THE POSSIBLE RENOPROTECTIVE EFFECT OF CURCUMIN ON ISCHEMIA-REPERFUSION INJURY AND TACROLIMUS INDUCED NEPHROTOXICITY IN RENAL CORTEX IN ADULT MALE ALBINO RAT: A LIGHT AND ELECTRON MICROSCOPIC STUDY

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ABSTRACT

Curcumin is a polyphenolic phytochemical, has been used for decades and it exhibits anti-inflammatory, anti-carcinogenic and anti-oxidative properties. The present study aimed to evaluate the histological changes induced by ischemia-reperfusion (I/R) and tacrolimus treatment in rat kidney and the possible protective role of curcumin. Thirty adult male albino rats were divided into five main groups. The control group (group I) was divided into three subgroups (Ia, Ib and Ic). Subgroup Ia used as negative control, subgroup Ib were subjected to Sham operation and subgroup Ic received curcumin orally. Group II underwent to renal ischemia-reperfusion (I-R), group III received tacrolimus orally, group IV were subjected to I-R pre-treated with curcumin orally, and group V were subjected to tacrolimus pre-treated with curcumin. The specimens were processed for histological and utrastructural examinations. Light and electron microscopic examinations of group II showed renal ischemia-reperfusion revealed tubular dilation, loss of brush border, desquamation of tubular epithelial cells with irregular folded pyknotic nuclei while group III showed characterized histologically by tubular cell flattening, swelling mitochondria, dilated RER, cytoplasmic vacuolization and necrosis.

Groups IV and V showed that pretreatment with curcumin were significantly reduced the histologic evidence of renal damage. Our findings suggest that curcumin has a positive contribution as a dietary supplement for a longterm strategy to minimize tacrolimus nephrotoxicity and ischemia-reperfusion renal damage.

INTRODUCTION

Renal ischemia/reperfusion (I/R) injury, which occurs during renal transplantation, shock and kidney sections, is a major cause of acute renal failure with increased morbidity and mortality (Fouad et al., 2010). It has been estimated that ischemic 'nsult, especially during renal transplantation, is responsible for 20-30% of primary graft dysfunction (Fouad et al., 2010). Reperfusion of ischemic renal tissue initiates a complex series of cellular events that eventually lead to necrotic and apoptotic renal cell death. The exact molecular mechanisms underlying ischemia/repefusion (I/R) renal injury are not fully understood (Weight et al., 1996). Several factors contribute to the pathogenesis of ischemia/reperfusion injury, including ATP depletion, phospholipase and protease activation, increased endothelin-1 formation and neutrophil infiltration (Weight et al., 1996; Walker et al., 2001 and Fouad et al., 2010). Also, reactive oxygen species (ROS) play a key role in this process (Sussman and Bulkly, 1991). However, increased generation of reactive oxygen species and pro-inflammatory mediators in the reperfusion phase seems to play a crucial role. Several antioxidants and anti-inflmmatory agents were found to be effective in reducing renal injury resulting from ischemia/reperfusion

Tacrolimus (FK506) is a potent immunosuppressive agent that is effective in allograft prophylaxis after organ transplantation. However, its clinical use is limited by nephrotoxicity, that characterized by a hemodynamic change, renal vasoconstriction, dose-related and reversible. On the other hand, chronic FK506-induced nephrotoxicity is thought to be progressive and irreversible (Tamada et al., 2003). The precise mechanisms of FK506-induced nephrotoxicity are not completely understood (Andoh et al., 1995).

Medicinal plants have recently become a focus of interest because they may play key roles in treating ischemic renal disease (Aggarwal and Harkumar, 2009). Curcumin (diferuloyl methane) is the yellow pigment of turmeric in curry, and it is derived from the rhizome of plant curcuma longa (Bayrak et al., 2008). Curcumin is widely used as spice and it has been known to have anti-inflammatory, anti-cancer, antioxidant and several other activities (Bayrak et al., 2009). Curcumin exerts proimmune activity in several autoimmune disorders and has been reported to scavenge free radicals and to inhibit nitric oxide synthase activity and the lipoxygenase and cycloxygenase activities (Jones and Shoskes, 2000). A body of accumulated evidence suggests that curcumin is a potential anti-inflammatory and antioxidant agent that could suppress the induction of cytokines, the recruitment of immune cells and the progression of tissue damage (Sharma, 2006).

The aim of this work is to evaluate the antioxidant effects of curcumin and assess whether curcumin contributes to controlling important factors that have roles in aggravating renal I/R-injury and

nephrotoxicity.

MATERIALS AND METHODS

Thirty adult albino rats, weighing approximately 200gms each, were used in this study. All animals were kept under the same hygienic conditions and received balanced diet and water. The animals were divided into five main groups as follow:

- **Group I (Control group):** Consisted of 15 rats, were subdivided into 3 subgroups; 5 animals each (Ia, Ib and Ic):
  - **Subgroup Ia:** Non-operated and non-treated animals used as negative control.
  - **Subgroup Ib (Sham-operated animals):** the animals in this group were sham operated with the exposure of both the renal pedicles, but were not subjected to any ischemia reperfusion (Williams et al., 1997).
  - **Subgroup Ic:** the animals received curcumin 200mg/kg/day (Sigma chemicals USA) was suspended in 0.5% carbory methyl cellulose and administered orally for 7 days (Bayrak et al., 2008).
- **Group II:** Consisted of 5 animals were exposed to bilateral I/R, the rats were subjected to 45 min of bilateral renal pedicles occlusion (Fouad et al., 2010).
- **Group III:** Consisted of 5 animals received tacrolimus (FK506) Fujisma Pharmaceutical Co. Ltd, Japan, at a daily dose 3.2 mg/kg/day once intramuscularly (i.m.) dissolved in physiological

saline for 7 days (Wang et al., 2001).

