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Review Paper

Pharmacological Evaluation of *Boswellia Serrata* on Docetaxel Induced Kidney Toxicity in Experimental Rats

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ABSTRACT

Nephrotoxicity is defining as rapid deterioration in the kidney function due to toxic effect of medications and chemicals. There are various forms, and some drugs may affect renal function in more than one way. Nephrotoxins are substances displaying nephrotoxicity. Different mechanisms lead to nephrotoxicity, including renal tubular toxicity, inflammation, glomerular damage, crystal nephropathy, and thrombotic microangiopathy. The traditional markers of nephrotoxicity and renal dysfunction are blood urea and serum creatinine which are regarded as low sensitive in the detection of early renal damage. Thus, the detection of the initial renal injures required new biomarkers which are more sensitive and highly specific that gives an insight into the site of underlying renal damage. Kidney injury molecule-1, Cystatin C, and neutrophil gelatinase-associated lipocalin sera levels are more sensitive than blood urea and serum creatinine in the detection of acute kidney injury during nephrotoxicity..

INTRODUCTION

Here's a **comprehensive review style summary** focused on **pharmacological evaluation of *Boswellia serrata*** in the context of **docetaxel-induced kidney toxicity in experimental rats** — including relevant mechanisms, evidence from related nephrotoxicity models, and implications for future research.

Importance of Renal Toxicity Assessment

Nephrotoxicity, also known as renal toxicity, is a continuing concern during drug development. Studies have shown that numerous substances, such as toxic chemicals and medications, can induce kidney toxicity by one or more common pathogenic mechanisms. Generally, renal toxicity refers to acute kidney injury and chronic kidney

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disease. Importantly, once a human is diagnosed with acute kidney injury after exposure to toxic chemicals, it means that the rapid loss of renal function and the precursor of acute renal failure. While, chronic kidney disease indicates it is a long process that may result in end-stage kidney disease and requiring dialysis or kidney transplant. Therefore, it is critical to determine the potential kidney toxicity of new drugs before clinical trials.

Background & Rationale

Docetaxel (DTX) is a widely used chemotherapeutic agent for multiple solid tumors, but its clinical use is limited by **organ toxicities**, including kidney (renal) damage. In experimental rats, DTX has been shown to induce nephrotoxicity characterized by *oxidative stress*, *inflammation*, *apoptosis*, and *autophagy* in renal tissue, leading to impaired renal function and histopathological alterations. A protective agent ideally should counteract these molecular events.

Boswellia serrata (BS) is a traditional medicinal resin known for its **anti-inflammatory**, **antioxidant**, and **anti-fibrotic** properties, largely attributed to boswellic acids (e.g., AKBA, KBA). These active pentacyclic triterpenes modulate signaling pathways linked to inflammation (NF- κ B), oxidative stress, and extracellular matrix deposition.

Preclinical Evidence on Nephroprotection

Although **no direct published study** (as of now) explicitly evaluates *Boswellia serrata against docetaxel-induced nephrotoxicity* in rats, there is substantial evidence from **related nephrotoxicity models** supporting its potential protective effects:

1. Antioxidant and Anti-inflammatory Effects

- In a carbon tetrachloride (CCl₄)-induced nephrotoxicity model, BS gum resin extract significantly improved renal function, increased antioxidant capacity, reduced

oxidative stress markers (MDA), and decreased pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6, IL-8) and fibrogenic TGF- β . Histology also showed restoration of kidney architecture.

2. Reduction of Oxidative Stress & Inflammation in Other Models

- Diabetic rat models: BS reduced renal markers and oxidative stress (lower malondialdehyde, higher antioxidant enzymes) and prevented structural abnormalities in kidneys.
- Mercuric chloride-induced kidney damage: BS or its fractions prevented increases in nephrotoxic serum markers and preserved structural integrity in rats.
- Sepsis-associated renal injury: Animal studies report amelioration of sepsis-induced kidney dysfunction with BS extract.

