OPEM
www.opem.org

Oriental Pharmacy and Experimental Medicine 2006 **6(2)**, 108-111

KHUP

Protective effect of *Kundur* (*Boswellia serrata*) against mercuric chloride induced nephrotoxicity in rats

M Alam[1], K Javed[2] and MA Jafri[1]

[1]Department of Ilmul Advia (Pharmacology), Faculty of Medicine (Unani), Hamdard University, New Delhi-110062, India; [2]Department of Chemistry, Faculty of Science, Hamdard University, New Delhi-110062, India

SUMMARY

The effect of *Kundur* (oleo-gum resin of *Boswellia serrata*) and its fractions viz: methanol soluble (MS) and methanol insoluble (MI) were investigated on mercuric chloride induced nephrotoxicity in rats. The animals of group I and II were administered with 1% carboxymethyl cellulose (CMC) (1,000 mg/kg, p.o.) and the animals of groups III, IV and V were administered with *Kundur* (1,000 mg/kg, p.o.), MS (650 mg/kg, p.o.) and MI (350 mg/kg, p.o.) respectively for ten days. On 10th day a single dose of the mercuric chloride (3 mg/kg, s.c.) was also administered to all groups except the group I which received only 1% CMC (10 ml/kg, p.o.). After two days of mercuric chloride administration the blood samples of each animal were collected and analyzed for blood urea nitrogen and creatinine concentration. Rats fed with *Kundur* and MI fraction showed a significant prevention in the rise of serum markers while MS failed to prevent the rise of these serum makers. These results suggest that *Kundur* and MI fraction may have potential to reduce the nephrotoxicity in rats.

Key words: *Kundur* (*Boswellia serrata*); Mercuric chloride; Nephrotoxicity; Rats

INTRODUCTION

The effects of toxic metals on kidney have been known for many years, which occur as a result of occupational or therapeutic exposure to these agents. Heavy metals affecting renal functions are important in that they tend to accumulate in kidneys and may produce a broad spectrum of morphological and functional effects on kidneys. The kidneys may excrete metals in two ways. They may be filtered from blood by renal glomerulus or secreted directly into urine by transport across renal tubular lining cells from particular capillaries. Metals, which are filtered by the glomerulus, may be reabsorbed again by the cells and may be concentrated within the cell (Conner and Fowler, 1993).

Kundur (oleo-gum resin of *Boswellia serrata* Roxb, Family: Burceraceae) possesses antifungal (Garg, 1974), anticomplementary (Kapil and Moza, 1992), juvenomimetic (Dennis *et al.*, 1999) and anticarcinogenic properties (Huang *et al.*, 2000). Investigations on *Kundur* revealed its beneficial effects in immunomodulation (Sharma *et al.*, 1996), bronchial asthma (Gupta *et al.*, 1998), polyarthritis (Sander *et al.*, 1998), hepatitis C-virus (Hussein *et al.*, 2000), colitis (Gupta *et al.*, 2001) and crohn's disease (Gerhardt *et al.*, 2001).

Kundur is being used for various ailments such as dysentery, dyspepsia, lung diseases, haemorrhoids, rheumatism, urinary disorders and corneal ulcer in

*Correspondence: M Alam, B-4 Hamdard Flats, Pul Pehladpur, Tuglakabad, New Delhi-110044, India.
E-mail: mahealam_234@yahoo.co.in

Unani system of medicine for the last several years (Azam, 1885; Ibne, 1912; Ghani, 1917). It is also an ingredient in certain compound formulations viz: *Majoon Kundur, Majoon Murawwah-ul-Arwah, Dawa-ul-Kibrit* and *Habbe Suzak* of Unani medicine used in renal disorders (Lubhaya, 1979; Nigrami, 1995). Therefore, it was of great interest to determine the real efficacy of *Kundur*. In the present study, the effect of *Kundur* and its methanol soluble (MS) and methanol insoluble (MI) fractions were studied in mercuric chloride induced nephrotoxicity in rats.

MATERIALS AND METHODS

Plant material

Kundur (oleo-gum resin of *Boswellia serrata*) were procured from Qadimi Unani Dawakhana, Delhi and authenticated by Prof. S.H. Afaq at Department of Ilmul Advia (Pharmacology), Aligarh Muslim University, Aligarh. The voucher specimen (MA-K-02) of this drug is deposited at Department of Ilmul Advia (Pharmacology), Faculty of Medicine (Unani), Hamdard University, New Delhi-110062.

Drugs and chemicals

Mercuric chloride, carboxymethyl cellulose (CMC) and methanol were procured from CDH Ltd. India. The drugs were suspended in distilled water with 1% CMC.

Preparation of extracts

The procured material (*Kundur*) was further dried over calcium chloride in desiccator under reduced pressure. It was crushed thoroughly and exhaustively extracted with methanol by refluxing on boiling water bath for 10 min. It was filtered and residue was further extracted with methanol in similar conditions. The same process was also repeated third time. All the filtrates were mixed together and the solvent was removed by distillation method. The extract obtained after removal of methanol was coded as MS. The residue left on the filter paper (methanol insoluble) was coded as MI. The yields of MS and MI were found to be 65% and 35% respectively.

