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Moringa Oleifera Protective Effect Against DNA Damage from Hydroxychloroquine

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Abstract:

Background: The objective of this research was to investigate whether powdered Moringa oleifera leaves could offer protection to genetic material from hydroxychloroquine-induced damage in Male albino rats. They were given dry Moringa leaf powder with lunch for three weeks. Additionally, they were administered hydroxychloroquine treatment at various doses every day for five days. **Results**: The data indicate the presence of malondialdehyde (MDA) in serum. Liver DNA damage was examined using the Comet test and (SCGE) techniques in addition to assessing the superoxide dismutase (SOD) enzyme. MDA increased while SOD dropped otherwise. After the administration of powdered Moringa oleifera leaf, the activity of antioxidant factors was raised, and the MDA level decreased. It can be inferred from these findings that hydroxychloroquine is genotoxic at the dosages utilized, and the liver is a major target organ. In addition to exhibiting a protective role against HCQ-induced DNA damage, M. oleifera demonstrated slight genetic alterations. **Level of lipid peroxide (MDA):** The HCQ groups exhibited a substantial increase in lipid peroxide (malondialdehyde) activity when compared to the normal group. **Antioxidants (SOD):** It was discovered that the HCQ groups had markedly reduced superoxide dismutase (SOD) activity than the control group. Enzyme activity, however, was notably elevated in the M. oleifera-treated groups ($P = 0.001$).

Keywords: Moringa oleifera, DNA, antioxidant, Hydroxychloroquine.

Introduction:

For many years, the first-choice treatment for rheumatic disorders has been hydroxychloroquine, an antimalarial drug [1]. Hydroxychloroquine (HCQ) can have varying effects on the immune system, brain, intestinal tissues, liver, kidney, and other animal organs [2]. Furthermore, there is a negative correlation between the use of HCQ and the chance of developing chronic kidney disease (CKD) earlier, per [3]. There may be limitations to lupus nephritis flare-ups.

Additionally, earlier research on chronic kidney disease (CKD) examined the effect of HCQ [3]. A 25-year study of 256 lupus patients revealed a negative correlation between the use of HCQ and the occurrence of advanced chronic renal impairment. We believed that there was insufficient data to

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support HCQ's capacity to stop end-stage renal disease (ESKD), lupus nephritis flare-ups, or death. In order to determine if HCQ use and the risk of developing CKD in patients with SLE are related, we established a retrospective cohort to monitor data from a population-based statistics collection [3].

Moringa oleifera is a member of the Moringaceae family of plants. Its leaves are rich in alkaloids, carotenoids, flavonoids, phenolic acids, polyphenols, macronutrients, micronutrients, and vitamins [4]. The Moringa oleifera plant is therefore an excellent nutritional supplement for both people and animals. It has long been a component of traditional medicine and is used to treat a variety of ailments [5,6].

Procedures:

Plant: After being collected, fresh Moringa oleifera leaves were recognized and verified. The crushed leaves were allowed to dry in the shade on a dish before being utilized. Chemicals: Hydroxychloroquine sulfate ($C_{18}H_{26}ClN_3O$), utilized in this study, was supplied by EVA Group Limited in Egypt.

Experimental animals:

All tests were conducted using adult male rats weighing 180 grams, which were obtained from the Animal House at the Faculty of Science, University of Sabha, Libya. Each group of five rats was housed in each cage, which was maintained at a temperature of 24 ± 2 °C with a 12-hour light/12-hour dark cycle. They were given free access to water and a regular meal. The animals were kept in these typical settings for two weeks before the study to allow them to acclimate.

Experimental design:

Following the acclimation phase, the animals were randomly assigned to eight groups, each with five rats. As the control group, Group I rats were fed a typical diet. In Group II, the rats were fed a meal consisting of 2.7g/kg b.wt. of powdered Moringa oleifera leaves. The rats in Group III were given 1000 mg/kg b.wt. of HCQ orally daily for five days. Rats in Group IV were given 2.7g/kg b.wt. of powdered Moringa oleifera every day. Following three weeks of meal mixing, oral HCQ (1000 mg/kg b.wt) was given for five days. Group 5: For five days, the animals in this group received 500 mg/kg b.wt. of HCQ orally through a gastric tube. Group 6: This group was given 3 grams of Moringa oleifera powder per five rats with lunch for three weeks. Following that, animals were given hydroxychloroquine (HCQ) at a dose of 500 mg/kg body weight orally using a stomach tube for five consecutive days.

Group 7: This group received an oral dose of HCQ at 250 mg/kg body weight via a gastric tube for five days.

Group 8: These animals were fed 3 grams of Moringa oleifera powder per five rats with their lunch for a period of three weeks. After this period, they were administered HCQ at a dose of 250 mg/kg body weight daily by oral gavage for five days.

Gathering tissue and blood samples:

Rats were fasted for 12 hours at the end of the experiment before being put to death under chloroform anesthesia. Sterile syringes were used to draw samples straight from the heart. The blood was drawn into sterile, dry centrifuge tubes for biochemical analysis without the use of anticoagulants. After that, the liver was promptly removed, and any extra blood was cleaned out with ordinary saline solution. A little portion of it was removed, placed in tiny bags, and kept at -20 °C until the inspection date.

