Effect of oleo-gum-resin of *Boswellia serrata* (*Kundur*) on renal functions in Albino rats

Mahe Alam1*, K Javed 2, & MA Jafri 3

1Department of Ilmul Advia (Pharmacology), Faculty of Medicine (Unani), Hamdard University, New Delhi-110062
2Department of Chemistry, Faculty of Science, Hamdard University, New Delhi-110062, India
3Director, National Institute of Unani Medicine, Bangalore, Karnataka, India
E-mail: mahealam_234@yahoo.co.in

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Oleo-gum-resin of *Boswellia serrata* Roxb. (Burseraceae) locally called ‘*Kundur*’, is one of the ingredients in certain Unani formulations used in renal diseases. In the present study, the effect of *Kundur* and its methanol soluble (MS), and methanol insoluble (MINS) fractions were investigated on Gentamicin induced nephrotoxicity in Albino rats. The renal effects of *Kundur* and its fractions were studied by monitoring urea and creatinine blood levels.

Aminoglycoside antibiotics including Gentamicin are widely used in the treatment of Gram-negative bacterial infections. A major complication of the use of these drugs is nephrotoxicity. In the current study, treatment with *Kundur* its methanol soluble (MS) and methanol insoluble (MINS) fractions significantly prevented the rise in blood urea and serum creatinine levels. Our results suggest that *Kundur* and its (MS) methanol soluble fraction induced renoprotective action against Gentamicin induced nephrotoxicity probably due to the presence of compounds possessing antioxidant potential.

Keywords: Gentamicin, *Kundur*, Nephrotoxicity

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*Kundur* (Oleo-gum-resin of *Boswellia serrata*) is used for the treatment of various ailments such as dysentery, dyspepsia, lung diseases, haemorrhoids, rheumatism, urinary disorders and cornal ulcer in Unani System of Medicine and Ayurvedic System of Medicine for the last several years1-3. It is also an ingredient of certain compound formulations viz. *Majoon Kundur*, *Majoon Murawwah-ul-Arwah*, *Dawa-ul-Kibrit* and *Habbe Suzak* used in Unani medicine for the treatment of different renal disorders4-5. Various pharmalogically active chemical constituents were isolated from *Kundur*6-10.

*Kundur* is known to exhibit antifungal11, anti-complementary12, Juvenomimetic13, anti-inflammatory14-15 and anti-carcinogenic activities16. Earlier investigations also revealed that *Kundur* to possess immunomodulatory properties17, useful in bronchial asthma18, Polyarthritis19, Colitis20, Crohn's disease21 and against Hepatitis C-virus22.

Aminoglycosides including Gentamicin isolated from the *actinomycetes* were found effective against gram-negative bacteria, especially *Pseudomonas* species, and certain gram-positive bacteria. The major side effect of Gentamicin treatment is its nephrotoxic potential. Gentamicin was confirmed to cause acute renal failure and it induced dose-dependent cytotoxicity23.

The proximal tubule was the most common site for Gentamicin induced nephrotoxicity and renal carcinogenesis as confirmed in different animal models24-25. The Gentamicin induced nephrotoxicity was found to be mainly confined to the proximal convoluted tubules and pars recta, where it produced tubular cell necrosis26. However, the pathogenesis are yet to be elucidated27-30. The effects of Gentamicin accumulation by crossing apical membrane, its action on lysosomes, mitrocondrial, and plasma membrane structure and function were studied by several researchers31-36. Gentamicin treatment in rats was found to increase lipid peroxidation in renal cortex37, which was decreased by selenium38. These observations indicated a possible role of lipid peroxidation in aminoglycoside nephrotoxicity.
Usually for clinical studies, decline in glomerular filtration rate, serum creatinine and urea levels, N-acetylgalactosaminidase, proteinuria, β2-microglobulin, lysozymuria, and histopathological investigations are considered essential for patients to conclude possible nephrotoxicity. Based on the fact that reno-protective activity of Kundur has not been fully investigated, therefore, current study was designed to explore the effect of Kundur-treatment on kidney function in order to justify its use in different systems of medicine.

**Materials and methods**

*Kundur* used in the current study, was obtained from Qadimi Unani Dawakhana Ballimaran, Delhi, India. The authenticity of *Kundur* was established as Oleo-gum-resin of *B. serrata* by Prof. S H Afaq and Dr Mohinul Haq Siddiqui, Dept of Ilmul Advia, Ajmal Khan Tibbiya College, Aligarh Muslim University, Aligarh. The voucher specimen MA-K-02-03 of this drug was preserved at the Department of Ilmul Advia, Faculty of Medicine, Hamdard University, New Delhi, India.

