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Original Research Article

The Hepato and Reno Protective Role of Curcumin against the Alterations in Some Biochemical Parameter and Histological Damage Induced by Monosodium Glutamate in Male Albino Rats

Shaimaa Mohammed Ali Jasim[1*], Noor I. Abdul-Zahra[2]

[1]Faculty of Science, University of Kufa, Iraq, Najaf
[2]Technical Institute, Al-Furat Al-Awsat Technical University, Iraq, Najaf

***Corresponding Author:** Shaimaa Mohammed Ali Jasim
Faculty of Science, University of Kufa, Iraq, Najaf

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Abstract: The main objective of current research was to investigate toxicity effect of Monosodium glutamate and protective role of Curcumin on some blood biochemical parameters, body weight gain, relative organ weight and histopathological alterations in liver and kidney tissues in male albino rats. Twenty animals of male rats (*Rattus norvegicus*), their weight ranged from 111 to 165 gm. The animals were divided into four groups: Each animal group contained five rat, first group was control negative (-ve) administrated distilled water, the second group was control positive (+ve) administrated curcumin, third group was administrated by Monosodium glutamate (MSG) at dose 20 mg per one Kg and the forth group was administrated by Monosodium glutamate (MSG) at dose 20mg/Kg of body weight + curcumin at dose 100 mg per one Kg of body weight. All animal groups were administrated orally about 30 days. The study recorded significant $p \leq 0.05$ increment in liver and kidney function parameters included [Alanine transaminase (ALT), Aspartate aminotransferase (AST), Urea and creatinine] after oral administration of animals with MSG and MSG + Curcumin as a comparison with control groups. The study recorded significant decrement $p \leq 0.05$ in liver and kidney function parameters included ALT, AST, Urea and creatinine) in group was administrated MSG + Curcumin in comparison with group was administrated MSG only. Additionally, current study revealed histopathological changes in liver and kidney tissue in groups were administrated MSG and MSG+ curcumin compared with + curcumin compared with control groups. Furthermore, the study revealed that curcumin had protective effect and result in slight histopathological changes in liver and kidney tissue by reducing the damage and in group was treated by MSG+ curcumin for 30 days compared with MSG treated group.

Keywords: Monosodium glutamate, curcumin, hepatotoxicity, nephrotoxicity, biochemical parameters, histological damage.

INTRODUCTION

Commonly used as a flavor enhancer, monosodium glutamate (MSG) has been the subject of research due to possible neurotoxicity, which is linked to oxidative stress [1].

Food additive monosodium glutamate has been shown to have negative effects in both human clinical reports and animal model experiments [2].

Due to its high ability to enter our bodies without any limits and its presence in hundreds of food items on a daily basis, reports have indicated that MSG is toxic to humans and experimental animals. The chemical structure of MSG is the sodium salt of glutamic acid, one of the most abundant naturally occurring non-essential amino acids [3].

The using of monosodium glutamate in human feeding daily inducing many metabolic alterations, oxidative damage in different organs, inflammation and obesity [4].

Curcumin, a polyphenol derived from Curcuma longa, a perennial herbaceous plant in the Zingiberaceae family that is rhizomatous, has drawn interest from scientists across the globe due to its biological properties, which include anti-inflammatory, antioxidant, anti-apoptotic, antimicrobial, antiviral, and anti-carcinogenic effects [5].

Numerous advantageous physiological and pharmacological actions, including immunological modulation, metabolic regulation, antidepressant, and tissue protection, are exhibited by curcumin [6].

A herbal substance called curcumin helps repair damaged liver and kidney tissue and lowers elevated biochemical markers [7, 8].

By measuring liver and kidney function parameters, body weight, relative organ weight, and histologically examining changes in the liver and kidney cortex tissues of male albino rats, the primary goal of this study was to determine the potential protective and curative role of curcumin in enhancing cytotoxicity and preventing hepatic and renal injury caused by monosodium glutamate administration.

METHODOLOGY

The Treatments and Animals Grouping

This study was conducted in animal house and Genetics Laboratory that belong to Biology department - Faculty of Science \University of Kufa for the period from 18 February to 8 April 2023, forty-two male *Rattus norvegicus* animals, before the experiment began, they were housed in an animal house with typical light and dark cycles, food, and water supplements for at least two weeks. Their weight ranged from 130 to 292 grams.

