

Effects of Administration of Tramadol Hydrochloride on the Histological Structure of the Kidney and the Possible Protective Role of Curcumin in Adult Albino Rat

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Abstract

Introduction: Tramadol is a synthetic centrally acting analgesic with effects similar to those of codeine and 10 times less than morphine. Tramadol has a wide range of applications mostly in the treatment of moderate to severe, acute or chronic pain. Curcumin, the active component of *Curcuma longa*, has antioxidative, anti-fibrotic, anti-inflammatory and anti-proliferative properties.

Aim of the Work: The aim of the study was to detect the toxic effects of tramadol on the histological structure of the renal tissue in adult male albino rats and the possible protective role of curcumin against these effects.

Material and Methods: 30 adult albino rats were used. The animals were divided into three equal groups: Group I: (control group): Animals were given normal saline orally by intragastric tube in a dose of 25ml/kg every day for one month. Group (II): Animals were given Tramadol Hydrochloride in a dose of 25mg/kg orally by intragastric tube every day for one month. Group (III): Animals were given Tramadol Hydrochloride in a dose of 25mg/kg and Curcumin solution in a dose of 80mg/kg orally by intragastric every day for one month. At the end of the experiment, the rats were anaesthetized by ether then perfused with saline then with the appropriate fixator, the kidney was obtained and subjected to light and transmission electron microscopic studies.

Results: Tramadol caused damage, shrinkage and lobulation of renal glomeruli. It also caused dilatation in the distal and proximal convoluted tubules with loss of their brush borders as seen by light and electron microscope. Administration of curcumin improved the structure of the renal glomeruli, proximal and distal convoluted tubules.

Conclusion: Tramadol caused damage in the renal cortex with dilatation of tubules. The addition of curcumin partially improved these toxic effects.

Key Words: Kidney – Tramadol – Curcumin.

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Introduction

TRAMADOL is a centrally acting analgesic is widespreadly used throughout the world. It has opioid, noradrenergic and serotonergic properties. Various data suggest that, in addition to its analgesic effect, tramadol may have also antidepressant and anxiolytic-like effects [1]. Tramadol provides its analgesia through 3 mechanisms: mu-opioid binding (through its metabolite O-desmethyltramadol), serotonin reuptake inhibition (through (+)-tramadol) and nor-epinephrine reuptake inhibition [2].

The absorption of tramadol is 95-100% and the bioavailability is 70%. The bioavailability of tramadol is more than that of morphine (15-65%). When tramadol is used in multiple doses, its bioavailability increased to 100%. The complete absorption of tramadol takes place in the upper part of small intestine [3].

The metabolism of Tramadol occurs in the liver by cytochrome p450 enzyme system and its products are excreted through kidneys. Consequently the kidney is considered to be the primary target organ for tramadol toxicity. Its biotransformation occurs in the liver, firstly by the phase I reactions (mainly O-and N-demethylation) and secondly by the phase II reactions (mainly conjugation of O-and N-demethylated compounds), in turn about eleven and twelve metabolites are produced respectively [4].

Tramadol abuse, dependence as well as acute overdose-related deaths have been increasingly reported recently, especially in young male adults. Being an opioid, tramadol carries all the possible risks known from other opiates. Tramadol can

cause psychological and physical addiction similar to that seen with other opiates and opioids. Repeated tramadol administration in such patients might lead to accumulation of toxic metabolites in their bodies, increase the risk for pharmacokinetics interactions, and/or decrease the clearance of tramadol, thus increasing its potential for toxicity [5].

Curcumin is a natural phenolic compound isolated as a yellow pigment from turmeric (*Curcuma longa*), is extensively used as a spice and food preservative in India, China, and South East Asia [6].

Chemically, curcumin is a bis- α , β -unsaturated β -diketone (commonly called diferuloylmethane). Its contents of phenolic, β -diketone and the methoxy groups contribute to the free radical-scavenging activity of curcumin. Curcumin exists mostly in two forms, keto and enol [7].

Curcumin possesses several pharmacological properties including strong antioxidant, anti-inflammatory, antimicrobial, antiviral, antifungal, and wound-healing properties. It also decreases the level of lipid peroxides and regulates the activity of antioxidant enzymes such as reduced Glutathione (GSH), Superoxide Dismutase (SOD), and Catalase (CAT) [8].

Aim of the work:

The aim of the study is to detect the toxic effects of tramadol on the histological structure of the renal tissue in adult male albino rats and to detect the possible protective role of curcumin against these effects.

Material and Methods

The research was done in 2016. A total number of 30 adult male albino rats (average weight 200-250gm). Were brought from the Animal House of Sohag Faculty of Science. They were reared under the standard conditions of feeding, light-dark ratio and temperature.

Tramadol hydrochloride was obtained in the form of commercially packed tablets (Tamol-X) from Royal National Pharmaceutical Company. Each tablet contains 225mg of tramadol hydrochloride. The tablets (8 and 1/3 tablets) were grinded and dissolved in 500ml saline. Hence each rat received 6.25mg of the drug in 1.6ml of the prepared solution.

