

The study used completely randomized blocked design of six treatment groups replicated five times with each replicate having two rats. The descriptive statistics, test for significance in mean and turkey *post hoc* test were used to analyze the data. The rats were acclimatized for 14 days *prior* to randomization to six treatment groups of 10 rats each. Group 1 rats received normal saline (1ml) as the control. Groups 2 to 6 were the treated groups. Group 2 rats received CASEE (200mg/kg). Group 3 rats received MSG (8000 mg/kg) according to Obidike and Egbuonu (2019) while groups 4, 5 and 6 rats in addition to MSG (8000mg/kg) respectively received 200, 400 and 600mg/kg of CASEE. Experimental administration was orally by gavage and daily for 14 days. At the end of 14 days experimental period, the animals were sacrificed by cervical dislocation, and blood samples were collected by cardiac puncture into ethylene ditetra-acetic acid (EDTA) bottles (to obtain uncoagulated whole blood) and some in plane bottles (to obtain clotted blood). Uncoagulated whole blood samples were used for the determination of hematological parameters. Coagulated blood samples were further centrifuged at 3000 g for 15 minutes to obtain the serum for the determination of serum ALT, AST, urea and creatinine levels.

Uncoagulated whole blood samples as collected into EDTA bottles were left to rest at room temperature for about 15 minutes to ensure adequate stabilization of the cells (Muriithi *et al.*, 2015).

Determination of hematological parameters and some serum indicators of liver and kidney functions

The red blood cell white blood cell, hemoglobin, and packed cell volume, parameters were determined by methods as surmised recently (Egbonu and Amadi, 2021). The mean cell hemoglobin concentration, MCHC, was estimated as described recently (Alaabo *et al.*, 2022; Nwuke *et al.*, 2020) while the mean corpuscular volume, MCV and mean corpuscular hemoglobin, MCH were calculated as described by Alaabo *et al.* (2022). ALT and AST activity in the rats' serum were determined with Randox Kit based on the method of Reitman and Frankel (1957). Urea was determined by the Urease Berthelot method (Fawcett and Scott, 1960) while creatinine was determined by the direct endpoint method as described recently (Anuforo *et al.*, 2020).

Histological preparation and examination of liver and kidney

The liver and kidneys were prepared and examined for histological alterations as reported recently (Egbonu *et al.*, 2022). The photomicrographs of selected images were captured using a moticam 2.0 digital camera attached to a computer at $\times 400$ magnification.

Statistical analysis

The descriptive statistics and test for significance in mean of the data were by one-way analysis of variance (ANOVA) with the statistical package for social sciences (SPSS) version 22. The turkey *post hoc* test were used to identify the means that differ significantly at $P < 0.05$. Group results were expressed as mean \pm standard error of mean SEM ($n = 10$).

Results and Discussion

MSG significantly decreased ($P < 0.05$) HB, RBC, MCHC and MCH (pictogram, pg/dl) but increased ($P < 0.05$) WBC and MCV (femtolitres, fl) compared to others. It decreased ($P < 0.05$) PCV compared to others except group 6 rats (Table 1). As shown in Table 2, MSG increased ($P < 0.05$) in the serum indicator levels of liver function (ALT and AST) compared to others. It increased ($P < 0.05$) the serum indicator levels of kidney function (urea and creatinine) compared to other determined groups (1, 2 and 6). Liver histology of rats exposed to CASEE (200mg/kg, group 2) showed features comparable to that for control (group 1) with demarcated nuclei (N), and intervening sinusoids (S). Compared to others, MSG (800mg/kg, group 3) caused significant ($P < 0.05$) alterations in the liver histology of rats revealed by loss of sinusoidal spaces, dilated and congested central vein, V, with lipid inclusion (White arrow) and loss of sinusoidal spaces. Simultaneous exposure to CASEE (400mg/kg, group 5) markedly mitigated MSG effect on the rats' liver histology compared to CASEE (600 mg/kg, group 6 and 200 mg/kg, group 4) as revealed by minimal loss of

sinusoidal spaces and absence of lipid inclusions in the central vein, V. (Figure 1). Kidney histology of rats exposed to CASEE (200mg/kg, group 2) showed features comparable to that for the control (group 1) with intact Bowman's capsule and capillaries. Compared to others, MSG (800mg/kg, group 3) caused significant ($P < 0.05$) alterations in the kidney histology of rats revealed by widening of Bowmans space due to contraction of glomerulus and hypercellularity. Simultaneous exposure to CASEE (400 mg/kg, group 5) in contrast to CASEE (600mg/kg, group 6 and 200mg/kg, group 4), mitigated MSG effect as revealed by mild widening of Bowmans space due to minimal contraction of glomerulus and marked reduction in hypercellularity without overall loss of renal architecture (Figure 2).

