Original Article

Histological Study on the Effect of Curcumin and Curcumin Nanoparticles on Cadmium-Induced Liver Damage in Adult male Albino Rats

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ABSTRACT

Background: Cadmium (Cd) is a non-essential heavy metal that is toxic to humans. Liver damage is one of chronic Cd exposure's most serious side effects. Curcumin has antioxidant and anti-inflammatory characteristics that make it good preventive therapy. Unfortunately, it has poor bioavailability due to its low solubility in aqueous solutions. However, its nanoparticle formulations improve absorption by 10–14 times. Therefore, the present study was performed to evaluate the possible protective effect of curcumin and nanocurcumin on Cd-induced liver damage in adult male albino rats.

Materials and Methods: Forty-two male albino rats were used in this study. Rats were divided into 6 main groups. Cd-treated group received 5mg /kg Cd dissolved in saline orally, once daily alone or associated either curcumin or nanocurcumin dissolved in phosphate buffer in a dose 100mg /kg, orally once daily for 28 days. The appropriate controls were included. Animals were scarified and livers were harvested and processed for histological, immunohistochemical and morphometric assessments.

Results: Cd caused damage to liver tissues in the form of blood sinusoid congestion and hepatocyte vacuolation with pyknotic nuclei. Moreover, there was inflammatory cell infiltration and increased collagen deposition. Immunohistochemistry revealed a strong positive Bax immunoreactivity in cadmium group. Oral administration of curcumin and nanocurcumin significantly attenuated hepatotoxicity with a concomitant reduction in Bax immunoreactivity.

Conclusion: Administration of curcumin and nanocurcumin demonstrated beneficial effects on Cd-induced hepatic histological alterations. Moreover, nano curcumin administration showed a more ameliorative effect on the histological structure of Cd-induced hepatic toxicity.

Key Words: Bax, cadmium, curcumin, immunohistochemistry, nanocurcumin.

Revised: 14 April 2022, **Accepted:** 6 May 2022.

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ISSN: 2536-9172, December 2021, Vol. 5, No. 2

INTRODUCTION

Cadmium (Cd) is a non-essential heavy metal that is harmful to people and represents a risk to living creatures' growth and development[1, 2]. Cd is a hazardous metal that has also widely dispersed deadly ecological and modern toxicity widely recognized in food, soil, water, and air[3].

Liver is the most capable organ to detect oxidative stress. Liver is the most important organ detoxifying and metabolizing external substances[4]. According to prior studies, liver is the greatest and the primary site for storage of heavy metals in the body, followed by the renal tissue[5, 6]. Ingested Cd is only absorbed approximately 5% of the time, and it accumulates in the liver and kidneys[7]. Thus, liver and kidney damage is the most serious side effect resulting from chronic Cd exposure[8].

Although the bivalent cadmium cation is incapable of directly forming free radicals, after Cd exposure, there is increase in the production of reactive oxygen species (ROS) such as; superoxide radicals, hydrogen peroxide, and hydroxyl radicals[9, 10].

The protective impact of plant products or medicinal plants with antioxidant characteristics in lowering free radical-induced tissue damage has been in focus[11]. Curcumin, a yellowish pigment extracted from the Curcuma longa plant, has antioxidant and anti-inflammatory properties, making it an excellent preventive therapy[12].

Recently, curcumin has received a lot of interest, since it possesses a wide range of medicinal properties, including anticancer, antifibrotic, anti-inflammatory, antidiabetic, antibacterial, and antioxidant effects[13]. Curcumin inhibits inflammatory cytokines and reduces oxidative stress-mediated pathological conditions by scavenging reactive oxygen and nitrogen species. Moreover, it prevents lipid peroxidation and promotes biosynthesis of various cytoprotective and antioxidant proteins[14]. Furthermore, it can also chelate oxidative metal ions such as lead, preventing their accumulation in tissues and protect cells[15].

 DOI: 10.21608/jmh.2022.133655.1099

Curcumin has poor bioavailability due to its low solubility in aqueous solutions, despite its safety at high doses (up to 12 g/day). Its absorption is reduced, while its metabolism and systemic elimination are increased[16]. Several approaches have been proposed to overcome curcumin's low bioavailability and to get benefits from its prophylactic and therapeutic benefits. Nanotechnology has recently been used as the primary approaches to convert curcumin into nanoparticles. Curcumin's solubility and bioavailability in the body are enhanced by using nanoparticles with a size of 10–100 nm[17]. Nanoparticle formulations improve absorption by 10–14 times when compared to a similar dose of native curcumin.[18]

This study aims to investigate and compare the possible protective effect of curcumin and nanocurcumin on cadmium-induced liver damage in adult male albino rats.

MATERIALS AND METHODS

Drugs and chemicals:

1- Cadmium (cadmium chloride) particles were obtained from the analytical chemistry department, Faculty of Pharmacy, Beni-Suef University, Egypt. Cd was prepared according to[19]. Briefly, Cd was dissolved in saline and administered to animals orally by blind-ended tube in a dose 5 mg/kg, once daily for 28 days.

2- Curcumin powder was obtained from Sigma Corporation (St. Louis, Mo, USA). The required dose was 100 mg/kg[20], weighed using a digital scale, dissolved in phosphate buffer (PH 7.4), and given orally by blind-ended tube once daily for 28 days.

3- Curcumin nanoparticles were prepared in the Nanotechnology Unit, Faculty of Pharmacy, Beni-Suef University, Egypt. The required dose was 100 mg/kg[20], weighed, dissolved in phosphate buffer (PH 7.4), and given orally by blind-ended tube, once daily for 28 days.

Animals:

Forty-two male albino rats 5–6 months old, weighing 200–250 g were used in this study. The animals were housed in the Animal House of Faculty of Science, Beni-Suef University. Each group was housed in a separate cage with free access to food and at a constant temperature (22–24 °C) and light-controlled environment on an alternate 12:12 hours light-dark cycle. Rats were fed a conventional commercial pellet diet and acclimatized for one week before starting the experiment. Animals were treated in accordance with the animal rights committee's recommendations Faculty of Medicine, Beni-Suef University.

Experimental Design: (Fig.1, Table 1)

The animals were divided into 6 groups (7 rats each), and experiment was for 28 days:

1. Group I: Control group, received saline orally by a blind-ended tube once daily.

2. Group II: Curcumin-treated group, received 100 mg/kg curcumin, orally by blind-ended tube once daily.

3. Group III: Nanocurcumin-treated group, received 100 mg/kg nano-curcumin orally by blind-ended tube once daily[20].

4. Group IV: Cadmium treated group, received 5 mg / kg Cd orally by blind-ended tube once daily[19].

5. Group V: Cadmium-curcumin treated group, received 5 mg/kg of Cd concomitantly with 100 mg/kg of curcumin orally by blind-ended tube once daily.