Curcumin was obtained in powder form from El-Gomhouria Company. 3 grams were dissolved

in 300ml (saline and Acacia gum). Hence each rat received 20mg of curcumin in 2ml of the prepared solution.

The animals were divided into 3 groups; each of them consists of 10 rats.

Group (I) [control group]: Animals were given normal saline orally by intragastric tube in a dose of 25ml/kg body weight every day for one month.

Group (II) [tramadol treated group]: Animals were given Tramadol Hydrochloride in a dose of 25mg/kg body weight [9] orally by intragastric tube every day for one month.

Group (III) [tramadol-curcumin treated group]: Animals were given Tramadol Hydrochloride in a dose of 25mg/kg body weight and Curcumin solution in a dose of 80mg/kg body weight orally by intragastric tube every day for one month [10].

At the end of the experiment, the rats were anaesthetized by ether then perfused with saline then with the appropriate fixator (Formalin 10%). The abdomens were opened and the kidneys of the control and treated animals were extracted, cut, and processed for light and transmission electron microscopic studies.

For light microscopic study: The specimens were fixed in 10% neutral buffered formalin and processed for light microscopic study to get paraffin sections of 6 μ m thickness. Sections were stained with Haematoxylin and Eosin (H & E) and Masson's Trichrome stain.

For Transmission Electron Microscopic study (TEM): Specimens were cut in small pieces and fixed in 2.5% glutaraldehyde for 24 hours. Then specimens were washed by sodium cacodylate buffer solution, postfixed in 1% osmium tetroxide in sodium cacodylate buffer for two hours, then washed and dehydrated in ascending grades of alcohol, ethanol 30%, 50%, 70%, 95%. The specimens were embedded in Mollenhauer's Epon-Araldite formulation and the tissue blocks were polymerized in an oven. Blocks were trimmed with a razor blade and cutting was done by a glass knife in KLB ultramicrotome. Semithin sections were stained with Toluidine blue. Ultrastructural sections were mounted on copper grids, stained with Uranyl acetate and Lead citrate and ultrathin sections were examined by transmission electron microscope (Jeol-1010) in Assiut University.

Morphometric and statistical analysis:

Estimation of the mean diameters of the renal glomeruli, proximal and distal convoluted tubules (at magnification 400) was done. Measurements were performed in Haematoxylin and Eosin (H & E) sections, 2-3 sections per animal. In each section five measurements were obtained from five randomly chosen fields using image analysis system (digimizer version 3.7.2005-2010) med-calc software in the Anatomy Department at Sohag University.

Statistical analysis:

Statistical analysis of measurements of mean diameters of the glomeruli, proximal and distal convoluted tubules were done using SPSS software Version 16. Variables were represented by mean \pm SD (mean \pm standard deviation of mean). One way ANOVA was used to compare the means of these variables between different groups. Finally the significance was considered according to the level of significance *p*-value as follows:

$p > 0.05$ non significant.

$p \leq 0.05$ significant*.

$p \leq 0.01$ highly significant**.

$p \leq 0.001$ (***) \rightarrow Very high significant difference.

Results

*Group I (control group):**Histological study:*

Light microscopic sections showed that the renal cortex was formed of renal corpuscle, proximal and distal convoluted tubules Fig. (1).

The renal corpuscle was formed of a tuft of capillaries called renal glomerulus which was surrounded by a double layered cup called Bowman's capsule. Bowman's capsule consisted of two layers. The outer parietal layer was formed of simple squamous epithelium while the inner visceral layer had modified epithelial cells called podocytes. The space between the two layers was called the urinary space. The renal glomerulus contained capillaries and mesangial cells Fig. (2).

The proximal convoluted tubules appeared lined by cuboidal epithelium. The nuclei were spherical and basally located. The apical surface had a prominent brush border Fig. (3).

The distal convoluted tubules were lined by cuboidal epithelium. The epithelial cells lacked

the brush border. The nuclei were spherical and apically located. The cytoplasm was lighter in staining than those of proximal convoluted tubules Fig. (3).

The kidney sections revealed thin layer of collagen fibers around the glomerulus and inside it between mesangial cells. There were also few collagen fibers around the proximal and distal convoluted tubules Fig. (4).

Ultrastructural study:

The renal glomerulus appeared formed of a glomerular capillary and podocyte. The capillary was lined by endothelial cells. Between the endothelial cells, there were fenestrations. The podocytes had numerous pedicles from the cytoplasm interdigitating with neighboring podocytes. Small openings between the pedicles formed filtration slits. The basal lamina lied between the capillary endothelium and podocytes Fig. (5).

The proximal convoluted tubule was lined by epithelial cells which appeared oval in shape and contained a large rounded euchromatic nucleus. There were multiple elongated basally located mitochondria. The apical surface showed multiple closely packed microvilli forming the brush border. Some vesicles were observed Fig. (6). The distal convoluted tubule was lined by epithelial cell which showed large rounded euchromatic nucleus and multiple elongated mitochondria Fig. (7).

