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NEPHROPROTECTIVE EFFECT OF LEAVES OF DALBERGIA LATIFOLIA ON GENTAMICIN- INDUCED NEPHROTOXICITY IN RATS

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ABSTRACT

Objective: The main objective of the study was to evaluate the effects of methanolic extract of leaves of "Dalbergia latifolia" on gentamicin - induced nephrotoxic rats. **Methodology:** For nephrotoxicity, thirty rats were evenly divided into 5 groups. Group I and II served as untreated and diseased control, respectively while group III were the treated group with standard drug vitamin-E. Group IV and V served as the test groups, which were pretreated with 250 and 500 mg/kg body weight per day of "Dalbergia latifolia", 1hour before each dose of the nephrotoxicants. On the 11thday, blood samples for serum urea, serum uric acid, serum creatinine, total protein as well as ions like sodium, potassium and chloride and urine samples were collected for urinary creatinine, urinary uric acid, urinary urea, urinary total protein and the kidneys for histopathology were taken under inhaled diethyl ether anesthesia. **Results:** The extract shows significant nephroprotective activity in Gentamicin induced nephrotoxicity model as evident by a decrease in elevated serum creatinine, serum urea, total protein, serum uric acid, urinary urea, urinary creatinine, urinary uric acid, urinary total protein which was further confirmed by histopathological study as attenuation in tubular nephrosis, with no significant effect on ion levels and decrease in oxidative stress by increase in level of catalase, superoxide dismutase, glutathione peroxidase and decrease in levels of malondialdehyde. **Conclusion:** The results have shown that methanolic extract of Dalbergia latifolia can normalize the oxidative stress and attenuated tubular nephrosis and therefore it can be used as an effective nephroprotective agent against drug induced nephrotoxicity.

KEYWORDS: Dalbergia latifolia, gentamicin, nephroprotective activity, anti-oxidant activity.

I. INTRODUCTION

Kidney are bean shaped organ which always paired located just above waist, between peritoneum in the posterior wall of abdomen. Nephron is the functional unit of kidney that helps in removing waste from body by which urine is produced and finally ex created from body.[1] Kidney failure is a condition in which kidney will no longer work also called as end stage kidney disease. Kidney failure can be classified into two types acute and chronic kidney failure. Acute kidney failure is defined as measurable increase in serum creatinine concentration and drastic decrease in glomerular filtration rate, but the kidney function is reversible after over a period of treatment from weeks to days.[2] Whereas, chronic kidney failure is a irreversible damage to nephron in which around 75% of renal function is lost.[3] Toxicity of kidney is called as nephrotoxicity and the agents which produces such toxicity is called as nephrotoxicants.[4] Gentamicin is considered to be one of the most important anti biotic used in treatment of various types of infections caused by gram negative organisms but its used is limited because of nephrotoxicity and ototoxicity. Gentamicin molecules have cationic properties which facilitates binding to epithelial cells of proximal convulated tubules and by the virtue of there cationic properties they get accumulated easily in tubular cells to produce damage to tubular cells.[5] Dalbergia latifolia Roxb also called as Dalbergia emarginata with vernacular name beete in kannada , kala-shisham in hindi and with common name Bombay Blackwood, Indian Rosewood belonging to family Fabaceae.[6] Leaves are compound with odd pinnate leaflets and flowers are pure white with numerous lax pinnacles, flowering is seen during the month of September when the tree is full of leaf and fruiting occurs during the month of January – February, tree is large glabrous with single stem having characteristic smell. It contain dalbinol a new 12a-hydroxyrotenoid, sisafolin coumarin from seeds, - sitosterol, also contain dalbergichromene, lupeol, latifolin and dalbergin from bark of the tree, heartwood contains latinone, neoflavonoid dalcriodon and Latinone, a substituted phenanthrene-1, 4- quinone was isolated from Dalbergia latifolia.[7] Traditionally various species are reported to be used as aphrodisiac, abortifacient, expectorant, anthelmentic, antipyretic, appetizer, allays thirst, vomiting, burning sensation, cures skin diseases, ulcers, diseases of the blood, reduces obesity, used in leucoderma, dyspepsia, dysentery, for diseases of the eye and nose, syphilis, stomach troubles, leprosy, leucoderma, scabies and ringworm.[8]

The leaves are used as fodder and the plant is grown in coffee plantation as a shade tree. In addition, the bark of the tree contains tannins. Parts of the tree are reported to be useful as stimulant and appetizer helpful in dyspepsia, diarrhoea, leprosy, obesity and worms.[9]

Preliminary phytochemical screening reveals the presence of glycosides, tannins, steroids, flavonoids in various parts of Dalbergia latifolia.[10]

However, no work on nephroprotective activity has been reported on methanolic extract of leaves of Dalbergia latifolia. Therefore, the present study was designed for the evaluation of nephroprotective activity of leaves of Dalbergia latifolia.

