PRINT ISSN 1119-8362
Electronic ISSN 1119-8362

Full-text Available Online at
https://www.ajol.info/index.php/jasem
http://www.bioline.org.br/ja

J. Appl. Sci. Environ. Manage.
Vol. 26 (5) 949-954 May 2022

Effects of Aqueous Extract of *Moringa oleifera* on Phenylhydrazine-induced Liver Toxicity in Wistar Rats

OBAYUWANA, E; IMAFIDON, EO; ODIASE, DE; ALIH, OJ; NWEKE, SM; ENOGHASE, RJ; NDUBUISI, JPK; OKPAKO, RA

Department of Anatomy, School of Basic Medical sciences, College of Medical sciences, University of Benin, Benin City, Nigeria.
**Corresponding Author Email: obayuwanaedobor24@gmail.com*
Other Authors Emails: enduranceimafidon@gmail.com; daniel.odiase@uniben.edu; joyceechide@gmail.com; nwamgbadasamuelvic@gmail.com; enoghase41@gmail.com; johnnyken13@gmail.com; akpobome.okpako@bmedsci.uniben.edu

ABSTRACT: *Moringa oleifera* has been shown to have a variety of medicinal benefits, including hepatoprotective effects. Phenylhydrazine has been used to cause hepatotoxicity in experimental models. In this study, an aqueous extract of *Moringa oleifera* was used to evaluate the ameliorating properties of phenylhydrazine-induced liver damage by assessing liver enzymes and histoarchitecture employing twenty-five (25) mature Wistar rats were divided into five (5) groups. Group A received 1 ml distilled water, Group B received 50 mg/kg phenylhydrazine twice in 48 hours, Group C received 500 mg/kg body weight of *Moringa oleifera* aqueous extract for four (4) weeks, Group D received 50 mg/kg phenylhydrazine twice in 48 hours and 500 mg/kg body weight of *Moringa oleifera* aqueous extract for four (4) weeks, and Group E received 50 mg/kg of phenylhydrazine twice in forty-eight (48) hours and 70 mg/kg body weight of Silymarin for four (4) weeks. After the administration of phenylhydrazine, significant increases ($P<0.05$) in the mean concentrations of liver enzymes (ALP, AST, ALT) and total protein were observed, whereas treatment with *Moringa oleifera* resulted in a reversal of those parameters to values comparable to the control and the standard drug - Silymarin. Overall, the results showed that *Moringa oleifera* aqueous extract had considerable hepatoprotective capability against phenylhydrazine-induced hepatotoxicity.

DOI: https://dx.doi.org/10.4314/jasem.v26i5.23

Impact factor: http://sjifactor.com/passport.php?id=21082

Google Analytics: https://www.ajol.info/stats/bdf07303d34706088ffffbc8a92c9c1491b12470

Dates: Received: 21 February 2022; Revised: 13 April 2022; Accepted: 11 May 2022

Keywords: *Moringa oleifera*, Phenylhydrazine, Liver, Wistar rats.

Medicinal plants have long been recognized as being critical to the health of individuals and societies (Bruneton, 1993; Nku-Ekpang *et al*., 2021). Herbal medicines derived from plants are becoming more important in basic health care in many poor nations, and their worldwide commerce has expanded (WHO, 1996). *Moringa oleifera* is one of these plants. *Moringa oleifera* Lam. is a tropical and subtropical tree that grows widely. Commercial cultivation occurs in India, Africa, South and Central America, Mexico, Hawaii, and across Asia and Southeast Asia. It is known as the drumstick tree because of the shape of its immature seed pods, the horse-radish tree because of the flavor of ground root preparations, and the ben oil tree because of the oils generated from its seeds. Immature seed pods are consumed in some locations, while the leaves are commonly utilized as a basic meal because to their high nutritional value (Razis *et al*., 2014; Mbikay, 2012; Thurber and Fahey, 2009). The tree can reach a height of 10 to 12 m, with a spreading, open crown of drooping, brittle branches, feathery foliage with tripinnate leaves, and thick, corky, deeply fissured white bark. It is primarily appreciated for its edible fruits, leaves, flowers, roots, and seed oil, and it is widely utilized in traditional medicine across its native and introduced areas (Francis and Iogier, 1991; Jahn *et al*., 1986). Leaves of *Moringa oleifera* have been shown to have a favourable nutritional balance, containing vitamins, minerals, amino acids, and fatty acids (Moyo *et al*., 2011; Teixeira *et al*., 2014).