Previous study suggested CASEE-related nutritional and antioxidant potentials (Egbonu *et al.*, 2020). The present study explored the influence of CASEE on the hematologic, hepatic, nephrotic and histologic alterations caused by MSG overload in rats. This could serve as a prelude to minimizing its waste burden status through outcome that could provide insight to its possible exploitation as a plant-based pharmafood (dietary drug) against the widely used but potentially toxic food flavouring, MSG. Herein, as compared to others, MSG caused significant ($P < 0.05$) alterations in the determined hematologic, hepatic, nephrotic and histologic integrity in rats. This demonstrated and collaborates the adversity of MSG on these biofunctional and histologic integrity in rats. Consistent with the present study results, alterations in these profiles due to MSG assault in rats were reported recently (Airaodion *et al.*, 2019; Kianifard *et al.*, 2019). In agreement with Alaabo *et al.* (2022) and Imo *et al.* (2021), reduction in HB was associated with concomitant reduction in RBC and PCV levels as observed herein in the MSG-compromised rats. White blood cells in the MSG-treated rats increased in probable response to MSG related intoxication and stress as reported recently (Achi *et al.*, 2021; Imo *et al.*, 2021). Increased ALT and AST levels as in the MSG treated rats indicated compromised liver functions (Abdel-Ghaffar and Abdelghaffar, 2022; Egbonu *et al.*, 2022). Elevated urea and creatinine levels as in the MSG-treated rats indicated impaired renal/kidney functions (Ibrahim *et al.*, 2020; Anuforo *et al.*, 2020) due to retention of waste metabolites following increased proteolysis but decreased excretion rates (Shaikh and Gautam, 2014; Okpala *et al.*, 2014). Liver histology (with loss of sinusoidal spaces, dilated and congested central vein, lipid inclusion), and renal architecture (with widening of Bowmans space due to contraction of glomerulus and hypercellularity) in the MSG treated rats reported in this study, indicated compromised liver and kidney histology (Abdel-Ghaffar and Abdelghaffar, 2022). We hypothesized that dysregulation in hematologic, hepatic, nephrotic and histologic expression and functions could be co-probable mechanisms of MSG intoxication in rats and that sustained optimal regulation in these functions by

CASEE when taken together with MSG could indicate probable capacity of CASEE to protect against, or at least mitigate, MSG toxic manifestations in the rats.

The haematopoietic system is an important index of physiological and pathological status. Absence of treatment related changes indicated either none toxic influence on or none interference with the production of, the blood parameters assessed herein (Olugunagba *et al.*, 2017). A treatment related increase or decrease respectively in hematologic parameters suggested potential to spike or retard, respectively the blood and immunity functions *via* probable increase or decrease in the stimulation of erythropoietin release and subsequent production of red blood cell and hemoglobin (Achi *et al.*, 2021). Herein, CASEE (200 mg/kg) caused comparable effect on the hematologic function as in the control compared to MSG treated rats which suggests CASEE related optimization in the hematologic expression and functions in the rats. The outcome particularly tallied with that of Adebayo *et al.* (2010) which reported that ethanolic leaf extract of *C. albidum* significantly reduced WBC level in the rats. It is likely that CASEE did not stimulate WBC production and probably was not toxic to the rats since WBC count is a common immune function index that increases in response to treatment related intoxication or stress (Imo *et al.*, 2021; Achi *et al.*, 2021). This is in line with the suggestion following the outcome in MSG-treated rats as reported herein. Compared notably to MSG-treated rats, CASEE significantly ($P < 0.05$) and dose dependently increased the HB, RBC and PCV but decreased WBC in MSG co-treated rats. This could imply that CASEE can improve, and mitigate MSG effect on, the rats' hematology probably by sustaining the optimal response in the rats' hematologic expression and functions *via* spike in blood production and associated immunity to counter the MSG effect. Concomitant increase in RBC, Hb and PCV but decrease in WBC indicated stimulation of optimal blood production and immunity (Imo *et al.*, 2021).

