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Article

The Role of Vitamin C as a Protective Agent Against UVA Radiation Affecting Blood Counts and Liver Tissues in Experimental Rats

M. Adel Fawzy[1], Mona A.H. Yehia[2], Rana H.M. Khafaga[2], Sameh M. Elghnam[1,*], Mariam Y. Saad[1]

[1]*Physics Department, Faculty of Science, Alexandria University, Alexandria, Egypt.*

[2]*Medical Research Institute, Alexandria University, Alexandria, Egypt.*

[*] *Correspondence Address:*

Sameh M. Elghnam: Physics Department, Faculty of Science, Alexandria University, Alexandria, Egypt. Email address: sameh.elganam@alexu.edu.eg.

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ABSTRACT: This study aimed to use vitamin C as a protective agent to minimize the effects of ultraviolet radiation (UVA) damage rats' liver, lower oxidative damage and preserve cellular structure. 42 rats were divided into three groups; the control (GP-I) was neither subjected to UVA nor any treatment, GP II was divided into three subgroups were exposed to UVA (GP II-A) received low dose (88.52 J/cm^2), (GP II-B) received moderate dose (177.00 J/cm^2), and (GP II-C) received high dose (322.05 J/cm^2); (duration 24hr. /days). The third group was pre-treated with vitamin C 150 mg/kg for 8 weeks, followed by exposed to same doses of UVA as group II :(GP III-A), (GP III-B), and (GP III-C) The blood analysis was done using SysmecXP-300 for complete blood counts and Erba Chem7 for alanine transaminase (ALT), aspartate aminotransferase (AST). Also, the biochemical analysis of the Malondialdehyde (MDA) and Ferric Reducing Antioxidant Power (FRAP) levels were done on homogenate liver tissue. The liver tissue was prepared for examining under the light microscope and transmission electron microscopy. The results showed the exposure to the UVA induced a decrease in red blood cell counts (RBCs) and hemoglobin, an increase in liver enzymes and oxidative stress markers, degeneration in the liver tissue and destructive hepatocyte architecture. Supplementation of vitamin C mitigated these effects; it played a protective role on blood and liver tissues, reducing the harmful effect of UVA on blood parameters and recovering the degeneration of liver tissue.

1. INTRODCTION

Ultraviolet-A (UVA) radiation, with wavelengths ranging from 320 to 400 nm, is responsible for 90–95% of all UV radiation reaching the Earth's surface. They are present all day and can penetrate clouds and glass, creating constant exposure to dangers [1]. UVA (400–315 nm), UVB (315–280 nm), and UVC (280–100 nm) [1,2] can penetrate deeply into the body through the skin, causing alteration in the blood parameters and liver damage. It can influence red blood cells (RBCs) morphology and function and modify the hemoglobin structure and its ability to bind and release oxygen efficiently. Where RBCs (transports oxygen from the lungs to tissues and facilitate the removal of carbon dioxide and hemoglobin is the oxygen-carrying protein in red blood cells. Also, UVA radiation can influence White blood cells (Leukocytes)which are crucial components of the immune system, defending the body against infections. Moreover, UVA exposure can impact platelets (Thrombocytes) which play a key role in blood clotting and wound healing [2-4]. It is considered as a key player in immune function because it contains specialized cells called Kupffer cells that destroy pathogens and remove dead cells. It has exceptional regeneration ability, which is unique among human organs [5].

Elevated levels of liver enzymes, including AST (aspartate aminotransferase), ALT (alanine aminotransferase), GGT (gamma-glutamyl transferase), and ALP (alkaline phosphatase) are makers of liver injury and can indicate liver health issues and are linked to hypertension, diabetes, and nonalcoholic fatty liver disease [6,7]. UVA radiation induces oxidative stress, leading to liver damage, fibrosis, inflammation, and increased susceptibility to toxins, infections,

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and cancer risk. Plasma cells produce antibodies, aiding immune responses [6]. Oxidative stress, caused by an imbalance of free radicals as reactive oxygen species (ROS) and antioxidants, damages nucleic acids, proteins, and lipids, contributing to aging, cancer, and cardiovascular and neurological diseases [7]. Vitamin C, a water-soluble antioxidant, plays a critical role in several physiological processes such as the manufacture of collagen, carnitine, and neurotransmitters, which contribute to tissue repair and enzymatic function. Also, it is crucial for liver function and blood health. It increases antioxidant activity, detoxification, metabolism, and protein synthesis, it neutralizes free radicals and protects against ROS-induced cellular damage and controls lipid homeostasis in the bloodstream and liver. Furthermore, it boosts the immune system by supporting numerous cellular functions, such as phagocyte activation and lymphocyte proliferation. Also, it regenerates antioxidants, facilitates iron absorption by improving iron bioavailability, and decreases inflammation, which is a precursor to liver illnesses such as hepatitis and cirrhosis. Vitamin C is essential for maintaining overall health [8].

The purpose of this study is to look at the efficacy of vitamin C as a protective agent against UVA radiation effects on blood count, liver function, oxidative damage, and maintaining its cellular structure.

2. Materials and Methods

2.1. Radiation source

UVA lamps 40 watts, and 60 cm length model Black light 368 F40W/2FT/T12/BL368-made in Germany, has been used) and placed about 30 cm above the cover of the rat's cage. The UVA- lamp has been calibrated in the National Institute for Standards – NIS Radiometry Metrology Lab, Cairo. Reference Radiometry S480/268-UVA Report No. 7658/52T001/181/2023.

2.2. Experimental Design

The study included 42 male Sprague Dawley rats with weight range of about 200–220 gm. Their source is Egypt for Vaccines. These rats were divided into three main groups; the control group (Group I- contains 6 rats) was neither subjected to UVA radiation nor protective interventions, and the other two groups are divided into three subgroups(each group contains 6 rats) that were irradiated with artificially produced UVA (GP II-A) for low dose, (GP II-B) for moderate dose, and (GP II-C) for high dose; (duration 24hr. /days) as shown in Table 1.The third group was pre-treated with vitamin C 150 mg/kg for 8 weeks, followed by UVA exposure: (GP III-A) for low dose, (GP III-B) for moderate dose, and (GP III-C) for high dose; (duration 24hr. / days). They were given 150 mg/kg of Vitamin C daily for 8 weeks followed by exposure to UVA radiation with same exposure durations. The study was approved by the faculty of science Animal Care and Use Committee (ALEXU-IACUC) AU 04 23 10 31 1 06.