6. Group VI: Cadmium-nanocurcumin treated group, received 5mg/kg of Cd concomitantly with 100 mg/kg nanocurcumin orally by blind-ended tube once daily.

Table 1: Schematic diagram of the study protocol

Groups	No. of rats	Drugs	Route	Dose
I	7	Saline	Oral	Once-daily for 28 days
II	7	Curcumin	Oral	100mg /kg dissolved in phosphate buffer once per day for 28 days
III	7	Nanocurcumin	Oral	100mg /kg dissolved in phosphate buffer once per day for 28 days
IV	7	Cadmium	Oral	5mg /kg dissolved in saline once per day for 28 days
V	7	Curcumin	Oral	100mg /kg dissolved in phosphate buffer once per day for 28 days
		Cadmium	Oral	5mg /kg dissolved in saline once per day for 28 days
VI	7	Nanocurcumin	Oral	100mg /kg dissolved in phosphate buffer once per day for 28 days
		Cadmium	Oral	5mg /kg dissolved in saline once per day for 28 days

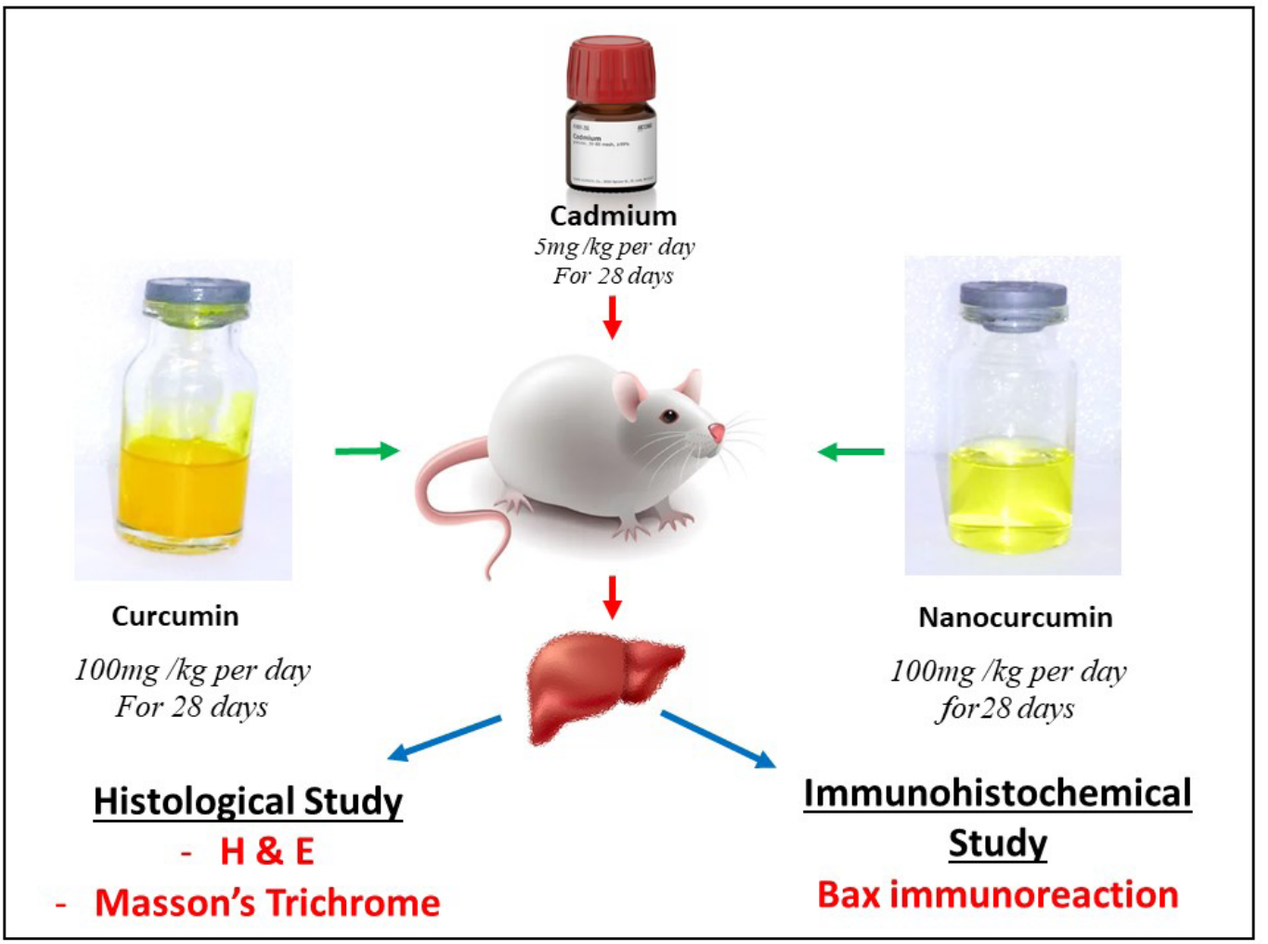


Fig. 1: Schematic diagram of experimental design.

On the last day of the experiment, rats were sacrificed under deep anesthesia by ether inhalation. The specimens were taken from the right lobe of the liver from all experimental animals. Liver tissues were fixed in 10% formol saline for 48 hours, dehydrated in ascending grades of alcohol, cleared in xylene, and embedded in paraffin. The following studies were carried out on paraffin blocks with 5 µ thick slices:

***A) Histological Study*:**

1. Hematoxylin and eosin (H&E)[21].

2. Masson's trichrome staining[22].

B) Immunohistochemical Study: to detect the apoptotic changes in liver cells[23]

Liver sections were dewaxed in xylene and hydrated through alcohol gradient. Endogenous peroxidase activity was blocked using hydrogen peroxide for 10 minutes followed by washing in Tris-buffered saline (TBS, pH 7.6) (Sigma-Aldrich) twice, for 10 minutes. Then, antibody nonspecific binding was blocked by incubation with protein blocking kit for 10-minute. Then, primary antibody rabbit anti-Bax antibody (Abcam-ab7977) was applied to sections (1:100 dilution) for 1 hour at room temperature. Then sections were washed in TBS for three times each 5 minutes and staining was completed using Novolink kits (Novolink Polymer Detection System, Catalogue number: RE7150-K from Leica), according to the manufacturer's instructions. Briefly, sections were incubated with post-primary for 30 minutes, followed TBS washing for 5 minutes and incubation with polymer for 30 minutes at room temperature. After, TBS wash, the reaction was developed with 3,3' diaminobenzidine. Sections were then counterstained with haematoxylin and dehydrated prior to mounting with DPX and coverslipped.