II. MATERIALS AND METHOD

a. Collection of plant material

The plant leaves of Dalbergia latifolia was collected from Kaimara forest region Chikmaglur District, Karnataka, India in the month of June 2017. This plant species were authenticated by Dr. Shiddamallayya N, Dr. V.Rama Rao, Dr.Sulochana Bhat, Regional Ayurveda Research Institute For Metabolic Disorders **(Central Council For Research In Ayurvedic Science, Ministry Of AYUSH, Govt. Of India)**.The plant was identified by a Botanist, and voucher specimen was deposited in Rajiv Gandhi University of Health Science and a copy has been preserved for the future reference at the Karnataka College of Pharmacy, Department of Pharmacology.

b. Preparation of methanolic extract of leaves

Methanolic extract of Dalbergia latifolia was obtained by soxhlet apparatus. Further, the obtained extract was dried with rotary evaporator. The percentage yield of extract was noted as 4.20% gm.[11]

c. Phytochemical analysis of successive extract of leaves of *Dalbergia latifolia*[12]

Table No: 1.

Sl. No.	Constituents	Tests	Result
1.	Flavonoid	Zinc Hydrochloric acid test	+
		Lead acetate test	+
		Shinodas test	+
		Ferric chloride test	+
2.	Sterols	Liebermann burchard test	+
		Salkowski test	+
3.	Terpenoids	Terpenoid test	+
4.	Alkaloids	Mayers test	-
		Wagers test	-
		Drangendoffs test	-
		Hagers test	-
		Tannic acid test	-
5.	Saponin	Foam test	-
6.	Tannin	Ferric chloride test	+
		Gelatin test	+
		Lead acetate test	+
		Alkaline reagent test	+
7.	Phenols	Ellagic acid test	+
		Phenols test	+
8.	Glycosides	Keller killiani test	+
		Concentrated sulphuric acid test	+
		Molischs test	+

Where:(+) Present and (-) Absent

d. Experimental animals

Wistar rats weighing between 150-200 gm and albino mice weighing between 20-25 gm were maintained in standard laboratory conditions at room temperature (25±2 °C) with 12 hr light/dark cycle. The animals were given pellet chow and water ad libitum except during experimentation. The study protocols were duly approved by the Institutional Animal Ethics Committee (IAEC) at Karnataka College of Pharmacy, Bangalore. Studies were performed in accordance with the CPCSEA guidelines (CPCSEA Reg No.1564/PO/RE/S/11CPCSEA).

e. Acute toxicity study

Acute toxicity study was conducted for the methanolic extract leaves of *Dalbergia latifolia* as per OECD guidelines 425 using Swiss albino mice. Each animal was administered methanolic extracts by oral route. The animals were observed for any changes continuously for the first 2 h and up to 24 h for mortality. There was no mortality and noticeable behavioural changes in all the groups tested. The extracts were found to be safe up to 5000 mg/kg b.w.[13]

Preparation of Dose

A dose of 1/10th and 1/20th of 5000mg/kg were considered to be high dose and low dose prepared by suspending in 2% tween 80. The doses were prepared as per the OECD guideline no. 425.

f. Experimental induction of gentamicin and their treatments with the extract

Group I-Control (untreated) treated with normal saline solution for 10 days.

Group II- Diseased control, rats were injected (I.P.) with GM only (80mg/kg body weight) for 10 days.

Group III–Rat was treated with vitamin E, 250 mg/kg as standard nephroprotective agent, one hour before the I.P. injection of GM (80mg/kg) for 10 days.

Group IV – Dalbergia latifolia low dose (250mg/kg body weight) one hour before the I.P. injection of Gentamicin (80mg/kg body weight) for (10 days).

