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**RESEARCH ARTICLE**

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# PROTECTIVE ROLE OF CURCUMIN ON GENTAMICIN INDUCED RENAL TOXICITY IN MALE ALBENO RATS

## ABSTRACT:

The effect of curcumin (CUR) on gentamicin (GM) induced nephrotoxicity in rats was studied. Forty albino rats were subdivided into four groups. Group (I) represented a control group. Group (II) received gentamicin sulphate (100 mg/kg BW) as interaperitoneal injection (i.p) once daily for 8 consecutive days. Group (III) received curcumin at the same dose for 15 days where animals were injected with GM at 100 mg/kg/day during the last 8 days of the treatment. Group (IV) received curcumin at oral dose of 100 mg/kg/day for 15 days. Nephrotoxicity was evaluated histopathologically by light microscopy and biochemically. Seum creatinine and urea levels and kidney, catalase (CAT) activity, malondialdehyde (MDA) level and urinary N-acetyl-β D-gluoseamindase (NAG) were assayed. The apoptotic fragments of DNA in kidney tissue were measured as optical density by Gel-pro-program. Gentamicin administration to rats significantly increased serum level of urea, creatinine and MDA and the activity of NAG but decreased CAT activity as compared with control. In addition, CUR administration with GM injections caused a significant decrease in serum urea, creatinine and MDA levels, and activity of NAG as compared with GM group (II). CUR administration increased CAT activity. Histological changes in the kidney group (II) showed tubular necrosis, which was ameliorated in group (III). GM decreases the intensity of DNA and induced apoptotic DNA fragment in group (II) where curcumin amelorate DNA damage in group (III). Curcumin treatment showed marked improvement of the biochemical, molecular and histopathological alterations induced by GM which pointed out the protective effect of curcumin against toxic effects of gentamicin on kidney tissue.

## KEY WORDS:

Gentamicin, Curcumin, Oxidative stress, Nephrotoxicity

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## INTRODUCTION:

Gentamicin (GM) is a cheap important and widely used antibiotic of aminoglycoside for the treatment of gram- negative bacterial infection. Its chemical stability and rapid bactericidal action have made it a drug of choice in a variety of clinical situation treatments (Ali, 2003). Nephrotoxicity is the main side effect that seriously limits its use. Gentamicin treatment causes acute renal failure with acute tubular necrosis in about 20% of the patient (Erdem *et al*., 2000). The toxicity of (GM) in the kidney seems to relate to the generation of reactive oxygen species (ROS) in these cells. ROS is believed to play a pivotal role in cellular damage and necrosis via several complex mechanisms including peroxidation of membrane lipids, protein carbonyltion and DNA damage (Parlakpimar *et al*., 2006). Also, ROS has been proposed as a causative agent of cell death in many different pathological states as well as in glomerular disease, renal ischemia and reperfusion injury, and various models of toxic renal failure (Al-Majed *et al*., 2002).

A large body of *in vivo and in vitro* evidence indicates that ROS are important mediators of GM induced nephrotoxicity (Kopple *et al*., 2002). Gentamicin has long been known to cause acute renal failure in patients, in addition to histological and functional signs of proximal tubule toxicity. The molecular mechanism of such changes still remains poorly defined. Gentamicin is almost entirely eliminated by the kidney, but a small toxic portion is selectively reabsorbed and accumulates in lysosomes of proximal renal tubular cells and cause apoptosis at clinically relevant doses (Servais *et al*., 2006). Several approaches involving the use of chemical compounds have been used to reduce (GM) nephroptoxicity. But little attention has been paid on the use of naturally occurring substances with potent antioxidant properties to protect against nephrotoxic damage induced by (GM).

In the light of this, we have explored the possible protective role of curcumin, a natural antioxidant substance, on (GM) induced

oxidative stress. Curcumin is a yellow coloured phenolic pigment gained from rhizome of turmeric *(Curcuma longa).* It is widely used as a spice and a colouring agent in several foods, as well as in cosmetics and drugs (Pedraza-Chaverrí *et al*., 2004). Pharmacologically, curcumin exhibits a wide range of effects including anti-inflammatory and anti-infection activities (Kalpana *et al*., 2007). Also, curcumin is reported to be a potent inhibitor of reactive oxygen species (ROS) formation (Venkatesan *et al*., 2000). Experimental studies with diabetic animals demonstrate that curcumin supplementation can suppress cataract development and collagen cross linking, promote wound healing and ameliorate renal lesions and lower blood lipids (Jain *et al*., 2006). Therefore, the present study, was designed to investigate the protective effects of curcumin on the experimentally (GM) induced renal toxicity.

## MATERIAL AND METHODS:

### I- Animal husbandry:

The present study was carried out using healthy adult male Wistar albino rats *(Rattus norvegicus)* of an average body weight equals 170 ± 20 gm. The rats were obtained from the breeding unit of the "Egyptian Organization for Biological Products and Vaccines" Helwan, Egypt. Animals were selected and housed in designed cages with hard wood chips. The rats were acclimated to the laboratory conditions, 25$^{o}$C and 12h light / dark cycle for one week. The rats were fed on a commercial rodent pellet diet manufactured by Egyptian company for oil and soap and supplied with tap water during the experimental period.