The leaves are up to 45 cm long, bipinnate or tripinnate, and alternately and spirally arranged on the branches. Pinnae and pinnules are opposed; leaflets

**Corresponding Author Email: obayuwanaedobor24@gmail.com*

are 1.2 to 2.0 cm long and 0.6 to 1.0 cm broad; lateral leaflets are elliptic, terminal leaflets are obovate; petioles of lateral leaflets are 1.5 to 2.5 mm long, terminal ones are 3 to 6 mm long. The leaflets are finely hairy, green and practically hairless on top, paler and hairless beneath, with red-tinged midveins, whole (not toothed) edges, and are rounded or blunt-pointed at the apex and short-pointed at the base. The twigs are coarsely hairy and green, eventually turning brown (Parrotta, 2004).

Furthermore, the leaves are said to contain antioxidant substances such as ascorbic acid, flavonoids, phenolics, and carotenoids (Alhakmani *et al*., 2013; Vongsak *et al*., 2014). *M. oleifera* formulations are utilized for antiinflammatory, antihypertensive, diuretic, antibacterial, antioxidant, antidiabetic, antihyperlipidemic, antineoplastic, antipyretic, antiulcer, cardioprotectant, and hepatoprotectant properties (Anwar *et al*., 2007; Mbikay, 2012; Razis *et al*., 2014). The compound phenylhydrazine hydrochloride (C6H8N2.Hcl) is largely utilized as an intermediate in the agricultural, pharmaceutical, and chemical industries, while its derivatives are used as antipyretics (Berger, 2007; Spivak, 2002).

Phenylhydrazine has been linked to decreased hemoglobin levels, red blood cell counts, and packed cell volume, as well as increased mean cell volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration, as well as extramedullary haematopoiesis in the spleen and liver (Unami *et al*., 1996). Phenylhydrazine also induces denaturation of cytoskeletal proteins, lipid peroxidation, ATP depletion, cation imbalances, and decreased membrane deformability (McMillan *et al*., 1998).

The objective of this study is to investigate the effect of aqueous extract of *Moringa oleifera* on phenylhydrazine-induced liver damage in mature Wistar rats.

MATERIALS AND METHOD

Plant material: Moringa Oleifera leaves were taken from a farm in Edo state, Nigeria's Ovia North East Local Government Area. A Plant Taxonomist from the Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin, Benin City, identified and validated the leaves, which were then air-dried for seven (7) days before being crushed into powder and weighed with an electrical weighing scale. Standard extraction procedures were used (Eze and Akonoafua, 2020).

Experimental animals: The experiment employed twenty-five (25) mature Wistar rats weighing between 190 and 220 g. The rats were obtained from the Department of Anatomy, School of Basic Medical Sciences, College of Medical Sciences, University of Benin, Edo State, and acclimatized for two weeks prior to the start of the study. During this time, the animals were given unlimited access to conventional animal feed (Top feed growers mash.) and clean water. Each animal procedure was carried out in accordance with established procedures and recommendations for the proper management and exploitation of laboratory animals employed for research (Buzek and Chastel, 2010).

Induction of hepatotoxicity: Hepatotoxicity was generated in the experimental rats using previously described procedures of Henneh *et al* (2021), in which the animals were given 50 mg/kg of phenylhydrazine orally twice in 48 hours.

Experimental design: The experimental design of the study is carefully presented in table 1.

Tissue collection, processing and staining: After four (4) weeks, the rats were anesthetized with chloroform and sacrificed. By making a midline incision in the ventral abdominal wall, each rat was sacrificed. The livers of each rat were instantly extracted. Blood was collected directly from the abdominal aorta to assess serum alanine aminotransferase (ALT), serum aspartate aminotransferase (AST), alkaline phosphatase (ALP), conjugated bilirubin, and total bilirubin. The liver tissues were fixed in 10% buffered formalin for 24 hours before being stained with haematoxylin and eosin and processed histologically. Tissue staining was accomplished using standard techniques (Drury *et al*., 1976).

