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Research Article

Renal Toxicity Induced by Nicotine in Male Albino Rats and Attenuation by Fenugreek Seeds and Curcumin

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Abstract

The present study aimed to evaluate the harmful effects of nicotine on serum urea, creatinine, and uric acid concentrations, and histological structure of the kidney, and assessment of the ameliorative effects of fenugreek seeds, and curcumin on renal toxicity induced by nicotine in male albino rats. 30 male F-344/NHsd Fischer rats, weighing from 180 to 200g were used in the present study. The animals were divided into five groups (6 rats for each); Group I (control group), Group II (nicotine treated group), Group III (nicotine/fenugreek seeds co-administered), Group IV (nicotine/curcumin co-administered), and Group V (nicotine/curcumin& fenugreek seeds co-administered). At the end of the experimentation and 24 hours after the last dose, all animals were anaesthetized with ether and blood samples were collected by heart puncture. The blood samples were collected in clean dry tubes. The allowed to clot at room temperature for about 30 minutes and centrifuged at 3000 rpm for 15 minutes then, serum was separated and kept in a deep freezer at -20°C until biochemical measurements were carried out. Animals were immediately dissected, and small pieces of the kidney were quickly removed and fixed in 10% formalin for histological examination. The results showed that the animals treated with nicotine for 4 weeks induced a significant increase in serum urea, creatinine, and uric acid concentrations compared with the control group. Also, administration of nicotine to rats induced a severe structural change in the renal tissues. Co-administration of nicotine with fenugreek and/or curcumin caused improvement in serum urea, creatinine, and uric acid concentrations and histological structure of the kidney when compared with nicotine group. It can be concluded that nicotine had a strong effect on the kidney function and histological structure of the kidney. The ingestion of fenugreek and/or curcumin attenuated the renal toxicity induced by nicotine. The current study suggests that fenugreek and curcumin may be useful in combating free radical-induced renal toxicity induced by nicotine.

Keywords: nicotine; renal toxicity; fenugreek; curcumin; co-administration; nephro-protective effect; male albino rats

1. Introduction

Nicotine is a naturally occurring alkaloid found primarily in the members of the solanoceous plant family such as eggplants, tomato, potato, tobacco, and green pepper (Siegmund *et al.*, 1999). It is one of hundreds of substances contained in cigarette smoke (Abdel-Aziz, 2010). It has been demonstrated that nicotine could be excreted through urine, feces, bile, saliva, gastric juice, sweat, and breast fluid (Seaton *et al.*, 1993). The level of renal excretion depends on urinary pH and flow. When 14C-nicotine is given to an animal, it has been shown that around 55% of the radioactivity is excreted in the urine. However, only 1% of the radioactivity was observed in the form of unchanged nicotine. This result demonstrates that nicotine is excreted following extensive metabolization. The urinary excretion of nicotine and its metabolites has been shown to be affected by ascorbic acid. It was reported that ascorbic acid increases the urinary excretion of cotinine and nicotine (Dawson *et al.*, 1999). Renal clearance of cotinine is much less than glomerular filtration rate (Benowitz et al., 1983). Nicotine and cotinine is also determined in the urine of infants who have mothers who smoke indicating that exposure of mothers to tobacco smoke affect the infants. In another study, the hypothesis that the rate of renal excretion of nicotine influences the nicotine intake during smoking was investigated. Researchers reported that the daily nicotine intake was 18% higher in persons with increased nicotine excretion and concluded that the rate of elimination of nicotine affects the rate of consumption (Benowitz and Jacob, 1985). The kidney of rats treated with 2.5 mg nicotine/kg of body weight, (5 days a week) for 22 weeks showed a cloudy swelling, medullary hemorrhage (Balakrishnan and Menon 2007).

Nicotine has been recognized to result in oxidative stress by inducing the generation of reactive oxygen species by various mechanisms (Yildiz *et al.*, 1998).

The overproduction of reactive oxygen metabolites and a reduction in antioxidant mechanisms have been reported due to acute or chronic smoke exposure (Van der Vaart *et al.*, 2004). The breakdown of membrane phospholipids and lipid peroxidation due to the generation of free radicals are expected to change membrane structure, fluidity, transport, and antigenic properties, all of which play an important role in the pathogenesis of organ disorders (Van der Vaart *et al.*, 2004; Sener *et al.*, 2007). High concentrations of nicotine were induced oxidative stress (Guan *et al.*, 2003). Nicotine administration induced a decrease in the activities of free radical scavenging enzymes catalase, superoxide dismutase, and glutathione reductase (Ashakumary & Vijayammal, 1996). Oxidative stress induced by nicotine occurs when there are massive free radicals or low antioxidant protection, and result in chemical alteration of biomolecules causing structural and functional change (Neogy *et al.*, 2008).

