

Nephroprotective Activity of Bark of *Artocarpus Heterophyllus* Lam

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Abstract

Nephrototoxicity is one of the major health problems of mankind as it is due to exposed of many kinds of therapeutic agents and xenobiotics. The present study was aimed to examining the possible nephroprotective role methanolic and aqueous extracts of *Artocarpus heterophyllus* bark against gentamicin induced nephrotoxicity. The plant extracts showed a remarkable nephroprotective activity against gentamicin induced nephrotoxicity. In gentamicin induced nephrotoxicity there is a significant elevation of uric acid, urea and creatinine level. Treatment with both the extracts (100mg/Kg and 200mg/Kg) significantly reduced the biochemical level in a dose dependant manner which proving it's nephroprotective activity. There was also significant increase in RBC count and haemoglobin level by both the extract. Histopathological study of kidney further confirms the activity.

Keywords: *Artocarpus heterophyllus*, Nephroprotective.

1. Introduction

The plants are most important wealth of the nature. They are using as the important source of drugs. Drugs that derived from phytochemicals are safer and cheaper. More than 65% of world populations depend on plant related medicines. The science of natural/traditional drugs has been evolved along with human civilization. During scientific knowledge accumulated, human we started deviating from the usage of traditional medicine to synthetic drugs. All these drugs of synthetic origin are chemical molecules and when they are administered to humans, they react with one or other endogenous substance to elicit their response. But along with the correction of the pathophysiological conditions these drug molecules also produce adverse reactions by interacting with other endogenous substances. This has become major difficulty in the treatment of many diseases. In addition the modern era of the globalization and

liberalization, the price of drug research on synthetic drugs is escalating in geometrical progression. This is affecting the prices of many essential drugs. Hence, new drug discovery are shifting to herbal medicines for safer and cheaper remedies to treat various ailments. To cope-up with the pace of the modern trend in drug research, we thought of turning our eyes towards the ancient system of medicine i.e. Ayurveda and native knowledge.

Since the tribal native practitioner of Manipur claimed that the bark of *Artocarpus heterophyllus* are highly useful in treatment of nephrotoxicity and we were in search for an alternative medicine for the treatment of kidney damage, this claim has attracted our attention and selected the plant for present study[1,2].

2. Material and Methods

2.1 Plant Material

Barks of *Artocarpus heterophyllus* Lam were collected from the forest of Manipur. The plant was authenticated by Dr. Biseshwori Thongam, Scientist, Plant Taxonomy, Medicinal plants and Horticultural resources division, IBSD, Dept. of biotechnology, Govt. of India, Imphal-795001, Manipur (IBSD/MPHRD/M/1008). The shade-dried bark were course powdered and this powder were packed in soxhlet column and extracted successively with petroleum ether, chloroform, methanol and aqueous. The extracts were concentrated under reduced pressure (bath temperature 50°C). The dried extracts were stored in air tight container in refrigerator below 10°C.

2.2 Experimental Animals

Albino rats (150-200gms) and albino mice (20-30gm) of either sex were procured from Sri Venkateshwara enterprises, Bangalore (IAE/SKIPS/2011/MAY15/I/12/RATS-96/MICE-36). After procuring the animals were acclimatized for 10 day's under standard husbandry conditions.

2.3 Determination of acute toxicity [3]:

The acute toxicity for methanolic and aqueous extracts of bark of *Artocarpus heterophyllus* was determined in albino mice, maintained under standard conditions. The animals were fasted overnight prior to the experiment. Fixed dose (OCED Guideline No. 420) method of CPCSEA was adopted for toxicity studies. There were no sign of toxicity for first 48 hours and no animal died on 14 day of study at a dose of 2000 mg/Kg.

2.4 Pharmacological evaluation [4-7]:

2.4.1 Evaluation of Nephro-protective activity in gentamycin-induced nephrotoxicity

Albino rats (Wistar Strain) of either sex weighing 150-200g were selected and divided into 7 groups of 6 animals in each. Group I: Rats orally received plain vehicle for 14 days. Group II: Received gentamycin control (60mg/kg b.wt/day) for 14 days. Group III: Received gentamycin Silymarin (25 /kg b.wt/day) for 14 days. Group IV: BMEAH (100 mg/kg) and gentamycin as group II. Group V: BMEAH (200 mg/kg) and gentamycin as group II. Group VI: BAEAH (100 mg/kg) and gentamycin as group II. Group VII: BAEAH (200mg/kg) and gentamycin as group II.