Table 1: Illustrates the accumulative radiation doses and exposure time.

Low dose -A in 5 days	Moderate dose- B in 10 days	High dose-C in 15 days
88.52 J/cm^2	177.00 J/cm^2	322.05 J/cm^2

2.3. Sample Preparation

Rats were fasted 24 hours before each designated time point and then they were given an Anesthetic of Isoflurane administered via intraperitoneal (IP) injection. The 3 ml of Blood was collected from the Cardiac aorta of the test subjects under Isoflurane anesthesia and in EDTA tubes to prevent clotting. The liver organs were removed from the rats by slitting their abdomens. It was cut into three parts; part for homogenate store at -80^{O}c, part put in the fixed agent (10% formalin) for proceeding paraffin sections. and third part put in 4% formal glutaraldehyde fixed for processing ultrathin section.

2.4. Blood Analysis

2.4.1. The Blood Counts

Blood samples for complete blood counts are collected in anticoagulant tubes (EDTA tubes) to prevent clotting. Sysmec XP-300 was used for complete blood counts.

2.4.2. The Liver Functions

The serum of blood samples from six animals for each group were collected in tubes. The samples were left for 20 min at 4^{o}C centrifuged at 3000 xg for 10 minutes using Hettich ZentrifugenTuttlingen centrifuge to obtain serum for assessment of liver function tests by Erba-chem7 at Nour-El-Ghad Laboratory in Damanhur Governorate. The principal reaction of the colorimetric determination of AST or ALT activity is based on the reaction of aspartate or alanine with α-ketoglutarate to form oxaloacetate or pyruvate hydrazine formed with 2, 4-dinitrophenylhydrazine [9].

2.4.3. Oxidative Stress Markers

Part of liver tissue was rinsed with saline, homogenized in a phosphate-buffered saline (PBS) solution (pH 7.4) at a 1:10 ratio, and used to measure Malondialdehyde (MDA) and Ferric Reducing Antioxidant Power (FRAP) levels, as a marker of oxidative stress. The absorbance measure was using a spectrophotometer.

2.4.3.1. Malondialdehyde (MDA)

Malondialdehyde determination as a marker of lipid peroxidation was determined according to the method of Draper and Hadley [10]. A 0.1 ml aliquot of the sample was mixed with an equal volume of SDS solution, followed by the addition of acetic acid, TBA, and distilled water. The mixture was vortexed, incubated in a boiling water bath for one hour, and cooled to room temperature. a standard curve prepared from TMP dilutions and normalized to tissue weight, expressed as nmol MDA per gram of tissue and absorbance at 532 nm.

2.4.3.2. Determination of Total Antioxidant Capacity (TAC)

The method used ferric reducing antioxidant power [11]. The Ferric reducing antioxidant power (FRAP). For the test, 7 µL of the sample was mixed with 200 µL of FRAP reagent and 10 µL of water in test tubes. All tubes were incubated at 37°C for 10 minutes, and absorbance readings were taken at 593 nm at zero time and after 4 minutes. A standard curve established using known concentrations of Fe^{2+} (100–1000 µmol/L).

2.5. Histopathological Techniques

2.5.1. Light Microscopic Technique

The liver samples were fixed with 10% formaldehyde, dehydrated in alcohol, and cleared in xylene. It was then impregnated in molten paraffin at 60 °C for 1-2 hours to form a paraffin block. The blocks were sliced into 5 µm thick slices, floated in a water bath, picked up in clean glass slides, and left at 40°C for dry and fixed portions. The histological alterations in liver tissues were investigated using paraffin sections and stained with hematoxylin and eosin (H&E) stain. The sections were deparaffinized with xylene, then rehydrated in alcohol, rinsed with hematoxylin stain, washed with tap water, and then rinsed with eosin. The slides were dehydrated in alcohol and then cleaned with xylene. DPX mounted the slides and protected them with coverslips to be ready for examination under light microscopy [12]. The histological technique of liver tissues was conducted at the Histochemistry and Cell **B**iology Department- Medical Research Institute - Alexandria University

2.5.2. Electron Microscope Technique

A section of the rat liver was prepared for electron microscopy. It was sliced into small pieces and fixed with 2% buffered glutaraldehyde, followed by dehydration with 1% osmic acid dehydrate agent was used before embedded in Araldite. Mixed rinses were produced by the araldite capsules. The capsule was created for cutting by Ultrathin-microtome and pinked up on a copper grade. The sample was then stained with uranyl acetate and lead citrate to examine the fine structures of the hepatocyte cells under the transmission electron microscopy. Then the copper grades carried out using a Joel electron microscopy model (JEOL-JSM-1400PLUS) at Faculty of Science, Alexandria University's.

2.6. Statistical Analyses

Data was loaded into a computer and evaluated with IBM SPSS software. The study t-test was used to compare two normally distributed quantitative data sets. To compare normally distributed quantitative variables across groups, use the F-test (ANOVA) with a statistical significance threshold of $P \leq 0.05$.

3. Results

3.1. Blood Analysis

The present study examined the impact of ultraviolet-A (UVA) radiation on hematological parameters in rats, with different exposure durations. The variations in hematological parameters were observed based on the exposure period and accumulative doses.

3.1.1. Red Blood Cells (RBCs)

The study investigated the impact of UVA radiation on male rats, with varying doses of exposure. The RBCs count significantly decreased in all exposure durations compared to the control group. Pre-treatment with vitamin C resulted in a mixed effect on RBC counts: low exposure (III-A) caused a decline in RBCs compared to the exposed group, while high exposure showed an improvement in RBC counts, although still lower than the control (**Figure 1A**).

