

## Protective Effect of Poly herbal Preparation Against Gentamicin Induced Nephrotoxicity in Female Rats

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### Abstract

Nephrotoxicity is the renal disorder which can be treated with the help of Medicinal plants. The current study was focused to recover gentamicin induced nephrotoxicity in female rats using mixture of six medicinal plants polyherbal formulation (HM) on the basis of literature survey. Polyherbal (HM) treatment shows significant dose-dependent improvement in the body weight, Hematological and biochemical parameter.

**Keyword:** Nephrotoxicity, Polyherbal mixture, Nephroprotective,

### Introduction

Nephrotoxicity is one of the most common kidney problems and occurs when body is exposed to a drug or toxin. Aminoglycoside antibiotics, especially, gentamicin (Abdet *et al.*, 2012). Despite rigorous monitoring, nephrotoxicity appears in 10-25% of therapeutic courses. Gentamicin mainly causes tubular toxicity; it is an aminoglycoside antibiotic used for the treatment of Gram-negative bacterial infections. Overdose of gentamicin causes renal damage (Sana *et al.*, (2015). It may give serious side effects while continuous consuming at higher concentrations. When kidney damage occurs, body unable to rid of excess urine and wastes from the body and blood electrolytes (such as potassium and magnesium) will all become elevated (Ramya, 2011). The use of herbs as nephroprotective is a major avenue in Indian perspectives particularly for treating kidneys damage, which require to be explored more successfully as there are many literatures available on these aspects. Ayurveda, an indigenous system of medicine, offers a vast scope of renal treatment for renal failure. Plants and other natural substances have been used as the rich source of medicine. Also, herbal drugs are more easily accessible. Medicinal plants are having curative properties and therapeutic values due to the presence of various complex phytochemical compounds (Jain and Agrawal, 2008). These

traditional medicines are assuming greater importance because of very effective, safer, locally available, and no side effects. In present study an attempt has been made to evaluate the nephroprotective activity of polyherbal formulation against gentamicin induced nephrotoxicity.

### Materials and methods

**Collection of plants:** Following listed plants were collected from North Maharashtra region during June 2009 to September 2009. The plants were identified by the taxonomists of Department of Botany, Moolji Jaitha College, Jalgaon, Maharashtra (India). Selected plants for nephroprotective activity listed are as Botanical Name followed by Family, Vernacular name, Part used; as under,

1. *Bauhinia recemosa* (Lam), Caesalpinaceae, Aapata, Stem bark
2. *Dolichos biflorus* (Linn.), Fabaceae, Kulitha, Seed
3. *Sphaeranthus indicus* (Linn), Asteraceae, Gorakhmundi, Flower
4. *Tectonagrandis* (Linn), Verbenaceae, Sag, Seed
5. *Tephrosia purpurea* (Linn), Fabaceae, Sharpunkha, Leaves
6. *Tribulus terrestris* (Linn), Zygophyllaceae, Gokhru, Fruit

### Poly herbal preparation (Herbal Mixture – HM)

Shade dried plant material pulverized using an electrically operated grinder. Equal quantities of the respective herbal powders were blended and then mixed with 1% Carboxy Methyl Cellulose for preparing the doses. The doses were prepared fresh daily, before administration; the rats were dosed at approximately the same time each day.

### Animals (Wistar rat)

Animals for the study were obtained from the National Biosciences, Pune. The animals were acclimatized to laboratory conditions (temperature: 22°C - 24°C, humidity: 65 - 70% and 12 h light and 12 h dark rhythm) prior to the start of the experiment in the CPCSEA registered (1062/CPCSEA/2007) Animal House of the

Department of Zoology, Moolji Jaitha College, Jalgaon and the protocol for experiment was approved from the Institutional Animal Ethics Committee (protocol number IAEC/04/CPCSEA/MJ/09-10).

**Methodology**

**Study plan: Animal experimentation**

Eight to twelve-week-old, either sex (weighing between 200-300 gm) Wistar rats were divided into following 6 groups.

- Group 1: Control - Treated with Saline
- Group 2: CMC - Treated with 1 % Carboxy methyl cellulose
- Group 3: GAG - Induced Nephrotoxicity, with gentamicin at 80 mg/kg b.w.
- Group 4: Herbal mixture I - Treated with HM250 mg/kg b.w.
- Group 5: Herbal mixture II - Treated with HM 500 mg/kg b.w.
- Group 6: Herbal mixture III - Treated with HM1000 mg/kg b.w.