Natural antioxidants strengthen the endogenous antioxidants defenses and restore the optimal balance by neutralizing reactive species (Ho *et al.*, 1994). Curcumin as one of the naturally occurring dietary substances has been used since ancient times for promoting human health (Joe *et al.*, 2004). It represents a class of anti-inflammatory and anti-oxidant reported to be a potent inhibitor of reactive oxygen species (ROS) formation (Venkatesan *et al.*, 2000). The effects of antioxidants on nicotine induced oxidative stress have been investigated (Gumustekin *et al.*, 2003, Helen *et al.*, 2003). Manikandan *et al*., (2011) found that curcumin affords curative role against nephrotoxicity induced gentamicin exposure and reduces gentamicin induced renal injury and this is supported by Biswas *et al*., (2005) who found that curcumin has anti-inflammatory and antioxidant properties with a potent ability to inhibit reactive oxygen species formation. Co-administration of curcumin with gentamicin in guinea pigs significantly improved the structural changes in the kidney and the blood urea, creatinine and uric acid were significantly declined compared with gentamicin treated group (Azab *et al.*, 2014).

Fenugreek (*Trigonella foenumgraecum*) is an annual herb belonging to Legume family; it is widely grown in India, Egypt, and Middle Eastern countries (Flammang *et al.*, 2004). It used both in medicine and with food as spice show antioxidant effect through their used in diabetes mellitus due to the presence of different active constituents such as flavonoids, alkaloids, vitamins and amino acids (Basch *et al.*, 2003). Dietary fenugreek seeds and onion caused a nephro-protective in diabetes treated groups (Pradeep and Srinivasan, 2018). El-Tawil, 2009 concluded that fenugreek would protect from oxidative damage and metabolic disturbances induced by ionizing irradiation. Nawasany *et al.* 2017 reported that herbs such as fenugreek are known to have a diuretic effect in cirrhotic ascitic patients.

Plant seeds and herbs are used for treatments of diseases in the folk medicine. Their use was increased in many fields due to their safetyness and its low side effects as compared with chemical drugs (Alhawari, 1986). Antioxidant potential of curcumin and fenugreek seeds in the amelioration of nicotine induced oxidative stress need thorough investigation because these natural antioxidants are components of many edible substances and has the potential for safe future use by humans. The evidence reporting the protective effect of curcumin and fenugreek seeds against nicotine induced nephro-toxicity are hardly found.

2. Objectives

The present study aimed to evaluate the harmful effects of nicotine on serum urea, creatinine, and uric acid concentrations, and histological structure of the kidney, and assessment of the ameliorative effects of fenugreek seeds, and curcumin on renal toxicity induced by nicotine in male albino rats.

3. Materials and Methods

3.1. Experimental animal

Animals which were used in this study were 30 male F-344/NHsd Fischer rats, weighing from 180 to 200g. Animals purchased from Animal Welfare House of Libyan National Medical Research Centre, Zawia, Libya. Rats were kept under standard veterinary hygienic conditions for cleanliness and health care and normal conditions through the whole experimental periods. Rats were separated in plastic cages, 6 rats per cage, and left one week of acclimation, before commencing the experiment. The rats were kept in a room under standard conditions of ventilation, temperature (25±4°C), humidity (65 ± 5 %) with light/dark cycle. A standard rodent pellet consisting of a mixture of protein, fat, fiber, and ash were used to feed the rats. Food and water were supplied ad-libitum.

3.2. Methods and Technique

3.2.1. The drug

Nicotine hydrogen tartrate salt (1-methyl-2-(3-pyridyl) pyrrolidine-bitartrate salt) will purchase from Sigma-Aldrich (St. Louis, MO, USA). Nicotine is a colorless organic Liquid. It was dissolved in physiological saline (0.9% sodium chloride) and was injected subcutaneously daily with 0.8 mg, nicotine/kg body weight for 30 days.

3.2.2. Curcumin, and Fenugreek seeds

Curcumin was given in diet as 20 g/kg diet daily for 30 days. Fenugreek seeds were finely grounded and added to the experimental diets as 7.5 g/kg diet daily for 30 days.

3.3. Experimental Design

After one week of acclimation, the animals were randomized and divided into five groups (6 male albino rats for each) as follow:

Group I (control group): This group included 6 animals that were injected subcutaneously with saline daily, provided with tape water and fed with normal diet for 30 days.

Group II (nicotine treated group): Male rats were injected subcutaneous daily with 0.8 mg, nicotine/kg body weight for 30 days.

Group III (nicotine/fenugreek seeds co-administered): The animals were injected subcutaneous daily with 0.8 mg, nicotine/kg body weigh concurrently with fenugreek seeds 7.5 g/kg diet daily for 30 days.

Group IV (nicotine/curcumin co-administered): The animals were injected subcutaneous daily with 0.8 mg, nicotine/kg body weigh concurrently with curcumin 20 g/kg diet daily for 30 days.

Group V (nicotine/curcumin& fenugreek seeds co-administered): The animals were injected subcutaneous daily with 0.8 mg, nicotine/kg body weigh concurrently with curcumin 20 g/kg diet and fenugreek seeds 7.5 g/kg diet daily for 30 days.

3.4. Blood Sampling:

At the end of the experimentation and 24 hours after the last dose, all animals were anaesthetized with ether and blood samples were collected by heart puncture. The blood samples were collected in clean dry tube and allowed to clot at room temperature for about 30 minutes and centrifuged at 3000 rpm for 15 minutes then, serum was separated and kept in a deep freezer at -20◦C until biochemical measurements were carried out.