### II- Experimental design:

At the end of acclimation period, the animals were divided to four groups, ten rats in each as:

**Group I:** received normal saline through intraperitoneal injections and served as a control group.

**Group II:** received gentamicin sulphate (100 mg/kg BW) through intraperitoneal injections once daily for 8 consecutive days.

**Group III:** treated with curcumin (100mg/kg BW) orally for 15 days and treated with gentamicin (100mg/kg BW) during the last 8 days.

**Group IV:** received curcumin (100 mg/ kg BW) orally once daily for 15 consecutive days.

The dose of GM was chosen based on the previous studies of Erdem et al., 2000. The dose of CUR was used in this study according to the previous study of Ali *et al*. (2005).

### III – Biochemical analysis and techniques:

Before sacrifice, rats were kept individually in metabolic cages for 24 h for collecting urine samples for estimation of renal enzyme (NAG) by the procedure of Gibey *et al*. (1986). Then, the animals were sacrificed and blood samples were obtained. After blood clotting, blood samples were centrifuged at 3000 xg for 10 min and sera were separated for determination of urea level according to the method of Patton and Crouch (1977) and serum creatinine level according to the method of Houot (1985). After dissection of animals, kidneys were excised from each animal, washed in 0.9% Nacl, the left kidney was frozen till further enzymatic analysis. The right one was divided into two parts, one of them for genetic analysis and the other part was fixed in 10 % formalin for the histological studies.

### Preparation of tissue homogenate:

After animal's dissection, weighted parts from left kidney from each animal in different groups were homogenized in deioninized dist water by tissue homogenizer to a final dilution 1: 10. The homogenates were frozen at 80°C for lipid peroxidation as malondialdehyde (MDA) determmation according to the method of Mihara and Uchiyama (1978) and catalase activity assayed according to the method of Aebi (1995).

### IV- Histopathological exanimation:

For microscopic evaluation, kidneys were fixed in 10% buffered formalin solution for 24 h at temperature of 37$^{o}$C, following dehydration in ascent series of ethanol (70, 80, 90, and 100%). Tissue samples were processed with paraffin wax. Sections (5 µm) were stained with hematoxyllin and eosin and were examined under light microscope.

### V- DNA fragmentation:

### DNA extraction:

DNA extraction and detection of apoptosis were done according to Salting out extraction method of Aljanabi and Martinez (1997) as modified by Hassab El-Nabi (2004).

### Agarose gel electrophoresis:

### Gel preparation:

Gel was prepared using 1.8% electrophoretic grade agarose (BRL) obtained from Hispangat D-1 LE, Spain. The agarose was boiled with tris borate EDTA buffer (1 × TBE buffer, 89 mM tris, 89 mM boric acid, 2 mM EDTA, pH 8.3) and then, 0.5 microgram / mL ethidium bromide was added to agarose mixture at 40$^{o}$C. Gel was poured and allowed to solidify at room temperature for 1 h before samples were loaded.

### Separation:

DNA was separated by horizontal electrophoresis with running buffer 1 × TBE (Tris-base, boric acid and EDTA) at a constant voltage (50 v) for 1.5 h using medium

electrophoresis cell (Bio-Rad power pac 300, USA).

- **Apoptosis analysis:**

Apopotic bands appeared and located at 200bp, 400 bp and 600 bp. The intensity of apoptotic bands could be measured by biogene software as a maximum optical density values.

## RESULTS:

No death or remarkable signs of external toxicity were observed in groups of rats that were given (GM) either alone or in combination with curcumin. Rats treated with gentamicin (100 mg/kg body weight) lost about 5.7% of their body weight as compared with that of control group. On the other hand, curcumin (CUR) treated rats gained about 2% of body weight compared with that of control group. However, rats given both GM and CUR lost 1.6%, as compared with control group. So the treatment with (CUR) partially minimized the reduction effect in body weight of GM treatment (Table 1).

Table 1. The effect of CUR on gentamicin induced changes in body weight, blood urea, and creatinine and NAG levels

| Parameters | Group I Control | Group II GM | Group III GM + CUR | Group IV CUR |
|---|---|---|---|---|
| Body weight (gm) | 196.01 ± 14 | 185.41 ± 10 | 193.45 ± 16 | 200.52 ± 18 |
| | 1000% | 94.3% | 98.4% | 102% |
| Urea (mg/dl) | 28.91 ± 4.3 | 61.71 ± 3.3[(a)] | 29.12 ± 2.8[(b)] | 27.53 ± 1.08 |
| Creatinine (mg/dl) | 0.43 ± 0.06 | 1.28 ± 0.25[(a)] | 0.53 ± 0.061[(b)] | 0.45 ± 0.09 |
| NAG (nmol/ml/hr) | 78.42 ± 2.5 | 224.48 ± 23.2[(a)] | 111.62 ± 15.6[(b)] | 75.21 ± 3.66 |

* Results are expressed as mean values ± SD, n = 10

(a) Significantly different from control (P<0.05)

(b) Significantly different from GM (P<0.05)

### The effect of CUR on GM treated rats on serum urea, creatinine levels, and NAG activity:

As shown in table 1, there was a significant increase in serum urea and creatinine level and NAG activity in rats of group (II) as compared with control. There was a significant decrease in serum urea and creatinine level and NAG activity in rats of group (III) as compared with group (II).