Alanine aminotransferase, ALT enzyme aids in the specific assessment of the extent of hepatic damage (Alshubaily and Almotairi, 2020) while aspartate aminotransferase, AST aids in the broad assessment of the extent of damage to the liver and other organs as the kidney (Egbuonu *et al.*, 2022). Increased ALT and AST indicated damage to the liver and probably resulted from compromised liver cell membrane permeability and attendant cellular seepage/leakage of the enzymes into the systemic bloodstream (Imo *et al.*, 2021; Abdel-Ghaffar and Abdelghaffar, 2022; Egbuonu *et al.*, 2022). Herein, CASEE (200 mg/kg) increased the ALT and AST levels above that of the control but below that of the MSG treated rats groups. This suggests that the apparent CASEE related adversity on the rats' liver function is probably less severe and negligible compared to that by MSG. The result was not in agreement with that of Adebayo *et al.* (2010) which reported a significant reduction in ALT and AST levels in rats but due to leaf (and not seed) extract of *C. albidum*. The result suggests

that CASEE may be hepatotoxic to the rats but can protect the liver of MSG-compromised rats in line with the report by Imo *et al.* (2021). CASEE (when exposed simultaneously with MSG) significantly ($P < 0.05$) and dose dependently diminished the MSG effect on the rats' hepatic function parameters. This indicated that CASEE (200 mg/kg) alone may not improve, but when taken together with MSG can mitigate MSG effect on the rats' hepatology *via* probable sustenance of optimal response on the rats' hepatologic expression and functions. This seemingly supported the suggestion herein of less severe and negligible adversity response of CASEE on the rats' liver.

Urea and Creatinine are waste products that are produced in the liver but serve as important markers of kidney function (Imo *et al.*, 2021). Herein, CASEE (200mg/kg) caused a significant ($P < 0.05$) reduction in the levels of urea and creatinine in the rats compared to control, MSG and MSG + CASEE at highest dose. This outcome was fairly consistent with the report by Adebayo *et al.* (2010) of significant reduction in creatinine level of rats following exposure to leaf extract of *C. albidum*. The result suggests that CASEE (200 mg/kg) improved these functional parameters of kidney function in the rats probably by preventing retention of waste metabolites (urea and creatinine) either *via* the reduction in their production rate or the optimization of their proper excretion. This agreed with the suggestion in the present report on MSG effect and was supported by earlier study reports (Shaikh and Gautam, 2014; Okpala *et al.*, 2014; Ibrahim *et al.*, 2020). CASEE (600mg/kg) significantly ($P < 0.05$) diminished the MSG effect on the urea level, but spiked that on the creatinine level, in the rats which suggests selective mitigation response on the MSG effect following concomitant exposure of MSG plus tested highest dose of CASEE in rats. This demonstrated that CASEE improved, and significantly but selectively reduced, the MSG effect in the rats' kidney function *via* probable concerted mechanism leading to selective beneficial response on the rats' nephrology. The urea and creatinine levels of rats in groups 4 (MSG + 200mg/kg of CASEE) and 5 (MSG + 400 mg/kg of CASEE) were not determined (following laboratory accident) which constitute significant limitation of this study to be addressed in future similar study.

Assessment of histological alterations of high metabolic organs complemented the determination of agent-related effect in experimental animal model (Kianifard *et al.*, 2019; Jubaidi *et al.*, 2019). Herein, liver and kidney histology of rats as assessed revealed that rats exposed to CASEE (200 mg/kg) had features comparable to that for group 1 as against that in MSG-treated rats. Significant histologic alterations in the rats' liver and kidney caused by MSG were significantly mitigated following simultaneous exposure to CASEE (at 400mg/kg and 600mg/kg for the liver) and CASEE (at 400mg/kg for the kidney). The observation suggests that unlike in the MSG treated rats reported herein which indicated compromised liver and kidney

histology of the rats (Abdel-Ghaffar and Abdelghaffar, 2022), CASEE showed overt but selective benefit respectively, and did not cause dose dependent mitigation of MSG-induced effect, on the rats' liver and kidney histology. The biochemical observations from this study supported the histological outcome which demonstrated that CASEE (200mg/kg) improved, and significantly but dose independently reduced, the MSG effect in the rats liver and kidney histology. This could be *via* concerted mechanism leading to beneficial response on the rats' liver and kidney histology.