Animals

Wistar albino rats (150 - 250 g) of either sex were obtained from central animals house, Hamdard University, New Delhi-62 and provided food and water *ad libitum*. All the animals were maintained under laboratory conditions. All studies were carried out using six rats in each group. The experiments were performed between 09:00 and 17:00 h. The animal ethics committee of Hamdard University approved the study protocol.

Experimental procedure

The animals of group I and II were administered with 1% CMC (10 ml/kg, p.o.) and the animals of groups III, IV and V were administered with *Kundur* (1,000 mg/kg, p.o.), MS (650 mg/kg, p.o.) and MI (350 mg/kg, p.o.) respectively for ten days. On 10th day a single dose of the mercuric chloride (3 mg/kg, s.c.) was also administered to all groups except the group I which received only 1% CMC (10 ml/kg, s.c.). After two days of mercuric chloride administration, blood samples of each animal were collected and analyzed for blood urea nitrogen (BUN) and creatinine concentration (Godkar, 1994).

Statistical analysis

All the values were expressed as mean ± S.E.M. Student's *t*-test was used to analyze significance of the two means. Probability level of less than 5% was considered as statistically significant.

RESULTS

Rats receiving mercuric chloride alone showed a significant increase in the levels of BUN (850%) and serum creatinine (289.9%) as compared to control (CMC treated rats, group I) ($P < 0.001$) while the rats fed with *Kundur* showed a significant prevention in the rise of BUN (94.40%) and creatinine (132.73%) ($P < 0.001$). MI fraction showed highly

Table 1. Effect of *Kundur* and its fractions (MS and MI) on BUN and creatinine in mercuric chloride induced nephrotoxicity.

Groups	Doses	N	BUN (mg/dl) Mean ± S.E.M.	Creatinine (mg/dl) Mean ± S.E.M.
I	CMC (1,000 mg /kg)	6	6.16 ± 0.37	2.38 ± 0.13
II	CMC + M. chloride (3 mg/kg)	6	$52.36 \pm 4.07^{a,***}$	$6.90 \pm 0.40^{a,***}$
III	*Kundur* (1 gm/kg) + M. chloride (3 mg/kg)	6	$8.75 \pm 0.76^{b,***}$	$0.90 \pm 0.04^{b,***}$
IV	MS (650 mg/kg) + M. chloride (3 mg/kg)	6	$51.08 \pm 5.68^{b,ns}$	$6.22 \pm 0.41^{b,NS}$
V	MI (350 mg/kg) + M. chloride (3 mg/kg)	6	$10.54 \pm 0.60^{b,***}$	$1.20 \pm 0.08^{b,***}$

$^{***}P < 0.001$ statistically significant (a vs. control and b vs. a). NS (Statically more significant). N, number of animals in each group. CMC (10 ml/kg), M.Chloride (3 mg/kg), *Kundur* (1,000 mg/kg), MS (650 mg/kg), and MI (350 mg/kg) doses were given to the above-mentioned groups.

significant reduction in the rise of BUN (90.52%) and serum creatinine (126.17%) ($P < 0.001$) while MS fraction failed to prevent the rise of these serum markers ($P > 0.05$). The results of the study are shown in Table 1.

DISCUSSION

The effects of mercurials (Hg) such as inorganic mercuric chloride and organic mercury such as methyl mercury on the renal proximal tubule cell epithelium have been studied for many years. Each chemical form of mercury shows some specificity for a different region of the proximal tubule. Acute exposure to mercuric chloride (2 - 3 mg) produces a highly selective necrosis of the S_3 segment of the proximal tubule (Rodin and Crowson, 1962; Taylor, 1965; Kempson *et al.*, 1977). This phenomenon is preceded by damage to the cell membrane (Gritzka and Trump, 1968; Ganote *et al.*, 1981), mitochondrial structure and function and loss of cellular control over intracellular Ca_2^+ concentrations (Trump *et al.*, 1984).

Kundur is a plant exudates of *B. serrata* and its constituents can be grouped in it oil terpenoids and gum. In the present study *Kundur* was extracted in methanol and all the essential oils and terpenoids are easily soluble in methanol. Recently it is also reported that essential oil of *B.serrata* demonstrated antioxidant activity (Baratta *et al.*, 1998). Based on the above evidence it may be conducted that *Kundur* may show nephroprotective effects through its antioxidants activity of essential oil which is present in *Kundur*.

In view of the above discussion rats fed with *Kundur* and MI fraction showed a significant prevention in the rise of serum markers while MS failed to prevent the rise of these serum makers. These results suggest that *Kundur* and MI fraction may have protective effects on S_3 region of proximal tubule. Thus the reported claim about this drug may be validated by this study. Although further investigations are necessary to elucidate the mechanisms by which *Kundur* prevents the rise of these serum markers.

CONCLUSION

The results of this investigation reveal that *Kundur* and methanol insoluble fraction contains pharmacologically active substance (s) with nephroprotective properties. Thus we presume that *Kundur* can be developed for renal disorders. But to reach any conclusive decision more detailed phytochemical studies are necessary to identify the active principle and exact mechanism of action.

