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Protective Effect of *Panax* ginseng extract on Renal Functions Altered by Mercuric Chloride in Albino Rats

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Abstract : Liver and kidney are specific organs which play an active role in biotransformation and detoxification mechanisms. Ant adverse effect of chemicals or heavy metal can cause the delay or fade in these mechanisms. Present study was designed to find out the protective effect of *Panax* ginseng extract on renal functions altered by mercuric chloride (heavy metal) in albino rat. Fifty albino rats were divided into 10 groups. Five groups for acute study and five groups for sud-acute study viz. control group (Tween 20 and distilled water), mercuric chloride treated group (0.926 mg/kg body wt. for acute and 0.044 mg/kg body wt. for sub-acute group after calculated LD_{50} (9.26 mg/kg body wt.) by probit analysis (Finney, 1971)[1], *Panax* ginseng extract treated group (10 mg/kg body wt. for acute and sub-acute sets), mercuric chloride treated followed by *Panax* ginseng extract and *Panax* ginseng extract followed by mercuric chloride group. All doses were given orally by gavage tube. The result revealed that the serum urea and creatinine significantly increased in mercuric chloride treated group, while significantly decreased ($p<0.01$) in *Panax* ginseng extract group after acute and sub-acute treatment. The biochemical estimation is also confirmed by nephropathological aspect. However, the *Panax* ginseng extract treated followed by mercuric chloride group is more prominent than the mercuric chloride treated followed by *Panax* ginseng extract group. It can be concluded that *Panax* ginseng extract had a protective nature on renal functions against mercuric chloride toxicity in albino rats.

Key words : mercuric chloride, *Panax* ginseng extract, urea, creatinine, gavage tube

INTRODUCTION

Human activities have drastically altered the biochemical and geochemical cycles by intoxication of various synthetic chemicals. These chemicals have basically affected major organs (Kidney, Brain & Liver) of the body. Kidney is a major vital organ of the body which regulates the excretion, osmoregulation like major activities in the body. Any alterations in the kidney or the parts of kidney due to induction of chemicals, metabolites and plant product, produce improper renal functioning. Out of these chemicals mercuric chloride (heavy metal) affects severely inhibiting renal functions. Hepatic and renal toxicity have been reported either in workers or in experimental animals exposed to chromium VI [1-3]. On the other hand, there is a growing evidence in the literature that *Panax* ginseng extract, the well known traditional herbal remedy used in Chinese medicine for thousands of years, possess an array of interesting pharmacological effects, such as cardioprotective, vasorelaxant, antistress and stimulating action on the central nervous system[4]. Hence present study is designed to find out the curative effect of *Panax* ginseng extract on renal functions altered by mercuric chloride intoxication.

MATERIAL AND METHODS

Experimental animals

Rattus norvegicus weighting approximately (120-130) gm of both the sex were procured from inbreed colony and acclimatized to the laboratory condition for 2 weeks. The animals were fed with a standard balanced diet (Hindustan Lever Ltd, Bombay) and water was provided *ad libitum.*

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Experimental compound

Experimental compound (mercuric chloride) was obtained from Bayer India Ltd. Bombay. The acute oral LD_{50} was determined on albino rats. The mercuric chloride was dissolved in distilled water of pharmaceutical quality and introduced by gavage tube. The data were analyzed by probit analysis[5] for LD_{50} determination (Table 1). Rats from the control set were given distilled water only.

Therapeutic actions of *Panax* on renal function damage by mercuric chloride ($HgCl_2$)

Animals were divided into 5 groups of 5 rats each. Group I (normal) received 1 ml of distilled water and 10 µl tween-20, group II received *Panax* ginseng extract (10 mg/kg b. wt), group III received mercuric chloride after LD_{50} (9.26 mg/kg b. wt.) determination for acutely (0.926 mg/kg b. wt.) and sub-acutely (0.044 mg/kg b. wt.) sets, group IV received *Panax* ginseng extract followed by mercuric chloride while group V received mercuric chloride followed by *Panax* ginseng extract. The details of group and treatment are given below. Animals were sacrificed 24 hrs after the last treatment. The blood was collected directly from ventricle of heart with a sterilized syringe. Serum was collected for different biochemical analyses. Urea[6] and creatinine[7] activities were determined spectrophotometrically (Cintra-5).

Statistically significant values between experimental and control values were calculated according to Fisher's student 't' test.