Physiological study:

Superoxide dismutase (SOD) and malondialdehyde (MDA) levels in serum are assessed in this investigation.

Genetic studies:

Genetic Analysis: The Comet Assay, also referred to as alkaline single-cell gel electrophoresis (SCGE), was employed in this study (comet test) [7,8].

Analyzing statistics:

The results were expressed as mean ± standard deviation and analyzed statistically using ANOVA followed by Duncan's post hoc test. This parametric approach was applied to assess the variability both within and between groups to determine significant differences. A p-value of less than 0.05 was considered significant. The data analysis was conducted using SPSS software (Version 20), and the results were found to be statistically significant.

Results:

1. Antioxidant Enzymes (Stress Marker)

Superoxide dismutase (SOD):

Table 1 shows that the dosages of the HCQ group were statistically different from those of the groups treated with Moringa oleifera. The Moringa oleifera-treated groups that received different doses of hydroxychloroquine showed a substantial increase in comparison to the groups that received different doses of hydroxychloroquine, as shown in Figure 1 (P value < 0.001).

2. Lipid Peroxidation Product (Oxidative Stress Marker)

- Malondialdehyde (MDA):

Furthermore, Table 1 showed that the doses of the HCQ groups differed significantly from those of the control group. The mean and standard deviation (S.D.) of serum levels of superoxide dismutase (SOD) (U/mL) and malondialdehyde (MDA) (nM/mL) were recorded for rats treated with Moringa oleifera and various doses of hydroxychloroquine, along with the control groups.

Table 2 shows that Alterations were also observed in the damage percentage. Following treatment with Moringa oleifera, measurements were taken for percentage, tail length, percentage of DNA in the tail, and tail moment.

-Figure 1 illustrates an increase in serum activity of SOD in the different treatment groups, with a P value <0.05, when comparing those treated with Moringa oleifera to those treated with hydroxychloroquine at different dosages.

-Figure 2, which shows the MDA serum activity of the different treatment groups, shows a highly significant increase (P value < 0.01) when comparing groups treated with Moringa oleifera to those treated with hydroxychloroquine at different dosages.

Figure 3 shows "The extent of DNA damage in the livers of rats from the different study groups was assessed using various parameters from the single-cell gel electrophoresis (comet assay). These measurements included tail length, tail moment, tail DNA percentage, and percentage of tailed cells (Figure 3).

The results demonstrated that hydroxychloroquine (HCQ) administration led to a marked increase in the frequency of tailed nuclei, tail length, tail DNA percentage, and tail moment in rat liver cells compared to the control group. Patients who underwent M. oleifera medication had a statistically significant reduction in liver DNA damage and all single-cell gel electrophoresis (comet test) parameters as compared to those who got HCQ injections.

Figure (3A) demonstrated that, in comparison to the control group, tail length increased statistically significantly (P<0.05) in groups that received a dosage of Moringa for three weeks after the administration of different HCQ doses (1000, 500, and 250 mg/kg). The mean tail lengths for the different doses were around 3.66, 2.79, and 2.08, suggesting some healing, but not as much as typical.

In Figure 3B, the mean tail DNA percentage reflects the average amount of DNA that migrated out of the nucleus during electrophoresis(head) among the 50 to 100 cells analyzed in the experiment.

The tail DNA percentages of the other research groups grew considerably (P <0.05), whereas the mean for the control group was 0.79%. Compared to the groups that got injections of varying quantities of HCQ, the group that underwent Moringa treatment had a significantly reduced proportion of tail DNA (P<0.05).

The mean tail moment for each group, indicating the average number of DNA strand breaks per nucleus, as compared to the control group.

The findings for these parameters showed that MO decreased the amount of damage caused by HCQ, which was also evident for the tail DNA percentage.

Table 1 presents the mean values and standard deviations (S.D.) for these measurements." levels of superoxide dismutase (SOD) (U/mL) and malondialdehyde (MDA) (nM/ml) in rats treated with M. oleifera and administered different dosages of hydroxychloroquine, as well as the control groups.

All data are presented as mean ± standard deviation (S.D.).

Clusters / Parameters	SOD Mean ± S.D. (U/mL)	MDA mean ± S.D. (nM/ml)
Control	203.58 ± 46.48^{b}	16.86 ± 3.22^{a}
Moringa oleifera	139.06 ± 36.68^{a}	16.86 ± 5.08^{a}
HCQ(1000mg/kg)	214.60 ± 28.44^{c}	25.42 ± 5.14^{a}
MO+HCQ(1000mg/kg)	137.24 ± 30.19^{a}	27.24 ± 13.01^{b}
HCQ (500mg/kg)	183.52 ± 53.38^{a}	27.70 ± 6.89^{b}
MO+ HCQ(500mg/kg)	130.52 ± 24.56^{a}	29.05 ± 4.77^{b}
HCQ(250mg/kg)	125.62 ± 39.31^{a}	28.36 ± 5.12^{b}
MO+HCQ(250mg/kg)	104.16 ± 37.04^{a}	36.36 ± 8.99^{c}
P-value(P)	**0.001*****	**0.003****
Decision	*****=Ex-Sig (P<0.001)**	****=Very-Sig (P<0.01)**

Double asterisks () indicate highly significant differences (P < 0.01), while triple asterisks (*) represent extremely significant differences (P < 0.001) compared to the control group. Each treatment group included five animals. Superscript letters (e.g., a, b, c) within the same column indicate statistically significant differences at P < 0.05.