Table 1: Table showing experimental design

Groups	DOSAGE
Group A	Received 1 ml distilled water only for four (4) weeks
Group B	Received 50 mg/kg of phenylhydrazine twice in forty-eight (48) hours
Group C	Received 500 mg/kg body weight of *Moringa oleifera* aqueous extract for four (4) weeks
Group D	Received 50 mg/kg of phenylhydrazine twice in forty-eight (48) hours and 500 mg/kg body weight of *Moringa oleifera* aqueous extract for four (4) weeks
Group E	Received 50 mg/kg of phenylhydrazine twice in forty-eight (48) hours and 70 mg/kg body weight of Silymarin for four (4) weeks

Photomicrography: A histopathologist examined the H&E stained liver slides using a Leica DM750 research microscope with a connected digital camera (Leica CC50). The tissues were photographed electronically at x400 magnification.

Statistical analyses: The IBM SPSS statistics application (Statistical Package for Social Science) Version 25 (SPSS, Inc., Chicago, Illinois, USA) was used to evaluate all of the data and create acceptable statistical values. Using a one-way analysis of variance, the values of the treatment groups were compared to those of the control group (ANOVA). P values less than 0.05 were considered significant. LSD was used as a post-hoc test.

RESULTS AND DISCUSSION

Photomicrographs of H&E-stained slides: Each photomicrograph taken at x400 magnification is a representative of each group. Plate 1 shows the liver of the control group showing normal histoarchitecture of the liver. They received 1 ml of water daily. Plate 2 shows the liver of the group that received phenylhydrazine only. Heavy periportal infiltrates of inflammatory cells, vascular ulceration and congestion, and necrosis were observed.

Table 2: Table showing results of liver function tests

	Control	Phenylhydrazine only	M. oleifera only	Phenylhydrazine + M. oleifera	Phenylhydrazine + Silymarin	P-value
ALP (U/L)	300.67±55.03	572.33±35.80*	365.00±94.40	371.33±36.77	283.67±49.47	0.037
ALT (U/L)	63.00±5.00	91.00±8.08*	64.00±8.74	53.00±5.69	42.67±5.55	0.001
AST (U/L)	118.33±21.85	233.67±51.49*	119.33±8.95	114.00±4.93	130.67±13.04	0.039
TP (g/dL)	7.27±0.20	8.47±0.43*	7.13±0.23	7.20±0.23	7.20±0.12	0.023

**Significantly different from the control group at P<0.05; The results are mean of rats in each group ± SEM*

Plate 2 is a photomicrograph of Group 3 **(***Moringa oleifera* only) showing normal histoarchitecture of the liver and comparable with the control group. Plate 4 is a photomicrograph of Group 4 (phenylhydrazine + *Moringa oleifera*). Kupffer cell activation and periportal lymphocytosis were seen, while the hepatocytes were normal. Plate 5 (Group 5) also shows Kupffer cell activation, periportal lymphocytosis and normal hepatocytes.

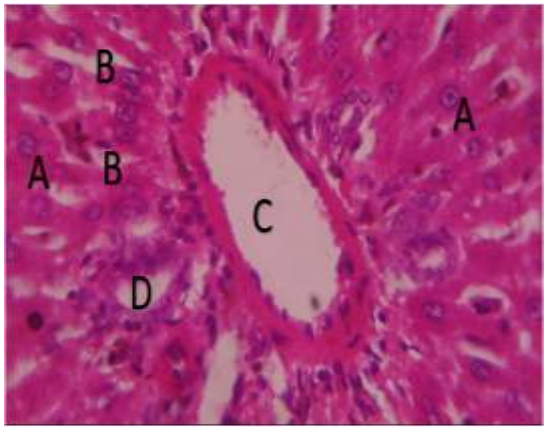

Plate 1: Control liver, composed of A: hepatocytes, B: sinusoids, C: portal vein and D: bile duct (H&E x 400)

The effects of *Moringa oleifera* on phenylhydrazine-induced toxicity in the liver of exposed Wistar rats were investigated and compared to the control group in the presence of a well-known standard drug, silymarin. The liver function test and histopathology data were used to assess the toxicity of phenylhydrazine and the effectiveness of *Moringa oleifera*. Liver function tests are an efficient modality for detecting hepatic impairment and are a useful screening tool.

