How to Cite:
Hussin, W. S. A., & Obeid, A. K. (2022). Assessment of moringa oleifera seeds extract effect on the adverse effects of levofloxacin drug induced liver injury. *International Journal of Health Sciences*, *6*(S6), 8335–8346. https://doi.org/10.53730/ijhs.v6nS6.12068

Assessment of moringa oleifera seeds extract effect on the adverse effects of levofloxacin drug induced liver injury

Wafia shaker Abdul Hussin
Department of Biology, College of Education for pure Sciences, Kerbala University, Kerbala, Iraq
Email: wafia.sh@s.uokerbala.edu.iq

Ashwaq Kadhem Obeid
Prof. Dr. Department of Biology, College of Education for pure Sciences, Kerbala University, Kerbala, Iraq
Email: ashwaq.kadhem@uokerbala.edu.iq

Abstract---The current study aimed to know the protective role of the cold aqueous extract of Moringa seeds against the toxic damages caused by levofloxin in male albino rats by studying biochemical parameters. 24 male white rats were randomly divided into four groups, comprising (6 animals per group). The first group (G1) as a control group was dosed orally and daily with physiological solution for 30 days, the second group (G2)) was dosed with levofloxacin at a concentration of 10 mg / kg of body weight, the third group (G3) was dosed with aqueous extract of Moringa oleifera seeds at a concentration of 350 mg / kg The fourth group (G4) was dosed with aqueous extract of Moringa oleifera seeds 350 mg/kg 4 hours before the administration of levofloxacin at a concentration of 10 mg/kg body weight. Male rats in all study groups were administered orally via the dosing tube, with one dose per day for 30 days. . Blood samples were collected in the four groups after one month of dosing to measure the level of Malona dialdehyde and glutathione, as well as the levels of liver enzymes aspartate transaminase (AST), alanine transaminase (ALT) and alkalinephosphatase (ALP). Where the results of the current study showed a significant increase at the level of $P \leq 0.05$) in the level of liver enzymes for group G2 compared with G1, and a significant decrease in $P \leq 0.05$) (G4) compared to G2. As for the level of antioxidant enzymes, the current study showed a high A significant decrease in GSH and a significant ($P \leq 0.05$) decrease in MDA in G3 compared with G1, and a significant decrease in GSH and a significant increase in MDA in G2 compared with G1.Results: The results of this study indicated the effectiveness of the aqueous extract

of Moringa oleifera seeds in inhibiting the activity of free radicals and neutralizing oxidative stress induced by levofloxin, which plays a major role in improving liver function and some functional parameters in male albino rats.

Keyword---moringa oleifera, seeds extract, adverse effects, evofloxacin, liver injury.

Introduction

Levofloxacin is a broad-spectrum fluorooquinles antibiotic with limited activity against anaerobic bacteria and an inhibitor of DNAgyrase and topoismerase as well as active against penicillin-resistant bacteria and effective in the treatment of respiratory infections and sinusitis (Croom and Goa, 2003), levofloxacin absolute. It is between (99 - 100%) in a tablet with a dose of 500 mg 750 mg of levofloxacin, and the absolute bioavailability in both of them is about 99% in the case of oral administration and this is evidence of complete absorption of the drug, that the drug levofloxacin is characterized by a long half-life, which ranges between 6- 8) an hour. Therefore, the drug is taken orally in the form of tablets at a dose of 750 mg, one per day (OMP Division, 2006). Fluoroculin drugs, including levofloxacin, are metabolized mainly in the liver and the degree of its metabolism is very low, and the percentage of its metabolites is about 5% of the amount of drug doses presented.

With diuresis, the process of excretion of levofloxacin from the body is mainly through the urinary system by removing it with the action of Glomerular filtration in the kidneys, as the rate of drug elimination from the body is between (6 - 8) hours after taking the dose orally or intravenously (Christ, 1990). Which cause the destruction of mitochondrial enzymes in addition to those released in the processing of RNA as a result of oxidative stress by these free radicals, causing cellular damage to various organs of the body, including the liver and kidneys (Coelho etal., 2010; Afolabi and Oyewo (2014, Schloss et al., 2018)). Medicinal plants are of great importance in the sciences of medicine and pharmacology and are a safe source for the pharmaceutical industry at the beginning of this century, which was accompanied by the great development in the fields of pharmacy, chemistry and the chemical drug industry (Jamshidi-Kia et al., 2018; am Ende and am Ende 2019).