Group V- Dalbergia latifolia high dose (500mg/kg body weight) one hour before the I.P. injection of Gentamicin (80mg/kg body weight) for (10 days).[14]

Groups IV and V rats were pre-treated with single daily orally dose of 250 mg/ kg and 500 mg/kg of Dalbergia latifolia 1 h before the intraperitoneal injection of 80 mg/kg bodyweight per day of gentamicin for 10 days.

On days 0 and 11 of the experiment, the rat weights were measured, respectively, with Digital weighing balance. The absolute and change in weights in reference to the initial weight per group were calculated.

g. Collection of blood

At the end of the study, blood was collected from rat by cardiac puncture under mild ether anesthesia. Collected blood samples were allowed to clot for 10 min at room temperature and they were centrifuged at 3000 rpm for 10 minutes.[15]

h. Collection of urine sample

The experimental animals were transferred to the separate metabolic cages after the last day administration. Twenty-four hour urines were collected. A drop of conc. HCl was added to the collected urine. This prevents the growth of microbes and also prevents metal hydrolysis. The collected urine was measured and transferred to a cleaned airtight container and used for the urine analysis.[16]

i. Parameters to measured

Blood sample was collected for analysis of serum creatinine, blood urea nitrogen, serum uric acid, serum total protein, serum potassium, serum sodium, serum chloride whereas urine sample was collected for analysis of urinary creatinine, urinary urea, urinary uric acid, urinary total protein and kidney's were isolated for histopathological and anti-oxidant studies.

j. Collection of tissue for histopathological and anti-oxidant studies

The rats were sacrificed by cervical dislocation under light ether anesthesia. The left kidney was quickly removed for homogenate preparation. The right kidney was then quickly removed and preserved in 10% formalin solution for histopathological examinations.

k. Histopathological studies

Right kidney from every animal of each group was identified and carefully dissected and fixed 10% neutral buffered formalin overnight. Fixed kidney specimens were dehydrated in graded ethanol, cleared in xylene and infiltrated with paraffin wax using an automatic tissue processor. Processed specimens were embedded in paraffin wax using metallic blocks.5 µm thick sections of kidneys were taken in a rotary microtome. Sections were stained with Hematoxylin and Eosin counter stains (H&E) and observed at x400 magnification under a light microscope.[17]

l. Anti-oxidant studies

After the isolation of left kidney from each group, they were quickly transferred to ice cold phosphate buffered saline (PBS pH-7.4). It was maintained free of blood and other tissue fluids and weighed. The kidneys were nicely chopped with surgical blade into small slices. Then the pieces were placed in ice cold 0.25M sucrose solution quickly placed on a filter paper. After that crushed and homogenized in ice cold tris HCL buffer of strength 10Mm of pH-7.4 to a concentration of 10% w/v. The obtained homogenate was centrifuged at 7000rpm for 25 minutes under normal conditions. The clear supernatant fluid was used for the purpose of estimation of different kidney anti-oxidant enzymes. Super oxide dismutase was estimated by using kakkar et al method,[18] Catalase was estimated using Sinha et al method,[19] Lipid peroxidation assay carried out as per huge and aust,1978 method,[20] glutathione peroxidase measured by the method of Rotruck et a/., 1973.[21]

m. Statistical analysis

The results are expressed as mean ± S.E.M from n=6 rats in each group. The significance of difference among the groups was assessed using one-way analysis of variance (ANOVA) followed by Tukey's test compared between Normal control (Untreated) v/s all groups $p<0.05$ were considered significant.

III. RESULTS

Effect of 10 days of oral administration of methanolic extract of Dalbergia latifolia on Average body weight and kidney weight in gentamicin induced nephrotoxic rats

Table 1 and Table 2 shows the effect single oral daily administration of MEDL (250 & 500 mg/kg bodyweight) on average body weight and kidney weight in gentamicin (80 mg/kg body weight) treated nephrotoxic rat respectively. As indicated in table 1 due to repeated intra peritoneal injection of gentamicin (80mg/kg body).

Table No: 2.