Ethics Statement

Each animal experiment was conducted in compliance with the guidelines for the use and care of laboratory animals, as authorized by the Central Committee for Bioethics at Kufa University. The transportation, care and use of animals should be in accordance with the Animal Act 1953 (Revised 2006), Wildlife Conservation Act 2010 and other applicable federal laws and state enactment, guideline and policies.

Experimental Design

There were four groups in use. Four rats in group one received distilled water as their only food and were not given any medication. While the second group received curcumin (100 mg /kg body weight) contained four rats. The third group received monosodium glutamate about (20 mg/kg body weight) composed of six rats, fourth group monosodium glutamate + curcumin for 30 days composed of six rats.

Chemicals

1. Monosodium glutamate solution

Chemical substance is used as food additive obtained from supermarket in Najaf –Iraq. It is crystal material so, it is grinding to powder form and dissolved in distilled water.

2. Curcumin Solution

One of the primary ingredients in the rhizome of Curcuma longa (L) and other Curcuma spp [9], used as coloring and food additive obtained from supermarket in in Najaf –Iraq. It is used as powder form and dissolved in olive oil to help its adsorption by animal intestine.

Blood Collection for Biochemical Assay

When the experiment is over (two weeks after acclimatization), 0.5 ml of ketamine and 0.1 ml of xylazine were used to create anaesthesia for the heart puncture used to obtain blood samples [10]. Four millilitres of blood were collected from each rat and dispensed in jel tubes. For the bending biochemical analysis, serum was separated by centrifugation at 3000 rpm for 10 min and kept at -80°C, the final result was expressed as IU/L for ALT and AST, mg/dL for urea and creatinine [11]. Clinical completely automatic biochemistry analyser Ds-26 (Sinnowa medical sciences & technology Co. Ltd., Jiangsu. China) was used to detect serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), urea, and creatinine.

Body Weight Gain Test

The body weight gain is the difference between final body weight (after experiment) and initial body weight (before experiment).

The Relative Organ Weight

The liver weight and kidney weight relative to the total body weight ratio was calculated using the Gornall *et al.*, (1949) [12], method. Relative organ weight equal organ weight / total body weight times 100.

Histopathological Study

According to Bancroft and Stevens (1999) [13], liver and kidney tissues were preserved in 10% formalin for at least 24 hours. Tissue specimens were then prepared to examine histological changes in the kidney cortex of experimental animals, embedded in paraffin, and cut into 6 mm-thick sections using a rotary microtome. The sections were stained with hematoxylin and eosin dyes, and a light microscope was used to analyse the histological changes in the kidney cortex and liver tissue.

Analytical Statistics

With the use of SPSS (statistical software for social sciences), the data were statistically evaluated. ANOVA and t-test are used for independent sample analysis. The mean ± standard deviation is used to present the results. A p-value of less than 0.05 indicated that the treatment differences were statistically significant.

THE RESULTS

Biochemical Assay

The current study's findings revealed important significant P≤0.05 increment in biochemical liver and kidney parameters ALT, AST, urea and creatinine in the group was administrated MSG and group was administrated MSG+ curcumin in comparison with the control groups was administrated distilled water and curcumin. While, the study observed significant decreasing P≤0.05 in biochemical both mentioned organs parameters ALT, AST, urea and creatinine in the group which was treated by MSG+ curcumin compared with group was administrated MSG only table 1.

Table 1: Effect of monosodium glutamate and curcumin on the biochemical parameters in male albino rats after 30 days of administration

Biochemical parameters Treatment	Alanine aminotransferase (ALT) U/L	Aspartate aminotransferase (AST) U/L	Urea mg/dl	Creatinine mg/dl
control – ve Distilled water	23.00±0.82a	12.75±0.96a	38.00±0.82A	0.77±0.09a
control + ve Curcumin	17.50±0.29b	20.50±1.29b	34.50±1.28B	0.85±0.05b
monosodium glutamate	37.25±1.71abc	41.50±1.29abc	49.75±1.71abc	2.80±0.21abc
monosodium glutamate + Curcumin	31.50±0.09abc	36.50±1.29abc	33.50±1.27abc	1.77±0.09abc

The values represented by mean ± standard deviation (Mean ± S.D), in the same column the small letters refer to significantly differences at P≤0.05 a: notable variation as compared to negative control. Significant differences between treatments and the positive control are denoted by letters b, c: significant difference in between treatments.

Body Weight Gain

The outcomes showed a significant P≤0.05 increment in the body weight in group was administrated MSG as comparison with the control groups.