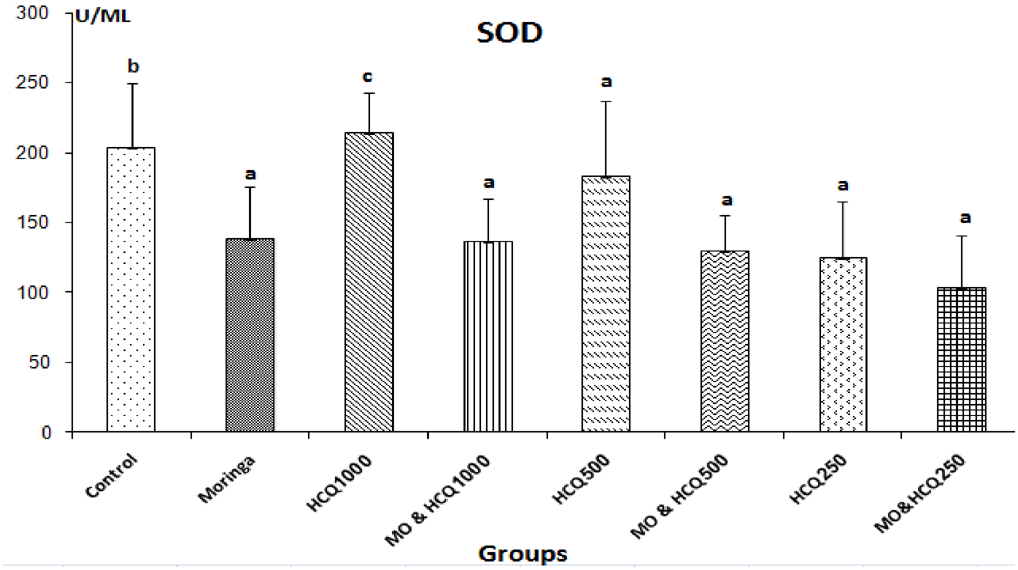

Figure 1: Superscript letters within the same row (e.g., a, b, e) indicate significant differences in serum SOD (superoxide dismutase) activity among the treatment groups (P < 0.05). HCQ refers to hydroxychloroquine, and MO denotes Moringa oleifera.

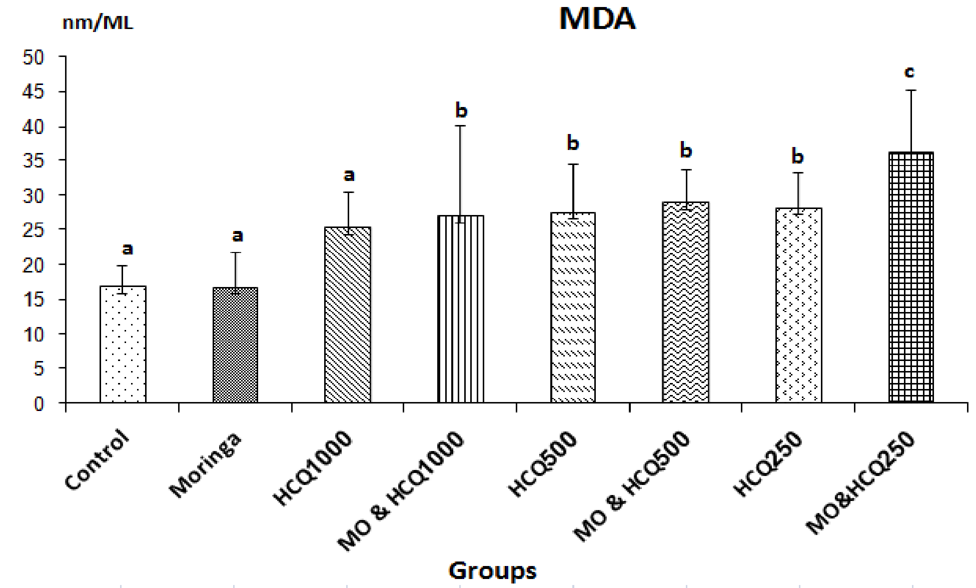

Figure 2: In this figure, the MDA (malondialdehyde) serum levels of different treatment groups are denoted by superscript letters (a, b, e) within the same row, indicating statistically significant differences (P < 0.05). HCQ stands for hydroxychloroquine, and MO represents Moringa oleifera.

Genetic Analysis: Single-Cell Gel Electrophoresis (Comet Assay)

Table 2 presents the findings of the comet assay performed on rats that received Moringa oleifera and different concentrations of hydroxychloroquine (HCQ). The key indicators of DNA damage assessed were the length of the comet tail and the proportion of DNA present in the tail region. This analysis also included rats that had discontinued HCQ treatment, demonstrated distinct outcomes, with significant DNA damage observed in liver tissues, suggesting the liver as a principal target organ for HCQ-induced genotoxicity at the tested doses. Notably, Moringa oleifera exhibited a protective effect, reducing DNA damage both in mild cases and in those induced by HCQ (see Figure 6).