3.1.2. Hemoglobin (Hb)

UVA radiation caused a significant hemoglobin to decrease rats with accumulative exposure increased the dosage led to decreased hemoglobin levels, Hb of GP (II-C) < Hb of GP (II-B) <Hb of GP (II-A). Vitamin C pre-treatment slightly improved hemoglobin levels in low/moderate exposures GP (III-A; B) but showed a significant decrease in high exposure (GP (III-C)) compared to the control and the exposed groups, as shown in (**Figure 1B**).

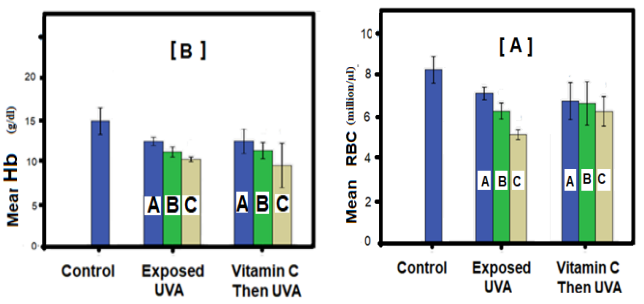


Figure 1. Bar chart, Show RBCs [A], and hemoglobin Hb [B] in daily groups (24hr/day) at different doses of exposure, and pre-treatment with vitamin C (150 mg/kg).

3.1.3. Platelets (PTL)

The study investigated the effect of UVA radiation on platelet (PLT) levels in blood samples from control and experimental groups. Results revealed a significant increase in platelet count in the exposed group, positively correlated with the UVA exposure duration (GP (II-A) < GP (II-B) < GP (II-C)), with higher doses leading to higher platelet counts. Vitamin C pre-treatment groups GP (III-A, B, and C) also resulted in significantly lower platelet counts than the exposed groups, although higher than controls, across all exposure durations (**Figure 2A**).

3.1.4. White Blood Cells (WBCs)

The study showed that UVA radiation exposure in male rats significantly increased WBC counts in a dose-dependent manner across groups GP (II-A)< GP (II-B)< GP (II-C), where higher dose of UVA led to high WBC counts, while Vitamin C pre-treatment mitigated this effect showing a noticeable decrease in WBCs than exposed groups, while remaining increased significantly than the control group across all exposure durations (**Figure 2B**).

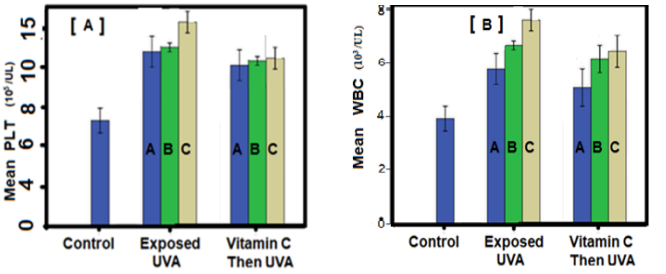


Figure 2. Bar chart, Show platelets [A], and WBCs [B] in daily groups (24hr/day) at different doses of exposure, and pre-treatment with vitamin C (150mg/kg).

3.2. Results of Liver Functions (ALT and AST)

UVA radiation significantly increased alanine aminotransferase (ALT) levels in rat blood samples. ALT levels followed this trend: exposed GP (II-A) < GP (II-B), and GP (II-A; B) > GP (II-C). Pre-treatment with vitamin C resulted in a significant decrease in ALT levels than exposed groups noticeably that the most significant reduction was in moderate exposure, though ALT levels remained higher than the control group (**Figure 3A**).

UVA radiation caused a significant increase in AST levels in exposed groups as follows:

(GP II-A < II-B < II-C), the higher exposure periods and cumulative doses led to progressively elevated AST levels compared to the control group. Vitamin C pre-treatment showed a protective effect, significantly lowering AST levels in low and moderate -exposed GP (III-A; B), particularly GP (III-A) was very close to the control group levels, although AST raised in GP (III-C), it decreased significantly compared to the corresponding exposed GP(II-C) (**Figure 3B**).

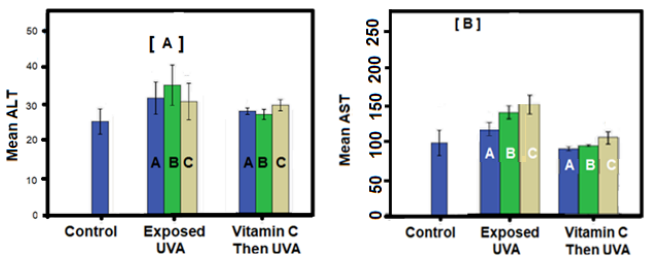


Figure 3. Bar chart, Shows ALT [A], AST [B]count in daily groups (24hr/day) at different doses of exposure and pre-treatment with vitamin C (150 mg/kg).

3.3. Oxidative Stress Markers

Table 2 illustrate the biochemical analysis of antioxidant parameters on homogenate liver tissue. The effects of UVA radiation on hepatic Malondialdehyde (MDA) levels in male rats showed an elevated MDA levels in the short term, decreasing in the intermediate term but remaining moderately higher than control in the long-term exposure. The vitamin C pre-treatment showed significant decreases in MDA during short and intermediate-term UVA exposure ($P< 0.05$). while at long term exposure MDA levels rose again exhibiting a highly significant increase ($P< 0.05$).

At the FRAR levels, the results showed a significant decrease observed in short-term exposure (P< 0.05). Intermediate and long-term exposures, while it was higher than short-term exposure. At pre-treatment with VIT C determined the decline in FRAR, which was increased gradually to reach the level close to the control group.