3.5. Determination of serum urea, uric acid, and creatinine concentration

Serum urea measurement was based upon the cleavage of urea with urease (Fawcett and Scott, 1960). Serum uric acid was determined (Fossatti *et al.*, 1980). Serum creatinine was measured without protein precipitation (Bartels *et al.*, 1972).

3.6. Histological Preparation

At the end of the experimentation and 24 hours after the last dose, all animals were anaesthetized with ether. Animals were immediately dissected, and small pieces of the kidney were quickly removed and fixed in 10% formalin. After fixation, specimens were dehydrated in an ascending series of alcohol, then kept in terpineol for three days to ensure complete dehydration and clearing purposes. Cleared specimens were rinsed in three changes of xylol before embedding in paraffin wax (m.p.56-58°C). Three sections of 5 microns thick were taken from each kidney sample, each being at a distance of at least 500 microns from the proceeding one and mounted on clean slides. For histological examination, sections were stained with Ehrlich's haematoxyline and eosin.

3.7. Statistical Analysis: -

Results were expressed as mean ± standard deviation, Data were analyzed by one way ANOVA. The difference between means ± SD was tested at P<0.05 using Duncan's multiple range test. In all statistical tests, the probability level of P<0.05 was considered significant.

4. Results

4.1. Effect of administration of nicotine, and co-administration of nicotine with fenugreek seeds, nicotine with curcumin and nicotine with fenugreek seeds, and curcumin on the serum urea, creatinine, and uric acid concentrations in male rats.

Serum urea, creatinine, and uric acid concentrations of the different groups are shown in table .1 and figures (1-3). Male rats that received intraperitoneal injection of nicotine only (0.8 mg/kg body weight /day) for 30 consecutive days had significantly (*P<0.01*), increased in serum urea, creatinine, and uric acid concentrations when compared with the control group.

Co-administration of 0.8 mg, nicotine/kg body weight subcutaneously with fenugreek seeds 7.5 g/kg diet daily for 30 consecutive days resulted in a significant (*P<0.01*) increase in serum urea, and creatinine, and at (*P<0.05*) in uric acid concentrations as compared to the control group. On the other hand, co-administration of fenugreek seeds with nicotine significantly (*P<0.01*) decreased serum urea, creatinine, and uric acid concentrations when compared with nicotine group (Table.1& Figures 1-3).

Co-administration of 0.8 mg, nicotine/kg body weight subcutaneously with curcumin 20 g/kg diet daily for 30 consecutive days caused a significant (*P<0.01*) increase in serum urea, creatinine, and uric acid concentrations as compared to the control group. Conversely, co-administration of curcumin with nicotine significantly (*P<0.01*) decreased serum urea, creatinine, and uric acid concentrations when compared with nicotine group (Table.1& Figures 1-2).

Co-administration of 0.8 mg, nicotine/kg body weight concurrently with curcumin 20 g/kg diet and fenugreek seeds 7.5 g/kg diet daily for 30 consecutive days were significantly (*P<0.01*) increased serum creatinine concentration when compared with the control group. On the other hand, the animals injected subcutaneous daily with 0.8 mg, nicotine/kg body weight concurrently with curcumin 20 g/kg diet and fenugreek seeds 7.5 g/kg diet daily for 30 consecutive days were showed a significant (*P<0.01*) decrease in serum urea, creatinine, and uric acid concentrations when compared with nicotine group (Table.3& Figures 1-3).

Groups / Parameters	Control	Nicotine	Nicotine+ Fenugreek	Nicotine+ Curcumin	Nicotine+ Fenugreek+ Curcumin
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD
Urea (mg/dl)	**27.00 ± 2.10**	**38.00 ± 1.10****	**30.67 ± 1.86$^{**\#\#}$**	**33.50 ± 1.76$^{**\#\#}$**	**28.83 ± 2.14$^{\#\#}$**
Creatinine (mg/dl)	**0.59 ± 0.12**	**1.24 ± 0.17****	**0.82 ± 0.04$^{**\#\#}$**	**1.00 ± 0.04$^{**\#\#}$**	**0.81 ± 0.04$^{**\#\#}$**
Uric acid (mg/dl)	**2.18 ± 0.25**	**4.53 ± 0.57****	**2.73 ± 0.27$^{*\#\#}$**	**3.32 ± 0.54$^{**\#\#}$**	**2.40 ± 0.14$^{\#\#}$**

*: Significant at (P<0.05) when compared with control group, **: Significant at (*P<0.01*) when compared with control group, ##: Significant at (*P<0.01*) when compared with nicotine group.