- **Group IV:** 5 animals received curcumin (200mg/kg/day) orally, 7 days prior to bilateral I/R.
- **Group V:** 5 animals received curcumin (200mg/kg/day) orally, 7 days prior to treatment with FK506 (3.2 mg/kg/day) intramuscularly for 7 days.

Surgical Procedure:

Ischemia-reperfusion was produced following overnight fasting; the animals were anaesthetized with intramuscular injection of ketamine (70mg/kg). The abdominal area was prepared with betadine, and sterile drapes were applied. A midline incision was made and ischemia was induced by bilateral renal pedicle clamping for 45 min (ischemic phase), using fine non-trumatic vascular clamps under sterile conditions. Warm saline was injected into the abdomen, which was temporarily closed. The rats were kept on a heat pad and body temperature was maintained at 37°C throughout the experimental procedure. The clamps were removed to start the reperfusion phase which lasted for 3h. the Sham operation was performed using the same surgical procedures except for occlusion of the renal pedicles. The rats were sacrificed after completion of the ischemia/reperfusion and the kidney specimens were obtained (Williams et al., 1997).

Biochemcial Evaluation Method:

Venous blood samples was collected from descendent aorta from all rats (control and experimental). This was done pre (baseline) and post

the experiment. After that serum was harvested immediately by centrifugation at 40°C and was stored at -30°C for biochemical analysis. Serum urea and creatinine levels were determined by standard colorimetric method using a 721 spectrophotometer (Thomas, 1998). The obtained data were expressed as mean ± standard deviation (SD). Data were analyzed using analysis of variance (ANOVA). Results were considered significant when probability (P) was <0.05 (Dawson and Trapp, 2001).

Histological Methods:

All animals were sacrificed after each of the durations and immediately the abdomen was opened and both kidneys were removed and processed for light and electron microscopic study.

(1) ***Light microscopic study:***

Paraffin sections of 5-7μm thickness were cut and stained with haematoxylin and eosin (H and E) (Drury and Wallngton, 1980).

(2) ***Transmission electron microscopic study:***

Very small pieces ($1mm^3$) were collected from renal cortex of both kidneys. Tissues were rinsed in phosphate buffer (pH 7.4), then fixed in 2% glutaraldehyde, post-fixed in 1% osmium tetroxide and dehydrated. After embedding in Epon, 0.5mm thick semithin sections cut and stained with toluidine blue for light microscopic evaluation. Ultra-thin sections from the selected areas were cut and stained with lead citrate and uranyl acetate (Hayate, 1981). The grids were examined and photographed with a Jeol 100S electron microscope in faculty of Medicine, Tanta University.

RESULTS

Biochemical Results:

There was no significant difference between the basline serum creatinine, urea in the control group and in the different groups. Animals in groups II and III exhibited significant increase in serum concentrations of creatinine and urea levels as compared to control animals, suggesting a significant decrease of glomerular function ($P<0.001$). Pretreatment with curcumin showed significantly improved urea and creatinine levels ($P<0.05$) (Table 1).

Table (1): Serum urea and creatinine levels in all groups.

Variable	Control	I/R	FK506	I/R+ curcumin	FK506 + Curcumin
Urea (mg/dL)	14.79±1.12	81.23±1.05[(b)]	79.33±1.03[(a)]	35.3±1.01	32.81±18.67
Creatinine (mg/dL)	0.50±0.07	2.02±0.06[(b)]	2.12±0.06[(b)]	1.71±0.55	1.72±0.52

Values are mean + SD.

a $p<0.001$ compared to control, I/R+ curcumin and FK506+curcumin.

b $p<0.05$ compared to control, I/R+ curcumin and FK506+curcumin.

Histological Results:

Light microscopic results:

- **Group I:** The renal cortex was formed of renal corpuscles, proximal and distal convoluted tubules. Each renal corpuscle consisted of a glomerular capillary tuft surrounded by Bowman's

capsule. The proximal convoluted tubules had a narrow lumen and lined by simple cuboidal epithelium with well developed brush border and large rounded nuclei. The distal tubule had wider lumen and appeared lined by low cubical epithelium with rounded nuclei (Fig. 1).

- **Group II (animals subjected to renal ischemia-reperfusion):** Examination of the renal cortex showed massive tubular distortion with wide lumina. Signs of necrosis in the form of epithelial degeneration, vacuolization, pyknotic nuclei and loss of brush border. Hyaline casts, desquamated cells were seen in tubular lumen with congested blood vessels (Figs 2,3).
- **Group III (animals received tacrolimus orally):** Sections of the renal cortex revealed tubular dilatation with epithelial cell necrosis and apparent increase in the size of renal corpuscle, apical blebbing, intraluminal sloughing of tubular epithelial cells and hyaline casts. Interstitial edema and mononuclear cells infiltration with congested blood vessles were observed (Figs 4, 5, 6).
- **Group IV (animals subjected to I-R pre-treated with curcumin):** Sections showed less cytoplasmic vacuolization and necrotic changes were hardly detected (Fig. 7).
- **Group V (animals subjected to tacrolimus pre-treated with curcumin):** Sections showed preservation of normal structure despite of the presence of minimal to mild luminal cast formation (Fig. 8).