C) Morphometric Study:

The area percent of stained collagen fibers and the area percent of Bax immunoreactivity in the liver sections of the studied groups were measured using a Leica Qwin 500 image analyzer computer system at Beni-Suef University's

Faculty of Veterinary Medicine (Leica Imaging Systems, Cambridge, England). The image analyzer included a Panasonic WV, GP 210 color video camera, a colored display, and a Leica IBM personal computer hard drive coupled to an Olympus BX41 microscope (Tokyo, Japan) and controlled by Lecia Qwin 500 software. The measurements were carried out in binary mode in 10 high power fields (HPF) in both the control and experimental groups.

STATISTICAL ANALYSIS

Analysis of variance (ANOVA) was used to compare the morphometric data of the different groups, followed by a post hoc Tukey test, using the statistical tool SPSS (Statistical Package for the Social Sciences) version 24. The data were presented as the mean ± standard deviation. When the *P-value* < *0.05*, the difference was judged statistically significant, and when the *P-value* < *0.001*, it was regarded as very significant[24].

RESULTS

No deaths were observed in all rats.

1- Hematoxylin and eosin:

Examination of the control group (group I), Curcumin-treated group (group II), and nanocurcumin-treated group (group III) displayed normal histological structure of the liver. The central vein surrounded by radiating hepatocytes and hepatic sinusoids between hepatocytes cords (Fig. 2).

Cadmium-treated group (group IV) showed remarkable disruption of the normal hepatic architecture with sinusoidal congestion and hepatocyte vacuolations (Fig. 3). Furthermore, liver showed; congested dilated central vein and degenerated vacuolated hepatocytes with pyknotic nuclei. Additionally, cellular infiltration and proliferation of bile ducts were noticed (Fig. 3).

Curcumin - cadmium treated group (group V) displayed normal histological architecture of the liver. However, vacuolated hepatocytes and congested blood sinusoids were seen. On the other hand, nanocurcumin - cadmium treated group (group VI) revealed normal histological architecture of the liver, with are normal with acidophilic hepatocytes radiating from the central vein. Although this treatment preserved normal hepatic structure, there was mild congestion of the central vein and mild dilatation of blood sinusoids (Fig. 4).

2- Masson's trichrome stained sections:

Liver sections from the control group, curcumin-treated group, and nanocurcumin-treated group displayed minimal collagen deposition. Contrary, liver from cadmium-treated group displaying extensive collagen deposition around the portal area. The liver of the curcumin -cadmium treated group and nanocurcumin - cadmium treated group displayed moderate collagen deposition (Fig. 5).

3- Immunohistochemistry results:

Liver sections from the control group, curcumin-treated group, and nanocurcumin-treated group displayed negative Bax immunoreactivity. Cadmium-treated group displaying strong positive Bax immunoreactivity in liver tissues. Livers from curcumin -cadmium treated group and nanocurcumin - cadmium treated group displayed weak positive Bax immunoreactivity (Fig. 6).

4- Morphometric results:

When compared to the control group, the mean area percent of Masson's trichrome stain in group IV increased significantly (*P<0.05*). When compared to group IV, the mean area percent of Masson's trichrome stain in the curcumin- cadmium treated group (group V) and cadmium-nanocurcumin treated group (group VI) decreased significantly (*P<0.05*). Furthermore, there was no significant difference between groups II and III and the control group in the mean area percent of Masson's trichrome stain (Histogram 1) (Table 2).

When compared to the control group, the mean area percent of Bax–immunopositive cells in group IV increased significantly (*P<0.05*). When compared to group IV, the mean area percent of Bax–immunopositive cells in the curcumin- cadmium treated group (group V) and cadmium-nanocurcumin treated group (group VI) decreased significantly (*P<0.05*). Furthermore, there was no significant difference between groups II and III and the control group in the mean area percent of Bax-immunopositive cells (Histogram 2) (Table 2).