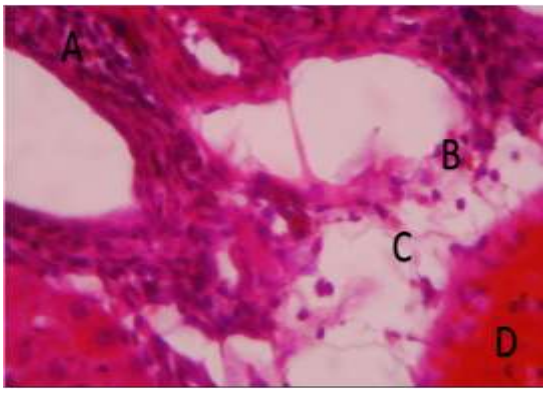

Plate 2: Rat given phenylhydrazine only, showing A: heavy periportal infiltrates of inflammatory cells, B: vascular ulceration, C: necrosis and D: vascular congestion (H&E x 400)

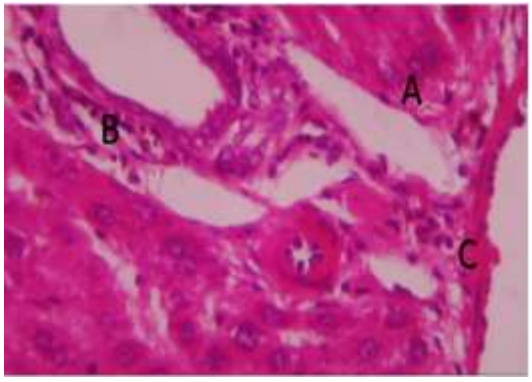

Plate 3: Rat given *Moringa oleifera* only, showing A: normal hepatocytes, B: periportal lymphocytosis and C: kupffer cell activation (H&E x 400)

Because the liver conducts so many activities, no one test can offer an accurate measure of the liver's function (Thapa and Walia, 2007). Phenylhydrazine was employed to generate hepatotoxicity in this investigation. While in the body, phenylhydrazine (C6H8N2) is harmful and damages various tissues (Giffin and Allen 1993; Mansuy *et al*. 1982).

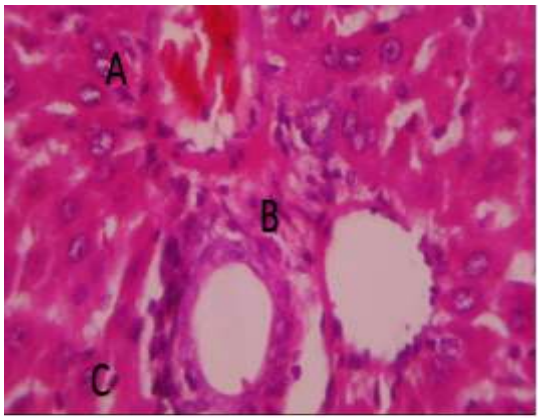

Plate 4: Rat given phenylhydrazine + *Moringa oleifera*, showing A: normal hepatocytes, B: periportal lymphocytosis and C: Kupffer cell activation (H&E x 400)

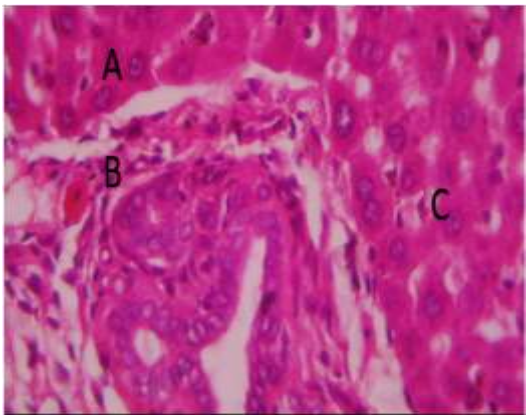

Plate 5: Rat given phenylhydrazine + Silymarin showing A: normal hepatocytes, B: periportal lymphocytosis and C: Kupffer cell activation (H&E x 400)