Electron microscopic results:

- **Group I:** Ultrastructural examination of the epithelial cells lining the proximal convoluted tubule with smooth rounded contour nucleus, well developed basal enfoldings with elongated mitochondria perpendicularly to the basement membrane (Fig. 9). In the distal convoluted tubules, the lining cells had apical nuclei, numerous mitochondria and few microvilli (Fig. 10). Normal architecture of the glomerulus, the basement membrane was composed of three layers, lamina dense and on its either sides, the lamina rara externa and lamina rara interna. The endothelium consisted of simple squamous layer of fenestrated cells (Fig. 11).
- **Group II:** Examination of the tubular epithelial cells of the renal cortex of I/R group revealed wide-spread vacuolization, swollen mitochondria with distorted cristae, irregular folded pyvnotic nucleus, dilated RER and loss of microvilli. Swollen micvovilli shedding into tabular lumen and apoptotic cells were noticed (Figs. 12, 13, 14, 15).
- **Group III:** Sections of renal cortex of tacrolimus-treated group revealed thickening of tubular basement membrane and necrosis of tubular epithelial cells with cytoplasmic vacuolization, dilated RER, swelling mitochondria and focal loss of microvilli. The common basement membrane of the filtration barrier in the renal corpuscles showed disrupted appearance of its layer and thickening in the lamina densa with apparent thining of the lamina rara externa and interna. Interstitial edema and mononuclear cell

infiltration were observed (Figs. 16, 17, 18, 19).

- **Group IV:** Ultrastructural examination of tubular epithelial cells of I-R pre-treated with curcumin group showed preservation of the normal structure of renal cortex (Fig. 20).
- **Group V:** Ultrastructural examination of tacrolimas pre-trated with curcumin group revealed restoration of normal structure of the convoluted tubules and focal thickening of the lamina densa is still present (Figs. 21,22).

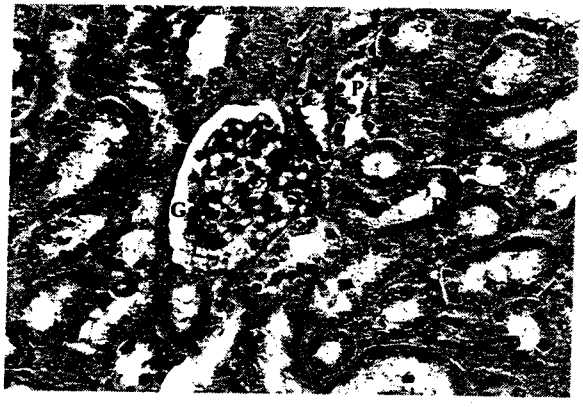

Fig. 1: Photomicrograph of a control rat renal cortex showing glomeruli (G), proximal convoluted tubules (P) and distal convoluted tubules (D). Hx. & E.; x 400

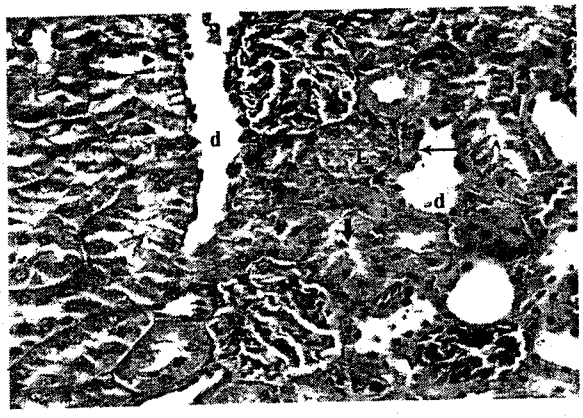

Fig. 2: Photomicrograph of a section in rat renal cortex underwent to renal ischemia-reperfusion (I-R) showing extensive tubular necrosis with dilatation (d), vacuolar degeneration (►)and epithelial desquamation (⟨). Notice, tubular cell atrophy (→) peritubular congested blood vessels (V), tubular lumen obstruction (L). Hx. & E.; x 400

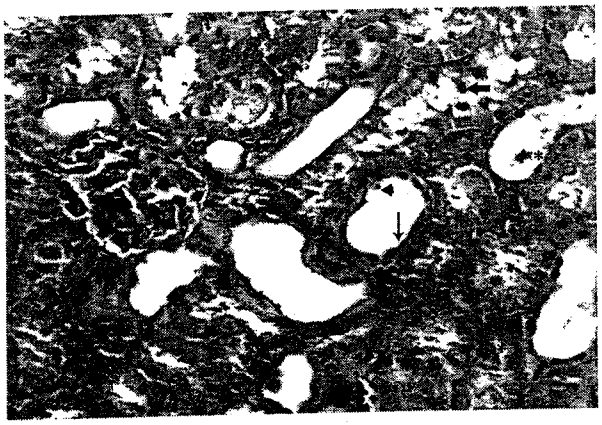

Fig. 3: Photomicrograph of a section in rat renal cortex underwent to renal ischemia-reperfusion (I-R) showing tubular cell flattening, pyknotic nucleus (►), loss of brush (→), widespread necrosis with tubular dilatation and epithelial desquamation (⇒). Notice intraluminal hyaline casts (⟨).Hx. & E.; x 400