Conclusion

The present study demonstrated that oral ingestion of CASEE (200mg/kg) resulted to a significant improvement of, while MSG (800mg/kg) compromised, the hematologic, hepatic, nephrotic and histologic integrity in rats. This may suggest that the CASEE possess hematopoietic activity of the blood cells relevant in management and prevention of agent-related blood depletion; immune stabilizing property relevant in normalizing immune response spiked in response to agent-related toxicity; hepatoprotective and nephroprotective properties relevant in maintaining bio-functional and histological integrity of the associated organs. It also demonstrated that oral ingestion of CASEE caused significant but selective dose dependent reduction in MSG effect in the rats *via* probable concerted mechanism leading to beneficial response on the rats' blood, immune, liver and kidney functions and associated organs histology. The dietary and pharmacologic implications of the results of this study in rats may be worthwhile and further studies are therefore required and recommended to elucidate the structure of the responsible bioactive compound (s), confirm the hitherto suggested probable mechanism (s) of action and address the noted shortcoming of this study.

References

Abdel-Ghaffar, W.H and Abdelghaffar, E.A. (2022). Pathophysiological effects of *Tamiflu* on liver and kidneys of male rats. *Beni-Suef University Journal of Basic and Applied Sciences*, 11(15): 1-14.

Achi, N. K., Onyedikachi, U. B. and Daniel-Igwe, G. (2021). Assessment of lipid, haemological and coagulation parameters following oral administration of *Ficus Capensis* in male albino rats. *Nigerian Agricultural Journal*, 52(1): 32-37.

Adebayo, A. H., Abolaji, A. O., Opata, T. K. and Adegbenro, I. K. (2010). Effects of ethanolic leaf extract of *Chrysophyllum albidum* G. on biochemical and haematological parameters of albino Wistar rats. *African Journal of Biotechnology*, 9(14): 2145-2150.

Adebayo, A.H., Abolaji, A.O. and Kela, R. (2011). Hepatoprotective activity of *Chrysophyllum albidum* against carbon tetrachloride induced hepatic damage in rats. *Canadian Journal of Pure and Applied Sciences*, 5(3): 1597-1602.

Adebayo, O.I., Ezejiaku, B.C., Agu, V.A., Idowu, G.A. and Salau, B.A. (2019). Vitamin C protects against

monosodium glutamate-induced alterations in oxidative markers and ATPases activities in rats' brain. *Asian Journal of Biochemistry*, 15(1): 12-20.

Adekanmi, D.G. and Olowofoyeku, A.E. (2020). African star apple: Potentials and application of some indigenous species in Nigeria. *Journal of Applied Science and Environmental Management*, 24(8): 1307-1314.

Airaodion, A.I., Ogbuagu, E.O., Osemwowa, E.U., Ogbuagu, U., Esonu, C.E., Agunbiade, A.P., Okereke, D. and Oloruntoba, A. P. (2019). Toxicological effect of monosodium glutamate in seasonings on human health. *Global Journal of Nutrition and Food Science*, 1(5): 1-9.

Alaabo, P.O., Njoku, G.C. Oriaku, C.E., Iloanus, D.U., Ezech, C.J., Ugboaja, T.C., James, U.A., Ekwunoh, P.O. and Anyadike, N.N. (2022). Histological assessment and haematological parameters of honey on alloxan induced diabetic male albino rats. *International Journal of Biochemistry Research & Review*, 31(2): 17-26.

Alshubaily, F.A. and Almotairi, E.S. (2020). The hepatoprotective effect of *Moringa oleifera* leaf aqueous extract against cadmium-induced toxicity on male rats. *Journal of Biochemical Technology*, 11(1): 101-107.

Anuforo, P. C., Egbuonu, A. C. C. and Egu, E. U. (2020). *Terminalia catappa* flour extract mitigated monosodium glutamate-intoxicated rats' kidney biofunction and histology. *Journal of Phytopharmacology*, 9(3): 164-168.

Dandare, S. U., Mainasara, B. B., Magaji, U. F., Dandare, I.A., Lailaba, A. A. and Sadiq, M. E. (2017). *In vitro* antioxidant activity of *Chrysophyllum albidum* fruit. *Nigerian Journal of Basic and Applied Science*, 25(1): 17-22.