According to research, phenylhydrazine promotes oxidative stress, free radical generation, lipid peroxidation, oxidative destruction of spectrum cell membranes, and red blood cell lysis (Ferrali *et al*. 1997; Giffin and Allen 1993). Phenylhydrazine also promotes haemolysis (increases ferrous, ferritin, and erythropoietin levels), liver enlargement, and chronic failure (through hypertrophy of liver cells) (Ferrali *et al*. 1997; Goldberg and Stern 1975). According to our findings, phenylhydrazine substantially (p 0.05) raised the levels of ALP, AST, ALT and total protein, demonstrating hepatotoxicity. This is consistent with the findings of Zangeneh *et al* (2019), who conducted a similar research. Despite the hepatotoxic effects of phenylhydrazine, *Moringa oleifera* therapy has shown a positive chance that *M. oleifera* extract possesses hepatoprotective properties due to a considerable decrease in serum transaminases and ALP activity, as well as by avoiding the histological alterations found with phenlyhydrazine therapy. In another research, *Moringa oleifera* enhanced liver biochemical markers such as ALT and AST when compared to the acetaminophen-treated group (Fakurazi *et al*., 2008). Aminotransferases are a class of enzymes that catalyse the reversible transfer of an a-amino acid's amino acid group to an oxo acid. These enzymes are not typical plasma components, and their function outside of the organ of origin is unclear (James *et al*., 2003). The cytoplasm of hepatic parenchymal cells contains the most ALT (Okuda, 1997). AST, on the other hand, is present in the cytosol and mitochondria of hepatocytes, as well as cardiac muscle, skeletal muscle, the pancreas, and the kidney (Shyamal *et al*., 2006). As a result, measuring ALT is more liver-specific for determining hepatocellular damage (Shyamal *et al*., 2006). Despite this, AST is still widely used as a laboratory test to measure liver function since it is regarded as a sensitive sign of mitochondrial damage, particularly in the centrilobular areas of the liver (Panteghini, 1990). Meanwhile, ALP is an enzyme family that hydrolyzes phosphate esters at alkaline pH and is frequently employed as a diagnostic for cholestatic liver disease. The liver, however, is not the only source of ALP. Significant levels are also found in the bone, placenta, kidney, and gut (Gaw *et al*., 1998). The leakage of cellular enzymes into plasma is a classic indicator of hepatic injury or destruction (Ramaiah, 2007; Kumar *et al*., 2004). Furthermore, the presence or absence of particular enzymes in the circulation can be used to determine the amount and type of liver injury or damage (Kumar *et al*., 2004). In general, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) levels are often utilized as hepatotoxicity markers (Yanpallewar *et al*., 2002; Yen *et al*., 2007). Previous research found that the root and flower of *Moringa oleifera* reduced acetaminophen-induced ALT, AST, and ALP increase in rats and mice (Ruckmani *et al*., 1998). Meanwhile, another study found that *Moringa oleifera* leaves extract substantially reversed the rise of ALT, AST, and ALP levels caused by isoniazid to normal levels (Pari and Kumar, 2002). In a recent research, Nadro *et al* (2005) found that *Moringa oleifera* leaves extract inhibited the release of these enzymes from hepatocytes into the circulation in rats when triggered with a high amount of ethanol administration. Our findings are consistent with prior research, which suggests that *Moringa oleifera* may retain the structural integrity of hepatocytes when exposed to hepatotoxicants, hence reducing enzyme leakage into

plasma. The findings also revealed that the plant extract is just as efficient as silymarin in avoiding a rise in liver enzymes when exposed to a hepatotoxic dosage of acetaminophen. Silymarin is a well-known hepatoprotective medication that has been shown to reverse aberrant changes in these enzymes in drug-induced hepatotoxicity (Pradhan and Girish, 2006). The capacity of silymarin to operate as a radical scavenger, so preserving membrane permeability, is connected with its ability to prevent drug-induced hepatotoxicity (Song *et al*., 2006). Because of its known hepatoprotective activity, silymarin is utilized as a reference agent for comparing the hepatoprotective effects of plant principles (Dhiman and Chawla, 2005).

Conclusion: The aqueous extract of *Moringa oleifera* demonstrates significant hepatoprotective potentials, based on the above findings.

REFERENCES

Alhakmani, F; Kumar, S; Khan, SA (2013). Estimation of total phenolic content, in–vitro antioxidant and anti–inflammatory activity of flowers of *Moringa oleifera*. *Asian Pac J Tro Biomed*, *3*(8): 623-627.