3.4. Histopathological Findings

3.4.1. Light Microscopic Findings

The photomicrograph of paraffin sections was examined, and the normal liver tissue (Group I) appeared with hepatic lobules, hepatocytes, sinusoids, and the portal tract. Hepatocytes are polygonal cells arranged in plates or cords, with spherical nuclei. Sinusoidal blood drains into each lobule's central vein (**Figure 4A**). The photomicrograph of rats exposed to low UVA group (II-A) showed mild disorganized of liver tissue, few fibrotic cells, few vacuolated hepatocytes with round nuclei and eosinophilic cytoplasm (**Figure 4B**). At Group (III-A) treated with vitamin C (150 mg/kg for 8 weeks) and then exposed to low UVA radiation revealed promising regenerative changes areas of liver recovery with a portal tract surrounded by a few fibrotic cells and only a few necrotic hepatocytes are observed (**Figure 4C**).

Table 2: Distribute the MDA and FRAP of Control, Exposure UVA and Vitamin C groups

Study groups	Statistical Parameters	Control	Exposed UVA			Vitamin- C then UVA		
			A	B	C	A	B	C
Malondi-Aldehyde (nmol/g tissue)	x̄±SD	136.311± 26.46	193.913± 64.73	198.727± 44.64	239.674± 101.17	117.717 ± 109.03	120.130± 36.62	152.66± 60.48
	*p		0.036	0.142	0.056	0.000	0.000	0.004
Total Antioxidant (FRAP) (Conc/mg)	x̄±SD	37 ±3.17	32.2 ±6.2	31±2.4	30.9 ±3.4	35.1 ±2.2	36.6±2.8	36.9 ±3.8
	*p		0.027	0.071	0.079	0.939	1.000	0.682

* Statistically significant difference compared to control Results by test, $P \leq 0.05$.

The photomicrograph of rats exposed to UVA moderate exposure group (II-B) showed moderate histopathological changes, the bile ducts are surrounded by proliferating hepatocytes and fibrotic tissue with infiltrating lymphocytes form follicular patterns. Hepatocytes display vesiculated nuclei, eosinophilic cytoplasm, and necrotic features (**Figure 5A**). While the pretreatment vitamin C group (III-B) there was evidence of mild recovery in the liver tissue, as demonstrated by the dilated portal tract surrounded by a few fibrotic cells and infiltrating lymphocytes, the hepatocytes

have dark small, rounded nuclei and vacuolated cytoplasm and area with necrosis one (**Figure 5B**).

The photomicrograph of high UVA radiation exposed group (II-C) showed marked degeneration of liver tissue, a congested portal tract, surrounded by fibrotic tissue, proliferating bile duct epithelial cells, many hepatocytes displaying eosinophilic cytoplasm and dark, foci of aggregated follicular lymphocytes and fragmented nuclei (**Figure 6A**). The photomicrograph of group (III-C) which pretreatment with vitamin C demonstrated mild recovery of degenerated liver tissue, with moderately dilated portal tracts and bile ducts, the hepatocytes have dark round nuclei and homogenous cytoplasm, some necrotic nuclei, and pyknotic cells and narrow sinusoids was seen (**Figure 6B**).

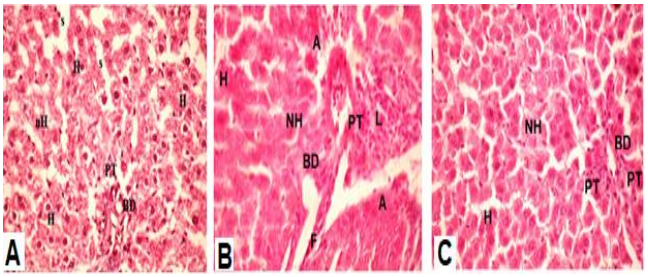


Figure 4. Photomicrograph of rats' liver paraffin section stained with H&E stains, X 400Magn. [A] control GP(I) liver, note portal tract (PT) with radiated hepatocytes cells have round dark nuclei and prominent nucleoli (H) and homogeneous cytoplasm, moderate dilated sinusoids (S) and few necrotic hepatocytes were seen (nH). [B] GP (II-A), shows degenerative liver tissue, dilated, congested, and attached to two portal tracts (PT) adjusted to the central vein (CV) and bill duct (BD), few fibrotic cells (F), infiltrating lymphocytes (L). Proliferating necrotic hepatocytes (NH) appeared with pale cytoplasm and others at the periphery with large round nuclei and eosinophilic cytoplasm (H).
[C] GP(III-A) shows the area of recovery of the liver tissue a portal tract (PT), few fibrotic cells. (F), infiltrating lymphocytes(L), The proliferated hepatocyte cells have round nuclei (H) with homogenous cytoplasm, and a few necrotic (NH).

3.4.2. The Electron Microscopic Finding

The electron micrograph studies illustrated the changes of the hepatocytes architecture, including mitochondria, rough endoplasmic reticulum (RER), Golgi complex and lysosmes. At three exposed durations of UVA radiation showed different sizes of mitochondria. fragmented Golgi apparatus accompanied by small lysosomes and lipid droplets near the thin cell membrane (**Figure 7 A-C**). At the pretreatment with vitamin C showed the recovering of hepatocyte in low UVA exposure and mild reorganized hepatocytes architecture appeared as a dense mitochondrion with varied sizes, small lysosomes migrating toward the cell membrane, and a large, acentric nucleolus, granulated chromatin (**Figure 7 D-F**).

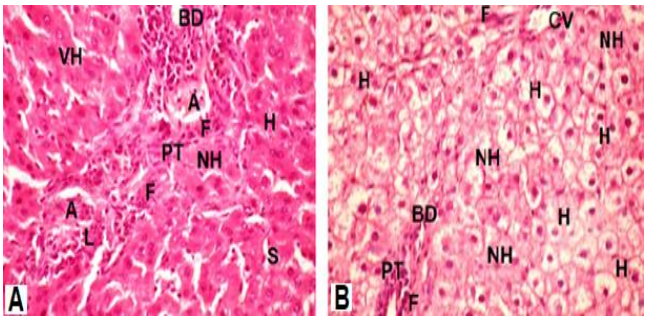


Figure 5. Photomicrograph of rats' liver paraffin section stained with H&E stains, X 400Magn. [A] (GPII-B), shows the part area of portal tract (PT), proliferating epithelial cells of bill duct (BD), thick artery surrounded with fibrotic cells (F) and infiltrating lymphocytes (L) form follicular shape. marked proliferating hepatocytes (H) with vesiculated nuclei (VH). Multi small dark nuclei with eosinophilic cytoplasm (H) and many necrotic ones (NH). [B] GP(III-B) Vitamin C shows mild recovery of the liver tissue bile ducts (BD) surrounded by a few fibrotic cells (F), infiltrating lymphocytes. (L). Crowded of proliferating hepatocytes and necrotic ones (NH).