Table.1: *Effect of administration of nicotine, and co-administration of nicotine with fenugreek seeds, nicotine with curcumin and nicotine with fenugreek seeds, and curcumin on the serum urea, creatinine, and uric acid concentrations in male rats.*

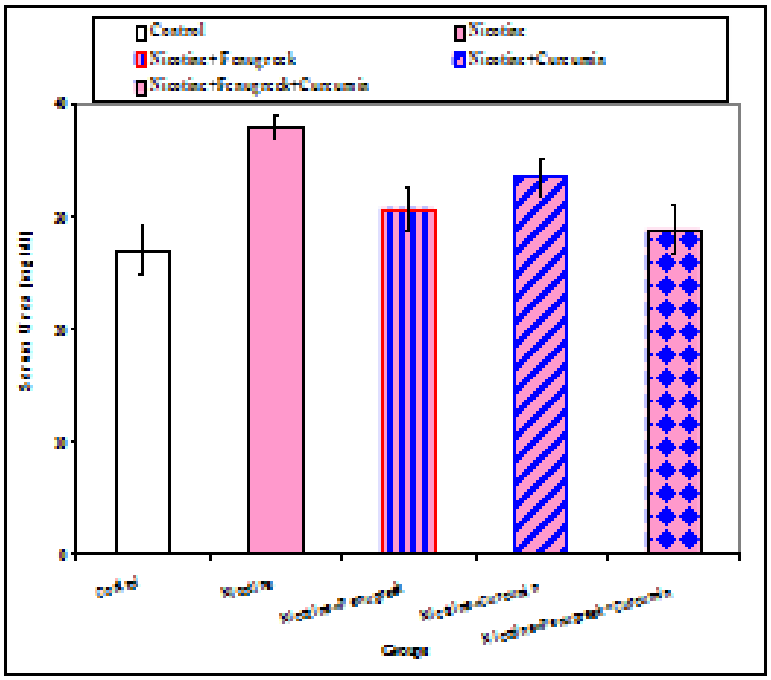

Figure.1: *Effect of administration of nicotine, and co-administration of nicotine with fenugreek seeds, nicotine with curcumin and nicotine with fenugreek seeds, and curcumin on the serum urea concentration in male rats.*

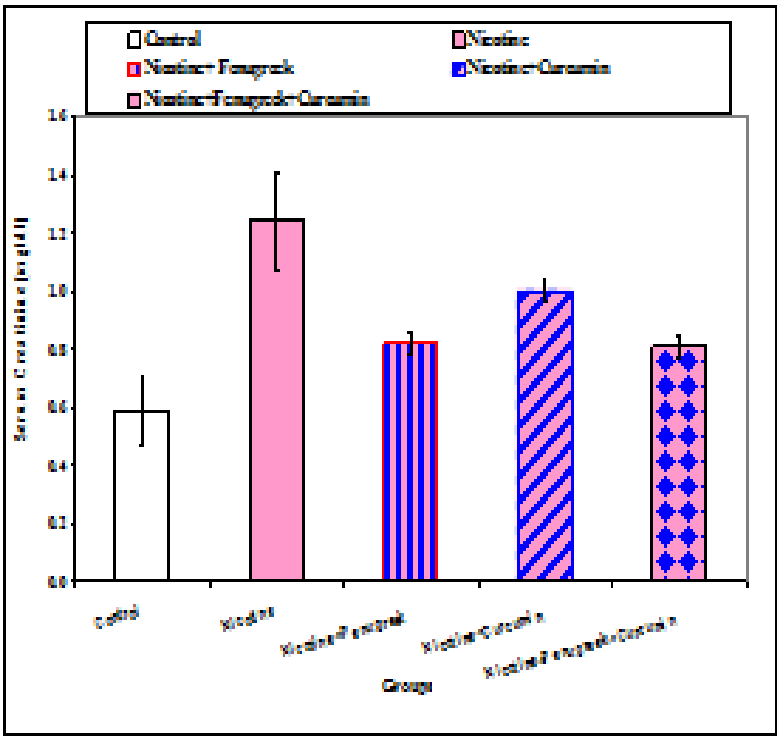

Figure.2: *Effect of administration of nicotine, and co-administration of nicotine with fenugreek seeds, nicotine with curcumin and nicotine with fenugreek seeds, and curcumin on the serum creatinine concentration in male rats.*

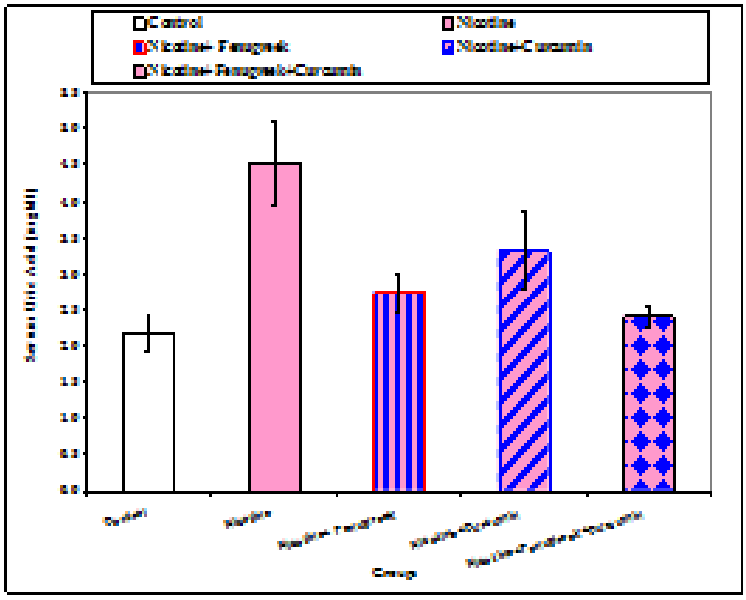

Figure.3: *Effect of administration of nicotine, and co-administration of nicotine with fenugreek seeds, nicotine with curcumin and nicotine with fenugreek seeds, and curcumin on the serum uric acid concentration in male rats.*

4.2. Effect of administration of nicotine, and co-administration of nicotine with fenugreek seeds, nicotine with curcumin and nicotine with fenugreek seeds, and curcumin on the histological structure of the kidney of male albino rats.