### The effect of CUR on GM treated rats on kidney CAT and lipid peroxidation:

As shown in figure 1 and 2, there was a significant increase in kidney MDA (P<0.05) as compared to the control group, while CAT activity was significantly decreased. Curcumin administration with (GM) caused significant decrease in MDA and increase in CAT activity in kidney when compared with group (II). Also, there were non significant changes between group (I) and group (III).

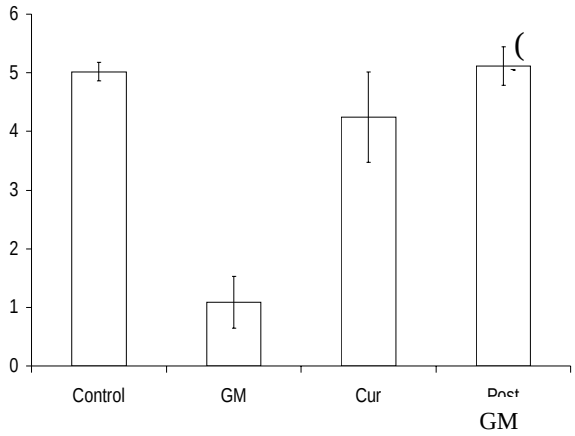



Fig. 1. Effect of curcumin on kidney CAT of gentamicin treated rats

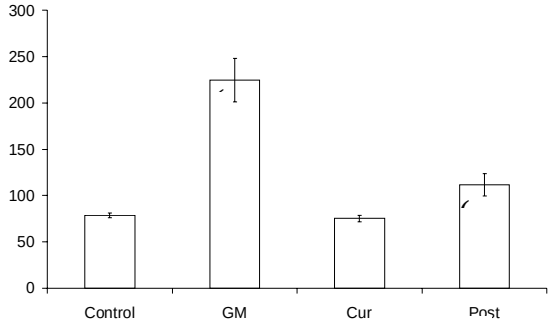



Fig. 2. Effect of curcumin on MDA of gentamicin treated rats

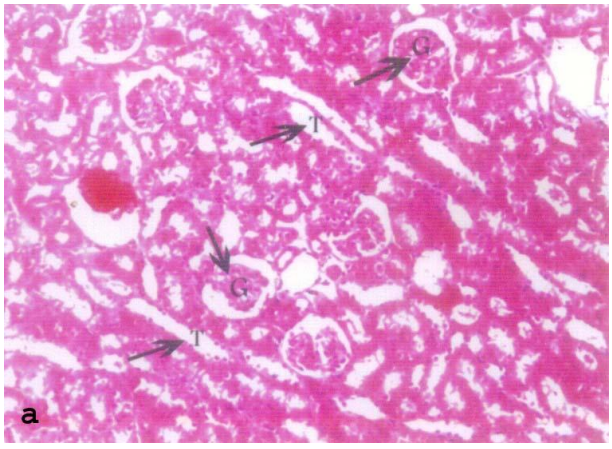
*Value are expressed as mean ± SD (mg/dl), n= 10

(a) Significantly different from control (P<0.05)

(b) Significantly different from GM (P<0.05)

### Effect of curcumin on GM treated rats, histological changes in kidney tissue:

Rats treated with gentamicin alone showed tubular necrosis and forming cellular casts and desquamation of tubular epithelia in the lumen as indicated in figure 3b. In addition, histological damage decreased after curcumin administration (Fig. 3d) where mild degenerative changes and reduced tubular vaculization appeared. Both control and only curcumin treatment showed no histopathological changes (Fig. 3a&c).