Sl. No	Groups	Average body weight (g) of rats	
		Day 0	Day 11
1	Control (normal saline 10ml/kg)	155.183±0.031	165.250±0.043
2	Gentamicin (80mg/kg)	183.167±0.021***	141.217±0.031***
3	Vitamin E(250 mg/kg) + Gentamicin (80mg/kg)	170.150±0.022###	175.183±0.031###
4	MEDL (250mg/kg) + Gentamicin (80mg/kg)	172.200±0.052###	160.267±0.033###
5	MEDL (500mg/kg) + Gentamicin (80mg/kg)	175.167±0.033###	170.233±0.021###

The data are expressed as Mean ±S.E.M (n=6 rats in each group).

***P<0.001 when compared with Normal Control.

###P<0.001 when compared with Gentamicin (80mg/kg) control.

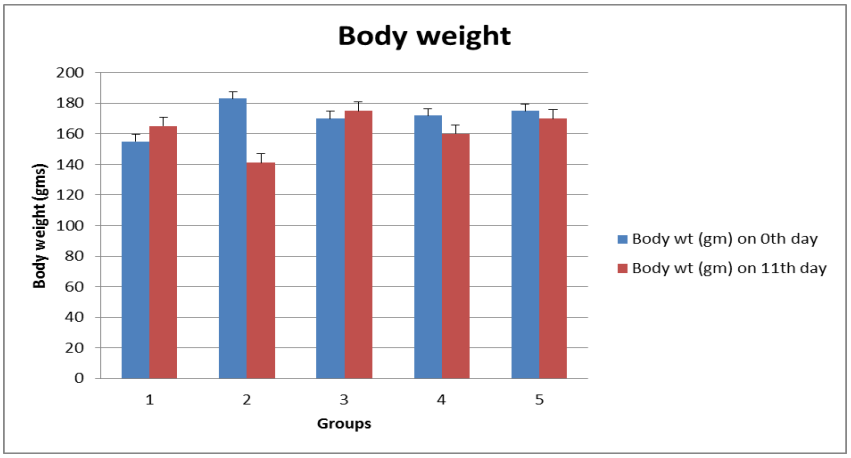


Figure no.1

***P<0.001 when compared with Normal Control.

###P<0.001 when compared with Gentamicin (80mg/kg) control.

Table No: 3.

Sl. No	Groups	Weight of wet kidney (gm)
1	Control (normal saline 10ml/kg)	1.322±0.006
2	Gentamicin (80mg/kg)	1.927±0.006***
3	VitaminE(250mg/kg)+Gentamicin(80mg/kg)	1.123±0.003###
4	MEDL (250mg/kg)+Gentamicin (80mg/kg)	1.520±0.003###
5	MEDL(500mg/kg)+Gentamicin (80mg/kg)	1.225±0.006###

The data are expressed as Mean ±S.E.M (n=6 rats in each group).

***P<0.001 when compared with Normal Control.

###P<0.001 when compared with Gentamicin (80mg/kg) control.

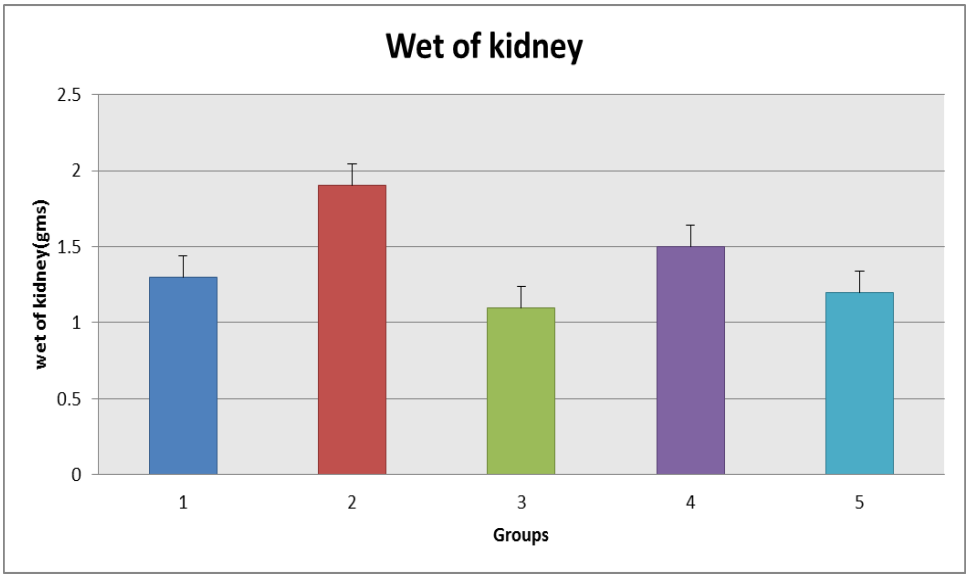


Figure No: 2.