4.2.1. Kidney sections of control rats:

The kidney sections of the control rat group showed normal histological architecture. The renal cortex was formed of renal corpuscles (glomerular tuft of capillaries surrounded by Bowman's capsule), proximal and distal convoluted tubules. The proximal convoluted tubules were lined by a cuboidal epithelium with basally located and spherical nuclei and prominent brush border at the apical surface. The distal convoluted tubules were lined by cuboidal epithelial cells that lacked a brush border. The nuclei were spherical and apically located with pale cytoplasm compared with proximal convoluted tubules (Figure. 4).

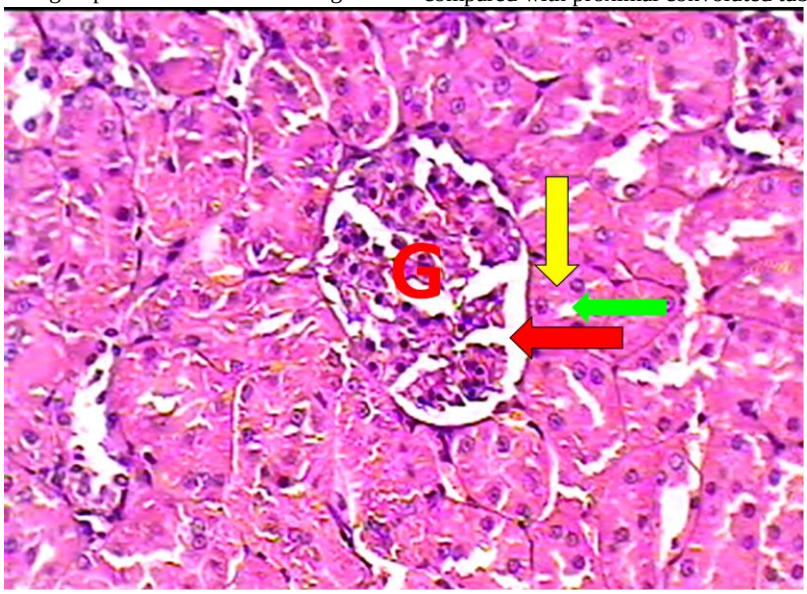

Figure 4. *Light micrograph of section in the Kidney of the control rat; Glomerular tuft of capillaries (G); Bowman's capsule (Red arrow); The proximal convoluted tubule was lined by a cuboidal epithelium with prominent brush border at the apical surface (Yellow arrow); Proximal convoluted tubule lumen (Green arrow); (H &E ×400).*

4.2.2. Kidney sections of nicotine treated rats:

Examination of kidney sections obtained from rats treated with nicotine show a marked tissue damage. The proximal convoluted tubules show a partial destruction of the brush border and desquamated cells were observed inside their lumens and presence of epithelial debris inside their lumens, some of which contained red blood cells. The cortex area of the kidney showed shrinkage of some glomeruli with wide capsular space, congestion of blood vessels and interlobular spaces (Figure. 5).

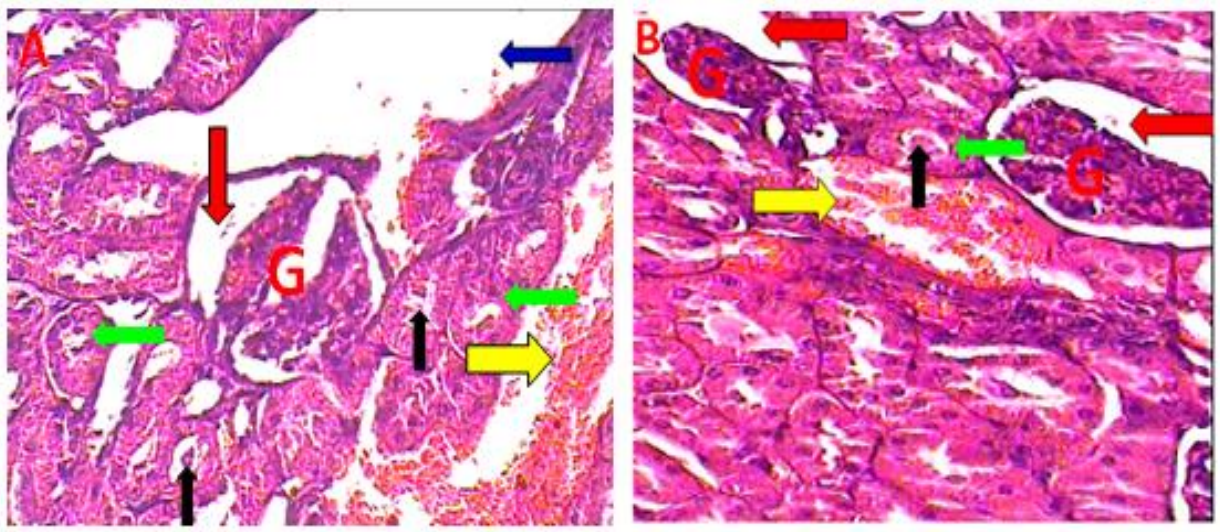

Figure 5. *Light micrograph of section in the Kidney of the Nicotine treated rat; A& B: Shrinkage glomerulus (G); Dilated Bowman's capsule (Red arrow); Dilated interlobular spaces and presence of red blood cells (Yellow arrows); The proximal convoluted tubule was lined by a cuboidal epithelium (Green arrow); Presence of epithelial debris inside the lumens of proximal convoluted tubules (Black arrows); Dilated interlobular spaces (Blue arrow). (H &E ×400).*