*Group II (tramadol group):**Histological study:*

After treatment with Tramadol, the renal cortex lost the normal picture. Some glomeruli were shrunken Fig. (8), while other glomeruli showed lobulation and destruction. The destruction was in the form of decreased number of podocytes and absent capillaries. Mesangial cells appeared normal Fig. (9). The proximal convoluted tubules were dilated with destruction of their brush border Figs. (8,10). Epithelial cells of proximal tubules showed vacuolation of cytoplasm and loss of nuclei Fig. (10). The distal convoluted tubules were also dilated Fig. (8).

Kidney sections showed marked increase of collagen fibers around the glomerulus and inside it. Deposition of collagen fibers mildly increased around the proximal and distal convoluted tubules after treatment with tramadol Fig. (11).

Ultrastructural study:

The renal glomerulus showed thickening in the basal lamina between the endothelial cells and

podocytes Fig. (12). The podocytes appeared normal with normal pedicles interdigitating with neighboring podocytes. The capillary was normal and was lined by endothelial cells.

The epithelial cell of the proximal convoluted tubule appeared with ill defined border. It showed a heterochromatic nucleus with ill defined nuclear border. The microvilli were destroyed with rarified cytoplasm Fig. (13).

The cells of the distal convoluted tubules appeared with ill defined border and the nucleus was heterochromatic and shrunken with irregular membrane. The cytoplasm was rarified with multiple elongated destructed mitochondria Fig. (14).

Group III (tramadol-curcumin):

Histological study:

After addition of Curcumin, most glomeruli restored their normal pictures. Some glomeruli were shrunken with dilated urinary space Fig. (15). Others appeared lobulated. The glomerulus showed a decrease in number of podocytes and capillaries with normal mesangial cells Fig. (16).

The proximal convoluted tubules showed mild dilatation Fig. (15) and partial destruction of the brush border Figs. (15-17). Some epithelial cells showed degeneration and loss of nuclei with vacuolation in the cytoplasm Figs. (16,17). The distal convoluted tubules were also dilated Fig. (15).

Sections showed normal distribution of collagen fibers around the glomerulus, inside it, and around proximal and distal convoluted tubules in a picture similar to control group Fig. (18).

Ultrastructural study:

The renal glomerulus showed the normal picture with normal thickness of basal lamina, normal

appearance of capillary cell. Podocytes showed normal pedicles interdigitating with neighboring pedicles Fig. (19).

Cells of the proximal convoluted tubule appeared oval in shape, some appeared with well defined border and showed heterochromatic shrunken nucleus with well defined nuclear membrane and few destructed mitochondria Fig. (20), while others showed ill defined border with large normal rounded euchromatic nucleus and well defined membrane and multiple normal elongated mitochondria Fig. (21). The microvilli appeared normal in some cells Fig. (20), and destroyed in others Fig. (21). The cytoplasm was rarified Fig. (20).

Cells of the distal convoluted tubule appeared rounded with well defined border and the nucleus was mildly shrunken with rarification of the cytoplasm and normal appearance of mitochondria Fig. (22).

Morphometric study:

- *Diameter of glomerulus:* (Table 1), Diagram (1): Mean glomerulus diameter in group II (382.44 pixels) showed a highly significant ($P=0.000$) decrease when compared with group I (673.08 pixels) and group III (505.88 pixels).
- *Diameter of proximal convoluted tubules:* (Table 1), Diagram (1): Mean proximal convoluted tubules diameter in group II (652.65 pixels) showed a highly significant ($p=0.000$) increase when compared with group I (358.04 pixels) and group III (305.31 pixels).
- *Diameter of distal convoluted tubules:* (Table 1), Diagram (1): Mean distal convoluted tubules diameter in group II (781.18 pixels) showed a highly significant ($p=0.000$) increase when compared with group I (288.43 pixels) and group III (317.56 pixels).

Table (1): Showing the mean diameter (in pixels) of glomerulus, proximal and distal convoluted tubules in control and experimental groups.

Parameters	Group I (Control)	Group II (Tramadol treated)	Group III (Tramadol-Curcumin treated)	P1 Value	p-Value	P2 Value
Diameter of glomerulus (Pixels)	673.08	382.44	505.88	0.001***	0.002**	0.000***
Diameter of proximal convoluted tubules (Pixels)	358.04	652.65	305.31	0.000***	0.823	0.000***
Diameter of distal convoluted tubules (Pixels)	288.43	781.18	317.56	0.000***	0.001***	0.000***

p_1 value : Comparison between Group I & Group II.

p_2 value : Comparison between Group I & Group III.

p -value : Comparison between Group I & Group III.

p, p_1 & $p_2 \leq 0.001$ (***) -* Very high significant difference.

$p_2 \leq 0.01$ (**) -* highly significant.

$p_2 > 0.05$ non significant.