Albino wistar rats of either sex weighing 175-250 gm were used in the present study. The animals were obtained from Hamdard University, New Delhi and the Animal Ethical Committee of Hamdard University approved the study protocol. The animals were randomly assigned to five separate groups. Six animals were allotted to each group. Throughout the study all animals were kept under standard laboratory conditions: Temperature 28±1°C, and 12 hr light/dark cycle. The experiments were performed between 09:00 and 17:00 hours. The animals were fed with standard diet (supplied by the New Maharashtra Chakan oil Mills Ltd., Mumbai) and water ad libitum.

*Kundur* was dried over calcium chloride (CaCl2) in a desiccator under reduced pressure. The dried oleo-gum-resin was crushed thoroughly and extracted with methanol by refluxing on boiling water bath for 10-15 minutes. It was filtered and the residue was further extracted with methanol two times. All the filtrates were combined together and the solvent was removed under reduced pressure. The extract obtained after removal of methanol was named as MS (Methanol soluble). The residue (Methanol Insolubile) left on the filter paper was named as MINS. The yields of MS and MINS were found to be 65% and 35%, respectively.

Carboxy methyl cellulose (CMC) and methanol were procured from Central Drug House, New Delhi, India, Gentamicin was obtained from Honyad Pharmaceutical Pvt Ltd. India. The drugs were suspended in distilled water with 1% Carboxymethyl cellulose (CMC).

**Experimental procedure**

The current study was designed for eight days.

- **Group I:** was given vehicle (1% CMC in D.W, 10 ml/kg/day, p.o.) and served as control. Distilled water was abbreviated as D.W. and body weight as b.w.
- **Group II:** was given vehicle (1% CMC in D.W 10 ml/kg/d, p.o.) and Gentamicin (100 mg/kg) for 8 days. It was Gentamicin group.
- **Group III:** The animals in group-III received *Kundur* (1 g/kg b.w/d) suspended in vehicle (10 ml/kg) and Gentamicin (100 mg/kg) for eight days.
- **Group IV:** The animals received methanol soluble (MS) *Kundur* fraction (650 mg/kg/b.w/d) suspended in vehicle (10 ml/kg) with Gentamicin (100 mg/kg) for eight days.
- **Group-V:** The animals received methanol insoluble (MINS) *Kundur* fraction (350 mg/kg b.w/d) suspended in vehicle (10 ml/kg) with Gentamicin (100 mg/kg) for eight days.

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

The effect of Oleo-gum-resin of *Boswellia serrata* (Kundur) and its fractions (MS and MINS) on renal function was examined in Gentamicin nephrotoxicity model. The daily subcutaneous administration of Gentamicin at 100 mg/kg for 8 days caused renal dysfunction in the rats as evidenced by statistically significant increase in blood urea (373.59%) and serum creatinine (170%) as compared with control. Co-administration of Kundur with Gentamicin subcutaneously prevented the rise (P<0.001) in blood urea (49.93%) and serum creatinine (8.21%). About 44.27% inhibition in the rise of BUN (Blood urea nitrogen) and (30.90%) inhibition in the rise of serum creatinine with MS treatment was observed. MINS treatment on higher dose caused a statistically, while (P>0.05) decrease in the studied parameters (Table 1).

Discussion

A relationship between oxidative stress and Gentamicin induced nephrotoxicity has been well documented in many experimental animal models. Administration of superoxide dismutase provides a marked protection against Gentamicin induced impairment of renal function. Co-administration of antioxidant, vitamin E and selenium was found protective against Gentamicin induced nephrotoxicity. It has also been reported that the essential oils of Kundur (*B. serrata*) demonstrated antioxidant activity comparable with α-tocopherol (vitamin E) and butylated hydroxyl toluene (BHT). The renoprotective activity shown by Kundur and its MS (Methanol soluble) fraction against Gentamicin-induced nephrotoxicity during current study, may be attributed to the chemical constituents of Kundur having antioxidative potential. It is worth mentioning that MINS (methanol insoluble) fraction also reduced serum creatinine level indicating its nephroprotective activity. During the current experiment it is fully justified that Kundur possesses renoprotective effect and further studies are warranted to explore its mechanism of action.

Conclusion

The results of our current study investigation revealed that essential oil of Kundur and the chemical constituents of its methanol soluble fraction are capable to reduce the nephrotoxicity caused by Gentamicin. However, to reach any conclusive decision before recommending Kundur in cases of renal disorders detailed phyto-pharmaco-toxicological studies are necessary to identify the active principle of Kundur and their exact mechanism of action.

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