Moreover, the study noticed significant decrement p≤0.05 in body weight in group was administrated MSG+ Curcumin in comparison with group was administrated MSG only table 2

Furthermore, the results of the study showed that curcumin could help prevent the body weight gain caused by MSG.

Table 2: Effects of curcumin and monosodium glutamate on male albino rats' body weight increase following 30 days of treatment

Treatments	Body weight gain (gm)
Control - ve Distilled water	26.25± 1.03a
Control + ve Curcumin	20.75± 0.89b
Monosodium glutamate	39.75± 1.20abc
Monosodium glutamate + Curcumin	18.00± 0.28abc

The values represented by mean ± standard deviation (Mean ± S.D), in the same columns the small letters refer to significantly differences at P≤0.05 a: notable variation as compared to negative control. Significant differences between treatments and the positive control are denoted by letters b, c: significant difference in between treatments.

Relative Liver and Kidney Organ Weight

The study indicated significant P≤0.05 increment in relative liver weight in group was administrated MSG and MSG+ curcumin as a comparison with control groups. While the results recorded significant P≤0.05 decrement in relative liver weight in group was administrated MSG+ curcumin as a comparison with group was administrated by MSG alone.

In addition, the study exhibited significantly decrement p≤0.05 in relative kidney weight in group was administrated MSG group as a comparison with control groups. While the results recorded significant P≤0.05 increment in relative kidney weight in group was administrated MSG + Curcumin compared with group was administrated MSG only table 3.

Table 3: Effects of curcumin and monosodium glutamate on male albino rats' relative organs weight increase following 30 days of treatment

Treatments	Relative liver weight %	Relative kidney weight %
Control - ve Distilled water	3.11± 0.32a	0.59± 0.01a
Control + ve Curcumin	3.47±0.49b	0.63± 0.04b
Monosodium glutamate	3.61±0.27abc	0.45±0.06abc
Monosodium glutamate + Curcumin	3.59±0.32abc	0.60±0.07bc

The Histopathological Study

Liver Tissue

The current study revealed foundation histopathological alterations which stimulated by monosodium glutamate treatment in liver tissue of male albino rats when they were administrated monosodium glutamate at dose of 20 mg/kg body weight for 30 days. The results also indicated the protective impact of curcumin at dose 100mg/kg and its capacity reduction the histological changes in the liver tissue as shown in figures 1 as well as 2.