Egbuonu, A.C.C, and Amadi, R.P. (2021). Ethanolic extract of ground *Vernonia amygdalina* stem exhibited potent antibacterial activity and improved hematological bio-functional parameters in normal and monosodium glutamate-intoxicated rats. *Journal of Applied Science and Environmental Management, JASEM*, 25(3): 311-317.

Egbuonu, A. C. C., Nwankwo, C. I., Chukwu, C.N., Alaabo, P. O. and Anoliefo, C. I. (2022). Amlodipine elicited dose-dependent benefit in rats' liver histology and some seric bioindicators following monosodium glutamate intoxication. *Nigerian Research Journal of Chemical Sciences, NRJCS*. 10(1): 171-181.

Egbuonu, A.C.C, Ubah, E.E. and Obidike, I.J. (2020). Physicochemical composition and antioxidant role of *Chrysophyllum albidum* seed endosperm in monosodium glutamate-intoxicated rats. *Asian Journal of Emerging Research, AJER*. 2(4): 212-222.

Ezeigwe, O. C., Nzekwe, F.A., Nworji, O. F., Ezennaya, C. F., Iloanya, E. L. and Asogwa, K. K. (2020). Effect of aqueous extract of *F. capensis* leaves and its combination with *C. aconitifolius* leaves on essential biochemical parameters of phenylhydrazine-induced anemic rats. *Journal of*