Anwar, F; Latif, S; Ashraf, M; Gilani, AH (2007). *Moringa oleifera*: a food plant with multiple medicinal uses. *Phytother Res*, *21*(1): 17-25.

Berger, J (2007). Phenylhydrazine haematotoxicity. *J Appl Biomed*, *5*(3): 125-30.

Bruneton, J (1993). *Pharmacognosie: phytochimie plantes médicinales* (No. 581.634 B7). New York, Lavoisier, 914.

Dhiman, RK; Chawla, YK (2005). Herbal medicines for liver diseases. *Digest Dis Sci*, *50*(10): 1807-1812.

Eze, GI; Akonoafua, KA (2020). Effect of Cymbopogon citratus aqueous extract on Areca catechu-Induced lesions in the liver of adult wistar rats. *Nig J Exp Clin Biosci*, *8*(1): 20.

Fakurazi, S; Hairuszah, I; Nanthini, U (2008). *Moringa oleifera* Lam prevents acetaminophen induced liver injury through restoration of glutathione level. *Food Chem Toxicol*, *46*(8): 2611-2615.

Ferrali, M; Signorini, C; Sugherini, L; Pompella, A; Lodovici, M; Caciotti, B; Comporti, M (1997). Release of free, redox-active iron in the liver and DNA oxidative damage following phenylhydrazine intoxication. *Biochem Pharmacol*, *53*(11): 1743-1751.

Francis, JK; Liogier, HA (1991). Naturalized exotic tree species in Puerto Rico. *General technical report SO-US Department of Agriculture, Forest Service, Southern Forest Experiment Station (USA)*.

Giffin, H; Allen, E (1933). The control and complete remission of polycythemia vera following the prolonged administration of phenylhydrazine hydrochloride. *Am J Med Sci*, *185*: 1-13

Goldberg, B; Stern, A (1975). The generation of O2- by the interaction of the hemolytic agent, phenylhydrazine, with human hemoglobin. *J Biol Chem*, *250*(6): 2401-2403.

Henneh IT, Agyei PE, Obese E, Biney RP, Antwi-Adjei M, Yahaya ES, Asiamah E, Acquah-Mills J, Boateng DO, Ekor M. Leaf and root bark extracts of Ziziphus abyssinica Hochst ex. A. Rich (Rhamnaceae) ameliorate hepatic, renal and splenic injuries induced by phenylhydrazine in rats. *J Basic Clin Physiol Pharmacol*. 2021; 32(1).

Jahn, SA; Musnad, HA; Burgstaller, H (1986). The tree that purifies water: cultivating multipurpose Moringaceae in the Sudan. *Unasylva*, *38*(152): 23-28.

James, LP; Mayeux, PR; Hinson, JA (2003). Acetaminophen-induced hepatotoxicity. *Drug Metabol Dispos*, *31*(12): 1499-1506.

Kumar, G; Banu, GS; Pappa, PV; Sundararajan, M; Pandian, MR (2004). Hepatoprotective activity of Trianthema portulacastrum L. against paracetamol and thioacetamide intoxication in albino rats. *J Ethnopharmacol*, *92*(1): 37-40.

Mansuy, D; Battioni, P; Mahy, JP; Gillet, G (1982). Comparison of the hemoglobin reactions with methyl-and phenyl-hydrazine: Intermediate formation of a hemoglobin Fe (II)-methyldiazene complex. *Biochem Biophy Res Comm*, *106*(1): 30-36.

Mbikay, M (2012). Therapeutic potential of *Moringa oleifera* leaves in chronic hyperglycemia and dyslipidemia: A review. *Front Pharmacol*, 3: 24.

Moyo, B; Masika, PJ; Hugo, A; Muchenje, V (2011). Nutritional characterization of Moringa (*Moringa*

oleifera Lam.) leaves. *Afr J Biotechnol*, *10*(60): 12925-12933

Nadro, MS; Arungbemi, RM; Dahiru, D (2006). Evaluation of *Moringa oleifera* leaf extract on alcohol-induced hepatotoxicity. *Trop J Pharmaceut Res*, *5*(1): 539-544.

Nku-Ekpang, OAT; Okon, UE; Beshel, FN; Ofem, OE; Nwaehujor, CO (2021). Antioxidant and hepatoprotective activities of harungana madagascariensis lam. Ex poir.(hypericaceae) ethanol leaf extract in phenylhydrazine-induced anaemia in wistar rats, *Pharmacol Online*, *3*: 778-787.