Right and left kidney were quickly dissected out from the albino rats after autopsy, fixed in Bouins fluid, dehydrated with alcohol series and processed with Delafield's haematoxylin eosin solutions.

Table 1. Toxicity evaluation of Mercuric Chloride for albino rat, *Rattus norvegicus* Specifying fiducial limits

Experimental individual	Compound	Regression equation	LD_{50} (mg/kg b.w.)	Variance	Fiducial limits
Rattus norvegicus	Mercuric Chloride	Y=5.146+3.410 (x-1.009)	9.26 mg	0.006	m_1=(±)0.972 m_2=(−)0.960

Table 2. Urea (mg/dl) in albino rat

Treatment duration	Treatment sets	Control	Mercuric chloride treated	*Panax* ginseng extract treated	Mercuric chloride treated followed by *Panax* ginseng extract	*Panax* ginseng extract treated followed by mercuric chloride
6 hrs		31.14±0.91*	47.33±1.20^d	27.0±0.57^a	44.76±0.463^d	43.1±0.115^d
12 hrs	Acute	31.78±1.22*	48.33±0.88^d	28.0±0.57^a	46.46±0.338^d	44.2±0.152^d
24 hrs		30.44±1.74*	49.66±0.33^d	24.93±0.23^b	47.5±0.264^d	44.83±0.120^d
7 days		32.87±2.18*	80.0±0.57^d	34.0±0.57^a	48.9±0.172^d	46.26±0.233^d
14 days	Sub-acute	33.63±2.34*	80.33±0.88^d	34.6±0.88^a	51.16±0.133^d	47.96±0.375^d
28 days		34.26±2.70*	82.33±1.20^d	35.66±0.33^a	52.93±0.145^d	50.03±0.08^d

Table 3. Creatinine (mg/dl) in albino rat

Treatment duration	Treatment sets	Control	Mercuric chloride treated	*Panax* ginseng extract treated	Mercuric chloride treated followed by *Panax* ginseng extract	*Panax* ginseng extract treated followed by mercuric chloride
6 hrs		0.812±0.115*	2.26±0.06^d	0.66±0.003^b	1.23±0.00^d	0.936±0.00^d
12 hrs	Acute	0.819±0.113*	2.70±0.05^d	0.59±0.003^d	1.26±0.005^d	0.953±0.00^d
24 hrs		0.857±0.134*	2.96±0.03^d	0.57±0.001^d	1.296±0.00^d	0.983±0.00^d
7 days		0.858±0.158*	3.16±0.08^d	0.59±0.00^c	1.366±0.00^d	1.01±0.00^d
14 days	Sub-acute	0.835±0.108*	3.53±0.08^d	0.72±0.00^b	1.416±0.00^d	1.063±0.00^d
28 days		0.7965±0.061*	3.73±0.12^d	0.74±0.00^a	1.47±0.00^d	1.10±0.00^d

*Mean±S.Em.

Significance level: a=>0.05, b=<0.05, c=<0.01, d=<0.001

RESULTS AND DISCUSSION

Biochemical alterations

In the mercuric chloride treated albino rats the level of serum urea and creatinine significantly increased ($p<0.001$) in acute and sub-acute sets (Table 2 and 3; Fig. 6 and 7). The rise of urea and creatinine levels in mercuric chloride treated albino rats compared to normal distilled water treated albino rats suggest that due to renal injury, glomerular filtration rate (GFR) and reabsoption process have been affected. Increased level of inorganic phosphate by mercuric chloride intoxication means decrease GFR and increase reabsoption by renal tubules. Reduction in GFR limits the renal excretion of phosphate, and develops hyperphosphatemia[3].

Increased levels of marker enzymes may be related to the extent of drug uptake by the cortex of kidney. The increased levels of urea and creatinine after mercuric chloride administration may indicate protein catabolism and kidney dysfunction[8], while considerable kidney damage leading to significant functional impairment, necrosis and loss of enzymes activity in the renal tubules under stress of chromium has earlier been reported [5,9].