The beneficial effects of medicinal herbs include the protective role of oxidative damage that stimulates oxidative stress, whether in cells or tissues, preventing the occurrence of various diseases such as cancer, diabetes, Alzheimer's and others in humans, as reactive oxygen radicals cause great damage to various components of the living cell such as lipids, Proteins, carbohydrates, and nucleic acids, RNA, and DNA, cause lipid peroxidation in cell membranes and break down DNA, as well as their role in damaging proteins and carbohydrates inside cells, which leads to the breakdown of different tissues and organs (Tsao et al, 2004). The body produces active oxygen radicals during natural cellular processes to perform its multiple functions or when exposed to various injuries, and the body can be protected from the damages of these free radicals through auto-

antioxidants or used as additives in food or pharmaceutical forms that work to inhibit enzymes involved in oxidation and displacement of radicals. The resulting free radicals and thus reduce their negative effects (source).

According to studies, medicinal plants contain numerous antioxidant chemicals, with Moringa oleifera Lam being the most important and effective of these species. It is a Moringaceae medicinal plant with micronutrient-rich leaves that include vitamins, phenolic acids, carotenoids, flavonoids, alkaloids, polyphenols, and minerals (Liang et al.,2020). This tree's entire life cycle is good for human consumption (Leone et al., 2015). In traditional medicine, it has also been used to treat a variety of ailments, including high blood pressure, sugar, heat, fat, heart tonic, blood circulation, immunity, antioxidant, tumors, infections, ulcers, convulsions, germs, fungi, depression, aging, anti-cancer, and diuretic. urine as a treatment for liver and kidney disorders) (Mbikay, 2012; AbdullRazis et al., 2014).

Materials and Working Methods

Experimental Animals

In this study, 24 adult male norvegicus Rattus white rats, whose weight ranged from (150-222) grams and their ages ranged between (14-10) approximately weeks, were used after they were brought from special breeding fields in the Holy Karbala Governorate. Its dimensions are (15 x 40 x 25) cm covered with metal sheets, and under appropriate laboratory conditions in terms of temperature (25-20°C), lighting duration 12 hours a day and good ventilation, its floor was spread with fine sawdust, the cages were kept clean, the floor was constantly changed and sterilized with disinfectants as well as continuous care By cleaning the irrigation bottles and the housing room, the animals were provided with water and the standard diet freely ad libitum for the duration of the rearing and research period. The rats were left to acclimatize for three weeks before the start of the experiment. All male rats were randomly divided into four main groups (6 rats / group): The group represented The first group (G1) as a control group was dosed with physiological salt solution only, while the rats of the second group (G2) were dosed with levofloxacin at a concentration of 10 mg / kg of body weight, while the rats of the third group (G3) were dosed with the extract of levofloxacin. Aqueous extract of Moringa oleifera seeds at a concentration of 350 mg / kg of body weight, while rats of the fourth group (G4) were dosed with aqueous extract of Moringa oleifera seeds at a dose of 350 mg / kg of body weight 4 hours before the administration of levofloxacin at a concentration of 10 mg / kg of body weight. All male rats were given a single dose by gastric tube for 30 days.

Preparation of the aqueous extract of Moringa oleifera seeds

Dry Moringa oleifera seeds were purchased from seed stores in Karbala - Iraq. The seeds were washed from the dust and impurities suspended in them and dried for four days at room temperature, after that they were ground by a medicinal herbs grinder to obtain a very fine powder. Use about 20 gm of dry seed powder and mix it with 200 ml of cold distilled water for 24 hours in At room temperature, the solution was filtered, and the extract was dried in an electric oven, after being

placed in sterile glass Petri dishes at 30 °C for 24 hours (Hernandez et al., 1994). The concentrated extract was stored until use during the study.

Anatomy of animals to collect samples

The animals were anesthetized using a piece of cotton containing a quantity of chloroform and placed in a transparent sealed box, then the animal was carried and quickly placed inside it and the lid was re-tightened and after making sure that it was anesthetized, it was taken out and blood was drawn from the heart directly through a heart puncture using a sterile medical syringe with wine 5 ml capacity To obtain the largest amount of blood, the blood samples were placed directly into sterile test tubes free of anticoagulant. For the purpose of obtaining the serum that was transferred to the small plastic tubes, the serums are stored in the refrigerator at a temperature of (-20) degrees Celsius until biochemical tests are performed on them (Moron et al., 1979), which included the estimation of both antioxidants Glutathione (GSH) and oxidative breakdown product Malondialdehyde (MDA). (Buege and Aust 1978) and level of liver enzymes (AST, ALT and ALP) (Belfield & Golderg, 1971; Bergmeyer & Rej, 1985)

Statistical Analysis

The statistical analysis of the results was carried out using the program (Statistical Analysis System (SAS) version 9, the results were expressed in terms of the mean and standard error (Mean ± SE), the data analysis of the tables was carried out using the t-test, and analysis of variance (ANOVA) as well as using the least significant difference Least Significant Difference (LSD) at the level of probability ($p \leq 0.05$) (SAS, 2012).