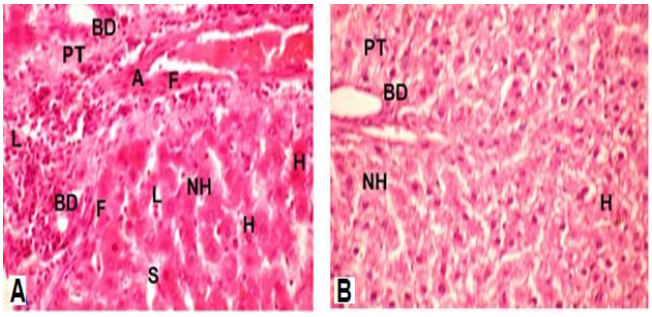


Figure 6. Photomicrograph of rats' liver paraffin section stained with H&E stains, X 400Magn. [A] GP (II-C), shows dilated and congested portal tract (PT) surrounded with fibrotic cells. (F), numerous infiltrating lymphocytes (L) and proliferated epithelial bile duct epithelial cells (BD). Area of necrotic hepatocyte nuclei with eosinophilic cytoplasm (NH), a dark nuclei hepatocyte, foci of the aggregated follicular lymphocytes (L) infiltrating lymphocytes. [B] GP(III-C) shows recovery of liver tissue, portal tracts (PT), bile ducts (BD), few necrotic nuclei, other hepatocytes have dark round nuclei with homogenous cytoplasm, and narrow sinusoids.

4. Discussion

UVA rays, the longest wavelength in the ultraviolet spectrum, account for 90-95% of UV radiation reaching Earth's surface. They have both beneficial and harmful biological effects, including deeper penetration into the skin, and damaging connective tissues and blood vessels [7]. The liver is a crucial organ in the immune system, responsible for metabolic activities such as fat breakdown, energy extraction, vitamins, minerals, and toxin clearance. The liver is also responsible for regulating glucose, protein, and lipid metabolism, waste breakdown, and tissue nourishment.

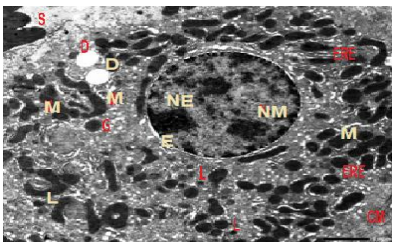
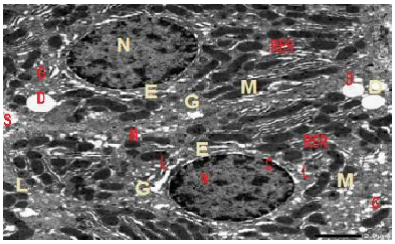
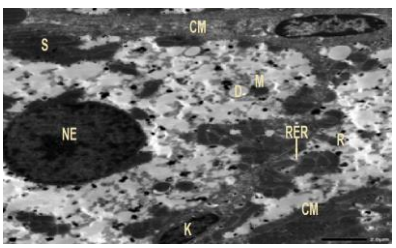
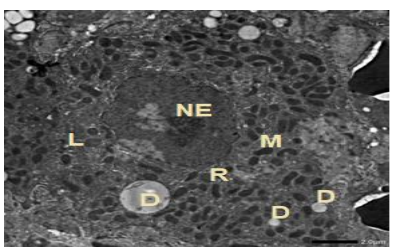
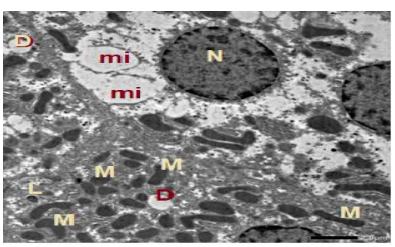
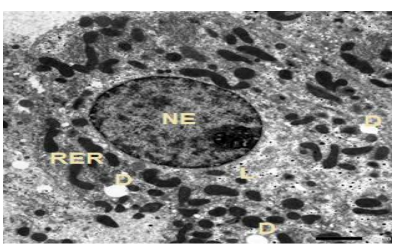
Durations	UVA radiation	Vit C pre – UVA exposure
Low 5 days exposure		
	[A] Shows one hepatocyte has small size of the mitochondria (M) associated with shorted RER grouped at periphery cytoplasm. A light cytoplasm with many microsomal ER(MR), many different size lysosomes (L) spread in cytoplasm with many fragmented Golgi complex and droplet lipid (D) particles were present at the thick cell membrane at width sinusoid with RBC cell. The dark nuclei (N) with segmented nucleolar matrix (NE), and small fragmented chromatin with dilated nuclear envelop was seen.	[B] Show the recovering of hepatocytes have different sizes of the mitochondria (M) associated with shorted RER cisternae grouped at periphery cytoplasm. A light cytoplasm with free ribosomes (R), many small lysosomes (L) and few droplets lipid (D) particles were present at the thin cell membrane. The recovering dark nuclei (N) with acentric prominent nucleolus (NE) and granulated chromatin and regular nuclear envelops was see.
Moderate (10 days exposure)		
	[C] Show one hepatocyte has small size mitochondria (M) associated with shorted RER grouped at periphery cytoplasm. a light vacuolated cytoplasm with many microsomal ER(MR) and free ribosomes (R), many different size lysosomes (L) and droplet lipid (D) particles was present at the thick cell membrane at narrow sinusoid with Kupffer' cell. The dark nuclei (N) with acentric prominent nucleolus (NE), small, granulated chromatin and irregular nuclear envelop was seen.	[D] Show marked recovery of hepatocytes have elongated to rounded mitochondria (M) increased in number, associated with RER and grouped at the periphery of the cytoplasm. The cytoplasm has free ribosomes (R), many small lysosomes (L), and few large droplet lipid (D) particles present at the thin cell membrane. The recovered dark nuclei (N) with a centric prominent nucleolus (NE), a light matrix, and a mildly regulated envelope were seen.
High (15 days exposure)		
	[E] Shows the binucleated hepatocyte has different sizes of the mitochondria (M) associated with shorted RER grouped at periphery cytoplasm. A vacuolated cytoplasm with free ribosomes (R), many small lysosomes (L) and droplet lipid (D), width microsomes were present. The dark nuclei (N) with fragmented chromatin and regular nuclear envelop was seen.	[F] Shows the recovering of hepatocytes that have different sizes of mitochondria (M) associated with shorted RER cisternae grouped at periphery cytoplasm. A light cytoplasm with free ribosomes (R), many small lysosomes (L) and few droplets lipid (D) particles were present at the thin cell membrane. The recovering dark nuclei (N) with acentric prominent nucleolus (NE) and granulated chromatin and regular nuclear envelopes were seen.