In young albino rats, nephrotoxicity was produced by injecting gentamycin (60 mg/kg) for 14 days intraperitoneally (I.P). The animal of control groups received equal volume of distilled water.

During the investigation, the rats were kept up under standard diet and water. The blood was collected from the

retro orbital plexus of the rats of all groups and on the 15th day of the dose administration, under light anesthetic ether. The blood sample centrifuged at 3000 rpm for 30 min to separate the serum. The serum was subjected for different biochemical parameters, like blood urea and serum creatinine.

The blood samples collected from the animals were subjected to centrifugation at 3000 rpm for 30 min to separate the serum. About 5-500µl of serum sample was collected for the estimation of biochemical parameters, was transferred to each of the pediatric sample cups. Then, these cups and the working reagent bottles (25 ml) corresponding to the bio-chemical parameters were placed at their respective positions in the rotor system of the Autoanalyser. After 30 min of programming the test parameters, the corresponding parameter values of the different serum samples displayed were recorded.

3. Result and Discussion

The results of the study specify that the aqueous and methanolic extracts of bark, *Artocarpus heterophyllus* posses nephroprotective activity (Table 1). The elevation of serum urea, and creatinine, on gentamicin treated rats indicate kidney damage, the decreased concentration of these parameters in the extract treated rats at 100 and 200 mg/ kg indicates protection of the kidney as urea and creatinine excreted through renal route (Figure 2 & 3).

Nephrotoxicity produced by gentamicin caused significant reduction in levels of Hb and RBC when compared to the normal control groups. *Artocarpus heterophyllu* extracts significantly improve the decrease in these parameters which significantly elevate Hb and RBC values (Figure 4 & 5). These results suggest that the plant contain phytoconstituent which can enhance erythropoiesis by increase the level of erythropoietin synthesized by kidney.

In this study, the nephroprotection produced by bark extracts of *Artocarpus heterophyllus* was confirmed histopathologically by the decreased damage appeared in the kidney tubules of treated rats which revealed recovery of many tubules from the nephrotoxic effect produced by gentamicin (Figure 1).

The phytochemical studies reveal the presence of flavonoids and polyphenolic compound in the bark extract [8-14]. These polyphenolic compounds are responsible for antioxidant activity. The plant posses the anti oxidant activity [15]; which may also be responsible for nephroprotective activity.

Table 1: Effect of aqueous and methanolic extract of *Artocarpus heterophyllus* bark on Gentamicin induced Nephro-toxicity in rats

Group	Blood urea (mg/dl)	Serum creatinine (mg/dl)	RBC (million cells/mm ³)	Haemoglobin (g/dl)
Normal control	33±1.328	1.12±0.0269	8.39±0.2567	13.9±0.2817
Toxic control (Gentamicin- 60 mg/kg)	71.3±0.3033	2.13±0.0251	5.29±0.0298	8.26±0.3326
Std (Silymarin-25 mg/kg)	35.6±0.8869***	1.14±0.0244***	8.27±0.0543***	13.1±0.3483***
BMEAH (100 mg/kg)	51.11±0.2369***	1.65±0.0323***	7.17±0.0305***	13.11±0.5280***
BMEAH (200 mg/kg)	38.2±1.469***	1.20±0.0286***	7.91±0.0961**	13.72±0.5743***
BAEAH (100 mg/kg)	57.6±0.3276***	1.73±0.0374***	6.97±0.0313***	13.06±0.5007***
BAEAH (200 mg/kg)	45.51±0.3382***	1.30±0.0290***	7.23±0.0305***	13.53±0.4865***

Values are the mean ± S.E.M., n=6. ***P <0.001, **P <0.01, *P <0.005 (Vs.toxic control)