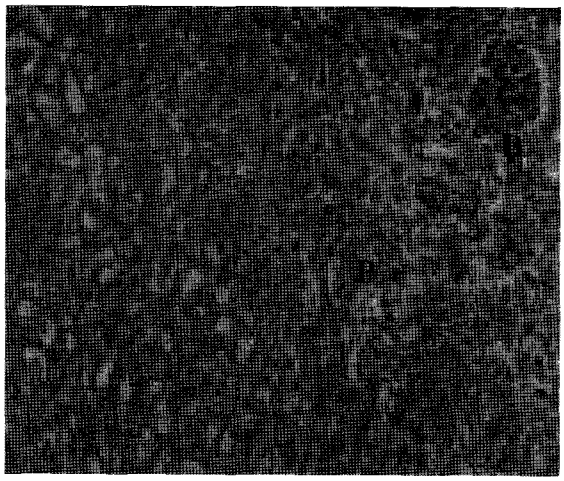

Fig. 1. Showing section of kidney [Control] emphasizing Bowman's capsule (B), glomerulus (G) and proximal convoluted tubules (P) with no sign of pyknosis.

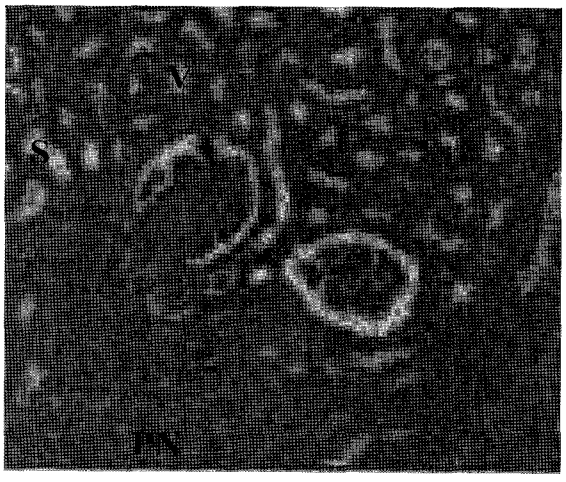

Fig. 2. Showing section of kidney [mercuric chloride treated] emphasizing changes at proximal convoluted tubule level at the site of brush border alongwith pyknotic nuclei (PN) and clearcut spaces (S) and vacuole formation (V).

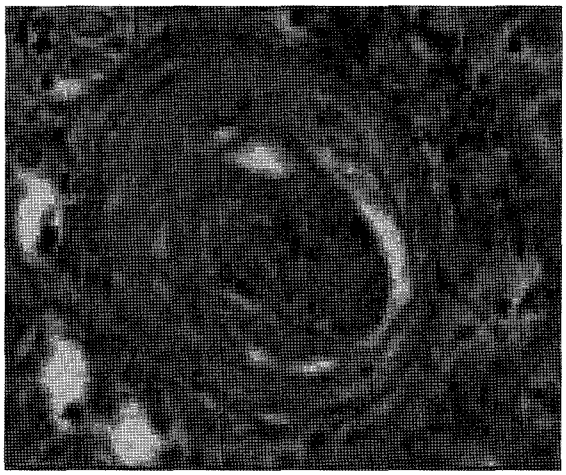

Fig. 3. Showing section of kidney [*Panax* ginseng extract treated] emphasizing anatomical details almost similar to control.

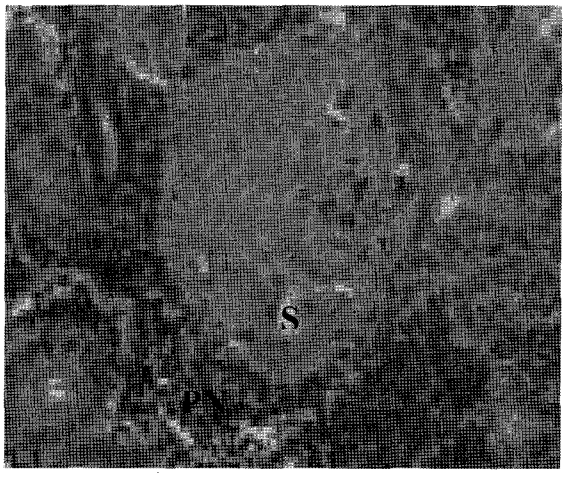

Fig. 4. Showing section of kidney [mercuric chloride followed by *Panax* ginseng extract] emphasizing moderate renal damage with greater number of pyknotic nuclei (PN) at proximal convoluted tubule level, spaces (S), however with lesser magnitude compared to Fig. 2.

The toxic effect of mercuric chloride may thus be due, to the production of oxidative stress on kidney as well as generation of reactive oxygen species producing a number of toxic reactions.

In the *Panax* ginseng extract treated albino rats the level of urea and creatinine significantly decreased acutely and sub-acutely, this may probably be due to natural antioxidant potential of *Panax* ginseng extract and generation of oxygen radicals. The present results indicate the beneficial effect of *Panax* ginseng extract in combating nephrotoxicity, as the levels of urea and creatinine approaches normal values.