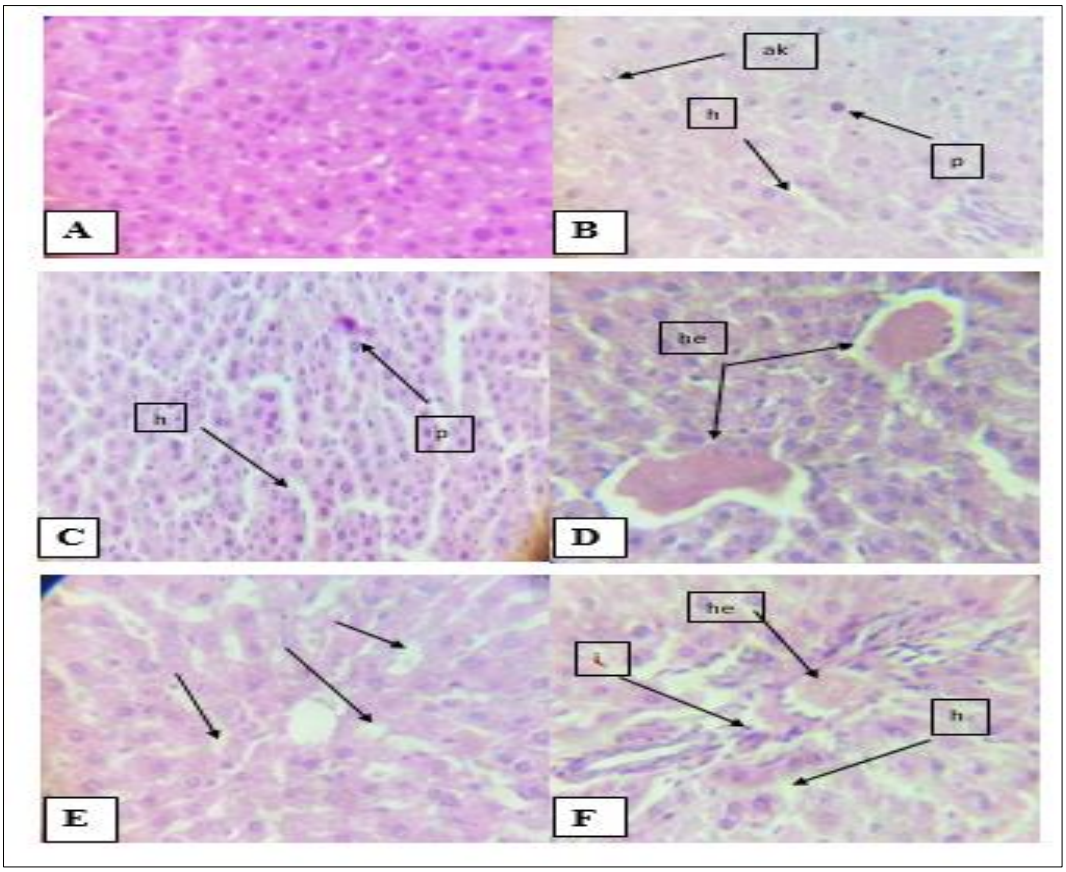

Figure 1: Cross section of liver tissue of male albino rats, A: From control -ve group showing normal architecture without changes, B: showing activated kupffer cells (ak), pyknotic cells (p) and hypertrophic hepatic cells (h) C: showing pyknotic cells (p) and hypertrophic hepatic cells (h) D: showing hemorrhage in blood vessels (he) E: hypertrophy, apoptotic and vacuolated in cell cytoplasm (arrowed). F: showing hemorrhage in blood vessels (he), infiltration of inflammatory cells (i) and hypertrophic cells. B-F from group treated by MSG. All animal tissue sections were stained by H&E and photographed at 400 X magnification.