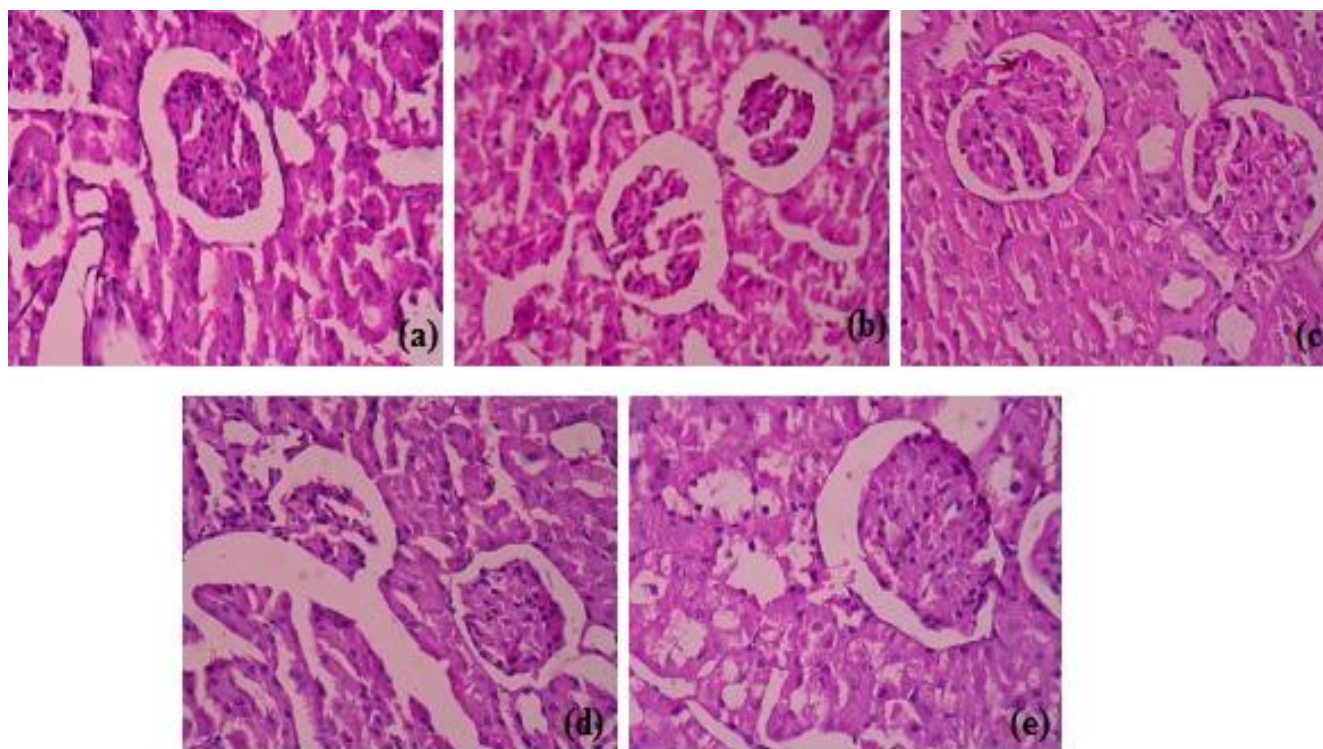


Figure 1: (a) Normal control (b) gentamicin 60 mg/kg (c) Silymarin 25 mg/kg (d) Bark methanolic extract 200 mg/kg (e) Bark aqueous extract 200 mg/kg

Group I: Normal control showed normal appearance of renal tissue architecture (Fig. 1a).

Group II: Negative control showed derelict architecture of renal parenchyma. The severe tubular congestion and glomerular congestion was observed. The moderate tubular cell swelling, loss of brush border, interstitial edema and also observed (Fig 1b).

Group III: Positive control showed intact architecture of renal parenchyma. In renal tubules and glomerules showed degenerative changes. Blood vessels and Interstitium were archetypal appearance (Fig 1c).

Group IV: Treatment done with BMEAH 200 mg/kg showed integral architecture of renal parenchyma. The tubular cells, cytoplasmic vacuoles are appeared normal. Glomerulus Bowman's space emerges intact. Most of the renal tubules show degenerative changes (Fig 1 d).

Group V: Treatment done with BMEAH 200 mg/kg showed integral architecture of renal parenchyma. Intact glomerulus renal tubules and some of the tubules are normal (Fig 1e).