These studies collectively support BS's nephroprotective potential through:

- ROS scavenging, enhancing endogenous antioxidant defenses
- Downregulation of pro-inflammatory cytokines
- Prevention of extracellular matrix buildup and fibrosis

Mechanistic Insights Relevant to Docetaxel Toxicity

DTX-induced nephrotoxicity shares several core pathological features with other nephrotoxic models where BS has shown benefit:

◆ Oxidative Stress

DTX elevates oxidative stress, depletes antioxidants, and increases lipid peroxidation in renal tissues — a key event leading to cell damage. BS compounds, especially boswellic acids, have free-radical scavenging activities that counter these effects.

◆ Inflammation



DTX triggers upregulation of pro-inflammatory mediators (TNF- α , IL-6). Boswellia's inhibition of NF- κ B and downstream cytokine production could counteract this inflammatory cascade.

◆ Apoptosis & Cell Death Pathways

Although direct evidence in DTX models is not yet published for BS, similar phytochemicals with antioxidant and anti-inflammatory roles have been shown to modulate apoptosis pathways in chemotherapy-induced organ toxicity models. Given boswellic acids' ability to influence signaling pathways like NF- κ B and possibly MAPK, BS could theoretically attenuate apoptosis linked to oxidative/inflammatory stress.

Pharmacological Evaluation Considerations

Active Constituents

The principal bioactives, especially **acetyl-11-keto- β -boswellic acid (AKBA)** and KBA, are key modulators of inflammatory and oxidative pathways.

Mechanisms of Interest

Potential mechanisms by which BS might protect against DTX-induced nephrotoxicity include:

1. **Antioxidant Activity** – enhancing glutathione and endogenous enzymes (SOD, catalase), reducing MDA
2. **Anti-inflammatory Action** – suppression of NF- κ B, reduction in TNF- α /ILs
3. **Antifibrotic Effects** – decreasing TGF- β and ECM deposition
4. **Cell Survival Pathways** – potential modulation of apoptotic regulators (Bcl-2 family) and stress-response signaling

These are inferred from studies in other nephrotoxic conditions where BS was beneficial.

Limitations & Research Gaps

✗ There are **no published studies directly testing Boswellia serrata against docetaxel-induced**

renal toxicity (verified through current literature searches).

✗ Most evidence is from **other nephrotoxicity models** (CCl₄, diabetes, heavy metals).

✗ Pharmacokinetic challenges (low bioavailability of boswellic acids) may limit clinical translation without formulation improvements.

✗ Dose optimization, timing of administration (prophylactic vs. therapeutic), and comparison with standard nephroprotective agents remain unexplored in the DTX context.

Future Directions

To establish *Boswellia serrata* as a protective agent for docetaxel-induced nephrotoxicity, future studies should:

✓ Conduct **controlled experimental rat studies** with DTX + BS co-treatment, evaluating:

- **Biochemical markers** (urea, creatinine, oxidative stress assays)
- **Inflammatory cytokines**
- **Histopathology of renal tissue**
- **Molecular signaling** (NF- κ B, TGF- β , apoptosis markers)

✓ Assess dose-response relationships and formulations that enhance **bioavailability**.

✓ Compare with established nephroprotective agents (e.g., silymarin) in head-to-head studies.

Kidney toxicity (nephrotoxicity) is damage to the kidneys from drugs, chemicals, or toxins, leading to a decline in kidney function, potentially causing acute kidney injury or chronic kidney disease. Common causes include certain antibiotics, chemotherapy drugs, heavy metals (mercury, lead), pesticides, and radiocontrast agents, while symptoms can range from fatigue and unusual bleeding to reduced urine output, with diagnosis often relying on blood tests like BUN, creatinine, and GFR. Treatment focuses on removing the

toxic substance and managing symptoms, though severe cases can be fatal

.Causes of Nephrotoxicity

- **Medications:** Antibiotics, anticancer drugs (e.g., cisplatin), some pain relievers, and anti-inflammatory drugs.
- **Chemicals & Heavy Metals:** Mercury, lead, cadmium, arsenic, ethylene glycol (antifreeze), and certain industrial solvents.
- **Natural Toxins:** Mycotoxins (from fungi) and plant toxins like aristolochic acids.
- **Other Substances:** Radiocontrast dyes used in imaging.