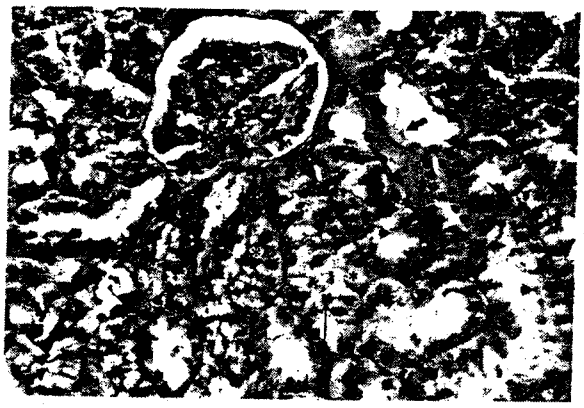

Fig. 4: Photomicrograph of a section in the renal cortex of rat treated with tacrolimus showing tubular dilatation with epithelial cells necrosis (⟨), cytoplasmic vacuolization (*), apical blebbing (►) and sloughing of tubular epithelial cells into the lumen (→).

Hx. & E.; x 400

Fig. 5: Photomicrograph of a section in the renal cortex of rat treated with tacrolimus showing tubular atrophy, necrosis of the epithelium with intraluminal hyaline casts (→) and increase in the size of renal corpuscle (*). Notice interstitial edema and mononuclear cell infiltration (C) with congested blood vessles (V).

Hx. & E.; x 400

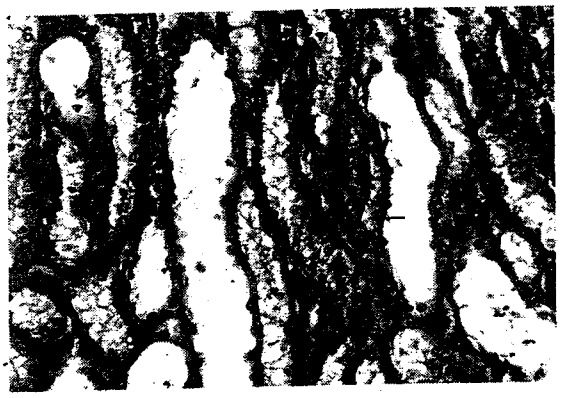

Fig. 6: Photomicrograph of a section in the renal cortex of rat treated with tacrolimus showing tubular dilatation with severe apical blebbing and hyaline casts (▶) with interstitial cell infiltration (→) and loss of normal tubular structure. Hx. & E.; x 400

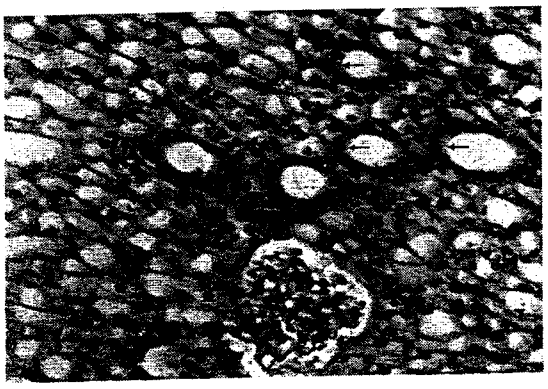

Fig. 7: Photomicrograph of a section in the renal cortex of rat subjected to I-R pre-treated with curcumin showing brush like edges of epithelial cells (→) of proximal convoluted tubutes, less cytoplasmic vacuolization and necrotic changes not observed. Hx. & E.; x 400

Fig. 8: Photomicrograph of a section in the renal cortex of rat subjected to I-R pre-treated with curcumin showing preservation of normal morphology of renal cortex with slight cast formation (→). Hx. & E.; x 400

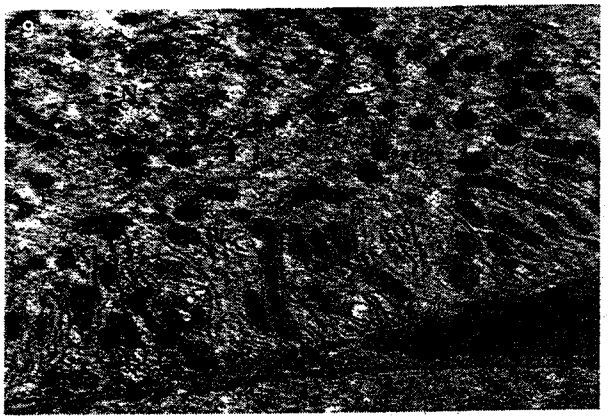

Fig. 9: Electron micrograph of a section in the renal cortex of control rat showing part of proximal convoluted tubule (PCT with intact basement membrane (▶), nucleus with smooth rounded contour (◊) and normal distributed chromatine (N), well developed basal infolding with elongated mitochondria oriented perpendicularly to the basement membrane (→).