4.2.3. Kidney sections of nicotine and fenugreek treated rats

Fenugreek seeds supplementation with nicotine treatment caused an improvement in the glomeruli that were clear as appeared less affected, markedly decreased the degree of injury and dilation of proximal convoluted tubules, tubules appeared normal except for the presence of few red blood cells in the interlobular spaces. Proximal convoluted tubules showed preserved brush border (Figure.6).

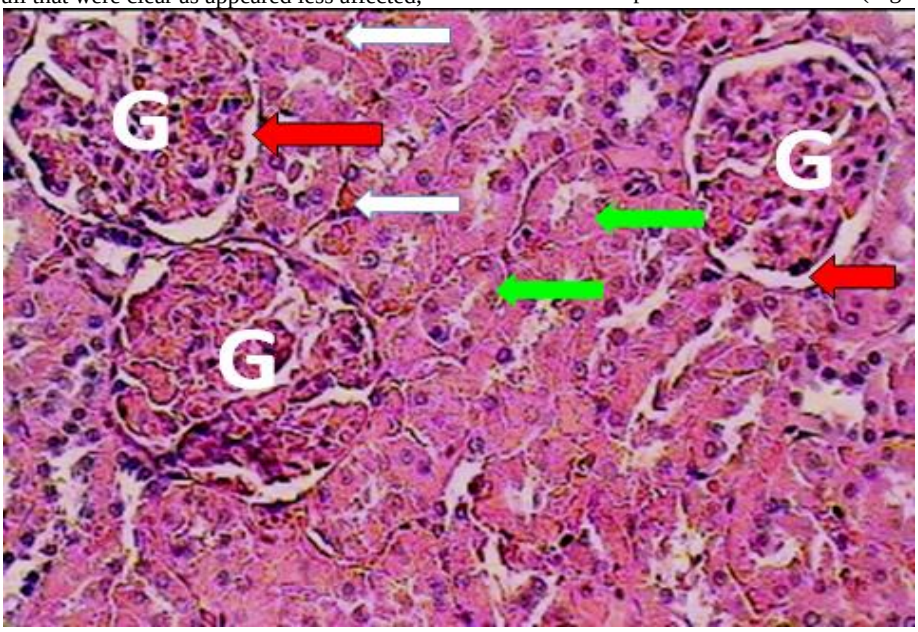

Figure 6. *Light micrograph of section in the Kidney of the Nicotine and fenugreek treated rat; Glomerular tuft of capillaries (G); Bowman's capsule (Red arrows); The proximal convoluted tubule was lined by a cuboidal epithelium with prominent brush border at the apical surface (Green arrows); Presence of few red blood cells in the interlobular spaces (White arrows) (H &E ×400).*

4. 2.4. Kidney sections of nicotine and curcumin treated rats

Giving the animal curcumin with nicotine for the same period, showed that A slightly improvement in the glomeruli that appeared more affected than fenugreek with nicotine group and less affected compared with nicotine group (Fig. 7).

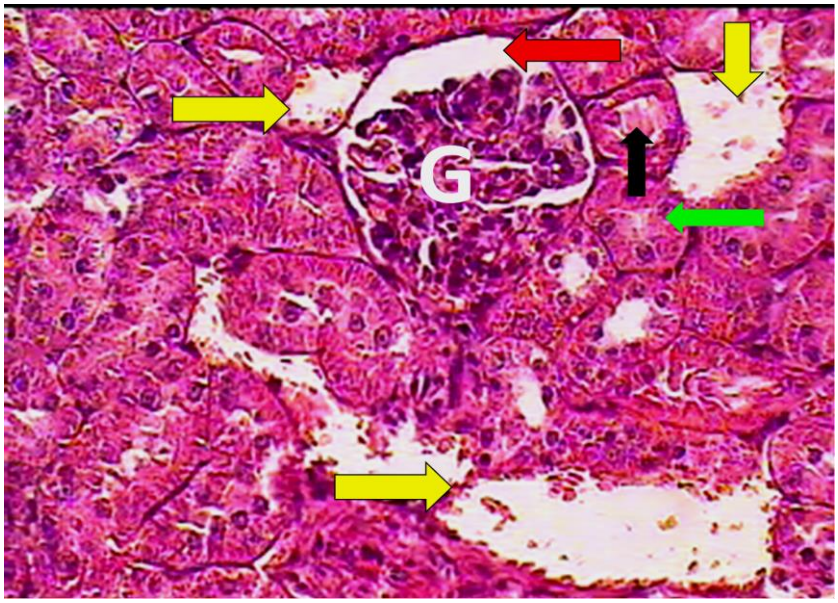

Figure 7. *Light micrograph of section in the Kidney of the Nicotine and curcumin treated rat; Glomerular tuft of capillaries (G); Slightly dilated Bowman's capsule (Red arrow); The proximal convoluted tubule was lined by a cuboidal epithelium with prominent brush border at the apical surface (Green arrows); Dilatated interlobular spaces and presence of red blood cells (Yellow arrows); Presence of epithelial debris inside the lumens of proximal convoluted tubules (Black arrow). (H &E ×400).*