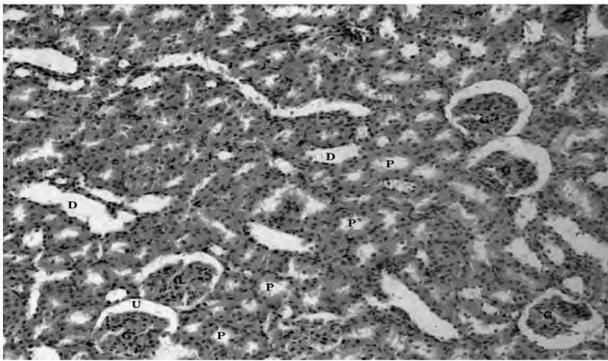


Fig. (1): A photomicrograph of a section of kidney of (group 1) control rat showing; renal Glomeruli (G), Proximal convoluted tubules (P) and Distal convoluted tubules (D) [Notice: Urinary space (U)] (H & E X200).

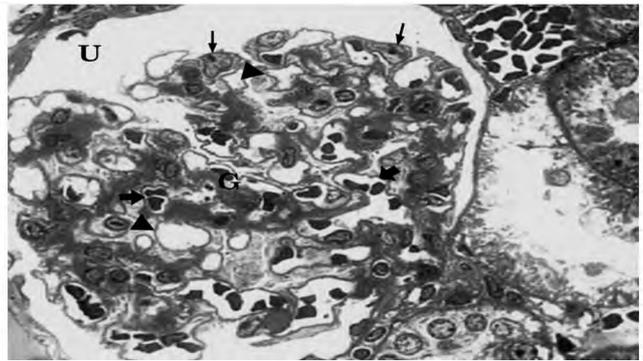


Fig. (2): A photomicrograph of semithin section in kidney of (group 1) control rat showing; renal Glomerulus (G) containing podocytes (thin arrows), mesangial cells (thick arrows) and capillaries (arrow heads) surrounded by Urinary space (U). (Toluidine blue X1000).

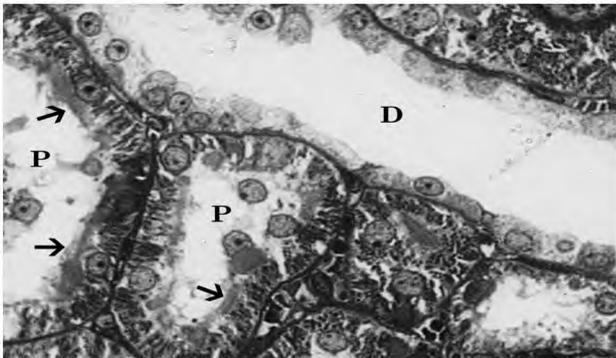


Fig. (3): A photomicrograph of semithin section in kidney of (group 1) control rat showing; Proximal convoluted tubules (P) with normal brush border (arrows) and Distal convoluted tubule (D). (Toluidine blue X1000).

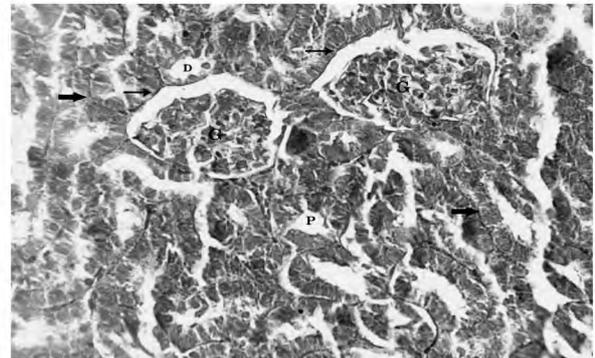


Fig. (4): A photomicrograph of a section of kidney of (group 1) control rat showing; normal distribution of collagen fibers around glomerulus (thin arrows) and inside it and around the Proximal (P) Distal (D) convoluted tubules (thick arrows). (Masson's trichrome X400).

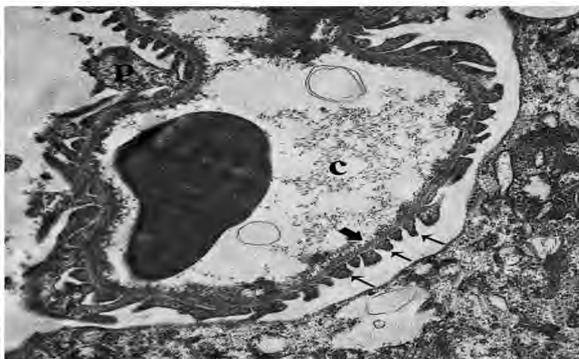


Fig. (5): An electron micrograph of a portion of renal glomerulus in kidney of (group 1) control rat showing; a glomerular Capillary (C) and an adjacent Podocyte (P). The capillary is lined by endothelial cells separated by fenestrations. The capillary endothelium rests on the basal lamina (thick arrow). The podocyte has multiple pedicles (thin arrows). (X10,000).