- Experimental Pharmacology*, 12: 191.
- Fawcett, J.K. and Scott, J.E. (1960). A rapid and precise method for the determination of urea. *Journal of Clinical Pathology*, 13: 156-159.
- Hajihassani, M.M., Soheili, V., Zarak, M.R., Sahebkar, A.H. and Shakeri, A. (2020). Natural products as safeguards against monosodium glutamate-induced toxicity. *Iranian Journal of Basic Medical Sciences*, 23: 416-430.
- Ibrahim, H.O., Osilesi, O., Muhammad, L.B., Orodele, K. and Olagoke, E.O. (2020). Hepatic- and renal protective effects of *Chrysophyllum albidum* (African star apple) fruit-skin supplementation on streptozotocin-induced diabetic rats. *Journal of Natural Sciences Research*, 10(6): 7-20.
- Imo, C., Arowora, K.A., Ezeonu, C.S., Ikwebe, J., Yakubu, O.E., Imo, N.G. and Danlami, G.C. (2021). Biochemical and histological effects of ethanolic extracts of fruits of *Xylopiya aethiopia* and seeds and leaves of *Piper guineense* on liver and kidney function in male albino rats. *Future Journal of Pharmaceutical Sciences*, 7(35): 1-12.
- Jimoh, W.A., Sodamola, M.D., Adebayo, M.D., Banjo, O.T., Ayoloja, A.A. and Adeleke, A.B. (2015). Histological changes in the liver and kidney of *Clarias gariepinus* fed *Chrysophyllum albidum* seed meal as maize replacer. *International Journal of Zoological Research*, 11(1): 28-36.
- Jubaidi, J.F., Mathialagan, R.D., Noor, M.M., Taib, I. and Budin, S.B. (2019). Monosodium glutamate daily oral supplementation: Study of its effects on male reproductive system on rat model. *Systems Biology in Reproductive Medicine*, 65(3): 194-204.
- Kianifard, D., Ehsani, A., Daneshgar, P.Z., Akbari, G. and Shoar, S.M.M. (2019). Effect of monosodium glutamate on testicular tissue of paclitaxel-treated mice: An experimental study. *International Journal of Reproductive Biomedicine*, 17(11): 819-830. doi: 10.18502/ijrm.v17i10.5492.
- Murriithi, N. J., Maina, G. S., Mugendi, N. M., Maina, M. B., Kiambi, M. J., Kelvin, J. K., Umar, A., John, K.M., Ann, W.N., Piero, M.N. and Eliud, N. M. (2015). Determination of hematological effects of methanolic leaf extract of *S. incanum* in normal mice. *Pharmaceutica Analytica Acta*, 6(10): 429-435.
- Musa, D. A., Iyeh, F., Ogbiko, C. and Nwodo, O. F. (2019). Effect of *Ficus capensis* chloroform extract and *Eucalyptus camaldulensis* n-hexane extract on blood glucose and lipids in normal Wistar rats. *Journal of Pharmacy & Bioresources*, 16(2): 173-177.
- National Research Council, NRC, USA (2011). Guide for the Care and Use of Laboratory Animals. 8th Edition, Committee for the Update of the Guide for the Care and Use of Laboratory Animals. Washington DC, USA: National Research Council, National Academies Press.
- Nwuke, C. P., Uhwo N. E., Uroko, I.R., Alaabo, P., Egbuonu C.A.C. and Ibeh, B. (2020). Acute anti-inflammatory and haematological effects of alkaloidal leaf extract of *Combretum dolichopetalum* (Engl & Diels). *Trends in Natural Products Research*, 1(1): 9-19.
- Obidike, I.J. and Egbuonu, A.C. (2019). Effects of ethanol extract of cocoa (*Theobroma cacao*) pod on normal and monosodium glutamate-intoxicated rats' hepatic histo-morphology, serum bio-functional parameters and serum antioxidant activities). *International Journal of Recent Research and Applied Studies*, 6, 11(1): 1-13.
- Ogunleye, F.A., Fapohunda, O. and Nwangwu, S. (2020). A Review on medicinal uses and pharmacological activities of African star apple (*Chrysophyllum albidum*). *Acta Scientific Pharmacology (ASPC)*, 1(4): 1-9.
- Okpala, J.C., Sani, I., Abdullahi, R., Ifedilichukwu, H.N. and Igwe, J.C. (2014). Effects of n butanol fraction of *Gongronema latifolium* leave extract on some biochemical parameters in CCl₄- induced oxidative damage in Wistar albino rats. *African Journal of Biochemistry Research*, 8(2): 52-64
- Olugunagba, M.O., Azubuike, C.P., Silva, B.O. and Sadiku, O. R. (2017). Characterization of *Chrysophyllum albidum* Linn (Family: Sapotaceae) endosperm seed gum for potential application as pharmaceutical excipient. *Tropical Journal of Natural Product Research*, 1(5): 217-222.
- Oputa, S.I., Mordi, R.C., Ajanku, K.O., Olugbuyiro, J.A.O., Oolurnshola, S.J. and Azuh, D.E. (2016). Phytochemical and antibacterial properties of ethanolic seed extracts of *Chrysophyllum albidum* (African star apple). *Oriental Journal of Physical Sciences*, 1(1 & 2): 05-09.
- Owoeye, O., Oluwagbemi, A.D. and Thomas, M.A. (2018). *Telfairia occidentalis* leaf extract mitigated monosodium glutamate-induced behavioural and histological alterations in rat hippocampus. *African Journal of Medicine and Medical Sciences*, 47: 405-413.
- Reitman, S. and Frankel, S. (1957). A colorimetric method for the determination of serum glutamate oxaloacetate and pyruvate transaminase. *American Journal of Clinical Pathology*, 28: 56-63.
- Salami, A.T., Famurewa, A. D., Omayone, T. P., Iyiola, T. F. and Olaeye, S.B. (2020). *Chrysophyllum Albidum* accelerates delayed gastric ulcer healing in rats through oxidative stress reversal and proton pump inhibition. *Nigerian Journal of Pharmaceutical Research*, 16(2): 163-175.
- Shaikh, I.A. and Gautam, R.K. (2014). Effect of organophosphate pesticide, nuvan on serum biochemical parameters of fresh water catfish *Heteropneustes fossilis* (Bloch.). *International Research Journal of Environmental Sciences*, 3(10): 1-6.

Table 1: Influence of *C. albidum* seed endosperm extract (CASEE) on altered hematologic bioindicators in MSG-compromised rats