4. 2.5. Kidney sections of rats treated with nicotine, fenugreek, and curcumin

Co-administration of nicotine with fenugreek seeds and curcumin restored the kidney tissues to the normal histological architecture. The renal cortex was formed of renal corpuscles, proximal and distal convoluted tubules. The proximal convoluted tubules were lined by a cuboidal epithelium with basally located and spherical nuclei and prominent brush border at the apical surface. The distal convoluted tubules were lined by cuboidal epithelial cells that lacked a brush border. The nuclei were spherical and apically located with pale cytoplasm compared with proximal convoluted tubules (Figure. 8).

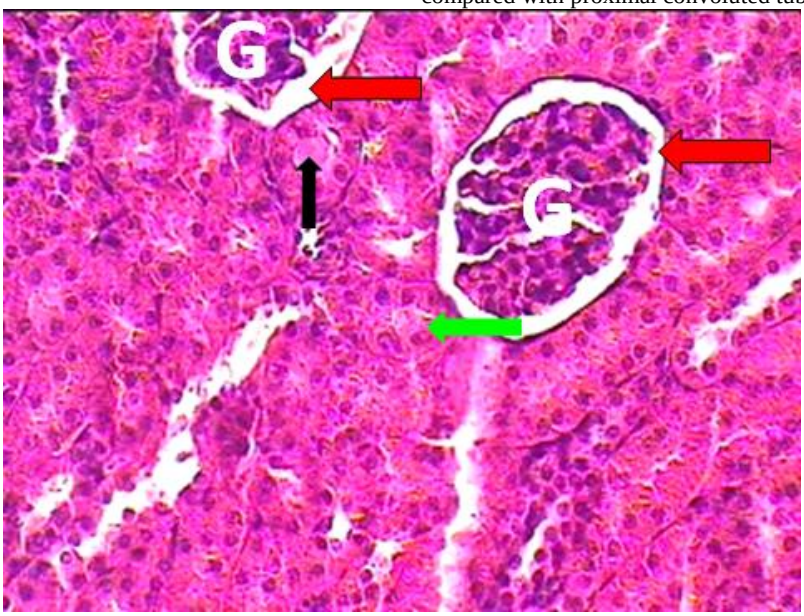

Figure 8. *Light micrograph of section in the Kidney of rat treated with nicotine, fenugreek, and Curcumin: It shows a normal glomerular tuft of capillaries (G), Bowman's capsule (Red arrow), The proximal convoluted tubule was lined by a cuboidal epithelium with prominent brush border at the apical surface (Green arrow); Presence of epithelial debris inside the lumens of proximal convoluted tubules (Black arrow). (H &E ×400).*

5. Discussion

Reduction of the ability of the kidney to eliminate the toxic metabolic substances is indicated by elevation of serum levels of creatinine and urea (Hummadi, 2012). Nicotine and its metabolites are eliminated from kidney, these organs are adversely influenced by nicotine. Therefore, this study investigated the possible protective effects of ingestion of fenugreek and curcumin on nicotine-induced renal toxicity in rats, by determining serum urea, creatinine, and uric acid. Membrane lipids are vital for the

maintenance and integrity of cell function, the breakdown of membrane phospholipids and lipid peroxidation due to the generation of free radicals are expected to change membrane structure, fluidity, transport and antigenic properties, all of which play an important role in the pathogenesis of organ disorders (Sener *et al.,* 2007).

In the present study, male rats that received intraperitoneal injection of nicotine only (0.8 mg/kg body weight/day) for 30 consecutive days had significantly (*P<0.01*), increased in serum urea, creatinine, and uric acid concentrations when compared with the control group. These results agree with the findings of several authors (Pramod Noborisaka *et al.,* 2006, Noborisaka *et al.,* 2012, El Sayed *et al.,* 2013, Okonkwo *et al.,* 2013, Azab, and Albasha, 2019). Ahmed *et al.,* 2015 recorded that the levels of urea and creatinine were significantly higher in smoker group when compared with the control group. In cases of acute and chronic renal diseases, there was an increase in renal retention of uric acid (Newman, and Price, 1998).

Nicotine increases plasma levels of vasoconstrictors including catecholamines, arginine, vasopressin and endothelin-1 (Gambaro *et al.,* 1998). It induces smooth muscle cell proliferation, and cigarette smoke damages endothelial cells (Pittilo *et al.,* 1990). The study of Black *et al.,* 1983 was attributed the renal vascular resistance to activation of the sympathetic nervous system. These effects could be attributed to changes in the threshold of renal blood flow, tubular reabsorption, and glomerular filtration rate (Zurovsky, and Haber, 1995).