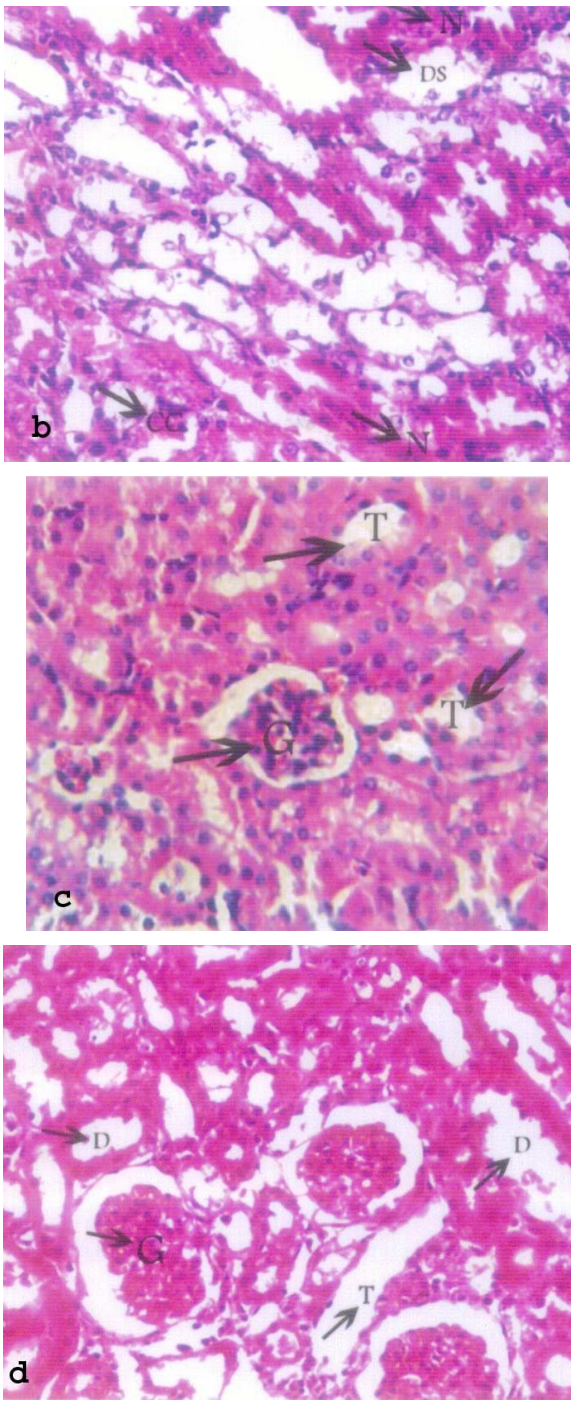


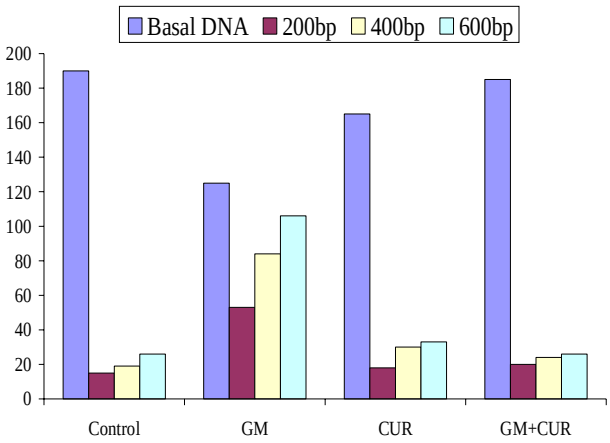

Fig. 3. Effect of curcumin on GM treated rats histopathological changes in kidney tissue

**a:** control, X10; **b:** gentamicin treatment X20; **c:** curcumin treatment X20; **d:** gentamicin + curcumin treatment X20.

G, glomeurli; T, renal tubules; D, degenerative changes in renal tubules; N, necrosis; CC, cellular casts; DS, desquamation of tubular epithelium. H & E

## DNA fragmentation:

Figure 4 shows the optical density of basal and apoptotic fragments of DNA at 200.400 and 600bp of kidney cells of different groups. The basal DNA decreased in rats treated with genetamicin while curcumin elevated the reduction of the intensity of DNA towards control. Gentamicine increased the intensity of apoptotic bands (Figs 4&5) 200.400 and 600pb with values 53, 84, 106 than control (15, 19 & 26), respectively. On the other hand, curcumin administration increased the optical density towards the control with values (20, 24, 26) at 200, 400 and 600pb, respectively.




| | *Basal DNA* | *200bp* | *400bp* | *600bp* |
|---|---|---|---|---|
| Control | 190 | 15 | 19 | 26 |
| GM | 125 | 53 | 84 | 106 |
| CUR | 165 | 18 | 30 | 33 |
| GM+CUR | 185 | 20 | 24 | 26 |

Fig. 4. Optical density of fragmented DNA in kidney cells

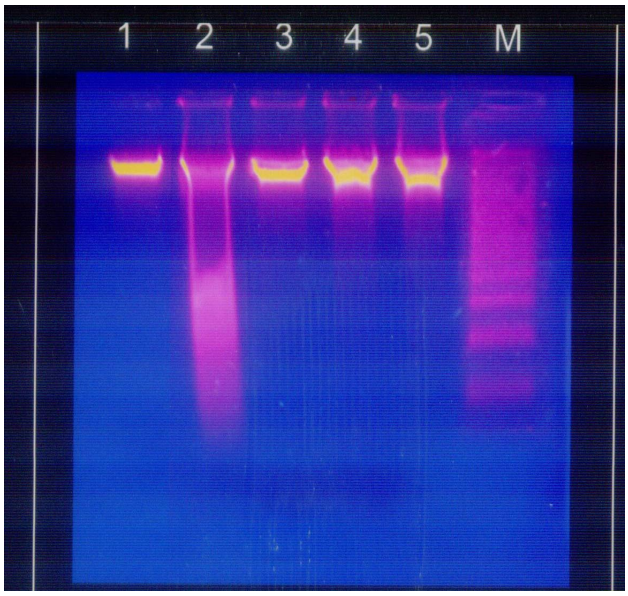



Fig. 5. Photograph of apoptotic DNA fragmentation in kidney cells of rats in different groups