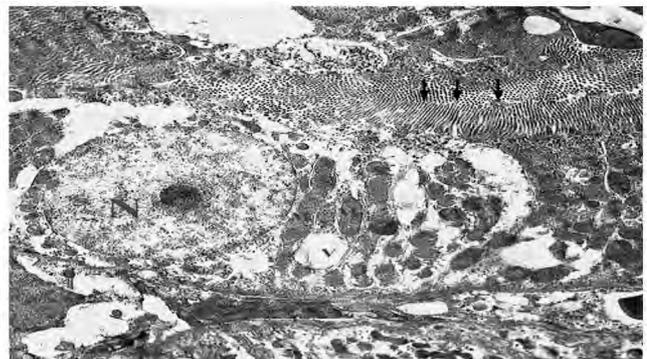


Fig. (6): An electron micrograph of a portion of proximal convoluted tubule in kidney of (group 1) control rat showing; a cell with a large rounded euchromatic Nucleus (N), multiple elongated basally arranged Mitochondria (M), Vesicle (V) and microvilli (arrows). (X4800).



Fig. (7): An electron micrograph of a portion of distal convoluted tubule in kidney of (group 1) control rat showing; 2 cells with 2 large rounded euchromatic Nuclei (N), multiple elongated Mitochondria (M). (X4800).

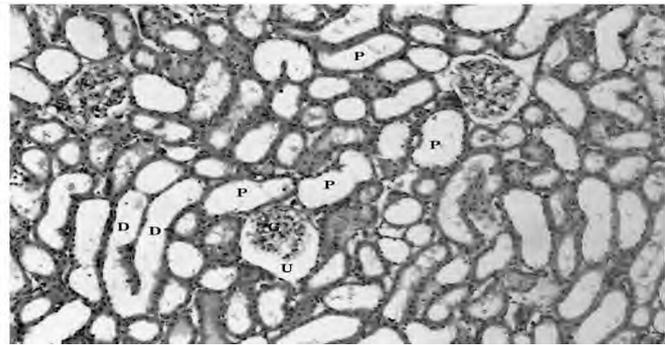


Fig. (8): A photomicrograph of a section of kidney of (group 2) tramadol treated rat showing; one shrunken Glomerulus (G), dilated Proximal convoluted tubules (P) with destruction of brush border and Dilated distal convoluted tubules (D). (H & E X200).

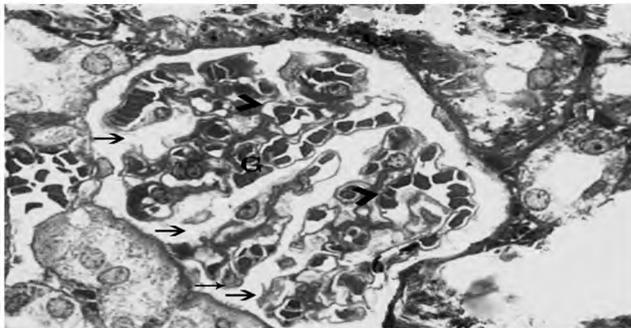


Fig. (9): A photomicrograph of semithin section in kidney of (group 2) tramadol treated rat showing; lobulation and destruction in the renal Glomerulus (G) (thick arrows), decreased number of podocytes (thin arrow), absent capillaries. [Notice: Mesangial cells (arrow heads)] (Toluidine blue X1000).

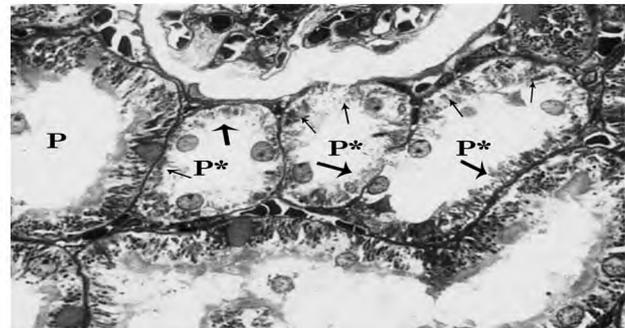


Fig. (10): A photomicrograph of semithin section in kidney of (group 2) tramadol treated rat showing; loss of brush border of Proximal convoluted tubules (P*) (thick arrows). Epithelial cells showed vacuolation of cytoplasm and loss of nuclei (thin arrows). (Toluidine blue X1000).

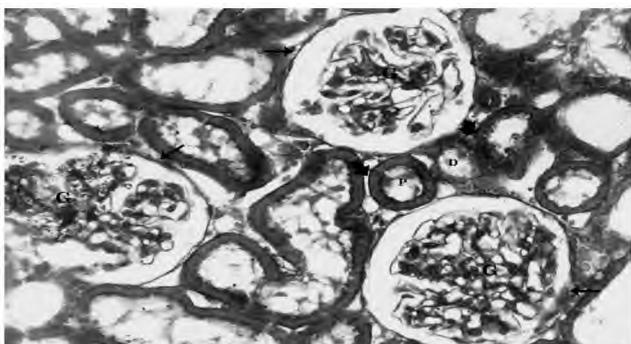


Fig. (11): A photomicrograph of a section of kidney of (group 2) tramadol treated rat showing; increase in distribution of collagen fibers around glomerulus (thin arrows) and inside it and around the Proximal (P) and Distal (D) convoluted tubules (thick arrows). (Masson's trichrome X400).



Fig. (12): An electron micrograph of a portion of renal glomerulus in kidney of (group 2) tramadol treated rat showing; thickening in the basal lamina (thick arrows). [Notice: Normal Podocyte (P) with normal pedicles (thin arrows) and normal glomerular Capillary (C). (X10,000).