Parameters	Groups					
	1	2	3	4	5	6
WBC ($\times 10^3/\mu\text{L}$)	7.78 \pm 1.02 ^d	6.36 \pm 0.48 ^b	28.07 \pm 2.58 ^f	7.26 \pm 1.16 ^c	5.93 \pm 0.30 ^a	10.76 \pm 0.33 ^e
PCV (%)	48.5 \pm 3.84 ^e	48.25 \pm 3.32 ^d	46.5 \pm 1.52 ^b	50.75 \pm 3.12 ^f	48.0 \pm 3.37 ^c	45.25 \pm 2.10 ^a
HB (g/dl)	13.55 \pm 0.91 ^d	13.0 \pm 0.21 ^e	9.85 \pm 0.61 ^a	11.17 \pm 0.78 ^d	10.95 \pm 0.66 ^c	10.85 \pm 0.33 ^b
RBC ($\times 10^6/\mu\text{L}$)	7.67 \pm 0.54 ^b	8.08 \pm 0.48 ^e	6.89 \pm 0.40 ^a	8.23 \pm 0.83 ^f	7.89 \pm 0.38 ^d	7.73 \pm 0.21 ^c
MCV (fl)	63.17 \pm 1.01 ^e	58.6 \pm 1.57 ^b	67.72 \pm 2.24 ^f	62.14 \pm 3.75 ^d	60.67 \pm 1.36 ^c	58.47 \pm 0.21 ^a
MCH (pg/dl)	17.71 \pm 0.60 ^f	14.37 \pm 0.98 ^d	13.59 \pm 1.02 ^a	13.74 \pm 0.70 ^b	14.04 \pm 1.32 ^c	16.86 \pm 0.58 ^e
MCHC (g/l)	28.01 \pm 0.70 ^e	22.81 \pm 1.74 ^c	21.18 \pm 0.90 ^a	22.26 \pm 0.30 ^b	23.27 \pm 2.51 ^d	28.92 \pm 1.44 ^f

Results represent mean \pm S.E.M of group serum results obtained (n = 10). Mean values in the same row, having different letters of the alphabet, are statistically significant at P < 0.05. (Control group =1, CASEE (200 mg/kg) group = 2, MSG group = 3, MSG + CASEE (200 mg/kg) group = 4), MSG + CASEE (400 mg/kg) group = 5 and MSG + CASEE (600 mg/kg) group = 6)

WBC= White blood cell. PCV = Packed cell volume. HB = Hemoglobin. RBC = Red blood cell. MCV = Mean corpuscular volume. MCH = Mean corpuscular hemoglobin. MCHC = Mean cell hemoglobin concentration.

Table 2: Influence of *C. albidum* seed endosperm extract, CASEE, on altered hepatic and nephrotic bioindicators in MSG-compromised rats

Groups	ALT (IU/L)	AST (IU/L)	Urea (mg/dl)	Creatinine (mg/dl)
1	24.00 \pm 1.08 ^a	102.0 \pm 4.30 ^a	69.76 \pm 9.35 ^c	1.26 \pm 0.03 ^b
2	30.00 \pm 1.08 ^c	124.5 \pm 3.50 ^b	58.66 \pm 15.17 ^a	1.24 \pm 0.05 ^a
3	41.50 \pm 2.21 ^e	158.25 \pm 2.78 ^e	112.21 \pm 4.03 ^d	1.42 \pm 0.03 ^c
4	40.75 \pm 3.63 ^d	160.50 \pm 3.42 ^f	ND	ND
5	28.50 \pm 2.32 ^b	141.00 \pm 4.24 ^d	ND	ND
6	42.25 \pm 3.47 ^f	133.30 \pm 11.55 ^c	67.61 \pm 5.21 ^b	1.55 \pm 0.03 ^d

Results represent mean \pm S.E.M of group serum results obtained (n = 10). Mean values in the same column, having different letters of the alphabet, are statistically significant at P < 0.05. ND = Not determined, Control group =1, CASEE (200 mg/kg) group = 2, MSG group = 3, MSG + CASEE (200 mg/kg) group = 4), MSG + CASEE (400 mg/kg) group = 5 and MSG + CASEE (600 mg/kg) group = 6.

ALT = Alanine aminotransferase. AST = Aspartate aminotransferase.