**Lane 1:** control, **Lane 2:** GM treated for 8 days by 100 mg/kg/day, **Lane 3:** CUR only for 15 days by 100 mg/kg /day, **Lane 4 &5:** GM + CUR treatment M 1 K b p ladder.

## DISCUSSION:

Nephrotoxocity incused by GM is a complex phenomenon characterized by an increase in blood urea, serum creatinine concentration and severe proximal renal tubular necrosis followed by deterioration and

renal failure (Nagai and Takano, 2004). It has been consistently shown that treatment with antioxidants can ameliorate the nephrotoxicity of gentamicin (Koyner *et al*., 2008), and the value and utility of gentamicin in clinical practice would be greatly increased (Ali *et al*., 2005). In the present study, we focused on the effect of curcumin on the renal damage and oxidative injury by gentamicin. Results of the present study indicate that gentamicin administration brought about a subtle but significant decrease in body weight of experimental animals treated with GM as compared with control. When CUR was simultaneously given with GM, the reduction in body weight following GM treatment was alleviated. Our results are in agreement with those reported by Ali *et al*. (2005).

Elevated blood urea is correlated with increased protein catabolism (Harper, 1979). Therefore, the high level of blood urea noted in this investigation results from either increased breakdown of tissue, or impaired excretion. The blood urea and creatinine levels increased after the kidneys were failed to remove them and other waste products from the blood. So, in this study, the elevation in blood urea and creatinine levels in GM treated rats is considered as suitable markers of renal dysfunction. This result is in agreement with reports of Shifow *et al*. (2000), Kopple *et al*. (2002) and Paralakapimar *et al.* (2006). Our results showed that curcumin treatment significantly attenuated the GM mediated increase in urea and creatinine levels. This effect may be related to the antioxidant properties of curcumin since it has been found that ROS may be involved in the impairment of glomerular filtration rate (Pedraza-Chaverri *et al*., 2000).

The protective effect of curcumin via scavenging of the ROS is well documented (Gafner *et al*., 2004). In the current study, GM gave alone induced oxidative stress which results in lipid peroxidation causing increase in MDA levels and decrease in antioxidant enzymes CAT. CAT is a hemoprotein which catalyses the reduction of hydrogen peroxide and protects the tissues from highly reactive hydroxyl radical (Rajasekaran *et al.*, 2005). The reduction in the activities of this enzyme could reflect the adverse effect of GM. Furthermore, the curcumin treatment would prevent CAT activity decreased induced by gentamicin. The protective effect might be due to ability of CUR to inhibit hydrogen peroxide-induced oxidative injury in renal cell line as has been elucidated by Cohly *et al.* (1998). It is reasonable to assume that curcumin is able to suppress nephrotoxicity in kidney as it was demonstrated in the studies with adriamycin (Venkatesan *et al*., 2000), GM (Farombi and Ekor, 2006), and cyclosporine (Tirkey *et al*., 2005).

Oxidative stress can promote the formation of variety of vasoactive mediators that can affect renal function and decrease the glomerular capillary ultrafiltration coefficient; and thus reducing glomerular filtration rate (GFR). In this study, it has been shown that GM, at 100 mg/kg, significantly increased the level of lipid peroxidation products (MDA) suggesting the involvement of oxidative stress**.** In addition, the effect of GM and elevation of the lipid peroxidation product, MDA, were reduced by CUR treatment. The present results showed that CUR decreases lipid peroxidation possibly by its antioxidant activity. Rukkumani *et al*. (2003) reported a protective effect of CUR on circulating lipids in plasma and on lipid peroxidation products in alcohol and on polyunsaturated fatty acid induced toxicity. The renal tissue is the main source of the excreted urinary enzymes, and the evaluation of the activities of these enzymes and endogenous metabolites is known to be a good and sensitive method to measure the tubular cell integrity (Kuzniar *et al*., 2006). NAG (alysosomal enzyme) is basically found in renal tissue and its greatest activity is in this organ. Although it exists in blood circulation, its presence in urine origimates from the kidney since its high molecular does not let it pass through the glomerulus even in pathological condition of increased glomerular permeability. The urinary activity of this enzyme correlates with severity of renal injury; hence it is used as a marker for assessment of renal injury due to nephrotoxic drugs (Lafayette *et al*., 1997). NAG activity was significantly increased by gentamicin treatment; this result is in agreement with Attessahim *et al*. (2003), Maldonado *et al*. (2003), and Wiland and Szechcimiski (2003).