Mic. Mag. x 2500

Fig. 10: Electron micrograph of a section in the renal cortex of control rat showing part of distal convoluted tubule (DCT) with numerous mitochondria (→), apical nucleus (N) few microvilli (MV) and intact basement membrane (⟨).Mic. Mag. x 1500

Fig. 11: Electron micrograph of a section in the renal cortex of control rat showing part of a podocyte with primary (pr) and discrete foot processes (F). Note: the three layers of the common basement membrane. Lamina rara externa (Lre), lamina densa (Ld), and lamina rara interna (Lri) and endothelial cells which appeared fenestrated (⟨)

Mic. Mag. x 1500

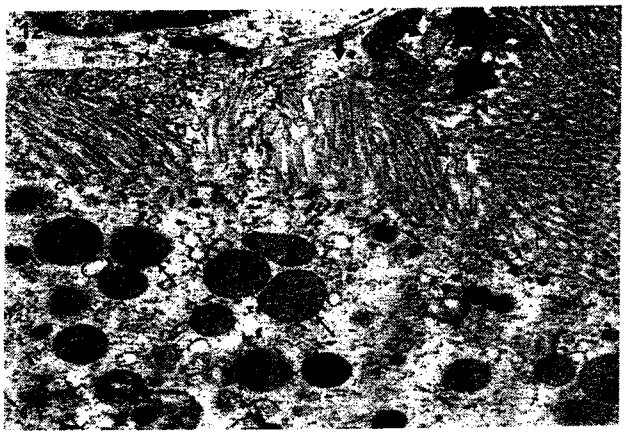

Fig. 12: Electron micrograph of a section in the renal cortex of rat underwent to renal ischemia-reperfusion (I-R) showing swollen mitochondria with vacuolated appearance (→), and other with distorted cristae (▶) in the tubular epithelium. Notice swollen microvilli shedding into tubular lumen (⟨). Mic. Mag. x 3000

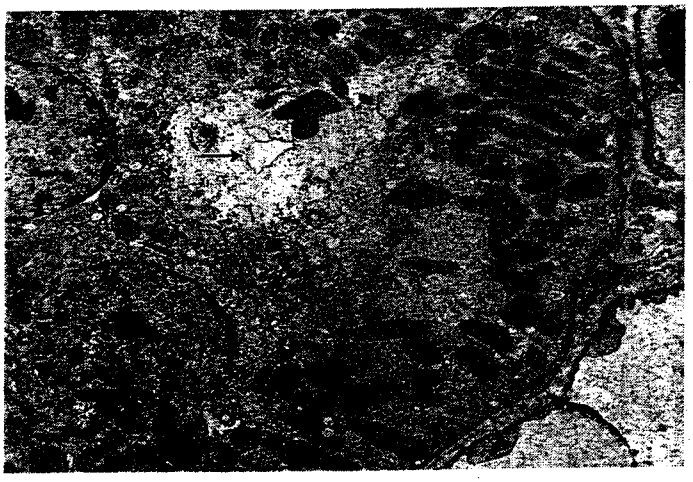

Fig. 13: Electron micrograph of a section in the renal cortex of rat underwent to renal ischemia-reperfusion (I-R) showing loss of microvilli with irregular lumen (→), irregular folded pyknotic nucleus with dense clumped marginal chromatine (N).Mic. Mag. x 1500

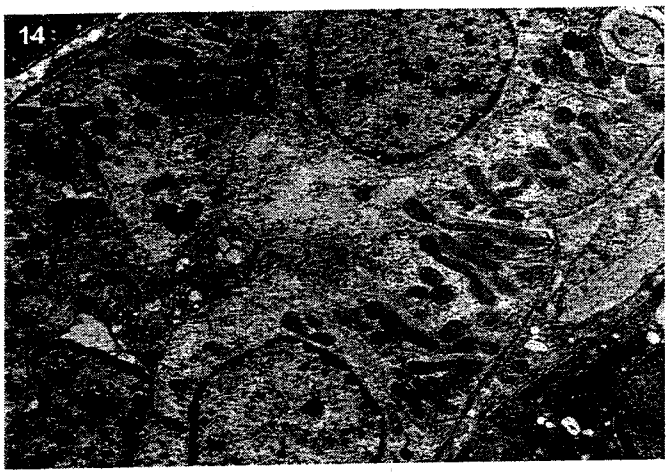

Fig. 14: Electron micrograph of a section in the renal cortex of rat underwent to renal ischemia-reperfusion (I-R) showing wide-spread cytoplasmic vacuolization (→) and loss of normal tubular structure.

Mic. Mag. x 1500

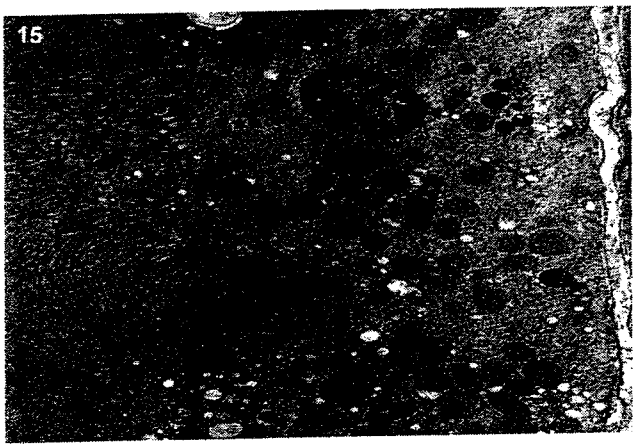

Fig. 15: Electron micrograph of a section in the renal cortex of rat underwent to renal ischemia-reperfusion (I-R) showing an apoptotic cell with shrunken nuclear profile with dense masses of chromatine (►), tubular cells with apical microvilli (() and numerous dilated RER (→). Mic. Mag. x 2000