Results and Discussion

Biochemical study

Effect of aqueous extract of Moringa oleifera seeds on the level of malondialdehyde (MDA and glutathione) GSH in the serum of healthy white male rats treated with levofloxacin

The results of the current study, as in Table (1), showed a significant decrease ($P \leq 0.05$) in the levels of GSH glutathione (29.90 ± 0.47) and a significant increase in MDA (21.53 ± 0.55) in the G2 group treated with levofloxacin at a concentration of 10 mg/kg of weight. body and for 30 days (positive control) compared with G1 group (negative control) (43.35 ±0.96), (12.81 ± 0.40), respectively. Table (1) indicated that there was a significant increase ($P \leq 0.05$) for group (G3) in the level of GSH glutathione in group (G3) (45.85 ±0.50), and a significant decrease ($P \leq 0.05$) in the level of MDA (11.61 ± 0.42, compared to the negative control group (G1). The results of the current study for group (G4) also showed a significant ($P \leq 0.05$) increase in the level of GSH glutathione (37.04 ± 0.48), and a significant decrease ($P \leq 0.05$) in the level of MDA (15.69 ± 0.34) compared with the G2 group.

This decrease in the level of glutathione GSH and the increase in the level of MDA in our current study we extend this result with the study of Pouzauaud and his

group, (2006) in a significant decrease in the level of glutathione GSH and an increase in MDA in rats treated orally with levofloxacin at a concentration of 40 mg/kg for a period of time. 14 days, and also agreed with Gupta and his group (2007), who conducted a study on white rats, and recorded a significant increase in the levels of MDA for rats treated orally with levofloxacin at a concentration of 20 mg/kg for 7 days. The antioxidants, including Glutathione, are among the antioxidant defense systems that work to protect the body from free radical damage, and oxidative stress often occurs due to its insufficiency (Nirmala et al., 2011). Glutathione is a short peptide consisting of three amino acids and is found in different organisms (Xu et al., 2017). The increase in oxidative stress leads to an increase in free radicals and, as a consequence, an increase in the rate of consumption of glutathione, which is one of the most important non-enzymatic antioxidants in the removal of free radicals and their products (Chaudiere et al., 1999); al., 2003 (Bartosikova).

In oxidative stress in many pathological conditions that stimulate it, the activity of free radicals increases by increasing their superiority over antioxidants, causing an increase in lipid peroxides and then (MDA) and a loss of balance between the activity of free radicals and the activity of antioxidants, which causes the rapid consumption of the antioxidant defense systems, and this leads to Increased lipid oxidation process, tissue damage and loss of elasticity of cell membranes (Rahal et al., 2014), and the reason may be a state of oxidative stress that affects pancreatic Cells-β cells and insulin secretion and thus leads to a decrease in the concentration of insulin in the blood, and this stimulates and increases the activity of Fatty acetyl CoA oxidase that catalyzes fatty acid β-oxidation and increases H2O2 formation and ultimately increases lipid peroxidation rates and MDA production (Aju et al., 2019).

And that the increase in the level of GSH glutathione and the decrease in the level of MDA in the current study of the group dosed with aqueous extract of Moringa seeds is consistent with the study of Jahan and his group (2018) and also agreed with the study of Kumbhare and his group, (2012) where the extracts of Moringa plant (leaves, fruits, The seeds) are considered good antioxidants. In the case of comparing the antioxidant activity of Moringa oleifera seeds with palm oil, it appears that Moringa oleifera seeds are the best means for radical scavenging (Ogbunugafor et al., 2011), and a strong source of natural antioxidants, and its seed powder contains glucosinolates such as Glucomoringin, flavonoids such as (quercetin and kaempferol) and phenolic acids such as chlorogenic acid, in addition to vitamins including B, D, C, and E. (Yassa and Tohamy 2014), in our current study, the oxidative stress index (MDA) was significantly reduced in rats that were dosed with seed extract only, and that lipid peroxidation could directly reflect the state of free radicals, the degree of attack by free radicals to the cell and the degree of lipid peroxidation (Petrulea et al., 2012).