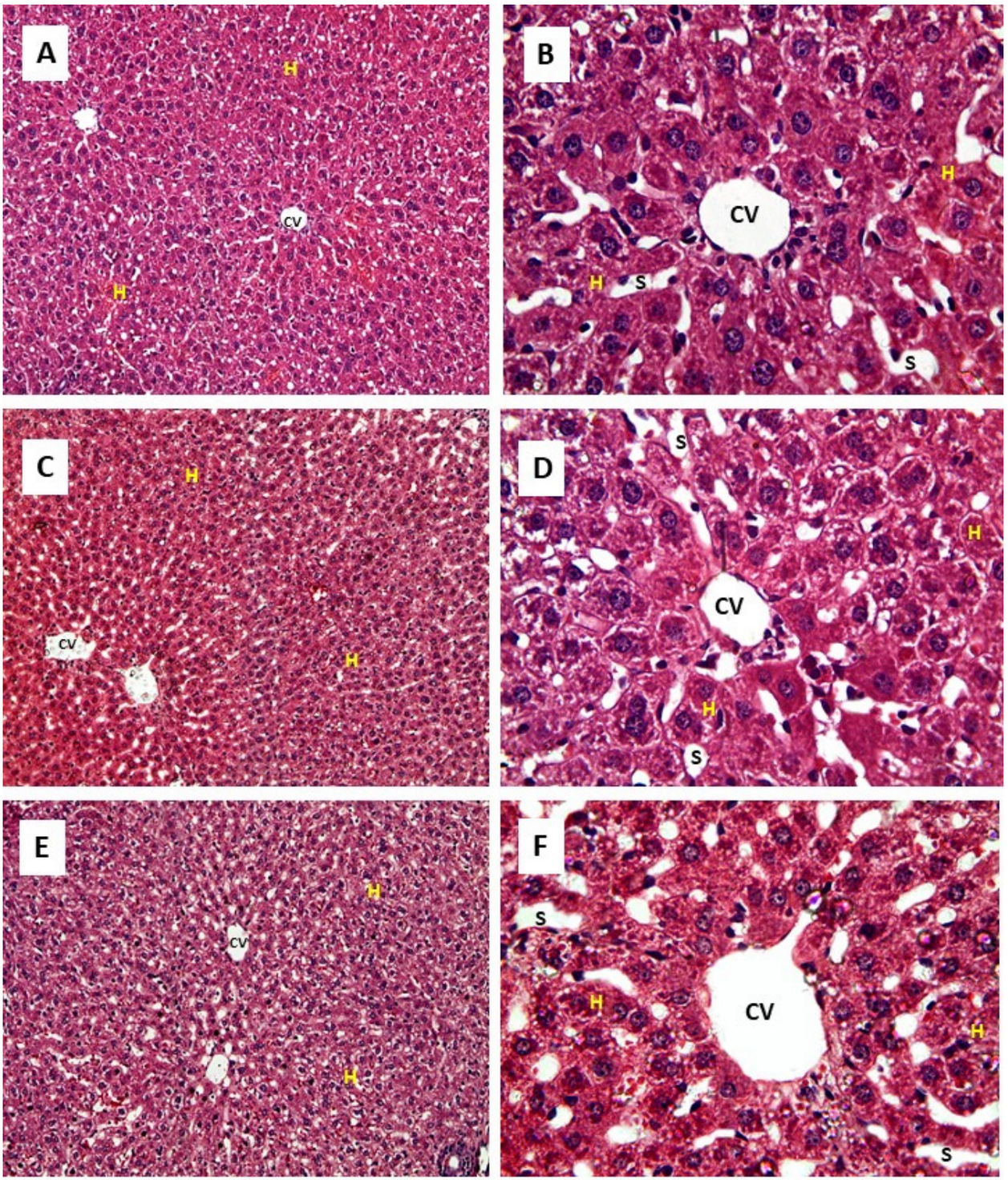


Fig. 2: Control group (group I) (A, B), Curcumin-treated group (group II) (C, D), Nanocurcumin treated group (group III) (E, F) displaying the normal histological structure of the liver. Hepatocytes (H) are radiating from the central vein (CV). Blood sinusoids (S) are present between the cords of hepatocytes. (H&E staining: A, C, E = X200, B, D, F = X400).

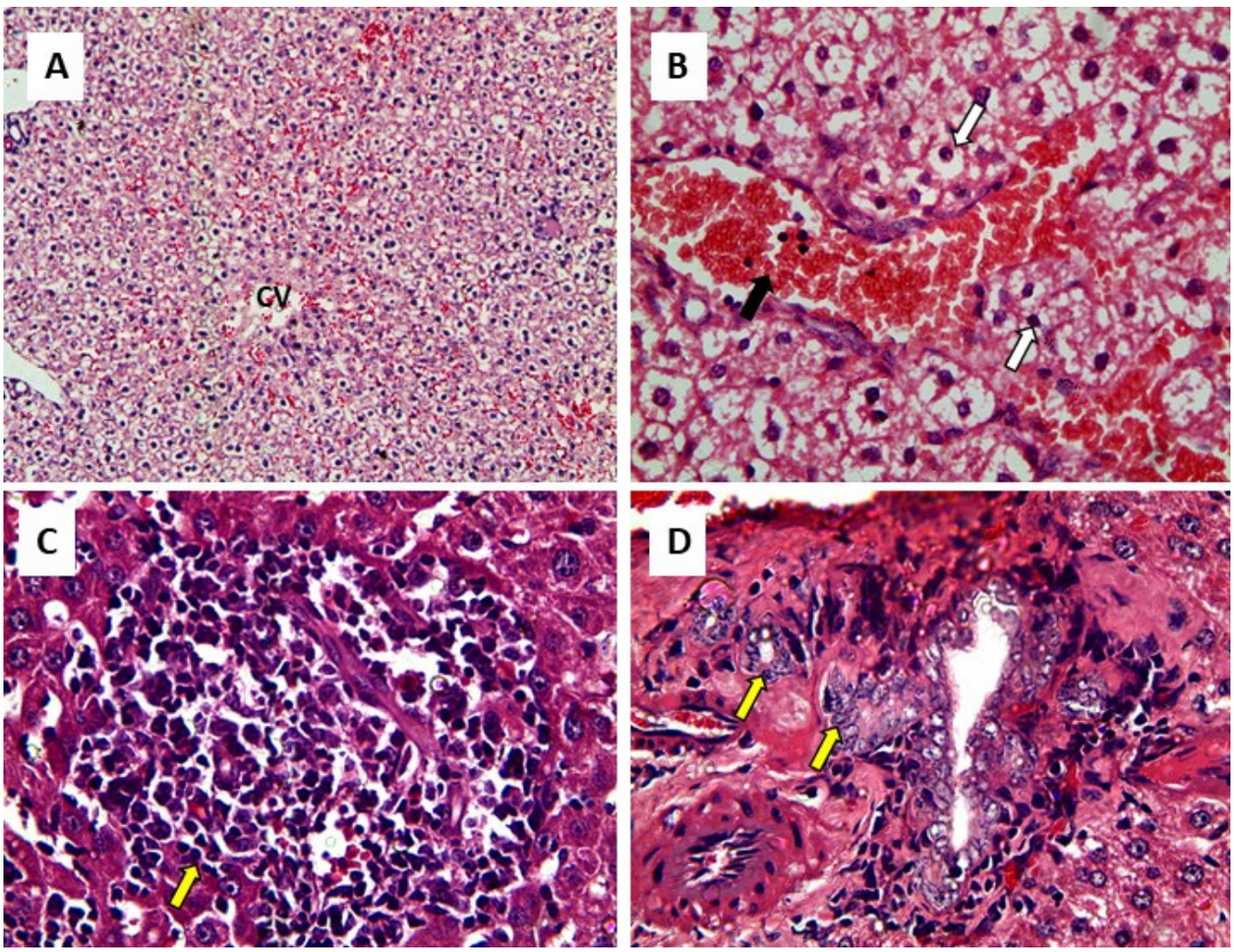


Fig. 3: Cadmium treated group (group IV) showing (A) Congestion of blood sinusoids and vacuolated hepatocytes. (B) Congested dilated central vein (black arrow) and degenerated vacuolated hepatocytes with pyknotic nuclei (White arrow). (C) Inflammatory cellular infiltration (Yellow arrow). (D) Bile duct proliferation (Yellow arrow). (H&E staining: A = X200, B-D = X400).