Fig. (13): An electron micrograph of a portion of proximal convoluted tubule in kidney of (group 2) tramadol treated rat showing; heterochromatic shrunken Nucleus (N) with ill defined nuclear border (thick arrow), destruction of the microvilli (arrows) and rarified cytoplasm (*). [Notice: Mitochondria (M)] (X4800).

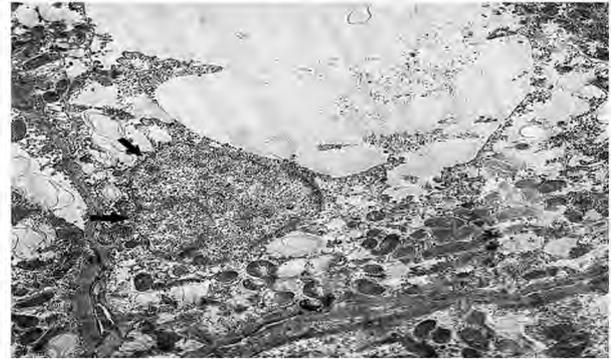


Fig. (14): An electron micrograph of a portion of distal convoluted tubule in kidney of (group 2) tramadol treated rat showing; a cell with heterochromatic shrunken Nucleus (N) with irregular membrane (arrows), and rarified cytoplasm (*). Mitochondria (M) are multiple elongated and destroyed. (X4800).

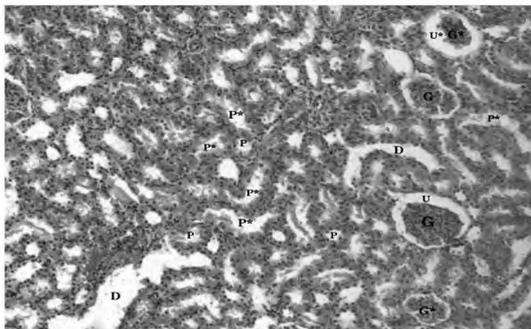


Fig. (15): A photomicrograph of a section of kidney of (group 3) tramadol-curcumin treated rat showing; two shrunken Glomeruli (G*) with dilated Urinary space (U*), dilated Proximal convoluted tubules (P*) with partial destruction of brush border and dilated Distal convoluted tubules (D). [Notice: Normal Glomerulus (G) and normal Proximal convoluted tubules (P)] (H & E X200).

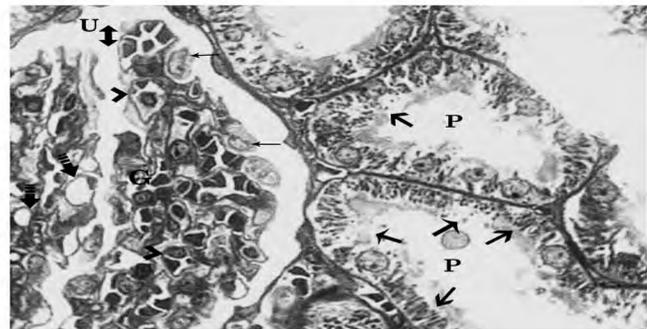


Fig. (16): A photomicrograph of semithin section in kidney of (group 3) tramadol-curcumin treated rat showing; lobulation in renal Glomerulus (G) (double head arrow). Decreased number of podocytes (thin arrows) and capillaries (dotted arrows) with normal mesangial cells (arrow head). Proximal convoluted tubules (P) showed partial loss of brush border and vacuolation of cytoplasm with loss of nuclei (thick arrows). (Toluidine blue X 1000).

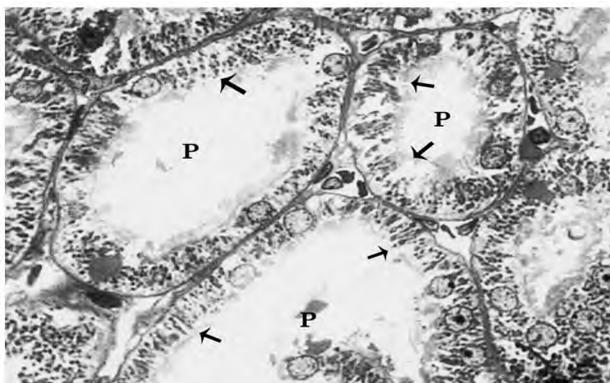


Fig. (17): A photomicrograph of semithin section in kidney of (group 3) tramadol-curcumin treated rat showing; partial loss of brush border of Proximal convoluted tubules (P) with loss of some nuclei of their cells (arrows). (Toluidine blue X 1000).