**Blood Collection**

On 15<sup>th</sup> day, blood samples from each group of animals were collected for serum biochemistry. The animals were mildly anesthetized using anesthetic ether before blood collection. Blood was collected from the retro-orbital sinus using heparinised capillaries (Remi, Mumbai).

**Body weight and feed consumption**

Body weight and feed consumption and observed for clinical signs of animals were recorded daily throughout the experimental period.

**Statistical analysis**

Statistical analysis of the data was performed by computing Analysis of variance (ANOVA) and Dunnett’s multiple comparison tests following the methods described by Chopda *et al.*, (2011).

**Results and Discussion**

At the 14<sup>th</sup> day of experiment the body weight (gm) decreased markedly in female group treated with gentamicin alone as compared to control group of animals. At 0 day - 229.30 ± 7.01, 7<sup>th</sup> day - 205.80 ± 1.53, and 14<sup>th</sup> day - 187.70 ± 3.67 control group (0 day 236.30 ± 2.07), (7<sup>th</sup> days 248.80 ± 1.01) and (14<sup>th</sup> 252.20 ± 3.76). On treatment with herbal mixture at 1000mg/kg b.w. an improvement in body weight at (0 day 241.20 ± 1.44), (7<sup>th</sup> day 218.20 ± 2.27) and (14<sup>th</sup> day 248.50 ± 7.38) gm body weight.

A significant reduction in feed consumption, compared to the control, was recorded in experimental group treated with gentamicin alone group (6.73 ± 0.12, 7.26 ± 0.11, 7.58 ± 0.79 gm on 0, 7<sup>th</sup> and 14<sup>th</sup> day respectively). In gentamicin + herbal mixture at a dose 250 and 500 mg/kg b.w. were significantly increased 7.800 ± 0.05, 8.35 ± 0.15, 8.31 ± 0.09 gm on 0, 7<sup>th</sup> and 14<sup>th</sup> day respectively (p < 0.001) as compared to gentamicin treated group. Whereas, in the group treated with gentamicin + herbal mixture at a dose 1000 mg/kg b.w. the feed consumption is increased in animal was 8.333 ± 0.12 gm, 9.31 ± 0.070 gm, 10.88 ± 0.10 gm which was parallel to that of the control group of animals 10.53 ± 0.06, 12.40 ± 0.25, 11.72 ± 0.10 gm on 0, 7<sup>th</sup> and 14<sup>th</sup> day respectively.

**Table 3 Body weight of ♀ rats of various days of treatment**

Day Group	0	7	14
Control	236.30 ± 2.07	248.80 ± 1.01	252.20 ± 3.76
CMC	237.30 ± 1.96	250.00 ± 0.89	254.50 ± 4.04
GAG	229.30 ± 7.01	205.80 ± 1.53***	187.70 ± 3.67***
HM-I	236.00 ± 3.26	213.00 ± 0.96	207.30 ± 2.49
HM-II	238.20 ± 3.19	212.80 ± 2.50	206.00 ± 1.43
HM-III	241.20 ± 1.44	218.20 ± 2.27	248.50 ± 7.38

HM – I = 250 mg/kg, HM – II = 500 mg/kg, HM – III = 1000 mg/kg  
Values are expressed as Mean ± S.E, (n=6) \*\*\*p < 0.001

**Table 4 Feed consumption in ♀ rats of various days of treatment**

Day Group	7	14	21
Control	10.53 ± 0.06	12.40 ± 0.25	11.72 ± 0.10
CMC	11.15 ± 0.45	12.40 ± 0.25	11.72 ± 0.16
GAG	6.73 ± 0.12	7.26 ± 0.11	7.58 ± 0.79
HM – I	7.31 ± 0.03	8.13 ± 0.12*	7.96 ± 0.18
HM – II	7.800 ± 0.05**	8.35 ± 0.15**	8.31 ± 0.09**
HM– III	8.33 ± 0.12***	9.31 ± 0.070***	10.88 ± 0.10***

HM – I = 250 mg/kg, HM – II = 500 mg/kg, HM – III = 1000 mg/kg  
Values are expressed as Mean ± S.E. (n=6) \*P<0.05, \*\*P<0.01, \*\*\*P<0.001