The results obtained by the present study showed that the male albino rats treated with fenugreek concurrent with nicotine injection exhibit a pronounced reduction in the nicotine induced increases of the serum urea, creatinine, and uric acid concentrations. These results are in agreement with that observed by El-Tawil, 2009 who found that fenugreek treatment has significantly attenuated radiation-induced oxidative stress in kidney tissues, which was substantiated by the significant amelioration of serum creatinine, and urea levels. The author concluded that fenugreek would protect from oxidative damage and metabolic disturbances induced by ionizing irradiation.

The present results showed that the male albino rats treated with curcumin concurrent with nicotine injection exhibit a pronounced reduction in the nicotine induced increases of the serum urea, creatinine, and uric acid concentrations. These results run parallel with that observed by many investigators (Manikandan *et al.,* 2011, Azab *et al.,* 2014). Manikandan *et al.,* 2011 found that curcumin affords curative role against nephrotoxicity induced gentamicin exposure and reduces gentamicin induced renal injury.

Azab *et al.,* 2014 was evaluated the effectiveness of curcumin against the histological and biochemical alterations of gentamicin induced nephrotoxicity in guinea pigs. In gentamicin treated animals, there were structural changes. The results showed that the serum urea, creatinine, and uric acid were elevated. The proximal convoluted tubules showed degenerated epithelial lining with disruption of their brush borders and presence of epithelial debris inside their lumens. The renal corpuscle appeared with degeneration of the glomerulus and disrupted Bowman's capsule. The afferent arteriole showed thickening in its wall and degeneration of endothelial lining with extensive perivascular infiltration of inflammatory cells. Massive interstitial hemorrhage was seen. Co-administration of curcumin significantly improved the structural changes in the kidney and the blood urea, creatinine and uric acid were significantly declined compared with gentamicin treated group.

In the present study, the examination of kidney sections obtained from rats treated with nicotine showed a marked tissue damage. The proximal convoluted tubules show a partial destruction of the brush border and desquamated cells and present of protein casts and debris were observed inside their lumens. The cortex area of the kidney showed shrinkage of glomeruli, congestion of blood vessels and between tubules**.** These results run parallel with that observed by Sener *et al.*, 2007 who reported that the sections of light microscopic examination of the kidney of Wister albino rats injected with 0.6 mg of nicotine hydrogen bitartarate/kg of body weight daily for 21 days showed a severe vasocongestion in the parenchyma, vacuolizations, and debris in the tubules compared with the control group. Also, Balakrishnan and Menon (2007) have reported that the kidney samples of rats administered nicotine showed cloudy swelling, medullary hemorrhage. In addition, the same results were recorded in the kidney tissues of rats treated with nicotine (Alkhedrawi, 2019).

The membrane phospholipids and lipid peroxidation may be breakdown due to the generation of free radicals which expected to change the membrane structure, fluidity, transport, and antigenic properties. (Van der Vaart, *et al*. 2004, Sener *et al*., 2007, Alkhedrawi, 2019)

The present study showed that the animals injected subcutaneous daily with 0.8 mg, nicotine/kg body weight concurrently with curcumin 20 g/kg diet and fenugreek seeds 7.5 g/kg diet daily for 30 consecutive days were caused a significant improvement in serum levels of urea, creatinine, and uric acid and the structural changes in the kidney when compared with nicotine group. These parameters and histological structure of the kidneys were nearly similar to that in the control groups. These results may be due to the additive antioxidant effect of fenugreek and curcumin together. Al Anany *et al.,* 2015 reported that treatment of adult male albino rats with curcumin or quercetin alone or in combination improved all parameters deteriorated by nicotine. Authors suggested that curcumin and/or quercetin exerts protective effects by improving the antioxidant system, inhibiting the oxidative stress induced by nicotine. Combined therapy with both curcumin and quercetin was much better than each one alone. Because, previous studies reported that natural antioxidants strengthen the endogenous antioxidants defenses from reactive oxygen species and restore the optimal balance by neutralizing reactive species (Albasha and Azab, 2014, Fetouh, and Azab, 2014). Curcumin has anti-inflammatory and antioxidant properties with a potent ability to inhibit reactive oxygen species formation (Biswas *et al.,* 2005). Curcumin represents a class of anti-inflammatory and anti-oxidant reported to be a potent inhibitor of reactive oxygen species formation (Venkatesan *et al.,* 2000). Fenugreek had a different active constituents such as flavonoids, alkaloids, vitamins and amino acids (Basch *et al.,* 2003). The ameliorative effect of fenugreek and curcumin against nicotine induced renal toxicity may be due to decrease nitric oxide production, uremic toxin, and increasing radical-scavenging enzyme activity through scavenging reactive oxygen and nitrogen species and chelating redex-active transition metal ions.

6. Conclusion

It can be concluded that nicotine had a strong effect on the kidney function and histological structure of the kidney. The ingestion of fenugreek and/or curcumin prevent the renal toxicity induced by nicotine. The current study suggests that fenugreek and curcumin may be useful in combating free radical-induced renal toxicity induced by nicotine.

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