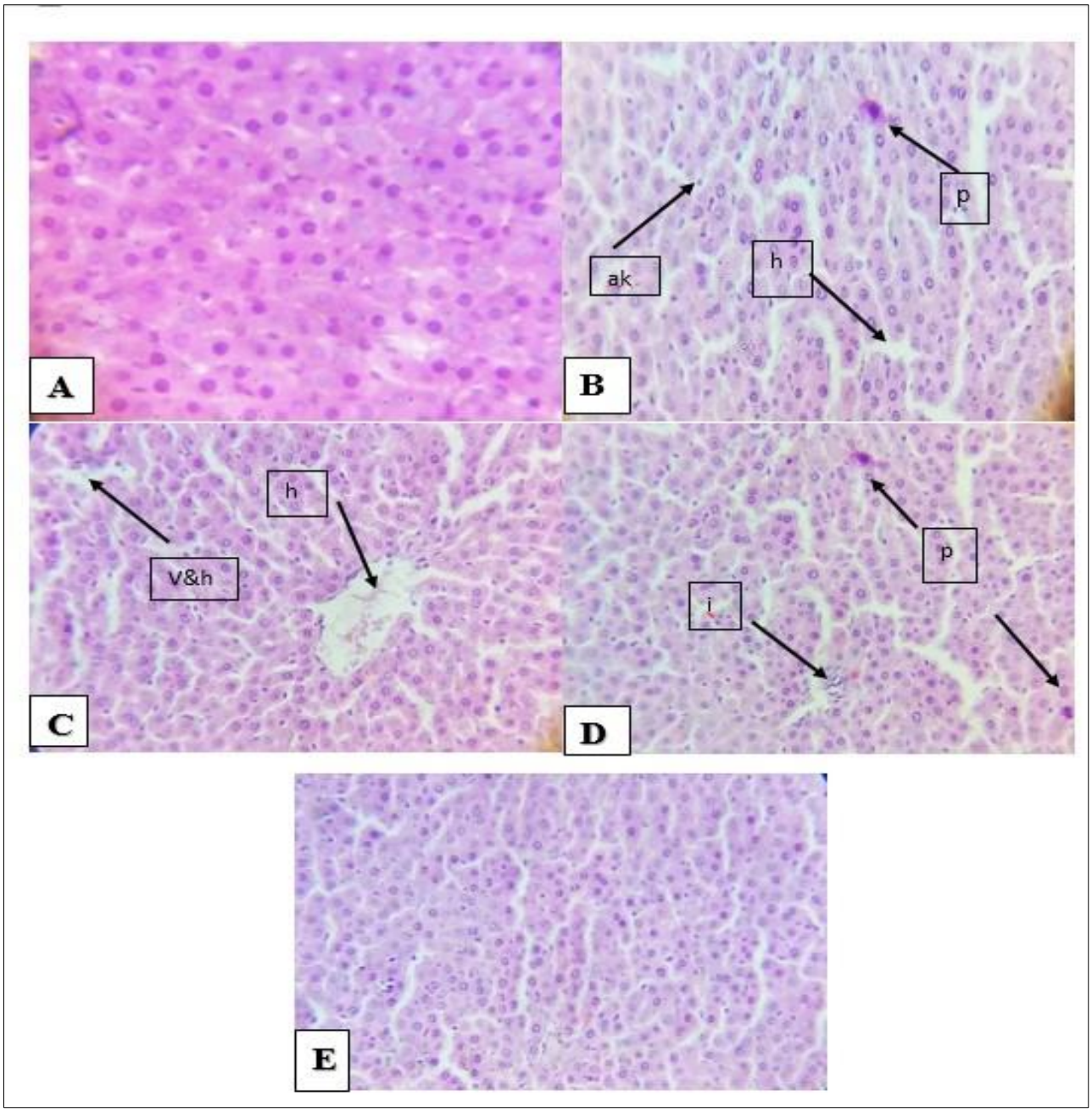

Figure 2: Cross section of liver tissue of male albino rats, A: From control+ve group showing normal architecture without changes, B: Showing apoptotic and hypertrophic hepatocytes (h) and activated kupffer cells (ak) and pyknotic cells (p) C: showing vaculation in cytoplasmic hepatocytes and hypertrophy (v) and little hemorrhage in blood vessels (h). D: showing pyknotic cells (p) and infiltration of inflammatory cells (i). E: showing liver section near to normal tissue B-E from group treated by MSG + curcumin. All animal tissue sections were stained by H&E and photographed at 400 X magnification.

Kidney Tissue

The current research revealed presence of histopathological changes in kidney cortex tissue induced by monosodium glutamate administration of male albino rats when they were administrated monosodium glutamate at dose of 20 mg/kg body weight for 30 days. The findings also elucidated the protective role of curcumin at dose 100mg/kg and its ability to improve the toxicity and histopathological changes in the renal tissue as shown in Figure 3 and 4.