Figure 7. The transmission electron microscopy photograph of rats' liver hepatocytes stained with uranyl acetate and lead citrate.

The present study examined the impact of UVA radiation on male rats' red blood cell counts and hemoglobin levels. Results revealed a significant declines, especially with continuous exposure (p=0.000), the UVA -induced oxidative stress resulted in hemolysis and lowered hemoglobin levels and RBCs causing anemia, which can lead to liver health troubles, such as reduced oxygen delivery, hypoxia, impairing lipid metabolism, hepatic steatosis or a fatty liver, and alter liver enzymes such as elevated ALT and AST, that the liver may partially take over hematopoiesis, causing liver enlargement and hemolysis [13]. In agreement to our results, oxidative stress and UVA radiation could impair bone marrow erythropoiesis, resulting in decreased hemoglobin synthesis, lowered blood levels, and activated inflammatory responses that further diminished red blood cell formation [14]. UVA radiation significantly affected the hemoglobin levels in male rats, particularly with prolonged exposure and led to oxidative stress, which altered various hematologic parameters, including erythrocyte counts. Hemoglobin levels vary based on the intensity and duration of exposure, with more pronounced effects occurring at higher doses or with extended exposure times. Continuous UVA radiation disrupted both blood health and physiological balance [15].

The present study revealed that preventative interventions with supplementation of vitamin C pretreatment could improve the UVA bad effects by reducing oxidative stress. Vitamin C pre-treatment has variable effects on red blood cell (RBC) count, low exposure showed a decline in RBC count less than the exposed group, while high exposure revealed a marked improvement in RBC counts, while it improved hemoglobin concentration in low and moderate exposure groups (III-A; B), but there was a significantly decreased in high exposure group (III-C). The present findings were maintained by other studies which reported that the pre-treatment with vitamin C in rats exposed to UVA radiation caused lower hemoglobin levels and raised red blood cell count [16,17]. However, extended UVA exposure can induce significant oxidative stress, resulting in damage to biological components such as lipids, proteins, and DNA while vitamin C pre-treatment has a significant influence on hemoglobin levels in UVA radiation-exposed persons by neutralizing reactive oxygen species, lowering oxidative damage, improving Hemoglobin stability, preventing hemolysis and impairing erythropoiesis [18]. The findings explored that UVA exposure duration had a considerable influence on hemoglobin levels, with longer doses resulting in more dramatic declines. This is consistent with prior studies, which found a dose-dependent connection between UVA exposure and oxidative stress indicators [19]. VitaminC, which is recognized for its antioxidant effects could also serve as a prooxidant, causing an increase in reactive oxygen species production and a decrease in hemoglobin [20]. This explains the decrease in hemoglobin in high doses of ultraviolet radiation although pre-treated with vitamin C, compared to the corresponding exposed groups. The present study revealed that UVA radiation had a significant impact on male rats' white blood cell (WBC) counts increased significantly with exposure dose. UVA radiation activates oxidative stress and inflammation, resulting in an increase in WBCs as part of the body's immunological response. The prolonged exposure impaired immunological homeostasis, which resulted in an increase in WBC counts (P=0.000), and indicated the immune system's reaction to continuous environmental stress. Pretreatment with vitamin C showed very slight improvement in low-exposed GP (III-A) rather than moderate and high-exposed GP (III-B; C), which may be offered limited immune protection. These findings were consistent with those of other study who discovered that vitamin C's antioxidant capabilities were dose-dependent under prolonged oxidative stress [21]. UVA radiation causes oxidative damage while vitamin C can reduce it. Pre-treatment with vitamin C improved antioxidant defenses in cells, particularly white blood cells, neutralizing reactive oxygen species and causing minor increases in WBC counts [22, 23].

At regard to the platelet counts, the present study revealed the significant impact of UVA radiation on platelet counts in rats, demonstrating a clear dependence on exposure duration. Low exposed (Group II-A) showed minor inflammatory responses, while moderate exposed (Group II-B) showed a marked increase in platelet counts, likely due to enhanced thrombopoiesis triggered by more severe inflammatory reactions. This underscores the relation between moderate UVA exposure and the body’s adaptive mechanisms to increase platelet production. However, high exposed (Group II-C) increased stress-related hematological changes, significantly increasing platelet counts (P=0.000) indicated that high UVA radiation may surpass the body's adaptive capacity, causing excessive platelet activation. Increasing platelet counts can form clots that impair blood flow to critical organs like the liver which can lead to worse ischemic disorders. These findings align with prior studies connecting increased platelets to inflammation and tissue damage, especially under radiation exposure [24,25]. Furthermore, a study connected UVA-induced oxidative stress to platelet activation and aggregation [26]. Whereas other studies found that prolonged UVA radiation induces systemic inflammation, hence increasing thrombopoiesis and platelet activation [27].