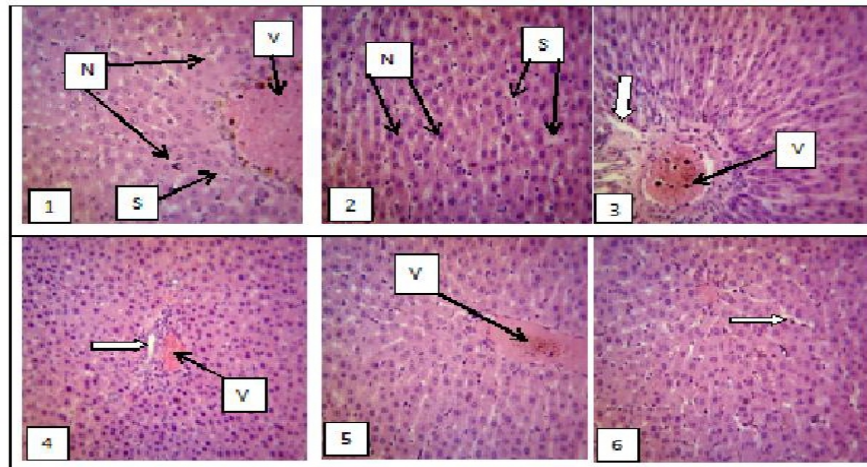


Figure 1: Photomicrograph of the influence of *C. albidum* seed endosperm extract, CASEE, on altered liver histology in MSG-compromised rats. N/B: Control group (1), CASEE (200 mg/kg) group (2), MSG group (3), MSG + CASEE (200 mg/kg) group (4), MSG + CASEE (400 mg/kg) group (5) and MSG + CASEE (600 mg/kg) group (6). Hematoxylin and Eosin (H & E) stained \times 400.

Notes: (N = Nuclei; S = Sinusoids; V = Central vein)

1: Normal liver histology with demarcated nuclei (N), intervening sinusoids (S) and normal central vein, V.

2: Liver histology comparable to that for group 1 with demarcated nuclei (N), and intervening sinusoids (S).

3: Compromised liver histology with loss of sinusoidal spaces, dilated and congested central vein, V, with lipid inclusion (White arrow).

4: Liver histology comparable to that for group 3 with loss of sinusoidal spaces, dilated central vein, V, and lipid inclusion (White arrow).

5: Markedly improved liver histology compared to that for group 3 with minimal loss of sinusoidal spaces and absence of lipid inclusions within the central vein, V, area.

6: Less compromised liver histology as compared to that for group 3 with minimal loss of sinusoidal spaces and minimal lipid inclusions (White arrow).

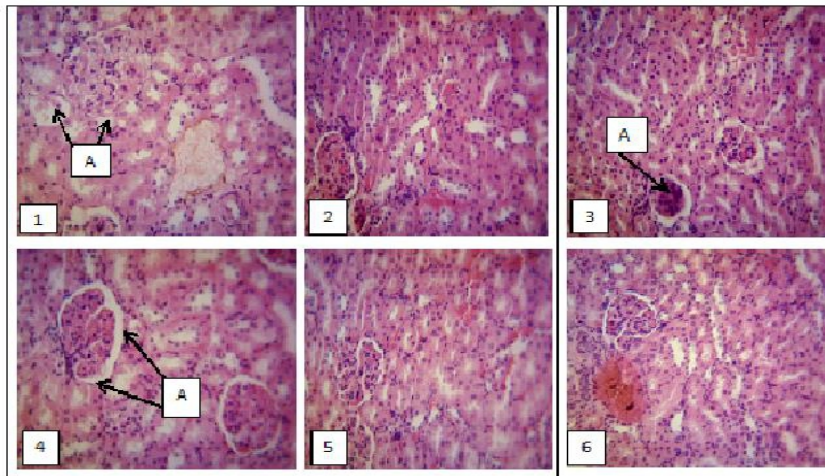


Figure 2: Photomicrograph of the influence of *C. albidum* seed endosperm extract, CASEE, on altered kidney histology in MSG-compromised rats. N/B: Control group (1), CASEE (200 mg/kg) group (2), MSG group (3), MSG + CASEE (200 mg/kg) group (4), MSG + CASEE (400 mg/kg) group (5) and MSG + CASEE (600 mg/kg) group (6). Hematoxylin and Eosin (H & E) stained $\times 400$.

Notes: (A = Glomerulus)

- 1: Normal kidney histology with Bowman's capsule and the capillaries forming a whole glomerulus (A).
- 2: Normal kidney architecture with Bowman's capsule and the capillaries intact.
- 3: Compromised renal architecture with widening of Bowmans space due to contraction of glomerulus and hypercellularity.
- 4: Compromised renal histology with widening of Bowmans space due to contraction of glomerulus and hypercellularity.
- 5: Improved renal histology compared to that for group 3 rats with mild widening of Bowmans space due to minimal contraction of glomerulus and marked reduction in hypercellularity without overall loss of renal architecture.
- 6: Compromised renal histology with widening of Bowmans space due to contraction of glomerulus and hypercellularity.