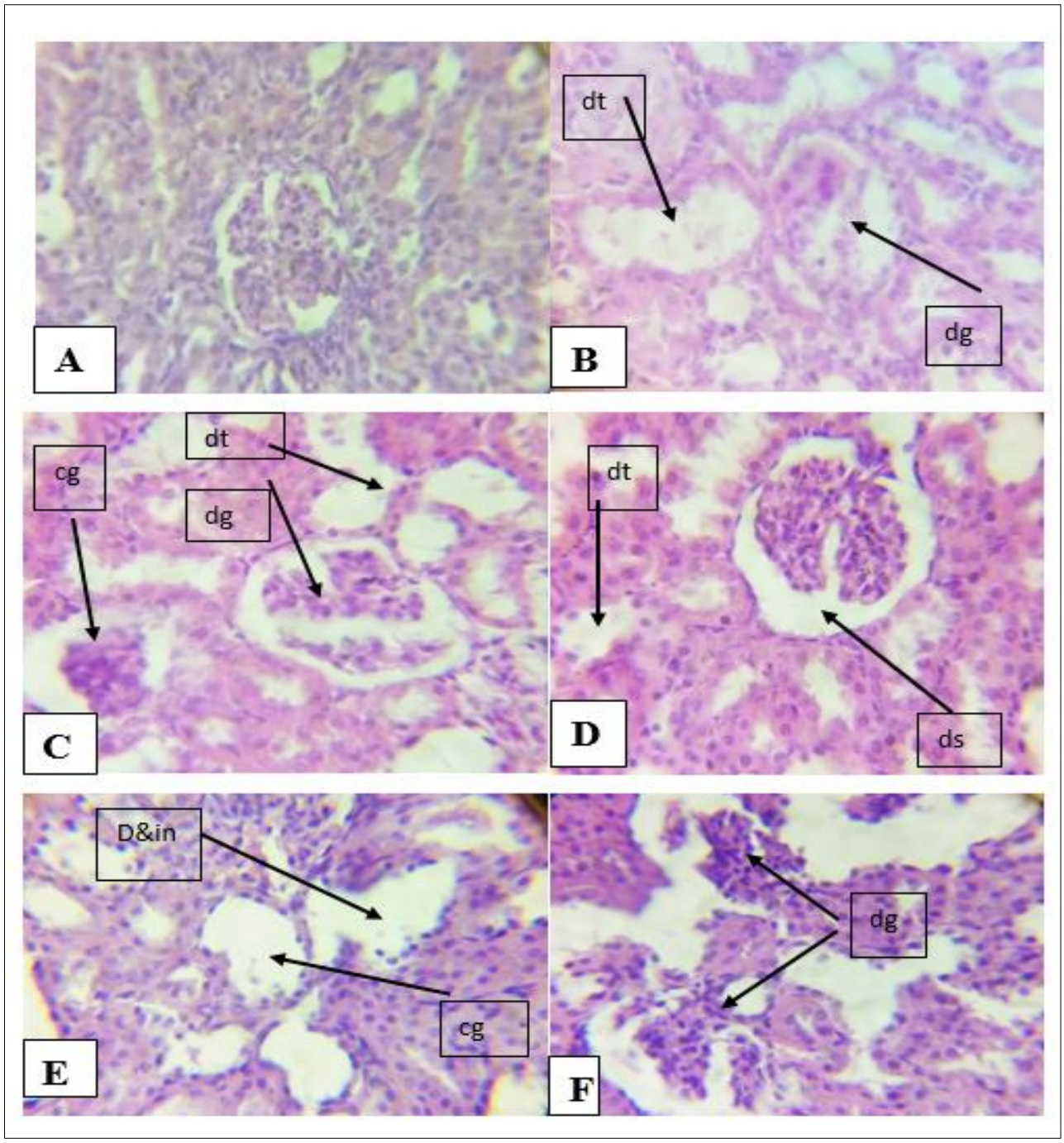

Figure 3: Cross section of kidney cortex tissue in male albino rats, A: showing normal architecture without changes from control –ve group, B: showing degradation in glomeruli (dg), dilation in tubules and degradation in lining epithelium cells (dt) C: showing congested glomeruli (cg) and dilation in renal tubules (dt) and degradation in glomeruli (dg) D: showing dilation in glomerulus capsule space (ds), dilation in renal tubules (dt) E: showing collapsed glomeruli (cg) , dilation in tubules and infiltration of inflammatory cells (d&in), F: showing dilation in capsule space and degradation in glomeruli (dg) B-F pictures from MSG treated groups. All animal tissue sections were stained by H&E and photographed at 400 X magnification.