The decrease in (MDA) is evidence of the high ability of Moringa seeds to inhibit the active oxygen and superoxide classes, and as a result, lipid peroxidation is reduced and prevents free radicals from destroying cell membranes, or this may be due to the high protective activity of Moringa seeds against oxidative stress because they contain flavonoids. Such as tocopherols, polyphenols, vitamins (Laandrault et al., 2001), and the results of our current study are in agreement

with what Shailaja and his group (2008) found, which indicated that the lack of formation of reactive oxygen species (ROS) leads to a decrease (tissue damage due to activity). The high concentration of the extract reduces the generation of oxygen radicals (ROS), and then the need for superoxide dismutase (SOD) and catalase decreases, and consequently the consumption of GSH glutathione decreases, and the efficiency of the redox cycle decreases due to the lack of appearance of oxidative damage to the cell wall. The reason for the decrease in the concentration of malondehyde may be due to the protective effect Moringa seeds are anti-oxidant because they contain phenolic compounds, in addition to containing effective biological compounds, including (glucos). inolates, isothiocyanates, thiocarbamates, and flavonoids).

Table 1
Effect of aqueous extract of Moringa oleifera seeds on the level of malondialdehyde (MDA) and glutathione (GSH) in the serum of healthy white male rats treated with levofloxacin. Transactions

N=6 average ± standard error

الكلوتاثيون GSH µmol/L	المالون ثنائي الديهايد MDA µmol/L	studied standards Means ± SE / Transactions	
43.35 ±0.96 C	12.81 ± 0.40 C	Negative control group (distilled water)	G1
29.90 ± 0.47 F	21.53 ± 0.55 A	Control group (positive) levofloxacin 10 mg/kg	G2
45.85 ±0.50 B	11.61 ± 0.42 D	Aqueous extract of Moringa seeds 350mg/kg	G3
37.04 ± 0.48 E	15.69 ± 0.34 B	Moringa seed aqueous extract 350 mg/kg + levofloxacin 10 mg/kg	G4

Different capital letters in the vertical direction indicate significant differences (P ≤ 0.05)

Effect of aqueous extract of Moringa oleifera seeds on the activity of ALP, AST, and ALT liver enzymes in the serum of healthy white male rats treated with levofloxacin

The results of the current study, as in Table No. (2), showed a significant increase at the level of probability (P ≤ 0.05) in the levels of liver enzymes (ALP, AST, ALT) in the second group (G2) dosed with levofloxacin at a concentration of 10 mg/kg for 30 days and as follows: : ALP((76.40 ± 1.92), AST (74.76 ± 1.69), ALT (71.06 ± 1.04) compared with the negative control group G1)) 48.48 ± 0.54)), (42.68 ± 1.01), (44.57 ±0.94), respectively. Our current study also recorded no significant differences ≤ 0.05 (p) in the levels of liver enzymes (ALP, AST, ALT) for the third group (G3), the group of rats dosed with aqueous extract of Moringa seeds at a concentration of 350 mg/kg for 30 days (46.87 ± 0.55), 41.52 ± 0.50), (43.97 ±0.94), respectively compared to the negative control group (G1)). The results of the current study also showed a significant decrease at the level of probability (P ≤

0.05) in the level of liver enzymes (ALP, AST, ALT) in the protective group ((G4 and as follows: ALP (57.70 ± 0.72)), AST 48.32 ± 0.93)), ALT (56.81 ± 0.88) compared with the positive control group (G2), respectively.

Liver enzymes (ALT, AST, ALP) are clinically important biomarkers for the detection of liver toxicity, as their level of activity is mainly related to the health of the body, and the control of the metabolism of proteins, carbohydrates and fats (Pandit et al, 2012). Organs are sensitive to oxidants by using it as a site for removing toxic substances and toxins from drugs and thus increasing their level to the normal limit when cellular damage is then carried into the blood. In the kidney, intestinal mucosal cells Braunwald et al., 2001; Longmore et al., 2004). The result of the elevated level of liver enzymes in the levofloxacin group in our current study agrees with the results of the study by Oda and his group, (2014), in which male rats were orally dosed with levofloxacin at a concentration of 10 mg/kg for 30 days, and also consistent with the study of Naik and Panda, (2007), which Their study was conducted on male albino rats that were orally dosed with levofloxacin at a concentration (5), 10 mg/kg) for 7 days, and with the study of researchers (Olayinka, et.al., 2015)) in their study of the effect of oral administration of levofloxacin at a concentration (5, 10, 20). mg/kg) after seven days of giving the dose to male albino rats.