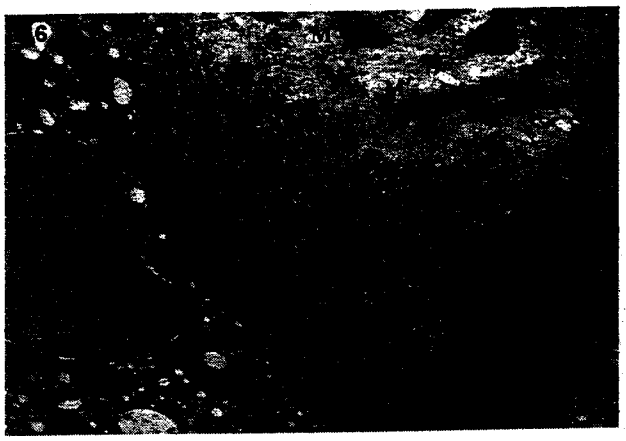

Fig. 16: Electron micrograph of a section in the renal cortex of rat treated with tacrolimus showing cytoplasmic vacuolization (►), dilated RER (→) and swelling mitochondria (M) of tubular epithelium. Mic. Mag. x 2000

Fig. 17: Electron micrograph of a section in the renal cortex of rat treated with tacrolimus showing thickening of tubular basement membrane (►) focal loss of epithelial microvilli with swelling mitochondria sloughed to the tubular lumen (→). Mic. Mag. x 1500

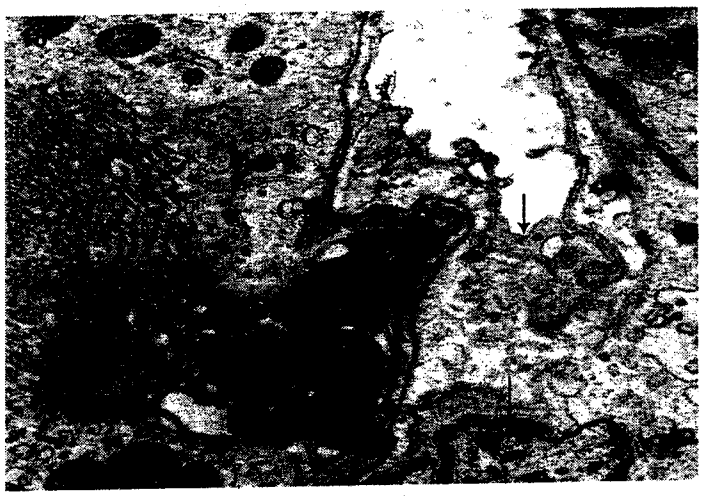

Fig. 18: Electron micrograph of a section in the renal cortex of rat treated with tacrolimus showing interstitial edema and mononuclear cell infiltration (→), swelling mitochondria (►) loss of normal basal infolding and necrosis of tubular epithelial cells (C). Mic. Mag. x 3000

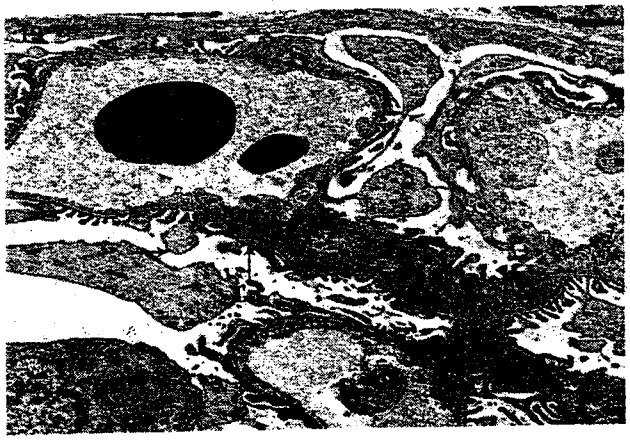

Fig. 19: Electron micrograph of a section in the renal cortex of rat treated with tacrolimus showing disrupted appearance of the layers of basement membrane (►) irregular thickening of the lamina densa (Ld) and apparent thining in lamina rara externa and interna are observed. Broadening and fusion of the feet processes of the podocytes can also be noted (→).Mic. Mag. x 1500

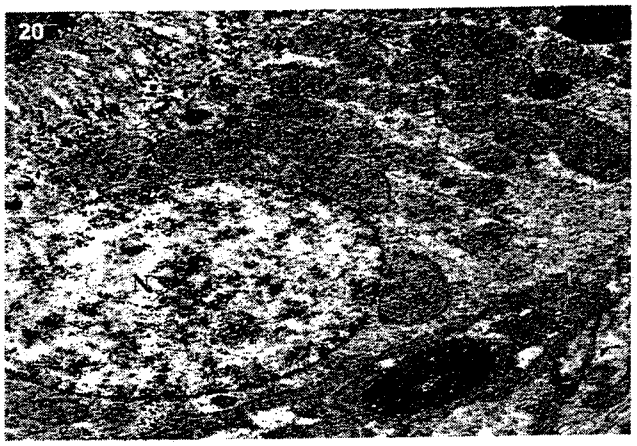

Fig. 20: Electron micrograph of a section in the renal cortex of rat subjected to (I-R) pre-treated with curcumin showing preservation of the normal structure of tubular epithelium without vacuolization, intact microvilli (→), normal mitochondria (►) with smooth rounded contour of the nucleus without abnormal chromatin distribution (N).Mic. Mag. x 2500