In the control and Moringa-only groups, most cells displayed intact nuclei without comet formation. The DNA retained its typical circular arrangement within the nucleus despite nuclear compaction (Figure 4).

In contrast, liver cells from rats treated with hydroxychloroquine (HCQ) at doses of 1000, 500, and 250 mg/kg body weight exhibited marked DNA damage. This was demonstrated by the appearance of a fluorescent tail extending from the nucleus, reflecting a higher level of DNA fragmentation (Figure 5). Table 2 outlines the variations in comet assay parameters—such as tail length, percentage of DNA in the tail, and tail moment—across groups receiving different HCQ doses, with or without Moringa oleifera supplementation.

Table 2 presents the findings of the comet assay performed on rats that received Moringa oleifera and different concentrations of hydroxychloroquine (HCQ).

Clusters	Length of Tail (PX)	DNA in the tail (%)	Moment of Tail
Control(G1)	1.95±1.99	0.79±1.89	0.02±0.07
Moringa(G2)	2.58±2.57	1.34±2.66	0.05±0.14
HCQ(1000mg/kg)(G3)	6.43±4.47	6.78±6.18	0.42±0.58
MO+HCQ(1000mg/kg)(G4)	3.66±2.92	2.94±3.79	0.12±0.21
HCQ (500mg/kg)(G5)	4.06±3.14	4.84±6.90	0.24±0.45
MO+ HCQ(500mg/kg)(G6)	2.79±2.55	2.38±4.05	0.11±0.25
HCQ(250mg/kg)(G7)	2.89±2.89	2.64±4.13	0.12±0.31
MO+HCQ(250mg/kg)(G8)	2.08±2.31	1.23±2.55	0.04±0.11
P-value (ANOVA), P	< 0.000***	< 0.000***	< 0.000***

The data are expressed as mean ± standard deviation (S.D.). All findings were statistically significant (***), with a P value less than 0.05 compared to the control groups.