Whereas the present study revealed that Vitamin C pre-treatment showed an increase in platelet counts than control group but decreased significantly than the corresponding exposed groups, indicating that these antioxidants played a protective and balanced role. This outcome was supported by findings from a study that discovered that vitamin C reduced platelet activation and aggregation by scavenging reactive oxygen species. Vitamin C may enhance the regulatory functions and demonstrate it can alter platelet levels during oxidative stress. It has been known that radiation can cause comparable immune responses, resulting in persistent inflammation and tissue damage [28]. Other studies discovered that exposure to high ultraviolet radiation (UVR) reduced immune function and increased systemic inflammation in animals. This emphasized the broader implications of UVA radiation exposure and the possible hazards to immunological health and organ function. The liver is an important organ in immunological system control and may develop inflammation and fibrosis due to chronic immune activation. Kupffer cells, critical in liver immunological responses, are susceptible to over-activation, leading to liver injury and inflammation. Persistent inflammation increases platelet counts, leading to clot formation and immune cell recruitment to the liver. This pro-inflammatory environment can cause hepatocellular injury,

fibrosis, and cirrhosis, which are linked to chronic liver dysfunction [29].

The present study revealed that UVA radiation significantly influenced liver function by elevating alanine aminotransferase (ALT) levels, a biomarker for hepatocellular injury. UVA exposure induced oxidative stress, resulting in ALT levels in exposed GP (II-A) being lower than GP (II-B), while ALT in exposed GP (II-A; B) was higher than in GP (II-C). Furthermore, a significant increase in AST levels was observed through exposure groups. The liver releases ALT and AST to repair itself following cellular injury, often associated with inflammation. UVA-induced oxidative stress damaged liver cells triggering persistent inflammation and fibrosis. Prolonged exposure and elevated ALT and AST levels can lead to cumulative liver damage, manifesting as cirrhosis, fibrosis, and scarring. Continuous hepatocellular damage from UVA exposure is a critical factor of liver failure, as it can cause microvascular injury, restricted blood flow, ischemia, micro thrombi formation, and an increased risk of liver failure caused exacerbation ALT and AST elevation and indicative of liver cell damage [25]. Ischemia further aggravates liver damage, raising ALT and AST levels and heightening the likelihood of liver failure. Continuous UVA exposure also disrupts key liver functions, such as detoxification, protein synthesis, nutrient metabolism, and overall metabolic balance, through oxidative stress and enzyme release [24,29]. While Vitamin C pre-treatment (Groups III-A, III-B, III-C) significantly reduced these effects, particularly in low-exposed (Group III-A), due to its antioxidant capacity to neutralize ROS and protect liver cells. Despite AST levels in Group (III-C) remaining elevated relative to the control, they were notably lower than in the high-exposed group GP(II-C), highlighting partial hepatoprotective effects that weaken with higher UVA doses.

The present study underscored the hepatoprotective effects of vitamin C pre-treatment in mitigating liver enzyme elevations in rats exposed to UVA radiation. Effect on ALT Levels. Vitamin C pre-treatment reduced the elevation in ALT caused by UVA exposure, correlating with exposure duration across all groups. Despite significant ALT increases in low (III-A) and high (III-C) UVA-exposure groups compared to controls; levels remained lower than in non-pre-treated groups (II-A, II-C). This suggests vitamin C's antioxidant properties preserve hepatocyte integrity by scavenging UVA-induced reactive oxygen species (ROS) [30,31]. Vitamin C pre-treatment was most effective in lowering AST, especially in low-exposure groups (III-A), where AST levels nearly normalized to control values. Even in high-exposure groups (III-C), AST levels were significantly lower than in non-pre-treated groups (II-C), demonstrating vitamin C role in mitochondrial protection and reduced oxidative damage [32] Vitamin C pre-treatment mitigated the oxidative stress, lipid peroxidation, and cellular damage caused by UVA radiation [33]. The dose-dependent AST reduction suggests vitamin C is most effective under lower oxidative stress conditions, consistent with its antioxidant activity's saturation kinetics [34]. Vitamin C's capacity to neutralize free radicals and reduce lipid peroxidation has been highlighted in prior studies, demonstrating its efficiency in preventing liver damage caused by oxidative stress [35,36] Overall, the study emphasized the complex interplay between oxidative damage and the body's adaptive responses, with vitamin C playing a crucial role in minimizing liver damage [37].

In addition, it is known that UVA radiation causes lipid peroxidation in cellular membranes, generating by products such as Malondialdehyde, which destroys cell structures and reduces antioxidant ability. These processes were amplified during longer exposures and higher radiation doses, leading to increasingly larger decreases in antioxidant levels in tissues. So, the present study of some lipid peroxidation effects by UVB radiation showed the MDA levels were dependent on the time and the amount of the exposure dose in rats were exposed to different UVA radiation durations and received vitamin C. The high significantly increase was in high exposure of 15 days UVA exposed, the result revealed a dose-dependent increase significantly across all exposure durations. And a direct correlation between UVA radiation and oxidative stress which highlights. The importance of minimizing prolonged exposure to UVA radiation to prevent oxidative damage is necessary. The supplement with the Vit C pre-treatment significantly lowered MDA levels during low and moderate UVA exposure. The protective effects of vitamin C were potential as antioxidants to combat oxidative stress. However, the high UVA exposure decreased its efficacy, indicating a saturation point beyond which its antioxidative characteristics may fail. Similarly, vitamin C's potent antioxidant activity at low and moderate levels reflects its ability to scavenge free radicals and mitigate oxidative damage [38]. Nonetheless, the considerable increase in MDA levels at high exposure suggests that its protective effect is limited, probably due to excessive oxidative stress that exceeds its neutralizing capabilities. [39]

Also, the present results revealed that FRAP levels were much lower in the group that received greater accumulative doses of UVA radiation than in the control group. This decrease highlights oxidative stress that UVA exposure causes depending on doses are cumulative and sustained. Oxidative stress may result from the liver's diminished capacity to neutralize reactive oxygen species (ROS) due to a decrease in FRAP. Cellular constituents such as proteins, lipids, and DNA may be harmed by this imbalance [40]. Resulting in chronic oxidative stress that depleted antioxidants in UVA-exposed tissues over time, an exposure to UVA radiation led to a reduction in antioxidant activity in a dose-dependent manner [15]. The biological systems used to reduce exposure duration and intensity of UVB radiation are necessary. Vitamin C, is a strong antioxidant, helps to counteract oxidative stress by scavenging free radicals and protecting liver cells. Its supplement can mitigate oxidative damage in rat liver tissues exposed to environmental contaminants. Vitamin C's preventive activity induced the hepatotoxic effects of UVA radiation, promoting liver function under oxidative stress situations [41].