Fig. 21: Electron micrograph of a section in the renal cortex of rat received tacrolimus pre-treated with curcumin showing focal thickening of tubular basement membrane is still present (►), mild improvement in the form of restoration of basal infolding and elongated mitochondria (→) of epithelial lining.
Mic. Mag. x 2500

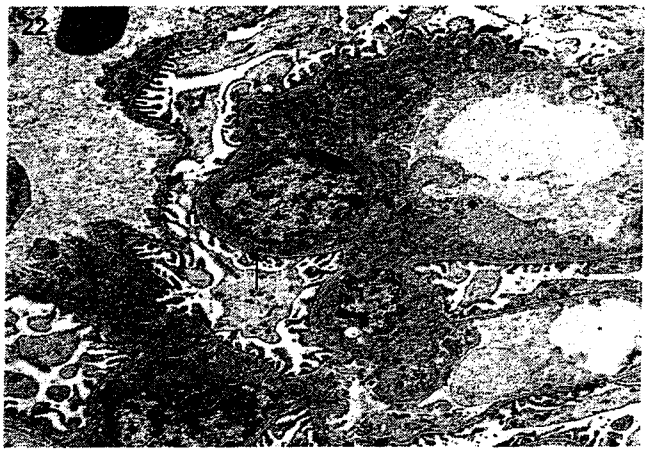

Fig. 22: Electron micrograph of a section in the renal cortex of rat received tacrolimus pre-treated with curcumin showing that focal thickening of the lamina densa is still present (→).Mic. Mag. x 1500

DISCUSSION

The present study was performed to investigate the possible protective role of curcumin on renal ischemia/reperfusion injury and FK506 nephrotoxicity. Renal ischemia/reperfusion (I/R), which is an important cause of renal dysfunction is inevitable in renal transplantation. surgical revascularization of the renal artery and partial nephrectomy (Yurdakul et al., 2010).

In the present study, group II (animals subjected to renal ischemia-reperfusion) and group III (animals received tacrolimus orally) showed significant increase in the serum concentration of urea and creatinine levels as compared to control group. Similar findings were also reported by others (Mollison et al., 1998; Tamada et al., 2003 and Fouad et al., 2010). They related these findings to tubular atrophy and tubule-interstitial ischemia. However, pre-treatment with curcumin significantly reduced the

ischemia/reperfusion and FK506 induced elevation in serum urea and creatinin. This is believed due to the ability of curcumin to atenuate oxidative and nitrative stress (Bayrak et al., 2008). In agreement with perivous studies ischemia/reperfusion group showed dilated renal tubules, vacuolation, luminal exfoliated cells, necrosis and disruption of brush border with loss of normal architecture (Mashiach et al., 2001; Avunduk et al., 2003; Yurdakul et al., 2010 and Fouad et al. 2010). They attributed these changes to a wide range of potential mechanisms that cause tissue damage mainly the oxidative mechanisms induced by neutrophils, which are concentrated in the area of ischemia, produce superoxide radicals which from releas reactive oxygen species (ROS).

Weight et al., (1996) proposed that polymorphonuclear leukocytes (PMNs) that are activated during ischemia, presumably by cytokines enter the kidney at the onset of reperfusion, causing tissue damage by releasing ROS. In addition some investigators explained these changes due to inflammation following ischemia mediated by neutrophils and T-cells infiltration with cellular activation and cytokines release (Jones and Shoskes, 2000). Also, they attributed these findings to lipid peroxidation and nitric oxide synthase activation by infiltrating macrophage that produce peroxynitrites which are highly cytotoxic in ischemia reperfusion injury. The ultrastructure of the current study illustrated swollen mitochondria with distorted cristae, shedding of microvilli, pyknotic nucleus with dense clumped marginal chromatin, wide spread cytoplasmic vacuolization, numerous dilated rough endoplasmic reticulum, loss of normal tubular structures and apoptotic cells can be detected. These results

were in agreement with other investigators who found that ROS induce cell injury through lipid peroxidation of the mitochondria (Avunduk et al., 2003 and Jones and Shoskes, 2000).

FK506 nephrotoxicity is the most frequent and serious adverse effect reported (MaCauley, 1993), however, little is reported regarding prevention of it's nephrotoxicity (Tamada et al., 2003). In the present study the histological changes observed in FK506 treated rats were tubular flattening and dilatation, with epithelial cell necrosis, cytoplasmic vacuolization with apical blebbing, intratubular hyaline casts with sloughing of epithelial cells and increase in the size of renal corpuscle. Also, interstitial edema, vascular changes, mononuclear cell infiltration were observed. Ultraslructural findings of FK506 treated rats showed sloughed swollen mitochondria in tubular lumen, dilated rough endoplasmic reticulum, increased thickness of glomerular basement membrane. These results are coincide with Mollison et al., (1998); Nakahama et al., (2000); Tamada et al., (2003) and Lioberas et al., (2008). Who attributed these changes to disturbance of renal hemodynamics due to release of vasoactive substances such as thromboxans and decrease in vasodilating factors such as prostacyclin. Wang et al., (2001) explained that the increased levels of nitric oxide in the FK506 nephrotoxicity. Tamada et al., (2003) stated that the tubulointerstatial changes may be due to increased nuclear factor kappa-β (NF-κβ) activation, a potent inflammatory inducer.