Signs & Symptoms

- Decreased urination or no urination
- Fatigue, weakness, confusion
- Nausea, vomiting, poor appetite
- Swelling (edema)
- Unusual bleeding or bruising
- Pain in the lower back or sides

Diagnosis & Management

- **Diagnosis:** Blood tests (serum creatinine, BUN, GFR) to assess kidney function, though these often show damage after it's already significant.
- **Treatment:** Stop the offending agent, supportive care, dialysis for severe cases, and management of underlying causes.

Risk Factors

- Pre-existing kidney disease
- Older age
- Dehydration
- Diabetes

DRUG PROFILE

Docetaxel

Brand Names- Beizray, Docivyx, Taxotere

Generic Name- Docetaxel

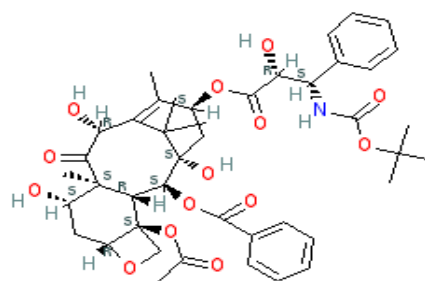
DrugBank Accession Number- DB01248

Background

Docetaxel is a clinically well-established anti-mitotic chemotherapy medication used for the treatment of different types of cancer, including breast, ovarian, and non-small cell lung cancer. Docetaxel is a complex diterpenoid molecule and a semisynthetic analogue of [paclitaxel](#). Docetaxel reversibly binds to micro tubulin with high affinity in a 1:1 stoichiometric ratio, allowing it to prevent cell division and promote to cell death. Compared to paclitaxel, docetaxel is two times more potent as an inhibitor of microtubule depolymerization. Docetaxel binds to microtubules but does not interact with dimeric tubulin. The use of docetaxel may lead to undesired outcomes such as hepatic impairment, hematologic effects, enterocolitis and neutropenic colitis, hypersensitivity reactions, fluid retention, second primary malignancies, embryo-fetal toxicity, and tumor lysis syndrome. Docetaxel was approved by the FDA in 1996 and is available in solution for injection for intravenous or parenteral administration.

Modality- Small Molecule

Groups- Approved, Investigational
Structure



Weight-Average: 807.8792g/Mol

Monoisotopic: 807.346605409g/Mol

Chemical Formula- C₄₃H₅₃NO₁₄

Synonyms -Docetaxel

Pharmacology: Docetaxel Is A Taxoid Antineoplastic Agent. It Promotes The Assembly



Of Microtubules From Tubulin Dimers And *Boswellia Serrata*
Stabilizes Microtubules By Preventing
Depolymerization.

Name	Indian frankincense
Scientific Name	<i>Boswellia serrata</i>
Common Name	Indian olibanum, Dhup, Salai, Salai guggul, Sallaki
Family	Burseraceae
Chemical Constituents	Oleo-gum-resin, β -boswellic acid, acetyl- β -boswellic acid, 11-keto- β -boswellic acid and acetyl-11-keto- β -boswellic acid



12 dark cycle. The animals will have free access to food pellet (Nav Maharashtra Chakan oil mills Ltd., Pune) and water *ad libitum*. All the experimental protocols will be approved by the Institutional Animal Ethics Committee (IAEC) of CPCSEA constituted under the guidelines of Committee for the Purpose of Control and Supervision of Experiment on Animals (CPCSEA).