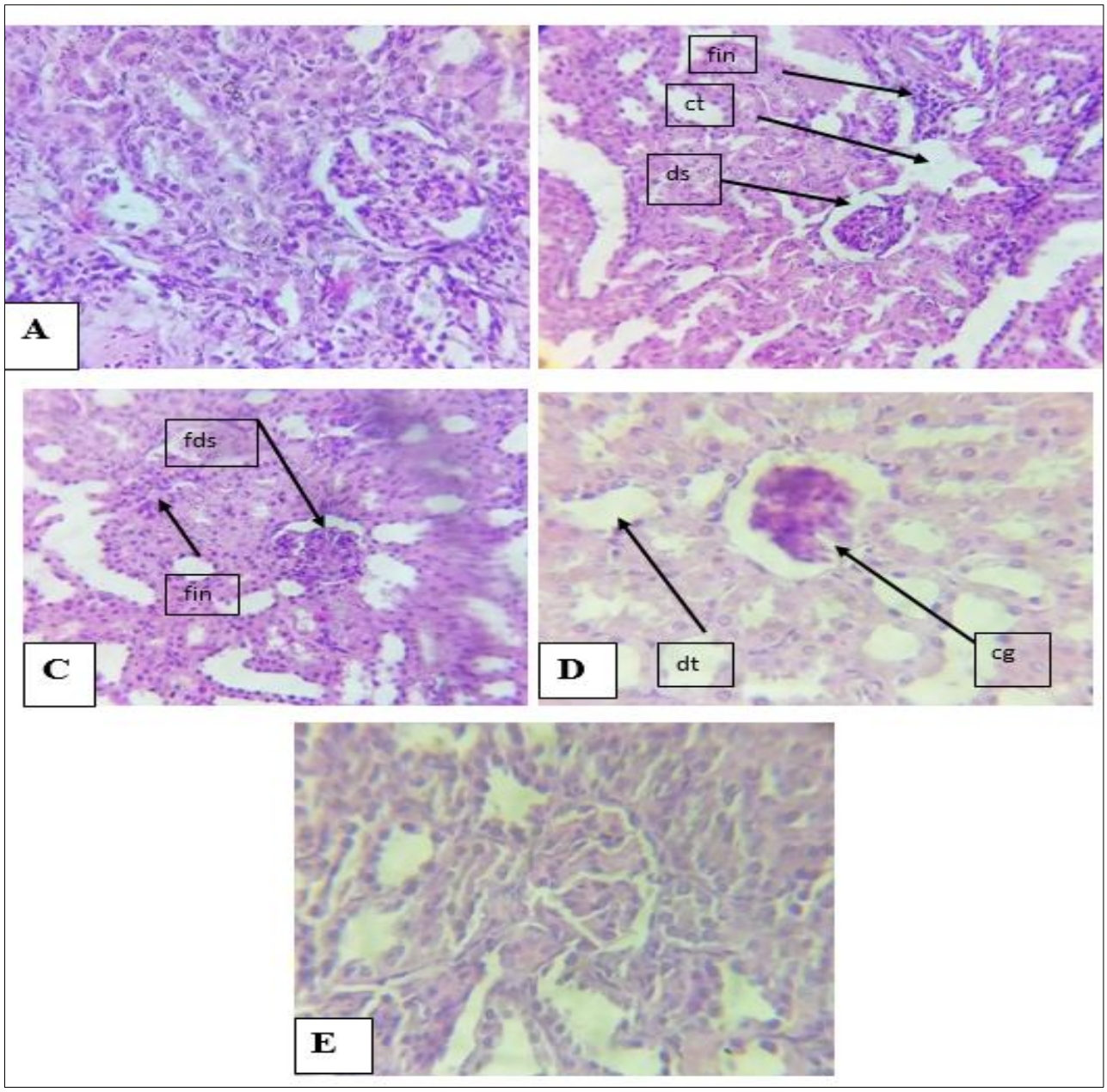

Figure 4: Cross section of kidney cortex tissue in male albino rats, A: showing normal architecture without changes from control group, B: showing collapsed renal tubules (ct) and little dilated glomerulus space (dg) and few infiltration of inflammatory cells (fin) C: showing few dilation in glomerulus space (fds), and few infiltration of inflammatory cells (fin). D: showing congested glomeruli (cg) and dilation of renal tubules (dt) E: showing semi normal kidney cortex. B-E pictures from MSG + curcumin treated group. All animal tissue sections were stained by H&E and photographed at 400 X magnification.

DISCUSSION

Biochemical Assay

The findings in table 1 were in agreement with [14], who reported that monosodium glutamate significantly affected the liver tissue and increased the serum liver function enzymes alanine aminotransferase, aspartate aminotransferase in Wistar rats. In addition, the results agreed with [15], who mentioned that MSG impaired the function of kidney to excrete toxic products leading to increase the serum urea and creatinine serum levels. Moreover, the outcomes were in similarity with [16], who demonstrated that hepatotoxic and nephrotoxic induced by MSG which may affect liver and kidney functions.

Furthermore, the results in table 1 agreed [17], who discussed how curcumin's modulation of oxidative stress regulators protects against disorders of the hepato-renal, biochemical profile, gene expression, and histological architecture.

The outcomes were in agreement with [18], who found that by influencing myeloperoxidase activity and the release of inflammatory cytokines in the tissues of the liver and kidney, curcumin may have anti-inflammatory and antioxidant benefits on liver and kidney damage. Additionally, it relieved the mice's symptoms while lowering their hepatic and nephritic biochemical indexes (ALT, AST, albumin and creatinine).

Body Weight Gain

The findings in table 2 were in agreement with [19], who demonstrated that MSG toxicity stimulated many deleterious impact on human health and physiological complication associated with are hypertension, obesity and impairment various organs function and endocrine system.

In addition, the results in table 2 were agreed with [20], who elucidated showed MSG-induced metabolic changes, inflammation linked to obesity, and decreased adiponectin were more pronounced in male mice. Moreover, the results supported by [21], who recorded the polyphenols in curcumin may offer benefits to fat tissue in obese individuals by reducing intracellular oxidative stress, lowering long-term low-grade inflammation, inhibiting the processes of lipogenesis and adipogenesis, and keeping preadipocytes from maturing into mature adipocytes. Furthermore, the findings supported by [22], who demonstrated dietary curcumin reduces fat mass, hepatic steatosis, and circulating lipopolysaccharide levels while improving insulin sensitivity in mice fed a high-fat diet, thereby protecting against obesity and associated metabolic diseases, supplementing with curcumin may change the metabolites and composition of the gut microbiota.