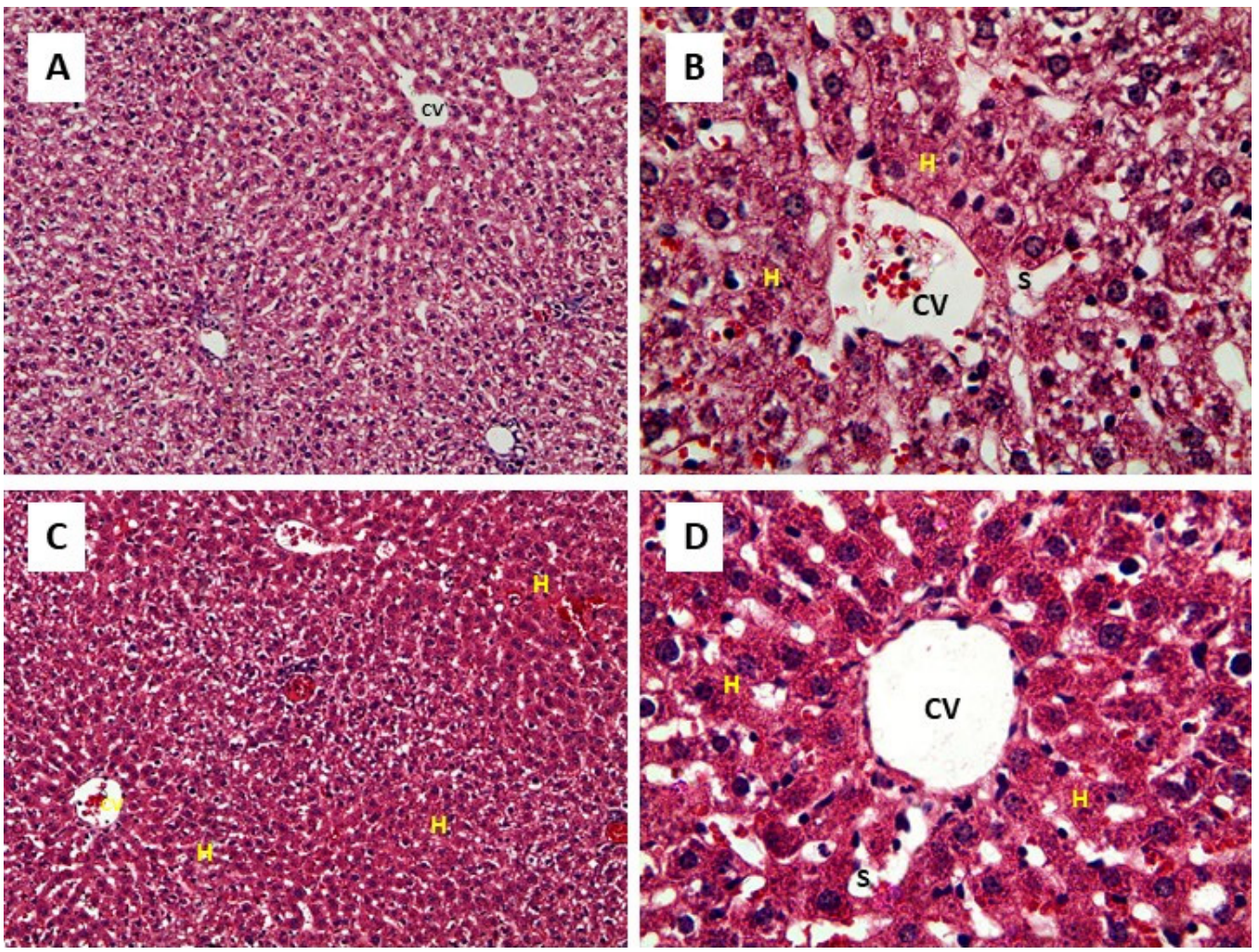


Fig. 4: Curcumin - cadmium treated group (group V) displaying (A) Normal histological architecture of the liver. (B) Vacuolated hepatocytes (H) are still seen with congested blood sinusoids (S). Nanocurcumin - cadmium treated group (group VI) displaying (C) Normal histological architecture of the liver with mild congestion of central vein (CV) hepatocytes (H) are normal (D) normal acidophilic hepatocytes (H) are seen radiating from the central vein (CV). Blood sinusoids (S) show mild dilatation. (H&E staining: A, C = X200, B, D = X400).