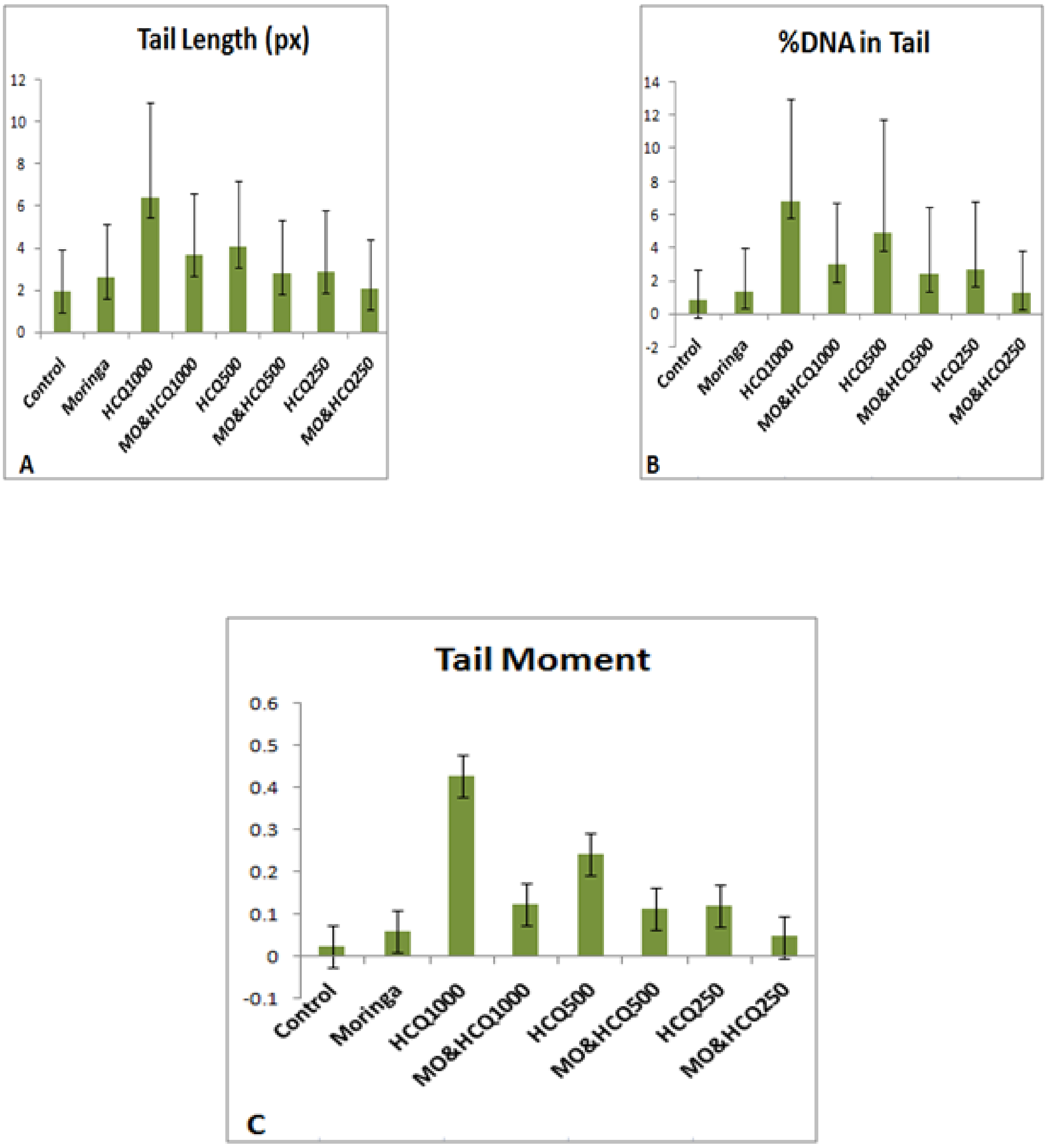

Figure 3 contains histograms representing the degree of DNA damage in liver cells of rats across the experimental groups. Panel A shows tail length, Panel B illustrates the percentage of DNA in the tail, and Panel C presents the tail moment, all based on the single-cell gel electrophoresis (comet assay) analysis. These measurements were obtained using an image analysis system applied to the comet assay.

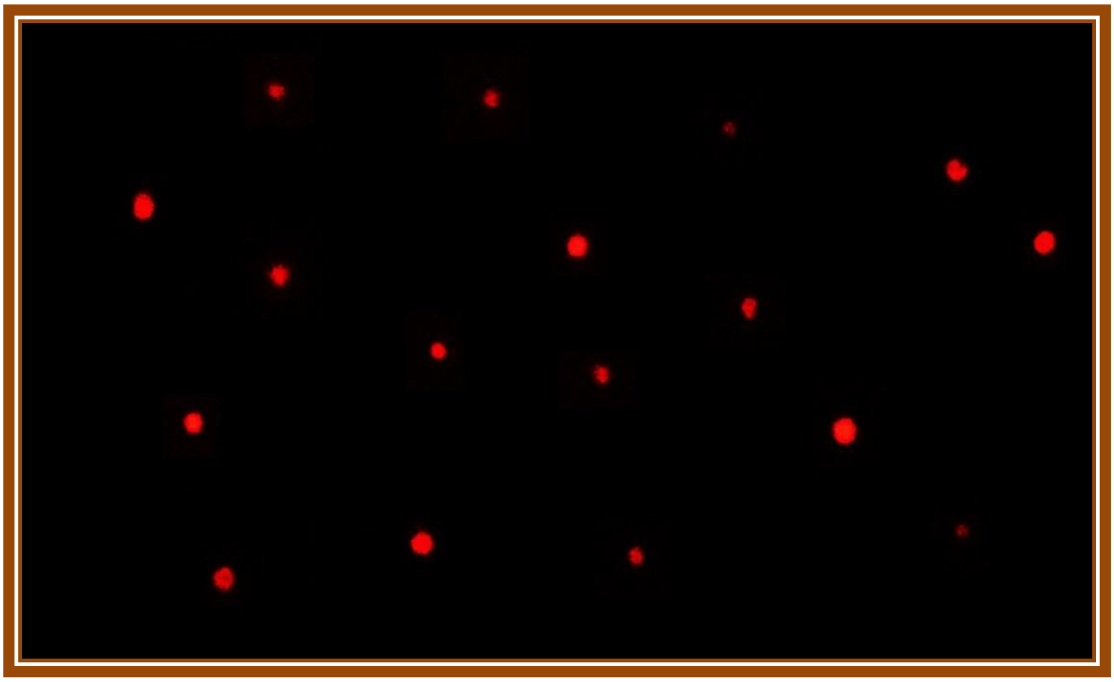

Figure 4: The DNA movement pattern of a rat liver cell stained with ethidium bromide illustrates the comet shape. Rats in the control and Moringa control groups showed comet morphology; intact DNA (%tail DNA <5%) was indicated by Grade 0.