The Relative Liver and Kidney Organ Weight

The results in table 3 were in agreement with [23], who recorded that MSG damages essential organs and raises the risk of some malignancies, increased endogenous antioxidants were observed in rats exposed to MSG-induced acute liver injury. Tissue examination of the rats revealed numerous vacuoles displayed in the cytoplasm, enlarged mitochondria, dilated endoplasmic reticulum, dilated blood sinusoids, and bundles of collagen fibers in the extracellular space. It's possible that the inhibition of inflammation led to this harm. In addition, the results supported by [24], who showed that MSG generated kidney failure, elevated toxicity and oxidative stress in animal organs, and caused extensive renal tissue loss with hypertrophy of the calyces, leaving surviving glomeruli lacking Bowman's capsule.

Moreover, the findings supported by [25] who demonstrated that use of curcumin improved kidney function and preventing kidney damage. As well as [26], who mentioned that curcumin improves kidney function and oxidative stress by lowering renal morphological damage and histological indicators of inflammation, fibrosis, and apoptosis.

Histological Study (Liver and Kidney)

The results in figure 1 and 3 were supported by [27], who reported preclinical research has linked MSG exposure to behavioural abnormalities as well as premalignant changes, low-grade inflammation, hepatotoxicity, and metabolic disruption. In addition, the outcomes were supported by [28], who significant histopathological alterations were observed in the liver tissues of the MSG-treated mice, in both the fetal and maternal liver tissues. The present research supported by [29], who revealed that exposure to MSG resulted in a number of histological and histochemical alterations in the hepatocytes' vacuolation, degenerative and necrotic areas, and atrophied hepatocyte size with pyknotic nuclei. These alterations were seen in the portal and centrolobular zones of the mother and fetal liver tissues of Wistar rats. Moreover, the results supported by [30], who displayed rat hepatocyte vacuolar degradation, congestion of the central veins and portal blood arteries, and infiltration of mononuclear cells following MSG treatment.

Furthermore, the results agreed with [31], who demonstrated MSG-induced oxidative stress amelioration and anti-apoptotic effects, such as reduced glycoprotein content and fibrosis in the number of apoptotic cells, caused histological abnormalities in kidney tissue. As well as the findings were in agreement with [32], that long-term MSG consumption causes kidney failure by decreasing the size of the glomeruli in renal corpuscles, increasing Bowman's space relative to the glomerular capillary lumen, and indirectly narrowing the glomerular capillary lumen.

Moreover, the results in figure 2 and 4 supported by [32], who demonstrated that Curcumin is hepato-protective due to its strong anti-inflammatory and antioxidant properties. In addition, the results in agreement with [33], who displayed curcumin reduced the hepatotoxicity and liver tissue changes in rats, including sinusoidal dilatation, inflammatory cell infiltration, congestion, and parenchymal necrosis.

Furthermore, the study in supported by [34], who recorded that curcumin and nano curcumin had better hepatoprotective impact in liver damage after rats exposure to parquets herbicide, most likely through modulation of oxidative stress and genes expression of nuclear factor erythroid 2-related factor 2pathway.

Additionally, the findings in figure 2 and 4 supported by [35], who showed that Curcumin exhibiting a protective effect against the formaldehyde-induced oxidative renal injury by improving the formaldehyde-induced renal degeneration.

Also, curcumin was found to prevent the reduction the activities of antioxidant enzymes (SOD, CAT and GSH-Px), while preventing NO levels.

Finally, the results supported by [36], who showed that curcumin significantly mitigated the negative effects of sodium arsenate on the diameter of the glomerulus and proximal tubule, glomerular area, and total antioxidant capacity, Curcumin also attenuated the histological alterations in rat's renal cortex tissue and compensated for the negative influence on lipid peroxidation and serum total antioxidant capacity.

CONCLUSION

The study can be concluded that curcumin can be used as antioxidant because, it has abundant beneficial properties for applications in food, the data showed it had potent protective impact against monosodium glutamate - induced cytotoxicity and histopathological changes in liver and kidney cortex tissue of male albino rats.

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