The results of the current study are also in agreement with the results of the study of Pratt and Kaplan (2000) and Nannipieri and his group, 2005)) if they all indicated a defect in liver function that led to a significant increase in liver enzymes (ALT, AST, ALP) in the blood serum. It also agrees with the findings of Farid and Hegazy, (2019) who reported that levofloxacin (40 mg / kg body weight) daily for two weeks was administered to albino rats who showed symptoms of impaired liver function and consequently increased AST, ALT activities. We also agree with the findings Ebenzer and his group, (2015), who reported a significant increase in enzyme activities in liver serum in rats when dosed with levofloxacin (10 mg/kg). Agree with Kim and his group (2003) where an increase in AST was observed in rats after administration of levofloxacin This may be due to damage to liver tissue due to alteration of membrane components in tissues, which led to the release of these enzymes into the blood and thus increase the level of serum enzyme activities. The enzymes leaked in high quantities from the liver tissues into the body fluids, especially the serum, and thus this high leakage reflects the damage done in the body tissues, specifically the liver, as it is the main organ responsible for processing toxins. T to which the body is exposed (Balta et al., 2019).

The reason for the high levels of liver enzymes in group (G2) treated with levofloxacin is due to oxidative stress caused by the generation of free radicals that cause lipid peroxidation, which is one of the important causes of damage and degeneration in liver cells. These enzymes inside hepatocytes are released into the bloodstream when the cell membrane is damaged Thus, their level in the blood plasma increases, and this may be due to an increase in the permeability of the liver cell membranes or cellular necrosis, and the release of these enzymes increases according to the severity of liver diseases and potential toxicity with an increase in various liver disorders and diseases and the infiltration of these enzymes into the blood circulation (Vahidi-Eyrisofla et.al. , 2015. And that their

release above normal physiological levels indicates a pathological condition that includes various bone disorders, jaundice (ALP), hepatitis ALT, and myocardial infarction (AST). The elevation in the activity of these enzymes by LFX may be a result of their release in response to tissue damage during Normal destruction of red blood cells, leukocytes and other cells such as liver cells (Singh et.al., 2011).

The current study also recorded Table (2) that there were no significant differences (P ≤ 0.05) in the levels of liver enzymes (ALT, AST, ALP) for group (G3) compared to the negative control group (G1), and a significant decrease in enzyme levels (ALT, AST, ALP) for group (G4) compared to positive control group (G2), where this study agreed with what Awodele and his group Sharifudin and (2012) and group 2013). and kaempferol), triterpenes, glycoside, alkaloid, sterols, , Quecer, tannin (Hamza 2010, Pari and Karthikesan 2007) which are found in large quantities in Moringa seeds, these compounds act to inhibit free radicals (ROS) and thus protect hepatocyte membranes and reduce enzymes Liver (Selvakumar & Natarajan, 2008), or because Moringa seeds contain highly effective and protective antioxidants, unsaturated fatty acids, and minerals (such as magnesium and zinc) in addition to protein as indicated by Auwal etal., 2013).

The results of our current study also agreed with the findings of Ashour and his group 2020, where the results of his study indicated a significant decrease in the enzymes (AST, ALT, ALP) due to the strong efficacy of Moringa seeds as antibacterial and antifungal, and this supports and enhances the results of the current study, that the role of the aqueous extract Moringa oleifera contributes to the repair of cell membranes and thus works to make the concentrations of liver enzymes (AST, ALT, ALP) withi n the normal level within the liver cells or by raising the level of antioxidants.

Table 2
The effect of Moringa seed aqueous extract on the activity of liver enzymes (ALT, AST, ALP) in the serum of healthy white male rats treated with levofloxacin

A LT U/L	AST U/L	ALP U/L	Studied / standards Means ± SE Transactions	
44.57 ±0.94 C	42.68 ± 1.01 CD	48.48 ± 0.54 CD	Negative control group distilled water)(	G1
71.06 ± 1.04 A	74.76 ± 1.69 A	76.40 ± 1.92 A	Control group (positive) levofloxacin 10 mg/kg	G2
43.97 ±0.94 C	41.52 ± 0.50 CD	46.87 ± 0.55 CD	Aqueous extract of Moringa seeds 350mg/kg	G3
56.81 ± 0.88 B	48.32 ± 0.93 B	57.70 ± 0.72 B	Moringa seed aqueous extract 350 mg/kg + Levo 10 mg/kg	G4

N=6 average ± standard error
Different capital letters in the vertical direction indicate significant differences (P ≤ 0.05)

References

Abdull Razis,A.F.; Ibrahim,M.D. and Kntayya,S,B. (2014). Health benefits of Moringa oleifera. Asian Pac J Cancer Prev. 15(20): 8571-8576.