***P<0.001 when compared with Normal Control.

###P<0.001 when compared with Gentamicin (80mg/kg) control.

Effect of 10 days of oral administration of methanolic extract of Dalbergia latifolia on serum parameters in gentamicin induced nephrotoxic rats

A significant increase (P<0.05) in blood urea nitrogen, serum creatinine, serum uric acid, total protein was seen in gentamicin treated group when compared with the control group and dose dependent decrease(P<0.05) in blood urea nitrogen, serum creatinine, serum uric acid, total protein was observed on animals pretreated with MEDL along with gentamicin. These values are tabulated below.

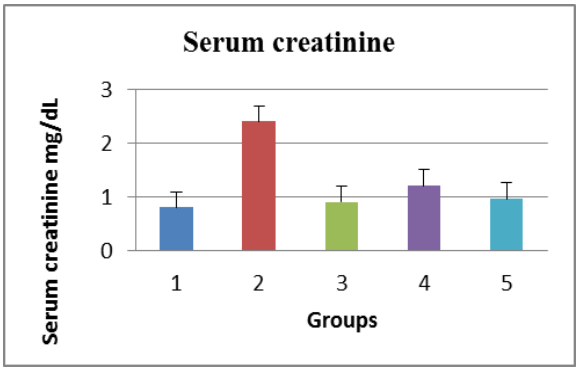
Table No: 4.

Sl. No	Groups	Serum creatinine	Blood urea nitrogen	Serum uric acid	Total protein
1	Control (normal saline 10ml/kg)	0.804±0.0008	46.063±0.013	1.705±0.001	6.030±0.015
2	Gentamicin (80mg/kg)	2.407±0.0006**	125.050±0.012**	3.105±0.001**	8.015±0.001**
3	Vitamin E(250mg/kg)+Gentamicin (80mg/kg)	0.905±0.0010##	44.057±0.011##	1.805±0.004##	6.206±0.001##
4	MEDL (250mg/kg)+Gentamicin (80mg/kg)	1.207±0.0007##	61.058±0.007##	2.105±0.001##	7.205±0.001##
5	MEDL (500mg/kg)+Gentamicin (80mg/kg)	0.964±0.0010##	43.060±0.012##	1.854±0.001##	6.404±0.001##

The data are expressed as Mean ±S.E.M (n=6 rats in each group).

**P<0.05 when compared with Normal Control.

##P<0.05 when compared with Gentamicin (80mg/kg) control.



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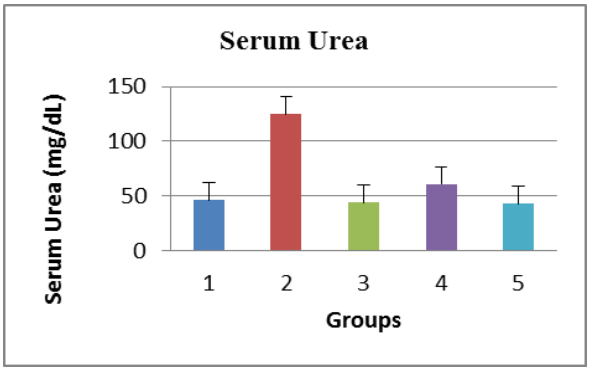

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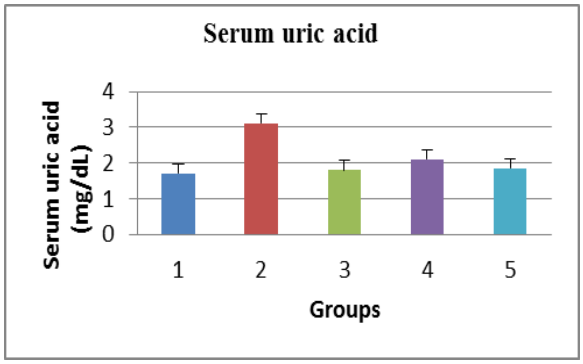