ACKNOWLEDGEMENTS

The authors are thankful to the authority of the institution for providing all kind of help needed.

REFERENCES

Azam K. (1885) *Akseer-e-Azam*, pp. 23-25, Maktaba Munshi Nawal Kishore, Lucknow, India.

Baratta MT, Dorman HJD, Deans SG, Figueiredo AC, Barroso JG, Ruberto G. (1998) Antimicrobial and antioxidant properties of some commercial essential oils, *Flavour Frag. J.* **13**, 235-240.

Conner EA, Fowler BA. (1993) Mechanisms of metal induced nephrotoxicity in toxicology of the kidney. IInd edition, edited by Jerry B. Hook and Robin S. Goldstein, pp. 437-457, Raven Press Ltd. New York.

Dennis TJ, Kumar A, Srimannarayana G, Raghunathrao D. (1999) Juvenomimetic activity of the gumoleoresin of *Boswellia serrata*. *Fitoterapia* **70**, 308-310.

Ganote CE, Reimer KA, Jennings RB. (1981) Acute Mercuric chloride nephrotoxicity: an electronic microscopic and metabolic study. *Lab. Invest.* **31**, 633.

Garg SC. (1974) Antifungal activity of some essential oils. *Indian J. Pharmacol.* **36**, 47-47.

Gerhardt H, Seifert F, Buvari P, Vogelsang H, Repges R. (2001) Effect of *Boswellis serrata* in crohn's disease. *Z. Gastroenterol.* **39**, 11-17.

Ghani MN. (1917) *Khazainatul Advia*, Part III, pp. 371-374, Maktaba Munshi Nawal Kishore, Lucknow, India.

Godkar PB. (1994) *Textbook of Medical Laboratory Technology*, pp. 174-175, Bhalani Publishing House, Bombay, India.

Gritzka, TL, Trump BF. (1968) Renal tubular lesions caused by mercuric chloride electronics microscopic observations degeneration of the pars recta. *Am. J. Pathol.* **52**, 12-25.

Gupta I, Gupta V, Parihar A, Gupta S, Ludtke R, Safayhi H, Ammon HP. (1998) Effect of *Boswellis serrata* gum resin in bronchial asthma. *Eur. J. Med. Res.* **3**, 511-514.

Gupta I, Parihar A, Malhotra P, Gupta S, Ludtke R, Safayhi H, Ammon HP. (2001) Effect of *Boswellis serrata* in chronic colitis. *Planta Med.* **67**, 391-395.

Huang MT, Bacdmaev V, Ding V, Liu Y, Xie JG, Ho CT (2000) Anti-tumor and anti-carcinogenic activities of triterpenoid, beta-boswellic acid. *Biofactors* **13**, 225-230.

Hussein G, Miyashiro H, Nakamura N, Hattori M, Kakiuchi N, Shimotohno K. (2000) Inhibitory effects of Sudanese medicinal plant extracts on hepatitis C-virus (HCV) protease. *Phytother. Res.* **14**, 510-516.

Ibne Sina. (1912) *Al-Qanoon Fit-Tibb*, Part II, p. 199, Nigar-e-Ashayat Main Chamber, Lahore, Pakistan.

Kapil A, Moza N. (1992) Anticomplementary activity of boswellic acid an inhibitor of C3-convertase of the classical complement pathway. *Int. J. Immunopharmacol.* **14**, 1139-1143.

Kempson SA, Ellis BG, Price RG. (1977) Changes in rat cortex, isolated plasma membranes and urinary enzymes following the infection of mercury chloride. *Chem. Biol. Interact.* **18**, 217.

Lubhaya R. (1979) *Delhi Ke Muntakhab Murakkabat*, p. 80, Goswami Pharmacy, Gali Qasimjan, Delhi, India.

Nigrami SMH. (1995) *Unani Advia Murakkaba*, pp. 110-303, Khalil Ahmad Mahmood Nagar, Lucknow, India.

Rodin AE, Crowson CN. (1962) Mercury nephrotoxicity in the rat I, Factors influencing the localization of tubular lesions. *Am. J. Pathol.* **41**, 297-314.

Sander O, Herborn G, Rau R. (1998) Resin extract of *Boswellia serrata* is useful supplement to established drud therapy of chronic polyarthritis, results of a double-blind pilot study. *J. Rheumatol.* **57**, 11-16.

Sharma ML, Kaul A, Khajuria A, Singh S, Singh GB. (1996) Immunomodulatory activity of boswellic acid (pentacyclic triterpene acids) from *Boswellia serrata*. *Phytother. Res.* **10**, 107-112.

Taylor NS. (1965) Histochemical studies of nephrotoxicity with sublethal doses of mercury in rats. *Am. J. Pathol.* **46**, 1-21.

Trump BF, Berezesky IK, Sato T, Laiho KU, Phelps PC, De Claris N. (1984) Cell calcium cell injury and cell death. *Environ. Health Perspect.* **57**, 281-287.