MATERIAL and METHODS

Animals:

Sprague Dawley rats weighing 180-220 g will be purchased from Global Bioresearch Solutions Private Limited, H No 251 Nhavi, Tal-Bhor, Dist-Pune; Pune. The animals will be housed in polypropylene cages and maintained under environmental condition of temperature 25 ± 1 °C and relative humidity of 45-55 % under 12h light:

Chemicals:

Standardized extract of *Boswellia Serrata* shall be purchased from Natural Remedies Private Limited, India. CoQ 10 (Coenzyme 10) capsules shall be purchased from Tata 1mg, India. Docetaxel shall be purchased from Otto Chemie Pvt. Ltd., India. All chemicals are analytical grade.

METHOD

Species/ Common name	<i>Common name: Rodent-Rat, Strain: Sprague Dawley rat</i>
Age/weight/size	5-6 weeks / 200-250 g /medium size
Gender	Male/female
Number to be used (year- wise breakups and total figures needed to be given)	36
Number of days each animal will be housed	07 days of quarantine=90 days of study

Proposed source of animal	Global Bioresearch Solutions Private Limited, H No 251 Nhavi, Tal-Bhor, Dist-Pune; Pune.
Registration number	2168/PO/Re/S/22/CPCSEA

Experimental study of standardized extract of *Boswellia Serrata* on docetaxel-induced kidney toxicity in laboratory rats

The effects of standardized extract of *Boswellia Serrata* and Coenzyme Q10 shall evaluate into following groups containing six rats in each group viz;

- Group I: Normal group: The rats will receive only vehicle (Distilled water, 10 mg/kg, p.o.) for 4 weeks.
- Group II: Vehicle control: The rats will receive docetaxel (DTX; 5 mg/kg weekly, i.p., for 4 weeks) and only vehicle (Distilled water, 10 mg/kg) for 4 weeks.
- Group III: Coenzyme Q10 (10) group: The rats will receive DTX (5 mg/kg weekly, i.p., for 4 weeks) and concomitant treatment with Coenzyme Q10 at a dose of 10 mg/kg, p.o., for 4 weeks.
- Group IV: *B. Serrata* (100) group: The rats will receive DTX (5 mg/kg weekly, i.p., for 4 weeks) and concomitant treatment with *B. Serrata* at a low dose of 100 mg/kg, p.o for 4 weeks.
- Group V: *B. Serrata* (200) group: The rats will receive DTX (5 mg/kg weekly, i.p., for 4 weeks) and concomitant treatment with *B. Serrata* at a medium dose of 200 mg/kg, p.o for 4 weeks.
- Group VI: *B. Serrata* (400) group: The rats will receive DTX (5 mg/kg weekly, i.p., for 4 weeks) and concomitant treatment with *B. Serrata* at a high dose of 400 mg/kg, p.o for 4 weeks.

Furnish details of injection schedule

A] For test drug:

Substances: Standardized extract *B. Serrata*

Dose: 100, 200, and 400 mg/kg

Sites: Oral

Volumes: Not more than 1-2 ml

Blood withdrawal: Yes

Volume: 0.3 ml

B] For test drug:

Substances: Coenzyme Q10

Dose: 10 mg/kg

Sites: Oral

Volumes: Not more than 1-2 ml

Blood withdrawal: Yes

Volume: 0.3 ml

CONCLUSION

The risk of nephrotoxicity depends on factors such as dosage, duration of exposure, patient age, pre-existing kidney disease, hydration status, and concurrent use of multiple nephrotoxic agents. Early recognition through monitoring of renal function tests, urine output, and clinical symptoms is essential for preventing irreversible injury. Preventive strategies include dose adjustment, adequate hydration, avoidance of unnecessary drug combinations, and regular follow-up in high-risk patients.

In conclusion, awareness, careful drug selection, patient education, and timely intervention are crucial in minimizing nephrotoxic effects and preserving kidney health. Early diagnosis and preventive measures significantly improve patient outcomes and reduce the burden of kidney disease.



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