This effect was alleviated by CUR treatment and this suggests that CUR may possess protective effect against GM – induced renal dysfunction. Aminoglycoside antibiotics have long been known to cause acute renal failure in both animal and human in association with histological and functional sings of proximal tubular toxicity. Yet, the underlying molecular mechanism still remains poorly defined. By using quantitative approaches, we now have demonstrated that apoptosis (i.e. the process of single programmed cell death) is an important cytotoxic mechanism in gentamicin treated proximal renal tubular cells (Saikumar and Venkatachalam, 2003). Apoptosis is known to be activated by a cascade of both extrinsic and intrinsic factors and to be placed under light genetic regulation. It has now been recognized as an important determinant of cell degeneration in many toxic events including several instances of nephrotoxicity caused by drugs (Lau, 1999). Aminoglycosides enter proxiaml tubular cells by pinocytosis from luminal pole and

accumulate in lysosomes, where they cause conspicuous phopholipidosis (Turrens, 2003). Reactive oxygen species (ROS) are important mediators of gentamicin-induced apoptosis. ROS generation is often responsible for the mitochondria-mediated signaling pathway of apoptosis. Gentamicin can induce apoptosis in LLC-PK1 (Lilly Laboratories, Culture- Pig Kidney type 1) cells through triggering the mitochondrial pathway and activating caspase-3(Servais *et al*., 2005). The result of the present study showed that gentamicin induced DNA damage and apoptosis in kidney cells. Also, in the present study, CUR has been found to inhibit the action of gentamicin induced apoptosis suggesting its influence as inhibitor of DNA damage. The protective ability of CUR was proved to be higher than that of the well-known biological antioxidants lipoate, alpha tocopherol and beta-carotene as indicated by Cheng *et al*. (2003).

The ability of CUR to protect DNA against GM seems to be related to its structure and may at least partly explain the therapeutic and other beneficial effect of this compound including anticarcinogenic and antimutagenic properties. The renal histological examination revealed more extensive and marked tubular necrosis in the GM treated kidney. Similar changes were also reported by Kumar *et al*. (2000) and Parlakpimar *et al*. (2004). They demonstrating structural changes in renal tissue of GM treated animals and its protection by various agents. Administration of CUR reversed kidney damage with reduction in tubular damage induced by GM. Similar result were acquired by Farombi and Ekor (2006) and Ali *et al*. (2005). In the light of biochemical and molecular results, as well as histopatholgical findings, the present study confirmed that CUR treatment possesses significant therapeutic effects.

## REFERENCES:


Aebi ME. 1995. Catalase. In: "Methods of Enzymatic Analysis vol. III. Enzymes oxidoreductases" (Bergmeyer J, Grabl BM eds), 3rd ed. Weinheim: Verlag-Chemie. Pp: 273-286

Ali BH, Wabel NAL, Mahmoud O, Mousa HM, Hashad M. 2005. Curcumin has a palliative action on gentamicin induced nephrotoxicity in rats. Fund. Clin. Pharmacol, 19(4): 473- 477.

Ali BH. 2003. Agents almeliorating or augmenting experimental gentamicin nephrotoxicity some recent research. Food Chem. Toxicol., 41: 147-152.

Aljanabi SM, Martinez I. 1997. Universal and rapid salt-extraction of high quality genomic DNA for PCR- based techniques. Nucleic Acids Res., 25(22): 4692-4693.

Al-Majed AM, Mostafa AC, Al-Rikabr AC, Al-Shabanah O. 2002. Protective effect of oral Arabic gum administration on gentamicin nephrotoxicity in rats. Pharmacol. Res., 46: 445-451.

Atessahin A, Karahan J, Yilmaz S, Ceribasi AG, Princci I. 2003. The effect of manganese chloride on gentamicin induced nephrotoxicity in rat. Pharmacol. Res., 46: 637-642.

Cheng AL, Hsu CH, Lin JK. 2003. Phase I clinical trial of curcumin, a chemopreventive agent, in patient with high-risk or pre-malignant lesions. Anticancer Res., 21: 2895-2900.

Cohly HHP, Taylor A, Angel MF, Salahydeen AK. 1998. Effect of turmeric, tumerin and curcunin on H2O2 induced renal epithelial (LLC-Pk1) cell injury. Free Radical Bio. Med., 24(1): 49-54.

Erdem A, Gundogan NU, Usmbuten A, Kilinc K, Erdem SR, Brozkurt A. 2000. The protective effect of taurine against gentamicin induced acute tubular necrosis in rats. Nephrol. Dial. Transpl., 15(8): 1175- 1182.

Farombi E, Ekor M. 2006. Curcumin almeliorate gentamicin induced renal oxidative damage in rats. Food Chem. Toxicol., 44(9): 1443 -1448.

Gibey R, Dupond JL, Peltier H, Lehl-Robery M,d Henry JC. 1986. An early and specific indicator of aminoglycoside nephrotoxicity: isoenzyme B of urinary N-acetyl-beta-D-glucosaminidase (NAG). Pathol. Biol., 34(5): 342-345.