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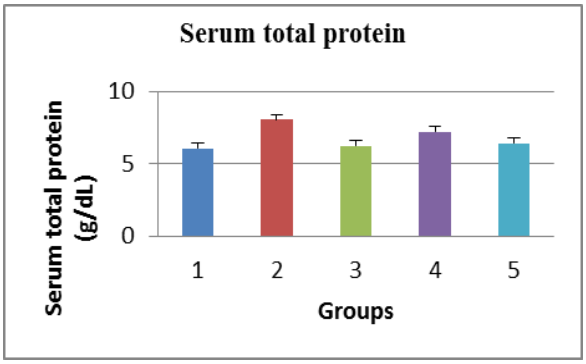


Figure No: 6.

**P<0.05 when compared with Normal Control.

##P<0.05 when compared with Gentamicin (80mg/kg) control.

Effect of 10 days of oral administration of methanolic extract of Dalbergia latifolia on serum ions in gentamicin induced nephrotoxic rats

No significant difference is seen among the groups of serum sodium and serum potassium but A significant increase(P<0.001) of serum chloride and serum potassium in

gentamicin treated group when compared with the control group and dose dependent decrease(P<0.001) in serum chloride was observed on animals pretreated with MEDL along with gentamicin.

Table No: 5.

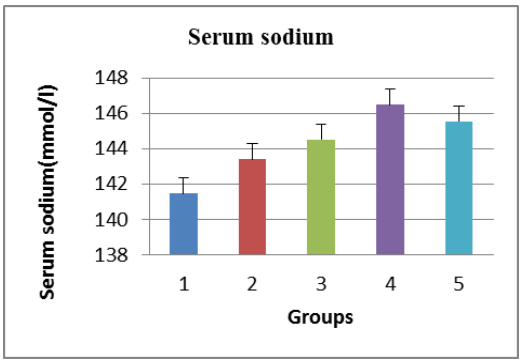
Sl. No.	Groups	Serum sodium	Serum potassium	Serum Chloride
1	Control (normal saline 10ml/kg)	141.460±0.142	4.763±0.057	190.313±0.078
2	Gentamicin (80mg/kg)	143.390±0.140	7.153±0.013***	238.423±0.147***
3	VitaminE(250mg/kg)+Gentamicin(80mg/kg)	144.517±0.134	4.615±0.004###	210.463±0.117###
4	MEDL (250mg/kg)+Gentamicin (80mg/kg)	146.488±0.141	5.137±0.012###	230.490±0.091###
5	MEDL(500mg/kg)+Gentamicin (80mg/kg)	145.542 ±0.162	4.913±0.004###	211.457±0.119###

No significant difference is found between groups when compared to normal and diseased group of serum sodium.

The data are expressed as Mean ±S.E.M (n=6)rats in each group(serum chloride and serum potassium).

***P<0.001 when compared with Normal Control.

###P<0.001 when compared with Gentamicin (80mg/kg) control.



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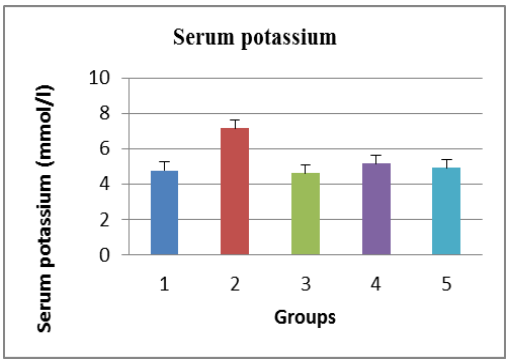

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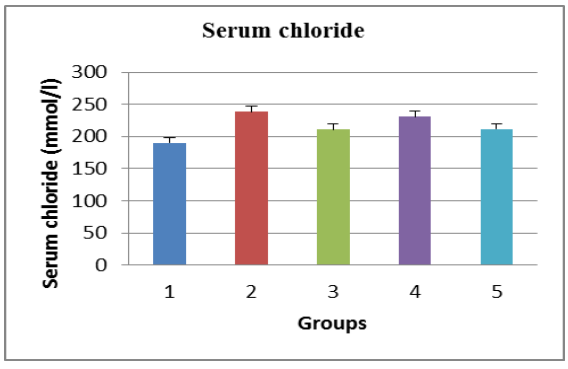


Figure No: 9.