Furthermore, the present histopathological results of rat hepatocytes exposed to high ultraviolet radiation revealed liver tissue damage and disorganized hepatocytes. The low exposure to UVA (Group II-A) revealed a degeneration of hepatic tissue, including vascular changes, fibrosis, inflammation, and hepatocyte damage characterized by necrosis and apoptosis, indicating the hepatotoxic consequences of extended UV exposure. This is consistent with other studies that recorded hepatocytes are vulnerable to oxidative damage and

inflammatory signaling brought on by UV light [23]. and the vascular changes, fibrosis, and hepatocyte necrosis due to low exposure to UVA [40]. This damage is due to reactive oxygen species overproduction, disrupting cellular homeostasis, causing lipid peroxidation, protein denaturation, and mitochondrial dysfunction. Also, the present study revealed that the treatment with vitamin C followed by low-dose radiation further enhanced liver repair appeared as minimal fibrosis and improved vascular remodeling. It was indicated that the highlighting of vitamin C's regenerative properties as antioxidant qualities may have been critical in neutralizing reactive oxygen species (ROS). This dual functioning is consistent with a study that reported the efficacy of vitamin C in decreasing liver damage in oxidative-stress-induced models [41].

The present study of reactive oxygen species (ROS), leading to oxidative stress, and lipid peroxidation, revealed significant structural damage and cellular abnormalities. The liver tissues showed pathological changes, including bile ducts surrounded by proliferating epithelial cells, fibrotic tissue, and lymphocyte infiltration forming follicular patterns. The study of the light and electron microscopy revealed that the hepatocytes exhibited vesiculated nuclei, eosinophilic cytoplasm, and necrotic features. The findings are consistent with earlier research demanded that the ROS-mediated tissue damage and inflammation after UVA exposure. These findings are consistent with previous research showing that ROS leading to oxidative stress, and lipid peroxidation, revealed significant structural damage and cellular abnormalities and causing inflammation, cellular damage, and even fibrosis in various organs [24, 40].The present study revealed that vitamin C treatment led to mild recovery, evidenced by mild dilated portal tracts and bile ducts with minimal fibrotic cells and infiltrating lymphocytes. Hepatocytes were densely packed but showed a mix of necrotic areas and healthy ones with dark, small, rounded nuclei and vacuolated cytoplasm. Vitamin C's capacity to scavenge ROS and promote collagen synthesis could have contributed to the reported benefits [41]. The present study revealed mild damage of liver tissue and subsequent recovery under different UVA exposure doses and pretreatment with vitamin C. The rats' liver tissues showed signs of chronic liver injury, including dilated and congested portal tracts, fibrotic tissue, biliary ductular reactions, and necrosis, indicating the liver's attempt to recover following injury. In addition, the electron microscopy study revealed the mild disorganization of mitochondria and small lysosomes byreducing the lipid droplet which was observed at low UVA exposure. Whereas at high UVA exposure the results revealed a less histopathological recovery of Vitamin C may be due to the secondary free radicals, which raise according to individual inequality of liver regeneration and antioxidant defenses, which produced the secondary free radicals, which raise according to individual variance in liver regeneration and antioxidant defenses; the finding was confirmed by the reduction induced in the antioxidant capacity studies.

These findings are consistent with the well-documented course of liver illnesses such as nonalcoholic steatohepatitis and biliary cirrhosis, in which inflammation and tissue remodeling are key to pathogenesis [42]. Also, inflammatory processes are marked by lymphocyte infiltration. Hepatocytes exhibit eosinophilic cytoplasm and fragmented nuclei, with necrotic areas indicating cell death that was given highlights of immune-mediated destruction in liver disease. Lymphocytic aggregation and sinusoidal dilatation are consistent with prior research relating inflammation to hepatocyte loss and fibro genesis [43]. Necrotic hepatocytes with eosinophilic cytoplasm and broken nuclei suggest severe cellular damage and apoptosis, which are hallmarks of hepatic necroinflammation [44]. The present study showed that in the pre-treatment with vitamin C followed by UVA Group (III-C) a recovery of degenerated liver tissue was seen such as a moderately dilated portal tracts and bile ducts, necrotic nuclei and hepatocytes with dark, round nuclei, homogenous cytoplasm, narrow sinusoids, and pyknotic cells. These changes suggest that vitamin C's antioxidant qualities help with cellular repair, hepatic injury resolution, and tissue homeostasis caused by UVA oxidative stress. Another study discovered that vitamin C can regenerate damaged liver tissue through lowering reactive oxygen species and increasing DNA repair in hepatocytes. Vitamin C pre-treatment of UVA radiation exposure could increase cellular turnover, which aided liver tissue repair [24]. In contrast, another study which revealed that high amounts of vitamin C mixed with UVA radiation may produce secondary free radicals, which raise concerns about pro-oxidants individual disparities in liver regeneration and antioxidant defenses, as well as variations in protocols (dose of vitamin C, UVA intensity, and length of therapy), are the causes of discrepancies [45,46].

5. Conclusion

UVA radiation can penetrate deeply into the body causing alteration in the blood parameters, liver functions and tissue structure. Vitamin- C can act as a protective agent against UVA-induced oxidative stress, improving blood counts and liver function, and promoting liver tissue and hepatocytes regeneration. Vitamin- C may be used as a therapeutic agent against UVA-induced hepatic damage, particularly at low-to-moderate exposure levels. Therefore, further research is needed to optimize dosing and explore complementary antioxidant strategies.

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