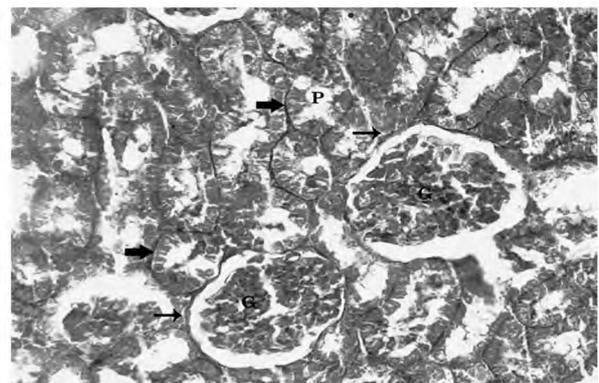


Fig. (18): A photomicrograph of a section of kidney of (group 3) tramadol-curcumin treated rat showing; normal distribution of collagen fibers around glomerulus (thin arrows) and inside it and around the Proximal (P) Distal (D) convoluted tubules (thick arrows). (Masson's trichrome X400).

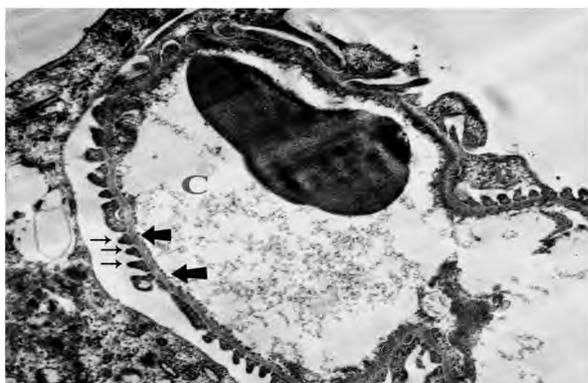


Fig. (19): An electron micrograph of a portion of renal glomerulus in kidney of (group 3) tramadol-curcumin treated rat showing; normal basal lamina (thick arrows), normal Podocyte (P) with normal pedicles (thin arrows) and normal glomerular Capillary (C). (X10,000).

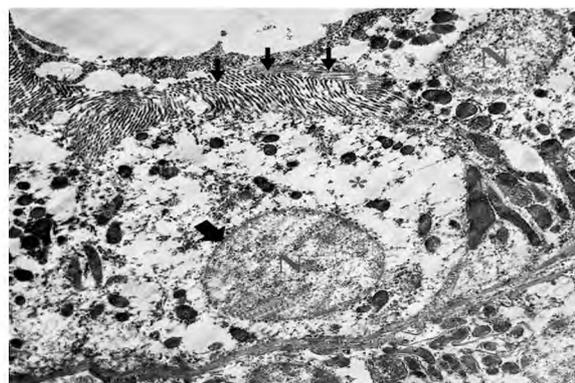


Fig. (20): An electron micrograph of a portion of proximal convoluted tubule in kidney of (group 3) tramadol-curcumin treated rat showing; epithelial cell with well defined border and heterochromatic shrunken Nucleus (N) with well defined membrane (thick arrow), normal microvilli (thin arrows), rarified cytoplasm (*) and destroyed decreased Mitochondria (M). (X4800).



Fig. (21): An electron micrograph of a portion of proximal convoluted tubule in kidney of (group 3) tramadol-curcumin treated rat showing; epithelial cell with ill defined border and normal large rounded euchromatic nucleus with well defined membrane (thick arrow) (N), destruction of microvilli (thin arrows) and normal multiple elongated Mitochondria (M). (X4800).



Fig. (22): An electron micrograph of a portion of distal convoluted tubule in kidney of (group 3) tramadol-curcumin treated rat showing; epithelial cell with well defined border and mild shrunken Nucleus (N) with well defined membrane (arrow), and rarified cytoplasm (*). [Notice: Multiple elongated Mitochondria (M)] (X4800).

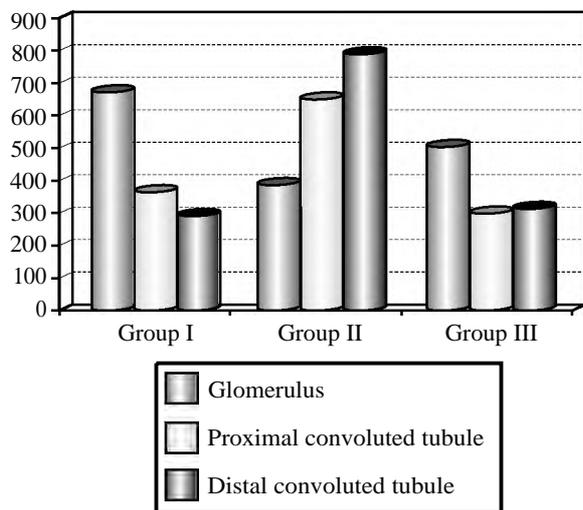


Diagram (1): Showing the mean diameter (in pixels) of glomerulus, proximal and distal convoluted tubules in control and experimental groups.

Discussion

These results of the effects of tramadol on the kidney in the present study were agreed with the previous results that showed that kidneys treated with tramadol had extensive changes in the form of atrophied glomeruli, wide urinary space, and degenerated tubules [11].

Another study about kidney also found atrophied glomerulus with collapsed tuft, wide Bowman's space, degenerated tubules, cellular infiltration and hemorrhage in tramadol treated rats [12].