Harper HA, Rodwell VW, Mayes PA. 1979. Metabolism of carbohydrates and lipid metabolism. In: "Review of Practical Physiological Chemistry". Los Altos, California: Lange Medical Publications, 370.

Hassab El-Nabi SE. 2004. Molecular and cytogenetic studies on the antimutagenic potential of engenol in human lymplocytes culture treated with depakine and apetryl drugs. J. Egypt. Ger. Soc. Zool., 43: 171-196.

Houot O. 1985**.** Interpretation of clinicial laboratory tests (Siet G, Henny J, Schielo F, Young DS. Eds). Biomedical publication, pp: 220-234.

Jain SK, Rains J, Jomed K. 2006. Effect of curcumin on protein glycosglation, lipid peroxidation, and oxygen radical generation in human red blood cells exposed to high glucose level. Free Radical Boi. Med., 41(1): 92- 96.

Kalpana C, Sudheer AR, Rajasekjaran KN, Menon VP. 2007. Comparative effects of curcumin and its synthetic analogue on tissue lipid peroxidation and antioxidant status during nicotine-induced toxicity. Singapore Med. J., 48(2): 124-130.

Kopple JD, Ding H, Letoha A, Ivanyi B, Qing DP, Dux L. 2002. L-carnitine ameliorates gentamicin induced renal injury in rats. Nephrol. Dial. Transplant., 17: 2122–2131.

Koyner JL, Sher AR, Murrary PT. 2008. Antioxidants: Do they have a place in the prevention or therapy of acute kidney injury? Nephron. Exp. Nephrol., 109(4): 109-117.

Kumar KV, Shifow AA, Naidu MU, Ratnakar KS. 2000. Carvedilol: a beta blocker with antioxidant property protects against gentamicin-induced nephrotoxicity in rats. Life Sci., 66(26): 2603-2611.

Kuzniar J, Marchewka Z, Krasnowski R, Boratynska M, Dlugosz A, Klinger M. 2006. Enzymuria and low molecular weight protein excretion as the differentiating marker of complications in the early post kidney transplantation period. Int. Urol. Nephrol., 38(3-4): 753-758.

Lafayette RA. Perrone RD, Levey AS. 1997. Laboratory evaluation of renal function. In:

"Disease of the Kidney. (Schrier RW, Gottschalk CW (eds.)". 6th edn. Little Brown. Boston. 1: 307-354

Lau AH. 1999. Apoptosis induced by cisplatin nephrotoxic injury. Kidney Int., 56: 1295-1298.

Maldonado PD, Barrera D, Medina-Campos ON, Hernadez-Pando R, Ibarra-Rubio ME, Pedraza-Chaverri J. 2003. Aged garlic extract attenuates gentamicin induced renal damage and oxidative stress in rats. Life Sci., 73(20): 2543-2556.

Mihara M, Uchiyama M. 1978. Determination of malonaldehyde precursor in tissues by thiobarbituric acid test. Anal. Biochem., 86(1): 271-278.

Nagai J, Takano M. 2004. Molecular aspect of renal handling of aminoglycoside and strategies for preventing the nephrotoxicity Drug Metab. Pharmacokinet., 19(3): 159 -170.

Patton CJ, Crouch SR. 1977. Spectrophotometric and kinetics investigation of the Berthelot reaction for the determination of ammonia. Anal. Chem., 49: 464–469

Pedraza-Chaverrí J, Barrera D, Maldonado PD, Chirino YI, Macías-Ruvalcaba NA, Medina-Campos ON, Castro L, Salcedo MI, Hernández-Pando R. 2004. S-allylmercaptocysteine scavenges hydroxyl radical and singlet oxygen *in vitro* and attenuates gentamicin-induced oxidative and nitrosative stress and renal damage *in vivo*. BMC Clin. Pharmacol., 4: 5-17.

Pedraza-Chaverrí J, Maldonado PD, Medina-Campos ON, Olivares-Corichi IM, Granados-Silvestre MA, Hernández-Pando R, Ibarra-Rubio ME. Garlic ameliorates gentamicin nephrotoxicity: relation to antioxidant enzymes. 2000. Free Radical Bio. Med., 29(7): 602-611.

Rajasekaran S, Sivagnanan K, Subramarian S. 2005. Antioxidant effect of *Aloe vera* gel extraction strepozotocin induced diabetes in rats. Pharmacol. Rep., 57: 90-66.

Rukkumani R, Balasubashini M, Menon VP. 2003. Protective effect of curcumin and photo-irradiated curcumain on circulatory lipid at preoxidation products in alcohol and poly unsaturated fatty acid induced toxicity. Phytother. Res., 17(8): 925 -929.

Saikumar P, Venkatachalam MA. 2003. Role of apoptosis in hypoxic/ischemic damage in the. Kidney Nephrol., 23: 511-521.