Afolabi O. K. and Oyewo E. B .(2014).“Effects of ciprofloxacin and levofloxacin administration on some oxidative stress markers in the rat,” International Journal of Biological, Veterinary, Agricultural and Food Engineering, vol. 8, no. 1, pp. 80–84, 2014.

Aju, B. Y., Rajalakshmi, R., and Mini, S. (2019). Protective role of Moringa oleifera leaf extract on cardiac antioxidant status and lipid peroxidation in streptozotocin induced diabetic rats. Heliyon, 5(12), e02935.

am Ende, D. and am Ende, M. T. (2019). Chemical engineering in the pharmaceutical industry: an introduction. Chemical Engineering in the Pharmaceutical Industry: Drug Product Design, Development, and Modeling, 1-17.

Ashour, Elwy A., Mohamed S. El-Kholy, Mahmoud Alagawany, Mohamed E. Ab. El-Hack, Laila A. Mohamed, Ayman E. Taha, Ahmed I. E. Sheikh, Vito Laudadio, and Vincenzo Tufarelli. (2020). “Effect of Dietary Supplementation with Moringa Oleifera Leaves and/or Seeds Powder on Production, Egg Characteristics, Hatchability and Blood Chemistry of Laying Japanese Quails.” Sustainability (Switzerland) 12(6):1–9.

Auwal,M.S.; Tijjani,A.N.; Sadiq,M.A.; Saka,S.; Mairiga,I.A.; A Shuaibu,A.; Adawaren,E. and Gulani,I.A. (2013). Antibacterial and haematological activity of Moringa oleifera aqueous seed extract in Wistar albino rats. Sokoto Journal of Veterinary Sciences. 11(1): 28-37.

Awodele, O., et al. (2012). Toxicological evaluation of the aqueous leaf extract of Moringa oleifera Lam. (Moringaceae)). Journal of

Balta, I., Sevastre, B., Mireşan, V., Taulescu, M., Raducu, C., Longodor, A. L., Marchiş, Z., Mariş, C. S., and Coroian, A. (2019). Protective effect of blackthorn fruits (Prunus spinosa) against tartrazine toxicity development in albino Wistar rats. BMC Chemistry, 13(1), 104.

Bartosikova, L., Necas, V., Suchy, R. and Franov, A. (2003b). Monitoring of antioxidative effect of morine alloxan-induced diabetes mellitus in the laboratory rat. Acta. Vet. 72 : 191-200.

Belfield, A., & Golderg, G. M. (1971). *Revised assay for serum phenyl phosphatase activity using 4-amino-antipyrine-Enzyme. 12*, 561–573.

Bergmeyer, H. U., & Rej, M. H. and R. (1985). INTERNATIONAL FEDERATION OF CLINICAL CHEMISTRY (IFCC) Scientific Committee, Analytical Section. J. Clin. Chem. Clin. Biochem., 24, 481–495.

Braunwald, K. ; Fauci, H. ; Kasper, L. ; Hauser, S. & Longo R. (2001). Jameson. Harrison's Principles of Internal Medicine. 15th Edition. McGraw-Hill, New York.

Buege, J. A. and Aust, S. D. (1978). Microsomal Lipid Peroxidation. Methods in Enzymology,52: 302-310.

Chaudiere.J , R. Ferrari-Iliou.(1999). Intracelluler antioxidants: from chemicalto biochemical mechanisms. Food Chem. Toxicol., 37: 949–962.

Christ W.(1990).Central nervous system toxicity of quinolones:human and animal findings.JAntimicrobChemother ;26 :219-25.

CoelhoJF, Pereira O, Picado B, Mendonsca P, Neves-Costa J, Neta J. (2010).Acute hepatitis associated with the use of levofloxacin. ClinTher.;23(10):1733-1737. Doi: 10.1016/j.clinthera..09.004 .

Croom, K.F.and Goa, K.L.(2003) . Levofloxacin .AReview of its vsein the terament of Bacterial in the united 63(24) : 2769 – 2802 .

Ebenzer, T.; Ayokanmi, O. and Olaniyi, S. (2015): influence of different doses of levofloxacin on antioxidant defense systems in rats. Adv. In Toxic, 20, 1-7.