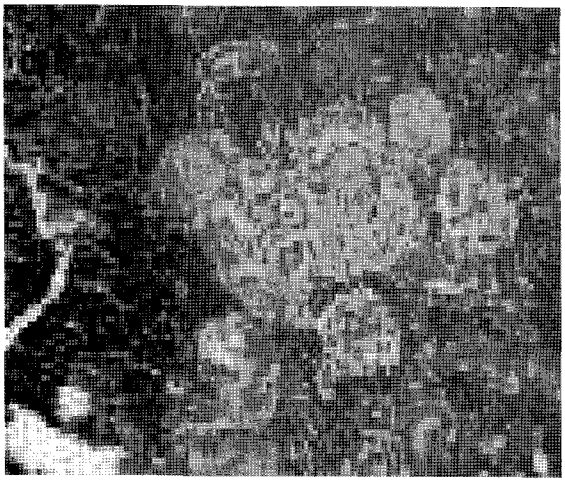

Fig. 5. Showing section of kidney [*Panax* ginseng extract followed by mercuric chloride] emphasizing minimal renal damage compared to Fig. 4.

Treatment of mercuric chloride followed by *Panax* ginseng extract and *Panax* ginseng extract followed by mercuric chloride resulted in significant improvement in kidney functions as indicated by the marked decrease in serum urea and creatinine levels and is in conformity to Yokozama *et al.*[10], who demonstrated that *Panax* ginseng extract and its active component, saponin, could significantly reduce the blood urea nitrogen and creatinine levels in the blood of nephrectomized rats. However, this reduction is better seen in *Panax* ginseng extract followed by mercuric chloride compared to mercuric chloride followed by *Panax* ginseng extract treatment in the present investigation. The nephroprotective effect by means of detoxifying excess urea and creatinine, its free radical scavenging property and its antioxidant property but the exact mechanism of the various effect is yet to be investigated for which isolation of the active ingredient is a must.

Nephropathological analysis

Mercuric chloride treated kidneys (Fig. 2) showed the shortening of the brush border, pycnotic nuclei, cytoplas-

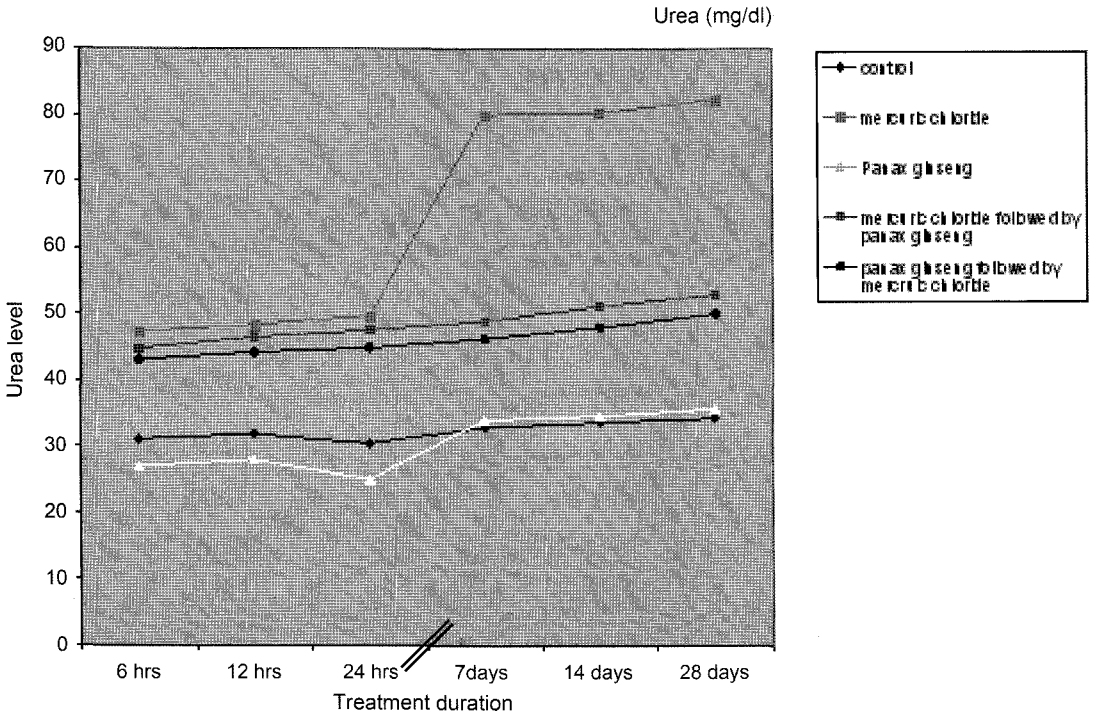

Fig. 6. Graph showing urea level in serum after acute and sub-acute studies.