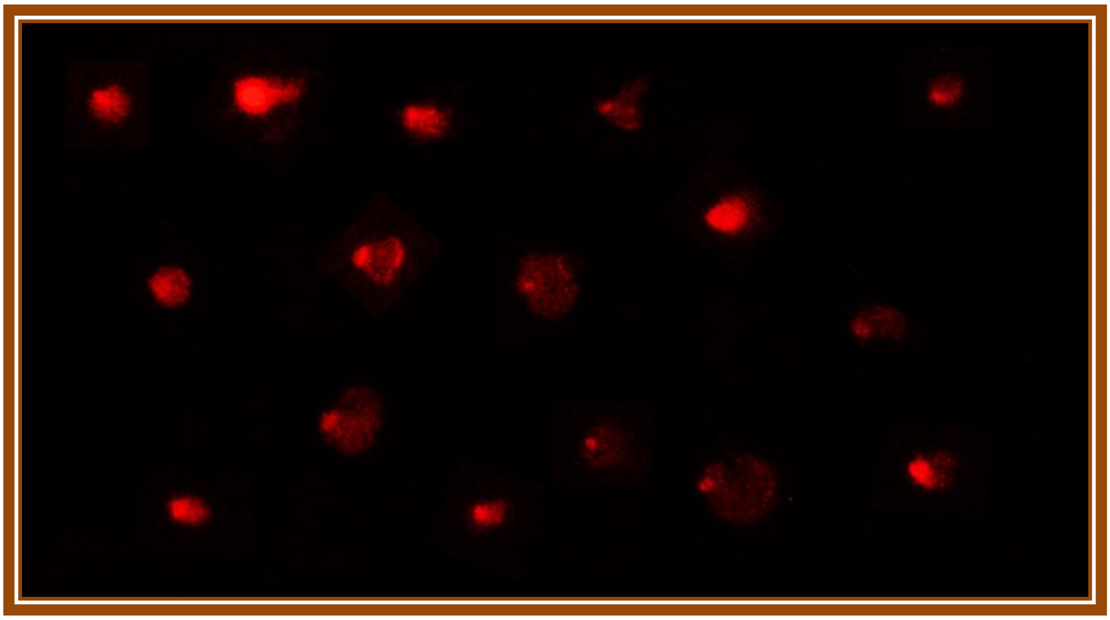

Figure 5: The DNA movement pattern of a rat liver cell stained with ethidium bromide illustrates the comet shape. Rats given different doses of hydroxychloroquine showed grade 2 comet morphology, which suggests substantial DNA damage (20–40%).

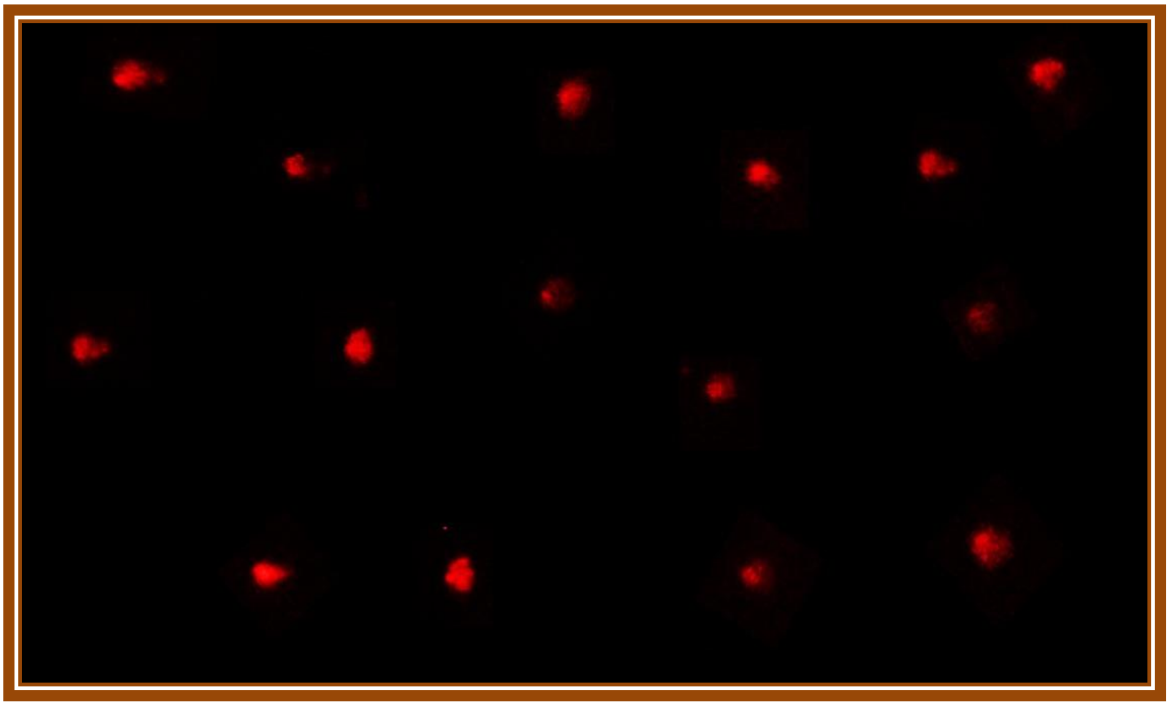

Figure (6): A comet morphology depiction showing the DNA movement pattern in rat hepatocytes stained with ethidium bromide. Mice treated with Moringa prophylactically and at different hydroxychloroquine dosages show a comet form, which suggests that Grade 1 mice have median DNA damage (DNA tail% 5–20%).

Discussion:

Systemic lupus erythematosus, rheumatoid arthritis, malaria, and other inflammatory diseases are all treated with HCQ [9,10]. In addition, it is used to treat HIV, SARS-CoV, influenza, and other viral illnesses. Recently, Several national and international medical organizations have authorized the limited use of hydroxychloroquine and chloroquine for treating COVID-19 in hospitalized patients [11,12].

This study primarily aimed to assess the protective and therapeutic potential of Moringa oleifera leaves in rats administered hydroxychloroquine using a rat model. Previous studies [13] found DNA damage in rat liver slices exposed to HCQ, suggesting that the chemical may cause genotoxicity, which would hinder the liver's ability to perform its synthesis activities.

The study's findings also show that the processes of antioxidant defense are made up of both enzymatic and non-enzymatic antioxidants, which are crucial for preserving physiological ranges of O2 and H2O2 as well as for eliminating peroxides produced by unintentional exposure to dangerous drugs. SOD is the primary enzyme antioxidant defense that shields the liver from oxidative damage caused by HCQ. The first line of defense against oxidative stress in an antioxidant device is SOD, which works by accelerating the transformation of Superoxide radicals (O_2^-) are converted into molecular oxygen (O_2) and hydrogen peroxide (H_2O_2) [14].