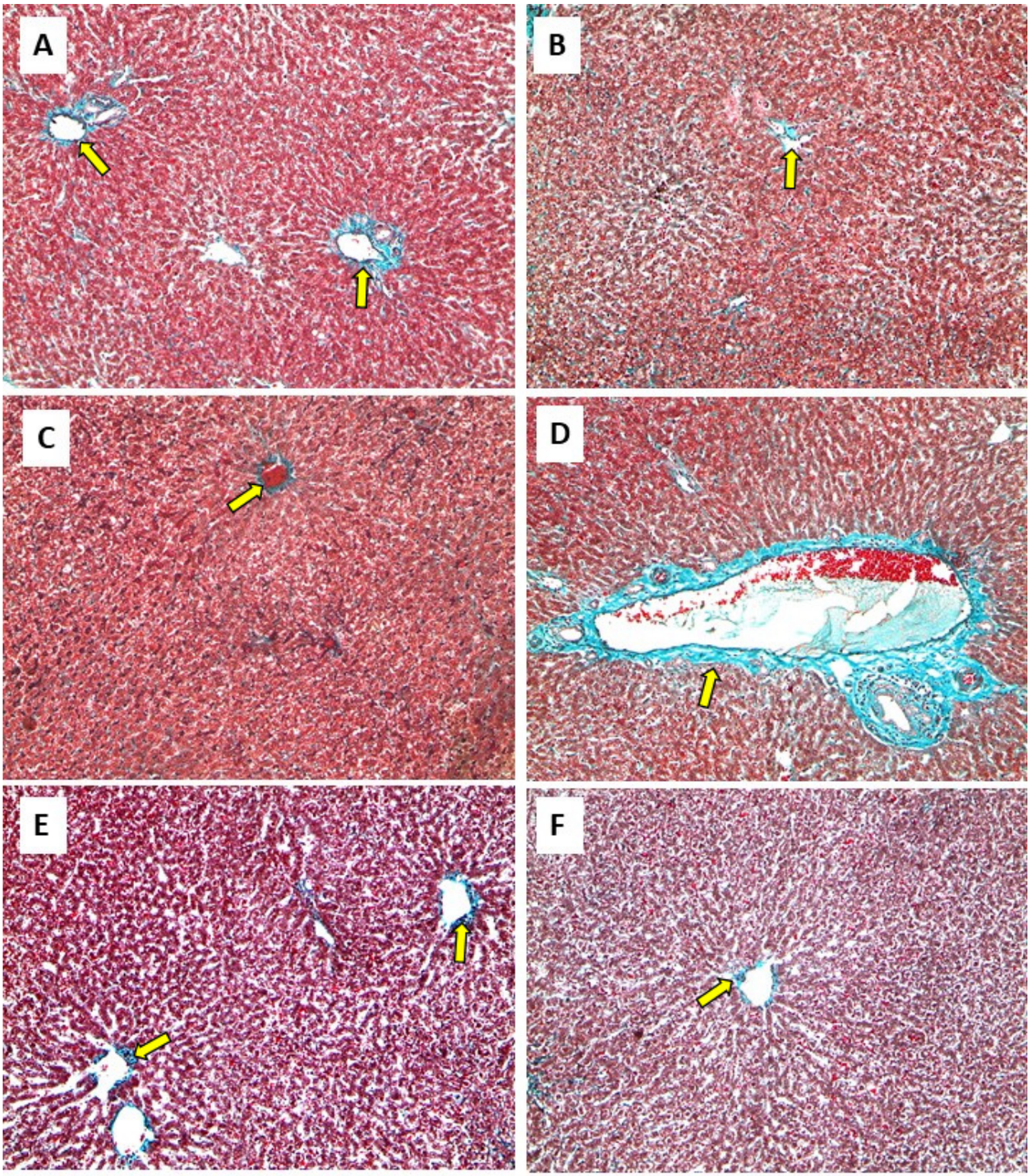


Fig. 5: Liver of control group (A), curcumin-treated group (B) and nanocurcumin - treated group (C) displaying minimal collagen deposition (Arrows). liver of cadmium-treated group (D) displaying extensive collagen deposition around the portal area (Arrows). Liver of curcumin - cadmium treated group (E) and nanocurcumin - cadmium treated group (F) displaying moderate collagen deposition (Arrows). (Masson's trichrome X200).

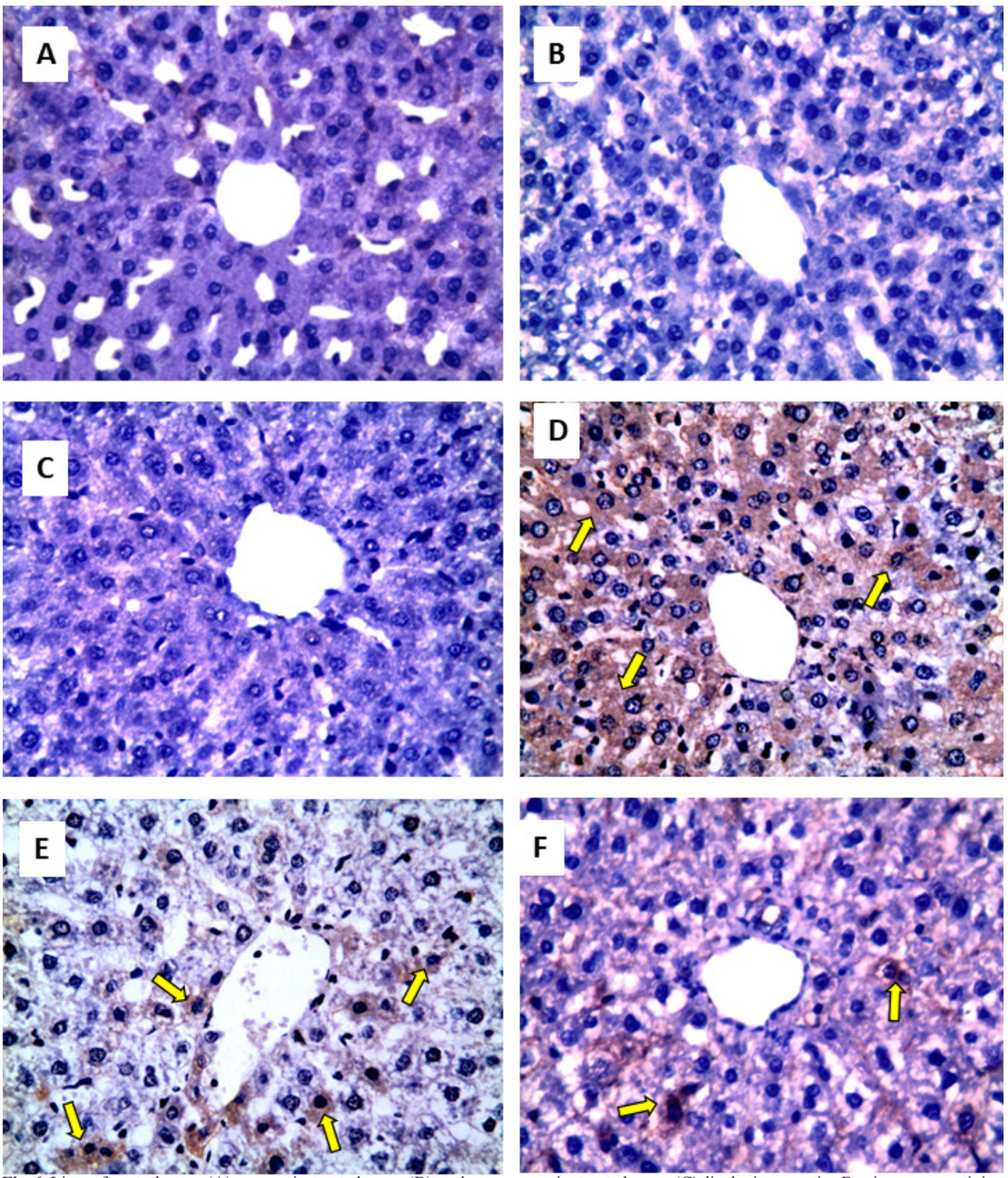
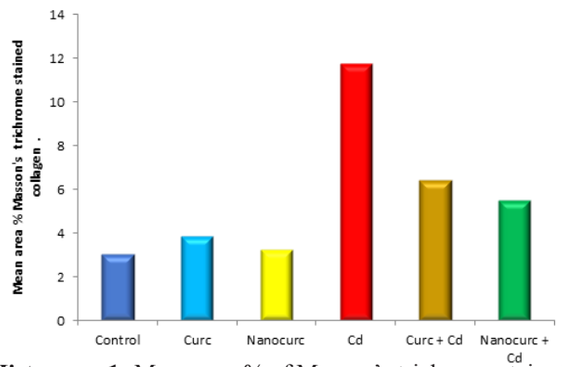


Fig. 6: Liver of control group (A), curcumin-treated group (B), and nanocurcumin -treated group (C) displaying negative Bax immunoreactivity. Liver of cadmium-treated group (D) displaying strong positive Bax immunoreactivity (Arrows). Liver of curcumin - cadmium treated group (E) and nanocurcumin - cadmium treated group (F) displaying weak positive Bax immunoreactivity (Arrows). (Bax immunoreactivity X400).