Servais H, Jossin Y, Van Bambeke F, Tulkens PM, Mingeot-Leclercq MP. 2006. Gentamicin causes apoptosis at low concentrations in renal LLC-PK1 cells subjected to electroporation. Antimicrob. Agents Chemother., 50: 1213-1221.

Servaisa H, Van Der Smissen P, Thiriona G, r Van der Essena G, Van Bambekea F, Tulkens PM, Mingeot-Leclercq MP. 2005. Gentamicin – induced apoptosis in LLC-PK1 cells: involvement of lysosomes and mitochondria. Toxicol. Appl. Pharm., 206: 321-333.

Shifow K, Kumar V, Naidur MVR, Ratmakar KS. 2000. Melatonin a pineal hormone with antioxidant property protects against gentamincin induced nephrotoxicity in rats. Nephron, 85: 167-174.

Tirkey V, Kaur G, Vij G, Chopra K. 2005. Curcumin a diferuloylnethare, attenuates cyclosporine induced renal dysfunction and oxidative stress in rat kidneys. BMC Pharmacol., 5: 189-196.

Turrens JF. 2003. Mitochondrial formation of reactive oxygen species. J. Physiol., 552: 335–344.

Venkatesan N, Durairaj Punithavathi D, Arumugam V. 2000. Curcumin prevents adriamycin nephrotoxicity in rats Braz. j. Pharmacol., 129(2): 231 -234.

Wiland P, Szechainiski j. 2003. Proximal tubule damage in patients treated with genatmicin or amikacin. Pol. J. phramacol., 55: 631 – 637.

## الدور الوقائى للكركم من التسمم الكلوى الناتج من عقار جنتاميسين في ذكور الجرذان البيضاء

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تم إجراء هذا البحث لإظهار مدى الأثار الجانبية لاستخدام الجنتاميسين كمضاد حيوى على الكلى وكذلك دراسة التأثير الوقائى للكركم كمانع طبيعى للأكسدة على الجرذ الأبيض. وقد أجريت الدراسة على 40 من ذكور الجرذان البيضاء. حيث تم تقسيمها على أربع مجموعات . المجموعة الأولى استخدمت كمجموعة ضابطة . المجموعة الثانية حقنت بمادة الجنتاميسين بتركيز 100مج/كجم لمدة 8 أيام متتالية . المجموعة الثالثة عوملت بالكركم عن طريق الفم بجرعة 100 مج/كجم لمدة 15 يوما متتالية . المجموعة الرابعة عوملت بالكركم لمدة 15 يوما وحقنت كذلك بالجنتاميسين بجرعة 100مج/كجم خلال 8 أيام الأخيرة من التجربة. وقد تم إجراء دراسات هستوباثولوجية ودراسات بيوكيميائية شملت قياس مستوى اليوريا والكرياتين فى المصل ، وقياس مستويات الكتاليز فى الكلية وانزيم إن استيل بيتا دى جليوكوامينديز (الناج) فى البول بالإضافة إلى إجراء دراسة وراثية لتحديد مدى تأثير وتحطم محتوى الدنا فى خلايا الكلى فى جرذان التجارب البيضاء. وأظهرت النتائج نقص في أوزان الجرذ التي عوملت بالجنتاميسن مقارنة بفئران المجموعة الضابطة وأيضاً لوحظ زيادة في أوزان الفئران التي عوملت بالكركم بمفردة مقارنة بالمجموعة الضابطة. لوحظ زيادة في أوزان المجموعة الرابعة التي عوملت بكل من الجنتاميسن والكركم مقارنة بالمجموعة الثانية التي عوملت بالجنتاميسن. لوحظ ارتفاع ذي دلالة إحصائية في مستوى اليوريا والكرياتين ومستوى المالونديالدهايد وارتفاع في مستوى NAG في فئران المجموعة الثانية المعاملة بالجنتاميسن بمفردها إذا ما قورنت بالمجموعة الضابطة وأيضاً لوحظ انخفاض في مستوى الكتاليز وحدوث تغيرات نسيجية مرضية في المجموعة الثانية إذا ما قورنت بالمجموعة الأولي. وقد حدث أيضا تكسير في الدنا (DNA) المعزول من خلايا الكلي وظهور تكسير الدنا المبرمج الأبوبتوسس Apoptosis في المجموعة الثانية المعاملة بالجنتاميسن بمفردها. لوحظ وجود إمكانية عالية للوقاية من الأضرار الناتجة من استخدام الجنتاميسن عند استخدام الكركم كمضاد أكسدة طبيعي حدث تحسن ملحوظ فى التكسير الحادث في الدنا وأيضاً حدوث تحسن في التغيرات البيوكيمائية محل الدراسة إلى الأمثل مقارنة بالمجموعة المعاملة بالجنتاميسن بمفرده. وقد أوضحت نتائج هذا البحث دور الكركم فى تقليل التسمم الكلوى المستحدث بالجنتاميسين وهذا من خلال وظيفته كمضاد قوى للأكسدة .

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