As demonstrated by a substantial decrease ($p<0.05$) in SOD activities, a major aldehyde linked to the peroxidation of organic tissue, and a large increase ($p<0.001$) in blood MDA ranges, the current study's findings demonstrated that HCQ management led to oxidative stress. [15] The latter may also play a role in the cells' ability to scavenge; hence, the overproduction of MDA was mediated by discounting their proposed values. [16] showed that HCQ treatment markedly enhanced ($p<0.001$) the activity of two antioxidant enzymes. in hepatic tissue: MDA and SOD, which our results supported.

The Comet test is an easy, quick, and sensitive way to find protein-DNA, DNA-DNA, alkali-labile points, and single-stranded breaks in single-cell cultures. Among the different types of DNA damage, the comet assay is a widely used technique to measure indicators such as tail length, the percentage of DNA in the tail, and tail moment [8]. Tail moment is calculated by multiplying tail length by the percentage of DNA in the tail, while tail DNA percentage represents the ratio of fluorescence intensity in the tail relative to the entire comet [17].

In this study, DNA damage from hydroxychloroquine (HCQ) treatment was evaluated by analyzing tail length and tail DNA percentage. The findings demonstrated that HCQ induced a significant, time-dependent increase in both indicators. According to the comet assay grading scale, Grade 0 represents no detectable tail, with increasing grades reflecting higher levels of tail DNA. Since HCQ did not lead to severe DNA damage, Grades 3 and 4 were not observed. Although none of the treatment groups exhibited severe damage, liver cells from rats treated with hydroxychloroquine (HCQ) showed a marked increase in both tail length and tail DNA percentage, as measured by single-cell gel electrophoresis (comet assay), a technique that assesses inborn damage.

This implies genotoxic damage. The induction of inborn damage was consistent across all groups that were analyzed.

The enhanced liver damage observed in this study may be related to the higher accumulation of HCQ within these tissues is promoted by membrane transport mechanisms. mechanisms that mediate the uptake of this hydrophilic emulsion [18].

This work used single-cell gel electrophoresis (comet test) to simplify some of the DNA changes that occur in rat liver cells following different HCQ boluses. The rat's situational behavior was preserved, and the DNA of the intact liver cells was firmly compressed. The nuclear DNA profile altered after HCQ, like A comet characterized by a bright head and an extended tail. The cells were assumed to contain normal DNA as a result. Using the Comet test, DNA breakage and DNA-protein crosslinks were found. Cross-links can fix chromosomal DNA and inhibit DNA mobility [19,20].

The formation of DNA breaks might be responsible for the increased DNA mobility in HCQ groups observed in our investigation. Crosslinks are relative lesions in terms of mutagenesis, and their induction may be the cause of the control group's reduced DNA mobility.

Rat liver DNA damage from HCQ was evident from the motley single-cell gel electrophoresis (comet test) features that were supplied by the image analysis software employed in this investigation. Tail length, tail time, tail probability of dogged cells, and tail chance of DNA in the tail were among them.

These measures showed a substantial increase when the HCQ groups were contrasted with the control group.

The quantity of DNA damage seen in the control group may have been caused by the body's estimated 10,000 oxidation hits per cell every day, as well as the fact that DNA is made up of more than 35 distinct kinds of oxidized bases [21]. Effective DNA-estate enzymes can repair the most recent damage, but some damage evades the estate and causes irreversible harm [22]. Together, the results of this study showed that M. oleifera shields DNA from HCQ-induced harm and shields the liver by lowering hepatic inflammation and oxidative stress. Because M. oleifera can change the liver and reduce the production of free radicals, it has been questioned whether further study is necessary to verify that the official tablet effectively treats liver diseases.

Conclusion:

The study's findings indicate that Moringa oleifera might protect rat liver cells against damage caused by hydroxychloroquine by reducing hepatic oxidative stress and liver inflammation.

Improved liver function, including the activity of liver enzymes produced by the liver cells, as well as an increase in the superoxide enzyme dismutase and a subsequent drop in malondialdehyde levels, which were advantageous to the liver cells (Cell Membrane), are examples of Moringa oleifera's antioxidant qualities. Additionally, DNA in its normal condition is visible in the plant Moringa oleifera.

Abbreviations and Acronyms:

HCQ = Hydroxychloroquine.

MO = Moringa oleifera.

SOD = Superoxide dismutase.

MDA = Malondialdehyde.

DNA = Deoxyribonucleic acid.

Conflict of interest: NIL

Funding: NIL

References:

[1]- Xin Qiao, Zhuo-Chao Zhou, and Rui Niu. (2019): Cheng 1* Hydroxychloroquine Improves Obesity-Associated Insulin Resistance and Hepatic Steatosis by Regulating Lipid Metabolism Department of Rheumatology and Immunology. Frontiers in J Pharmacology 12:120-126.

[2]- Sahraei, Z.; Shabani, M. and Shokouhi, S. (2020): Aminoquinolines against coronavirus disease 2019 chloroquine or hydroxychloroquine. Int J Antimicrob Agents 45:105.