Ethnopharmacology, 139 (2), 330–336.

extract on liver fibrosis in rats. Food and Chemical Toxicology : An

Farid, AS. and Hegazy, AM. (2019): Ameliorative effects of Moringa Oleifera leaf extract on levofloxacininduced hepatic toxicity in rats, Drug Chem. Toxicol. 1-7.

Gupta, A. Agarwal, J. Banerjee, and J. G. Alvarez.(2007) . "The roleof oxidative stress in spontaneous abortion and recurrent pregnancyloss: a systematic review," Obstetrical and GynecologicalSurvey, vol. 62, no. 5, pp. 335–347, 2007.

Hamza, A.A., (2010). Ameliorative effects of Moringa oleifera Lam seed

Hernández-Pérez, M., R. E. López-García, R. M. Rabanal, V. Darias, and A. Arias. (1994). "Antimicrobial Activity of VisneaMocanera Leaf Extracts." Journal of Ethnopharmacology 41(1–2):115–19.

International Journal Published for the British Industrial Biological

Jahan, Ismet Ara; M. Hemayet Hossain; Khondoker Shahin Ahmed; Zakia Sultana; Pizush Kanti Biswas and Katrun Nada. (2018). "Antioxidant Activity of Moringa Oleifera Seed Extracts." Oriental Pharmacy and Experimental Medicine 18(4):299–307.

Jamshidi-Kia, F., Lorigooini, Z. and Amini-Khoei, H. (2018). Medicinal plants: Past history and future perspective. Journal of Herbmed Pharmacology, 7 .

Kim, J.; Shin, D.; Ahn, T.; Ha, C. and Chung, M. (2003): 26-Week oral repeated dose toxicity study of the new quinolone antibacterial levofloxacin in rats. Food Chem. Toxicol. 41, 637-645.

Kumbhare, M. R., V. Guleha, and T. Sivakumar. (2012). "Estimation of Total Phenolic Content, Cytotoxicity and In–vitro Antioxidant Activity of Stem Bark of Moringa Oleifera." Asian Pacific Journal of Tropical Disease 2(2):144–50.

Laandrault, N., Pouchert, P., Ravel, P., Gase, F., Cros, G., and Teissedro, P. L., (2001). Antioxidant activities phenolic level of French wines from different varieties and vintages. J . Agr. Food Chem. 49:3341–3343.

Leone, A.; Spada, A.; Battezzati, A.; Schiraldi, A.; Aristil, J. and Bertoli, S. (2015): Cultivation, genetic, ethnopharmacology, phytochemistry and pharmacology of Moringaoleifera leaves: An overview. Int.J. Mol. Sci. 16: 12791– 835.

Liang, L. L., Cai, S. Y., Gao, M., Chu, X. M., Pan, X. Y., Gong, K. K., ... & Sun, K. L. (2020). Purification of antioxidant peptides of Moringa oleifera seeds and their protective effects on H2O2 oxidative damaged Chang liver cells. Journal of Functional Foods, 64, 103698

Longmore, P. ; Wilkinson, D. ; Rajagopalan, L. (2004). Oxford Handbook of Clinical Medicine. 6th Edition. Oxford University. press. London.

Macafarlane, A.; Bomford, G. and Sherwood, R. (2000): Liver Disease and Laboratory Medicine, ACB Ventures, London, UK.

Mbikay,M. (2012). Therapeutic potential of Moringaoleifera leaves in chronic hyperglycemia and dyslipidemia: a review, Frontiers in Pharmacology. 3: 24/12.

Moron, M.S.; Depierre, J.W. and Mannervik, B. (1979). Levels of glutathione, glutathione reductase and glutathione S-transferase activities in rat lung and liver. BiochimBiophysActa., 582: 67-78.

Naik and V. S. Panda. (2007) .“Antioxidant and hepatoprotectiveeffects of Ginkgo biloba phytosomes in carbon tetrachlorideinducedliver injury in rodents,” Liver International, vol. 27, no.3, pp. 393–399, 2007.

Nirmala, A., Saroja, S., & Devi, G. G. (2011). Antidiabetic Activity of Basellarubra and its Relationship with the Antioxidant Property.

Ogbunugafor, H. A., F. U. Eneh, A. N. Ozumba, M. N. Igwo-Ezikpe, J. Okpuzor, I. O. Igwilo, S. O. Adenekan, and O. A. Onyekwelu. (2011). “Physico-Chemical and Antioxidant Properties of Moringa Oleifera Seed Oil.” Pakistan Journal of Nutrition 10(5):409–14.