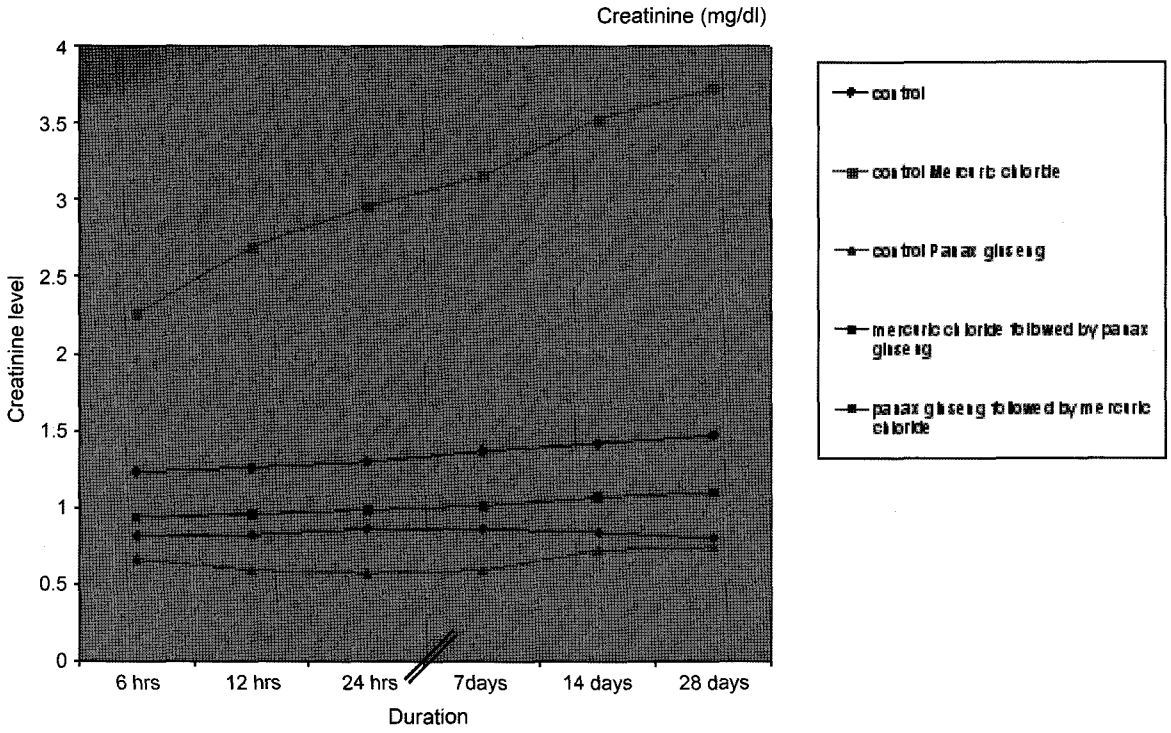

Fig. 7. Graph showing creatinine level in serum after acute and sub-acute studies.

mic debris in the vicinity of brush border as a result of the ruptured apical membrane of proximally placed tubular cells as compared to the control (Fig. 1). The rupture in the epithelium and pycnotic nuclei in the cytoplasm of distal tubular cells have also been observed. Excessive swelling and pycnotic nuclei have been detected in the cytoplasm of some proximal tubules and especially collecting tubules[11].

There has been significant regeneration of tubular epithelium of kidney after the administration of *Panax* ginseng extract (Fig. 3) due to antioxidant potential[5].

Although there have been individual differences, yet the damage to the kidney ranged from moderate to minimal in the albino rats administered with mercuric chloride followed by *Panax* ginseng extract (Fig. 4), while the damage in kidney was only minimal in the albino rats administrated with *Panax* ginseng extract followed by mercuric chloride (Fig. 5).

Hence on the basis of biochemical and nephropathological analysis it is evident that *Panax* ginseng extract followed by mercuric chloride is more potent than mercuric chloride followed by *Panax* ginseng extract treatment with regard to protection.

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