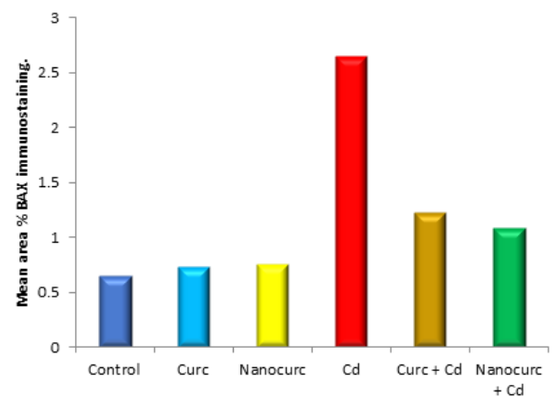
Table 2: Mean ± SD of the Area % of Masson's trichrome-stained collagen and BAX immunostaining of the liver of the six experimental groups.

Morphometrical parameters	Control	Curcumin	Nanocurcurcumin	Cd	Curcumin + Cd	Nano curcumin + Cd
Area % of Masson's trichrome stained collagen	3.04± 0.35	3.87± 0.55	3.24 ± 0.45	11.75 ± 0.66	6.41 ± 0.72*	5.52 ± 0.51#
Area % of BAX immunostaining	0.65 ±0.08	0.73 ±0.12	0.76 ± 0.06	2.65 ± 0.05	1.23 ± 0.03*	1.09 ± 0.04#

#: Significant with (Cd) Group IV
*: Significant with Group IV



Histogram 1: Mean area % of Masson's trichrome stained collagen



Histogram 2: Mean area % of BAX immunostaining

DISCUSSION

Cd is an environmental and industrial pollutant with a wide range of toxicological consequences. Cd has a significant impact on multiple organs, particularly the liver, in both humans and animals[25]. Cd's major target organ is the liver, which is very vulnerable to both acute and chronic Cd exposures[26].

In this study, light microscopic examination of liver sections from the control group (group I), curcumin-treated group (group II), and nanocurcumin-treated group (group III) revealed no differences in the histological structure. They showed normal histological liver structure similar to the normal control.

Meanwhile, light microscopic analysis of H&E-stained liver samples from group IV (cadmium treated rats) showed a remarkable histological alterations. They showed congestion of blood sinusoids and vacuolated hepatocytes. The congested dilated central vein and degenerated vacuolated hepatocytes with pyknotic nuclei were also detected. Additionally, cellular infiltration and proliferation of bile ducts can be noticed. These findings are in agreement with Duan *et al*., who showed that in Cd induces extensive liver damage, including congestion, cytoplasmic disintegration, nuclear debris, and enhanced inflammatory cell infiltration[25]. Similarly, Mohapatra *et al*. (2013), have reported that Cd administration to mice resulted in marked histological changes in hepatocyte including; disintegration, rupture of the cell membrane, cytoplasmic vacuolization, and nuclei pyknosis beside breakdown of hepatocytic plates[27].

Cd produced free radicals, which, could never be converted into less efficient or inefficient components in the biological system. Lipid peroxidation was also an outcome of these settings. Cd is produced in a radical manner through both indirect and direct methods. Each cell has a high concentration of glutathione (GSH). Furthermore, this substance is classified as a nonenzymatic biological antioxidant. Cd depletes GSH reserves in the liver by binding to GSH, and this depletion lowers GSHPx activity[28].

Cd also substitutes iron and copper in the cell by interacting with a variety of cytoplasmic & membrane proteins, resulting in an increase in these redox-active metals' levels. The Fenton reaction produces OH (hydroxyl) radicals directly when free redox-active metals are present[29].

The present study revealed that liver from curcumin - cadmium treated rats (group V) displayed normal histological architecture. However, there were still slight hepatocyte vacuolation and hepatic sinusoids congestion. This is in line with Widjiati1 *et al*., who showed that curcumin treatment of mice exposed to cadmium intoxication minimize the Cd induced hepatic damage and preserve hepatic histological architecture[30].

Curcumin is anti-inflammatory due to its ability to inhibit major inflammatory enzymes such as cyclooxygenase-2, lipoxygenase, and inducible nitric oxide synthase[31]. Curcumin is antioxidant as it has a suppressive effect on the formation of ROS and a stimulatory effect on endogenous antioxidant activity. Curcumin unique conjugated structure provides it with a typical radical-trapping properties as a chain-breaking antioxidant[32]. Thus, curcumin protect liver from Cd damage through stabilization of the cell membranes, protection from free radical damage, promotion of cell regeneration and limit transaminase release from the cell cytoplasm[33]. It also inhibits mitochondrial damage by promotion of cytochrome C transfer from mitochondria to the cytoplasm[34].

Curcumin low bioavailability and poor solubility limit its medicinal benefits. Thus, curcumin nanoparticles improve solubility and therapeutic index[35].

The present study revealed that concomitant administration of nanocurcumin along with cadmium (group VI) preserved the normal histological architecture of the liver with normal hepatocytes and mild congestion of the central vein and blood sinusoids. Recently, El-Gizawy *et al*. (2020) reported that nanocurcumin has hepatoprotective and therapeutic effects through structural and functional effects on the liver. They showed that nanocurcumin minimize hepatic cord disorganization, portal triad fusion, and central vein congestion, additionally, decrease liver function biomarkers. They attributed these effects to potent antioxidant and anti-inflammatory roles of nanocurcumin[36].

In the current work, Masson's trichrome showed that curcumin-treated group and nanocurcumin-treated group displayed minimal collagen deposition in the liver. Contrary, liver of cadmium-treated group displaying extensive collagen deposition around the portal area. Interestingly, curcumin-cadmium and nanocurcumin-cadmium treated groups displayed moderate collagen deposition. These findings were confirmed by the morphometrical and statistical results; there was a significant increase in the area percentage of collagen in group IV (cadmium treated group). Cd-curcumin and Cd-curcumin treatment preserved the liver and reduced Cd induced fibrosis by reducing collagen deposition. Cd-nanocurcumin was superior to curcumin in reducing collagen deposition in the e liver. Recently, Xu *et al*., reported that, chronic low-dose Cd exposure induced hepatotoxicity and hepatopathogenesis. Cd induces liver fibrosis through several mechanisms including, upregulation of fibrosis-related markers such as TGF-β1 and collagen-1, activation of hepatic stellate cells and exacerbation of inflammation, macrophage and dendritic cell infiltration[37]. Indeed, liver fibrosis is a critical risk factor for the development of cirrhosis and liver cancer. In agreement with our finding, Guo *et al*. (2018) showed that curcumin therapy significantly reduced collagen deposition in the liver and this effect was attributed to downregulation of transforming growth factor 1 (TGF-β1), the profibrotic factor and the most critical cytokine in the pathophysiology of tissue fibrosis, explains these findings[38].