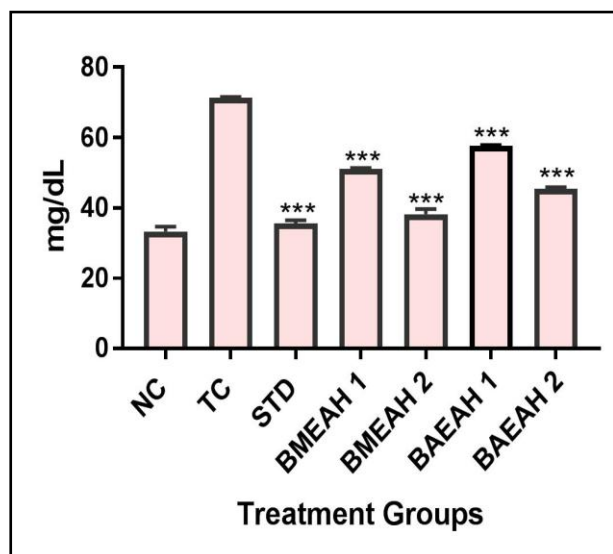


Figure 2: Effect of aqueous and methanolic bark extracts of *Artocarpus heterophyllus* on blood urea level

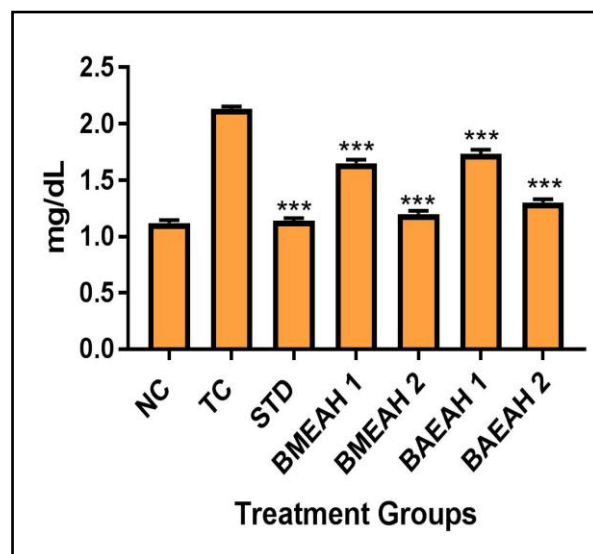


Figure 3: Effect of aqueous and methanolic bark extracts of *Artocarpus heterophyllus* on serum creatinine level

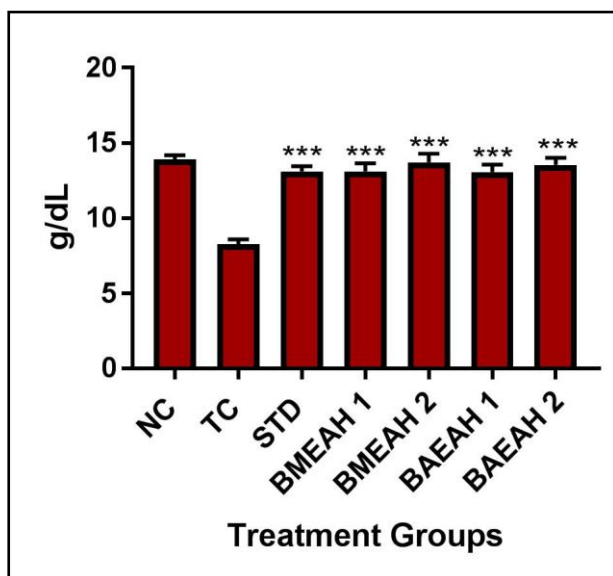


Figure 4: Effect of aqueous and methanolic bark extracts of *Artocarpus heterophyllus* on Hb level

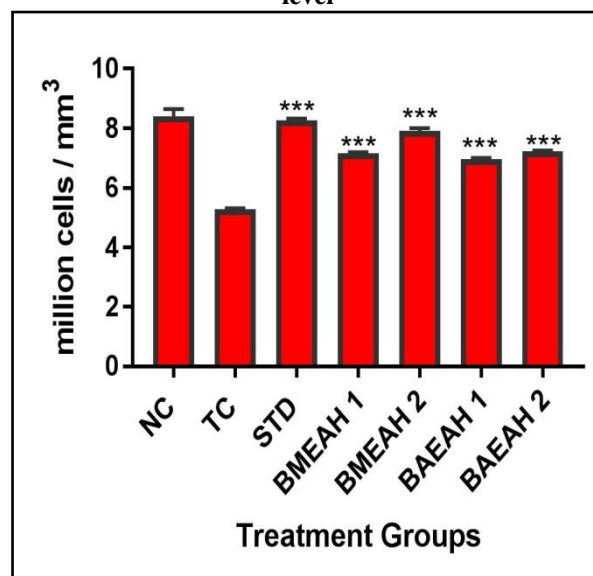


Figure 5: Effect of aqueous and methanolic bark extracts of *Artocarpus heterophyllus* on RBC count

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