Olayinka, E.; Ore, A. and Ola, O. (2014). Influences of different doses of levofloxacin on antioxidant defense systems and makers of renal and hepatic dysfunction in rats. Journal of Advances in Toxicology, Vol. 2015 Article ID, 385023: 7 pages.

OMP Division, (2006). LEVAQUIN®. Ortho McNeilPharmaceutical, Inc. Karitan, NewJersey, USA .

Pandit, A.; Sachdeva, T. and Bafna, P. (2012). Drug-induced hepato-toxicity: a review. Journal of Applied Pharmaceutical Science, 2(5): 233- 243.

Pari, L., and Karthikesan, K., (2007). Protective role of caffeic acid against alcohol-induced biochemical changes in rats. Fundamental & Clinical Pharmacology, 21 (4), 355–361.

Petrulea M, Muresan A, Duncea I. (2012). Oxidative Stress and Antioxidant Status in Hypo and Hyperthyroidism. In Antioxidant enzyme (ed Mohammed Amr El-Missiry. InTech Open Access publishers. DOI: 10.5772/51018); pp. 197-233.

Pharmaceutical Biology, 51 (3), 279–288.

Pouzauaud, M. Dutot, C. Martin, M. Debray, J. M. (2006).Warnet and P. Rat.Age-dependent effects on redox status, oxidative stress, mitochondrial activity and toxicity induced by fluoroquinolones on primary cultures of rabbit tendon cells. Comp Biochem Physiol. C. ToxicolPharmacol., 143: 232-241.

Pratt, D. and Kaplan, M. (2000). Evaluation of abnormal liver-enzyme results in a symptomatic patients. The New England Journal of Medicine, 342(17): 1266-1271.

Rahal, A., Kumar, A., Singh, V., Yadav, B., Tiwari, R., Chakraborty, S., and Dhama, K. (2014). Oxidative stress, prooxidants, and antioxidants: the interplay. BioMed Research International, 2014.

Research Association, 48 (1), 345–355.

SAS 2012. Statistical Analysis System, User›s Guide. Statistical. Version 9.1th ed SAS. Institute Incorporated Cary. N.C. USA.

Schloss M, Becak D, Tosto ST, Velayati A.(2018). A case of levofloxacin-induced hepatotoxicity. Am J Case Rep .;19:272-276. Doi: 10.12659/AJCR.907440.

Selvakumar, D. and Natarajan, P. (2008). Hepato-protective activity of Moringa oleifera Lam. leaves in carbon tetrachloride induced hepatotoxicity in albino rats. Pharmacognosy Magazine, 4:97-98.

Shailaja G. Mahajan; Ravindra G. Mali and Anita A. Mehta. (2008). “Protective Effect of Ethanolic Extract of Seeds of MoringaOleifera Lam Against Inflammation Associated with Development of Arthritis in Rats, Journal of Immunotoxicology, 4(1): 39-47.

Sharifudin, S.A., et al. (2013). Therapeutic potential of Moringa oleifera extracts against acetaminophen-induced hepatotoxicity in rats.

Singh, S.; Dimri, U.; Kataria, M. and Kumari, P. (2011). Ameliorative activity of withania somnifera root extract on paraquate-induced oxidative stress in mice. Journal of Pharmacology and Toxicology, 6(4): 433-439.

Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2022). Post-pandemic health and its sustainability: Educational situation. *International Journal of Health Sciences*, *6*(1), i-v. https://doi.org/10.53730/ijhs.v6n1.5949

Tsao, A.S., Kim, E.S. and Hong, W.K., 2004. Chemoprevention of cancer. CA: a cancer journal for clinicians, 54(3), :150-180.

Vahidi-Eyrisolfa, N.; Ahmadifar, M.; Eini, A. and Kalami, A. (2015). The study of levofloxacin effects on liver tissue in wistar rat. Journal of Liver, 4(1): 5 pages.

Wijayanti, N. (2021). Factors related to behavior the community in disposing of garbage. International Journal of Health & Medical Sciences, 4(1), 74-79. https://doi.org/10.31295/ijhms.v4n1.1226

Xu, D. P., Li, Y., Meng, X., Zhou, T., Zhou, Y., Zheng, J., ... & Li, H. B. (2017). Natural antioxidants in foods and medicinal plants: Extraction, assessment and resources. International journal of molecular sciences, 18(1), 96.

Yassa, HananDawood, and Adel FathyTohamy. (2014). "Extract of MoringaOleifera Leaves Ameliorates Streptozotocin-Induced Diabetes Mellitus in Adult Rats." ActaHistochemica 116(5):844–54.