It is well documented that curcumin is a better alternative therapy for liver fibrosis. It slows the evolution of fibrosis by reducing the expression of cytokines and chemokine genes in hepatic stellate cells (HSCs) that are directly linked to fibrosis and apoptosis. Curcumin has previously been found to diminish fibrotic damage and sinusoidal angiogenesis in rat livers with carbon tetrachloride-induced fibrosis. Curcumin inhibited the expression of several angiogenic markers in the fibrotic liver. It is hypothesized that, HSCs which are liver-specific pericytes, could be potential curcumin target cells. Curcumin reduces HSCs motility and the expression of vascular endothelial growth factor (VEGF) and also reduces new vascularization in the liver[39].

Recent studies provided evidence that, nanocurcumin is a promising therapeutic candidate with useful therapeutic capabilities such as anti-inflammatory, antioxidant, and antifibrotic properties, and it has potential for the prevention and treatment of a variety of human disorders[40].

Nanocurcumin significantly reduced the severity of liver necroinflammation, repressed HSCs activation, lowered collagen accumulation, and increased matrix metalloproteinases-2 in a previous study (MMP2)[41].

Bax protein was not detected in the livers from the control, curcumin-treated and nanocurcumin-treated groups. Contrarily, it was highly expressed in cadmium group. Interestingly, curcumin-cadmium and nanocurcumin-cadmium treated groups showed reduction in Bax protein expression in liver cells. Thus, Cd induced Bax expression and both curcumin and nanocurcumin counteract this and reduced the expression, with nanocurcumin having a superior effect to curcumin. In line

with our finding Duan *et al*., showed that Cd induced Bax, and caspases 3 and 9 overexpression through activation of mitochondrial pathway in liver cells[25]. Indeed, this provide evidence that Cd affect liver cell proliferation, differentiation, and death as documented recently, these are attributed to DNA repair, the formation of ROS, and the activation of apoptosis[42].

Therefore, curcumin could counteract the damaging effect of Cd on liver by reducing apoptosis, reducing oxidative stress and regenerating antioxidant enzymes[43]. Nanocurcumin, affect oxidative stress regulators and apoptotic gene expression, thus has preserve liver cells from the damage and is hepatic protectant[44].

Nanocurcumin is superior to curcumin because it has the potential to chelate and has a higher bioavailability than bulk curcumin. As a result of the invention of these drug delivery nanoparticles, the disadvantages associated with curcumin's limited bioavailability can be resolved, and there will be no need to increase the curcumin dose to achieve effectiveness[45].

Finally, the present study showed that both curcumin and nanocurcumin succeeded in reducing the damaging effect on rat liver and lowering oxidative stress induced by cadmium. In addition to that, nanocurcumin administration showed a more ameliorative effect on hepatotoxicity induced by Cd exposure than bulk curcumin and could be an excellent candidate for research exploring their potential preventive usage in people liable to Cd exposure due to environmental factors or the the nature of work.

CONCLUSION

Curcumin and nanocurcumin administration has a beneficial impact on Cd induced histological changes in the liver tissue Furthermore, nanocurcumin administration had a prophylactic effect by preserving liver structure and counteracting the damaging effects of Cd. Therefore, curcumin and nanocurcumin have a prophylactic role against Cd toxicity.

RECOMMENDATIONS

Anti-oxidant supplements such as curcumin and nanocurcumin should be used as protective measurements against cadmium toxicity. They could be added to the diet, especially in areas with a high environmental risk of

cadmium exposure.

CONFLICT OF INTEREST

There are no conflicts of interest.

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الملخص العربى

دراسة هستولوجية لتأثير جزيئات الكركمين و جزيئات الكركمين المعدة بطريقة النانوتكنولوجى على تسمم الكبد الناتج عن الكادميوم فى ذكور الجرذان البيضاء البالغه

الخلفية: الكادميوم معدن ثقيل غير أساسي سام للإنسان. ويعد تلف الكبد أحد أخطر الآثار الجانبية للتعرض المزمن للكادميوم. يحتوى الكركمين على خصائص مضادة للأكسدة ومضادة للالتهابات تجعله علاجًا وقائيًا جيدًا. ولكن لديه ضعف في التأثير البيولوجي بسبب انخفاض قابليته للذوبان في المحاليل المائية ، ومع ذلك ، فإن تركيبات الجسيمات النانوية تحسن الامتصاص بنسبة ١٠-١٤ مرة. لذلك ، أجريت هذه الدراسة لتقييم التأثير الوقائي المحتمل لجزيئات الكركمين وجزيئات الكركمين النانوية على تلف الكبد الناجم عن الكادميوم في ذكور الجرذان البيضاء البالغة.

الطرق: تم استخدام اثنان و أربعون من ذكور الجرذان البالغة وتم تقسيمها إلى ست مجموعات .عولجت الجرذان عن طريق الفم بـ ٥ مجم / كجم من الكادميوم المذاب في محلول ملحي مرة واحدة في اليوم بمفرده أو مرتبط بـ ١٠٠ مجم / كجم من الكركمين أو مع النانو كركمين ١٠٠ مجم / كجم مذاب في محلول فوسفات مرة واحدة يوميًا عن طريق الفم لمدة ٢٨ يومًا. تم تضمين الضوابط المناسبة. تعرض كبد الجرذان لدراسات نسيجية وكيميائية مناعيه وكميه قياسيه.

النتائج: تسبب الكادميوم في تدهور الأنسجة الكبدية على شكل احتقان في الشعيرات الدموية وخلايا الكبد المفرغة مع نوى مظلمه علاوة على ذلك كان هناك تسلل للخلايا الالتهابية وزيادة ترسب الياف الكولاجين. كشفت الكيمياء الهيستولوجية المناعية عن نشاط مناعي Bax إيجابي قوي في الفئران التي تعرضت للكادميوم. يؤدي تناول الكركمين والنانوكركمين عن طريق الفم إلى تخفيف السمية الكبدية بشكل كبير مع ما يصاحب ذلك من انخفاض في نشاط المناعة Bax.

الاستنتاجات: أظهر تناول الكركمين والنانو الكركمين تأثيرات مفيدة على التغيرات النسيجية التي حدثت في أنسجة الكبد بعد التعرض للكادميوم. علاوة على ذلك ، أظهر تناول الكركمين النانوي تأثيراً أكثر تحسناً على التركيب النسيجي للسمية الكبدية التي يسببها الكادميوم

الكلمات المفتاحية: الكادميوم ، الكركمين ، النانو كركمين ، باكس ، الكيمياء الهيستولوجية المناعية.