Okuda, K (1997). Hepatocellular carcinoma: clinicopathological aspects. *J Gastroenterol Hepatol*, *12*(9-10): S314-S318.

Panteghini, M (1990). Aspartate aminotransferase isoenzymes. *Clin Biochem*, *23*(4): 311-319.

Pari, L; Kumar, NA (2002). Hepatoprotective activity of *Moringa oleifera* on antitubercular drug-induced liver damage in rats. *J Med Food*, *5*(3): 171-177.

Parrotta, JA (2004). *Moringa oleifera*. *Enzyklopädie der Holzgewächse: Handbuch und Atlas der Dendrologie*, 1-8.

Pradhan, SC; Girish, C (2006). Hepatoprotective herbal drug, silymarin from experimental pharmacology to clinical medicine. *Ind J Med Res*, *124*(5): 491.

Ramaiah, SK (2007). A toxicologist guide to the diagnostic interpretation of hepatic biochemical parameters. *Food Chem Toxicol*. 45(4): 1551–1557.

Razis, AF; Ibrahim, MD; Kntayya, SB (2014). Health benefits of *Moringa oleifera*. *Asian Pac J Canc Prev*, *15*(20): 8571-8576.

Ruckmani, K; Kavimani, S; An, R; Jaykar, B (1998). Effect of *Moringa oleifera* Lam on paracetamol-induced hepatotoxicity. *Ind J Pharmaceut Sci*, *60*(1): 33.

Shyamal, S; Latha, PG; Shine, VJ; Suja, SR; Rajasekharan, S; Devi, TG (2006). Hepatoprotective effects of Pittosporum neelgherrense, *J Ethnopharmacol*, *107*(1): 151-155.

Song, Z; Deaciuc, I; Song, M; Lee, DYW; Liu, Y; Ji, X; McClain, C (2006). Silymarin protects against acute ethanol-induced hepatotoxicity in mice. *Alcoholism: Clin Exp Res*, *30*(3): 407-413.

Spivak, JL (2002). Polycythemia vera: myths, mechanisms, and management. *Blood, J Ame Soc Hematol*, *100*(13): 4272-4290.

Teixeira, EMB; Carvalho, MRB; Neves, VA; Silva, M; Arantes-Pereira, L (2014). Chemical characteristics and fractionation of proteins from *Moringa oleifera* Lam. leaves. *Food Chem*, *147*: 51-54.

Thapa, BR; Walia, A (2007). Liver function tests and their interpretation. *Ind J Pedia*, *74*(7): 663-671.

Thurber, MD; Fahey, JW (2009). Adoption of *Moringa oleifera* to combat under-nutrition viewed through the lens of the "Diffusion of Innovations" theory. *Ecol Foof Nutr*, *48*(3): 212-225.

Unami, A; Nishina, N; Terai, T; Sato, S; Tamura, T; Noda, K; Mine, Y (1996). Effects of cisplatin on erythropoietin production in rats. *J Toxicol Sci*, *21*(3): 157-165.

Vongsak, B; Sithisarn, P; Gritsanapan, W (2014). Simultaneous HPLC quantitative analysis of active compounds in leaves of *Moringa oleifera* Lam. *J Chromatograph Sci*, *52*(7): 641-645.

World Health Organisation (1996). Traditional Medicine. Fact Sheet N134. WHO, Geneva.

Yanpallewar, SU; Sen, S; Tapas, S; Kumar, M; Raju, SS; Acharya, SB (2003). Effect of Azadirachta indica on paracetamol-induced hepatic damage in albino rats. *Phytomed*, *10*(5): 391-396.

Yen, FL; Wu, TH; Lin, LT; Lin, CC (2007). Hepatoprotective and antioxidant effects of Cuscuta chinensis against acetaminophen-induced hepatotoxicity in rats. *J Ethnopharmacol*, *111*(1): 123-128.

Zangeneh, MM; Zangeneh, A; Salmani, S; Jamshidpour, R; Kosari, F (2019). Protection of phenylhydrazine-induced hematotoxicity by aqueous extract of Ocimum basilicum in Wistar male rats. *Compar Clin Pathol*, *28*(2): 331-338.