Chronic tramadol toxicity affected the kidney in the form of atrophied glomeruli with collapsed tufts, wide Bowman's space, degenerated tubules, and cellular infiltration [13]. That was explained by the toxicokinetic process of tramadol, since

30% of the drug is excreted through the kidney in an unchanged manner, while the rest are changed by the liver into active metabolites. These metabolites excreted by the kidney cause cellular damage leading to kidney dysfunction [14].

A previous study demonstrated the nephrotoxic effects of tramadol when given for 1 month, tramadol caused atrophy of the glomerulus with collapsed tuft, widening in Bowman's space, degeneration of tubules, cellular infiltration and hemorrhage. Thickening of the basement membrane of the renal corpuscles appeared by ultrastructural studies [15].

Effects of tramadol also were explained by previous studies that found that these toxic effects resulted of tramadol-induced lipid peroxidation of renal tissues. Lipid peroxidation of cell membranes leads to loss of membrane fluidity, changes in membrane potential and an increase in membrane permeability, all of which lead to alteration of the chemical compound of the cells [16].

The protective effect of curcumin against kidney damage was studied previously and was agreed with the results of the present study. Curcumin reduced these histopathological changes. It also reduced the increased serum urea nitrogen and creatinine levels. Curcumin decreased the lipid peroxidation and increased the enzymatic and nonenzymatic antioxidant system in kidney [17].

Curcuminoids exhibit a differential antioxidant activity in several in vitro and in vivo models by preventing lipid peroxidation. Curcumin is a bifunctional antioxidant because of its ability to react directly with reactive species due to presence of phenolic groups in its structure and to induce an upregulation of various cytoprotective and antioxidant proteins such as Superoxide Dismutase (SOD) and Catalase (CAT) [18].

A previous study reported that curcumin has a renoprotective effect by attenuating the inflammation. It blocks overexpression of inflammatory mediators such as TNF- α (tumor necrosis factor- α) and (IL-1 β) interleukin 1 β that stimulate leukocytes and vascular endothelial cells to release other cytokines. This occurs through activation of phospholipase 2 (PLP2) and COX-2, which are key regulators of inflammation and oxidative stress inductors [19].

Conclusion:

- Tramadol had a chronic toxic effect on the kidney in the form of glomerular damage and dilatation of proximal and distal convoluted tubules.

- Administration of curcumin to tramadol partially improved the renal glomeruli, proximal and distal convoluted tubules.

Recommendations:

More researches on the antioxidant effect of curcumin on different types of tissues and against different toxic drugs are recommended.

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تأثيرات إعطاء كلوريد الترامادول على التركيب النسيجي للكلية والدور الوقائي المحتمل للكركم في الفئران البيضاء البالغة

المقدمة: يعتبر عقار الترامادول من المسكنات الإصطناعية التي تعمل مركزيا على المخ ولها آثار مماثلة للكودين وعشر مرات أقل تأثيرا من المورفين. الترامادول لديه مجموعة واسعة من التطبيقات في علاج الألم المعتدل إلى الشديد والألم الحاد والمزمن. الكركم وهو العنصر النشط من نبات الكركم لونغا، لديه عدة خصائص كمضاد للاكسدة، مضاد للتليف، مضاد للإلتهابات ومضاد لتكاثر الخلايا.

الغرض من البحث: الهدف من هذه الدراسة الكشف عن الآثار السامة للترامادول على أنسجة الكلية والدور الوقائي المحتمل للكركم ضد هذه الآثار.

الآدوات والطرق: في هذه الدراسة تم استخدام ثلاثين من الفئران البيضاء البالغة وتم تقسيم الحيوانات إلى ثلاث مجموعات متساوية: المجموعة الأولى وتمثل المجموعة الضابطة وقد تم إعطاؤها محلول ملح بجرعة ٢٥ مل/كجم عن طريق أنبوبة المعدة يوميا لمدة ٣٠ يوم. المجموعة الثانية وتم إعطاؤها كلوريد الترامادول بجرعة ٢٥ مجم/كجم عن طريق أنبوبة المعدة يوميا لمدة ٣٠ يوم. المجموعة الثالثة تم إعطاؤها كلوريد الترامادول بجرعة ٢٥ مجم/كجم والكركم بجرعة ٨٠ مجم/كجم عن طريق أنبوبة المعدة يوميا لمدة ٣٠ يوم. وفي نهاية التجربة تم تخدير الحيوانات وأخذ الكلية وإعدادها للفحص بالميكروسكوب الضوئي والإلكتروني.

النتائج: لقد سبب الترامادول الضرر والإنكماش في الكبيبات الكلوية. كما تسبب في إتساع الأنابيب البعيدة والقريبة الملتوية كما يتضح من الفحص بالمجهر الضوئي والإلكتروني. إضافة الكركم أحدثت تحسن جزئي في هيكل الكبيبات الكلوية والأنابيب القريبة والبعيدة الملتوية.

الخلاصة: تسبب الترامادول في إلحاق الضرر في القشرة الكلوية مع توسع في الأنابيب. إضافة الكركم حسنت جزئيا من هذه الآثار السامة.