[3]- Pokroy-Shapira, E.; Gelernter, I. and Molad Y. (2014): Evolution of chronic kidney disease in patients with systemic lupus erythematosus over a long-period follow-up: a single-center inception cohort study. J Clin Rheumatol 33:649–652.

[4]- Leone, A; Spada, A; Battezzati, A; Schiraldi, A; Aristil, J. and Bertoli, S.(2015): Cultivation, Genetic, Ethnopharmacology, Phytochemistry and Pharmacology of Moringa oleifera Leaves: An Overview. Int J Mol Sci, 16:12791–12835.

[5]- Siddhuraju, P. and Becker, K. (2003): Antioxidant properties of various solvent extracts of total phenolic constituents from three different agroclimatic origins of drumstick tree (Moringa oleifera

Lam.) leaves. J Agricultural and Food Chemistry, 51(8): 2144– 2155.

[6]- Awad, H., Ibadi, E., Alrashedi, A. Reproductive toxicity induced by polyethylene glycol and possible protective mechanism of Moringa oleifera in male rats. *Journal of Medical and Life Science*, 2024; 6(3): 328-342. doi: 10.21608/jmals.2024.376125

[7]- Tice R. R.; Agurell, E.; Anderson, D.; Burlinson, B.; Hartmann, A.; Kobayashi, H.; Miyamae, Y.; Rojas, E.; Ryu, J.C. and Sasaki, Y. (2000): Single cell gel/single-cell gel electrophoresis (comet assay): guidelines for in vitro and in vivo genetic toxicology testing. Environmental and Molecular Mutagenesis 35:206-221.

[8]- Collins, A.R.; Oscoz, A.A.; Brunborg, G.; Gaivao, I.; Giovannelli, L.; Kruszewski, M.; Smith, C.C. and Štětina, R. (2008). The single-cell gel electrophoresis (comet assay): topical issues. J Mutagenesis 23:143-151

[9]- Borba, E. F; Turrini-Filho, J. R; Kuruma, K. A; Bertola, C; Pedalini, M. E; Lorenzi,M. C. and Bonfá, E. (2004): Chloroquine gestational use in systemic lupus erythematosus: assessing the risk of child ototoxicity by pure tone audiometry. Lupus PubMed 13: 223–227.

[10]- Takano, T.; Katoh, Y.; Doki, T. and Hohdatsu, T. (2013): Effect of chloroquine on feline infectious peritonitis virus infection in vitro and in vivo. J Antiviral Res. 99: 100–107.

[11]- Bensalah, N; Midassi, S; Ahmad, M.I. and Bedoui, A. (2020): Degradation of hydroxychloroquine by electrochemical advanced oxidation processes. Chem. Eng. J. 402:126-279.

[12]- Yameny, A. Characterization of SARS-CoV-2 Omicron XBB.1.5 sub-lineage: A review. *Journal of Medical and Life Science*, 2023; 5(2): 96-101. doi: 10.21608/jmals.2023.305080

[13]- Fernandez, A. P. (2017): Updated recommendations on the use of hydroxychloroquine in dermatologic practice. J. Am. Acad. Dermatol. 76 (6), 1176–1182.

[14]- Kirkman, H. N, Galiano, S., and Gaetani, G.F. (1987): The function of catalase bound NADPH. J. Biol. Chem., 262: 660-665

[15]- Glasauer, A. and Chandel, N.S. (2014): Targeting antioxidants for cancer therapy. Biochemical Pharmacology 92:90-101.

[16]- Koracevic, D; Koracevic, G; Djordjevic, V; Andrejevic, S. and Cosic, V. (2001): Method for the measurement of antioxidant activity in human fluids. J. Clin. Pathol. 54: 356–361.

[17]- Collins, A.R. (2004): The single-cell gel electrophoresis (comet assay) for DNA damage and repair. JMolecular Biotechnology. 26:249.

[18]- Tachampa, K.; Takeda, M.; Khamdang, S.; Noshiro-Kofuji, R.; Tsuda, M.; Jariyawat, S.; Fukutomi, T.; Sophasan, S.; Anzai, N. and Endou, H. (2008): Interactions of organic anion transporters and organic cation transporters with mycotoxins. J Pharmacological Sciences 30:215-220.

[19]- Merk, O. and Speit, G. (1999): Detection of crosslinks with the single-cell gel electrophoresis (comet assay) in relationship to genotoxicity and cytotoxicity. J Environmental and Molecular Mutagenesis 33:167-172.

[20]- Yousef, H.A.; Afify, A.; Hasan, H.M. and Meguid, A.A. (2010): DNA damage in hemocytes of Schistocerca gregaria (Orthoptera: Acrididae) exposed to contaminated food with cadmium and lead. J Natural Science 2:292-297.

[21]- Ames BN, Shigenaga MK, and Hagen TM (1993). Oxidants, antioxidants, and the degenerative diseases of aging. Proceedings of the National Academy of Sciences 90:7915-7922.

[22]- Jackson AL and Loeb LA (2001): The contribution of endogenous sources of DNA damage to the multiple mutations in cancer. Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis 477:7-21.