**Table 5 Hematological values in the ♀ rats after 14 days of drug treatment**

Group	HB (g/dl)	WBC (10 <sup>3</sup> /μL)	RBC (10 <sup>6</sup> /μl)	PCV (%)
Control	12.83±0.21	6.23±0.16	6.40±0.04	34.67±0.34
CMC	11.58±0.41	6.22±0.02	7.53±0.07	34.40±0.68
GAG	10.58±0.25	7.09±0.31	5.15±0.08	32.10±0.63
HM – I	11.60±0.30	6.33±0.28	5.45±0.17	30.33±0.53
HM– II	11.90±0.32*	6.28±0.19	5.40±0.15	32.45 ±0.93
HM– III	12.32±0.23**	6.24±0.17*	5.68±0.02**	35.13±0.29**

Hm – I = 250 mg/kg, Hm – II = 500 mg/kg, Hm – III = 1000 mg/kg  
Values are expressed as Mean ± S.E. (n=5). \*P<0.05, \*\*P<0.01, \*\*\*P<0.001

**Table 6 Biochemical parameters in female rats treated with Gentamicin and gentamicin + herbal mixture – Day 15**

Group	BUN	CRE	PRO
Control	16.90±0.58	0.84±0.01	6.28±0.01
CMC	16.82±0.48	0.83±0.01	6.23±0.007
GAG	160.7±0.62	3.79±0.01	5.89±0.20
GM + HM– I	157.9±0.77	3.52±0.16	6.03±0.007
GM +HM – II	148.8±0.48	1.82±0.15	6.12±0.005
GM + HM– III	91.86±2.29	0.96±0.005	6.23±0.003

GAG = Gentamicin alone group -80 mg/kg, CMC – 1% Carboxy Methyl Cellulose GM + HM – I = 250 mg/kg, GM + HM – II = 500 mg/kg, GM + HM – III = 1000 mg/kg, Values are expressed as Mean ± S.D. BUN- Blood urea nitrogen. CRE - Creatinine; PRO- Protein

**Hematological values in the ♀ rats after 14<sup>th</sup> day of drug treatment**

The values for RBC, Hb and PCV were significantly decreased in females administrated with gentamicin at a dose 80 mg/kg alone treated group of animals ( $5.15 \pm 0.08 \times 10^6/\mu\text{l}$ ;  $10.58 \pm 0.25\text{g/dl}$ ) and  $32.10 \pm 0.63\%$  respectively) as compared with control group of animals ( $6.40 \pm 0.04 \times 10^6/\mu\text{l}$ ;  $12.83 \pm 0.21 \text{g/dl}$  and  $34.67 \pm 0.34\%$  respectively). The changes in RBC ( $06.68 \pm 0.02 \times 10^6/\mu\text{l}$ ), Hb ( $12.32 \pm 0.23\text{g/dl}$ ) and PCV ( $35.13 \pm 00.29\%$ ) were revert significantly on co-administration of the herbal mixture at the dose 1000 mg/kg b.w.when compared with GAG group.

**Changes in biochemical values of ♀ rat after 14<sup>th</sup> day of drug treatment**

An increase in BUN, and creatinine,  $160.7 \pm 0.62 \text{mg/dl}$ , and  $3.79 \pm 0.01 \text{mg/dl}$  in gentamicin treated group compared to the control  $16.90 \pm 0.58 \text{mg/dl}$  and  $0.84 \pm 0.01 \text{mg/dl}$  confirming the nephrotoxicity induced by gentamicin. BUN  $91.86 \pm 2.29\text{mg/dl}$ , CRE  $0.96 \pm 0.005\text{mg/dl}$  were reach to normal level in herbal mixture treated group at the dose 1000 mg/kg b.w. while the level of protein decreased in GAG group of animals  $5.89 \pm 0.20\text{g/dl}$  compared to control group of animals.  $6.28 \pm 0.01\text{g/dl}$  reached to normal level in herbal mixture treated group at the dose 1000 mg/kg b.w  $6.23 \pm 0.003\text{g/dl}$ .

**Conclusion**

Promising results were obtained from the pharmacological study of the nephroprotective effects of different parts of herbal preparation are of effective reduction in elevated haematological and biochemical parameters and improvement in the renal cells were good indicators for nephroprotective activity.

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