Early study suggested that these changes due to accumulation of the FK506 in the cells causes delayed regeneration and morphological

changes of increased programmed cell death (apoptosis). Mitochondrial changes may be due to direct toxic effects of FK506 as reported by previous study (Andoh et al., 1995). Glomerular basement membrane thickening seen in the present study may due to increased deposition of glycoproteins (Hotta et al., 2001).

The renal tissues obtained from rats pretreated with curcumin demonstrated marked decrease in histological features of ischemia-reperfusion injury. This is in agreement with Shoskes (1998); Jones and Shoskes, (2000), Who explained current biochemical and morphological picture noticed in group IV on the basis that curcumin attenuated regulated upon activation, normal T-cell, cell expressed and secreated (RANTES) and marcrophage chemotactic protein-I (MCP-I). Other researchers reported that curcumin and related compounds inhibit free radical generation and act as free radical scavenger and antioxidants through prevention of lipid peroxidation (Bayrak et al., 2008).

Previous studies explained also, the protective effect of curcumin in I/R to a wide range of potential mechanisms (Shoskes 1998; Shahed et al., 2001 and Bayrak et al., 2008). Curcumin possess its role through suppression of tyrosin kinase pathways, inhibit smooth muscle prolferation, block T-cell proliferation, down regulate expression of proinflammatory mediators, adhesion molecules and growth factor receptor genes (Haung et al., 1992; Biswas and Rahman, 2008). Moreover, it was found that curcumin potientiates the effect of mycophenolate mofetil in prevention of immune injury (Shoskes et al., 2000). In the present study pretreatment with curcumin resulted in preservation of

histologic integrity in FK506 treated rats. Shoskes et al., (2000) stated that these results can be explained on the basis that curcumin exert its effect by blocking the induction of cytokines through the blockage of NF-κβ responsible for Fκ506 nephrotoxicity. Also, they reported that curcumin could reduce renal injury mediated through macrophages by interfering with nitric oxide synthase activity. Moreover, it was found that curcumin can scavenge free radicals and block the tyrosin kinase enzyme activity that is responsible for apoptosis in renal epithelial cells (Leclercqu et al., 2004).

In view of these findings, it is concluded that curcumin can ameliorate functional and histological changes in ischemia/reperfusion renal injury and tacrolimus induced nephrotoxicity.

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الدور الوقائى المحتمل للكركومين على الضرر الناتج عن الاحتباس وإعادة الإرواء الدموى على السمية الكلوية المستحدث بعقار التاكروليمس فى قشرة كلى الفأر البالغ الأبيض: دراسة بالميكروسكوب الضونى والميكروسكوب الإلكترونى

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يستخدم الكركومين منذ عقود طويلة فى علاج الالتهابات ، الأورام ومضادات الأكسدة ولذلك فإن هذه دراسة عن الدور الوقائى المحتمل لكركومين على تركيب قشرة الكلى فى حالات الاحتباس وإعادة الأرواء الدموى والسمية الكلوية الناتجة عن دواء تاكروليمس المثبط للمناعة . استخدم فى هذه الدراسة ثلاثون من ذكور الفئران البيضاء البالغة والتى قسمت إلى خمسة مجموعات:**المجموعة الأولى** (مجموعة ضابطة): والتى تم تقسيمها إلى ثلاث مجموعات فرعية: الفرعية الأولى مجموعة غير معاجلة والفرعية الثانية خضعت لعملية شام والفرعية الثالثة تم إعطاؤها الكركومين. **والمجموعة الثانية** هى مجموعة الإصابة بالإحتباس الدموى وإعادة الإرواء. **والمجموعة الثالثة** هى مجموعة أعطيت دواء التاكروليمس. **والمجموعة الرابعة** تم إعطاؤها الكركومين لمدة سبعة أيام قبل إحداث الاحتباس الدموى وإعادة الإرواء. **والمجموعة الخامسة** تم إعطاؤها الكركومين لمدة سبعة أيام ثم أعطيت عقار التاكروليمس. وقد تم إعداد الشرائح للدراسة الهستولوجية بواسطة الميكروسكوب الضوئى والإلكترونى وقد أظهرت النتائج وجود اتساع بالأنابيب الملتوية مع وجود نفايا خلوية فى تجويف الأنابيب بالإضافة إلى وجود تعرج بأغشية بعض الأنوية وانتفاخ فى الميتوكوندريا والشبكة الإندوبلازمية وظهور فجوات سيتوبلازمية . وقد بينت النتائج فى المجموعتين الرابعة والخامسة المعطاة الكركومين انخفاضا ملحوظا فى مظاهر تلف قشرة الكلى . ويستنتج أن الكركومين قد يكون اختيارا مناسبا فى العلاج الوقائى ضد الأضرار الناتجة عن الاحتباس الدموى وإعادة الإرواء والسمية الكلوية الناتجة عن عقار التاكروليمس المثبط للمناعة.