No significant difference is found between groups when compared to normal and diseased group(serum sodium).

The data are expressed as Mean ±S.E.M (n=6)rats in each group(serum chloride and serum potassium).

***P<0.001 when compared with Normal Control.

###P<0.001 when compared with Gentamicin (80mg/kg) control.

Effect of 10 days of oral administration of methanolic extract of Dalbergia latifolia on urinary parameters in gentamicin induced nephrotoxic rats

A significant increase(P<0.05) in urinary urea, urinary uric acid, urinary creatinine, urinary total protein, was seen in gentamicin treated group when compared with the control group and dose dependent decrease (P<0.05) in urinary urea, urinary uric acid, urinary creatinine, urinary total protein was observed on animals pretreated with MEDL along with gentamicin

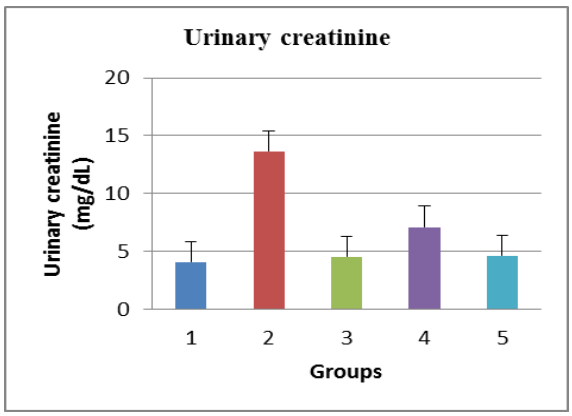
Table No: 6.

Sl. No	Groups	Urinary creatinine	Urinary urea	Urinary uric acid	Urinary total protein
1	Control (normal saline 10ml/kg)	4.092±0.033	34.692±0.085	10.235±0.089	1.470±0.006
2	Gentamicin (80mg/kg)	13.623±0.112**	91.662±0.114**	12.557±0.013**	2.848±0.011**
3	VitaminE (250mg/kg)+Gentamicin (80mg/kg)	4.535±0.012##	37.403±0.134##	10.547±0.013##	1.843±0.011##
4	MEDL (250mg/kg)+Gentamicin (80mg/kg)	7.115±0.041##	50.648±0.159##	11.552±0.012##	2.343±0.014##
5	MEDL (500mg/kg)+Gentamicin (80mg/kg)	4.648±0.012##	38.358±0.112##	10.747±0.012##	1.950±0.012##

The data are expressed as Mean ±S.E.M (n=6) rats in each group.

**P<0.05 when compared with Normal Control.

##P<0.05 when compared with Gentamicin (80mg/kg) control.



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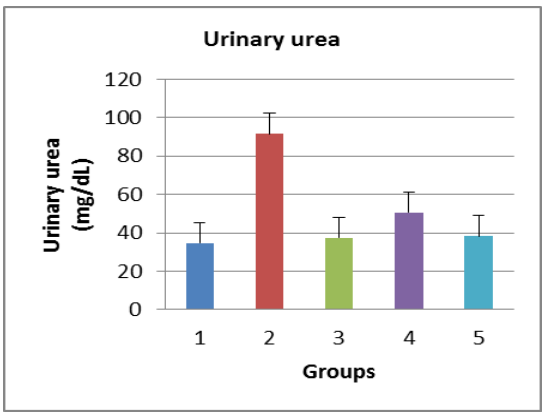

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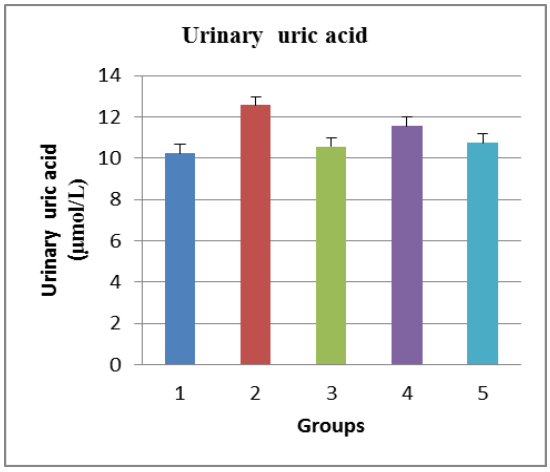

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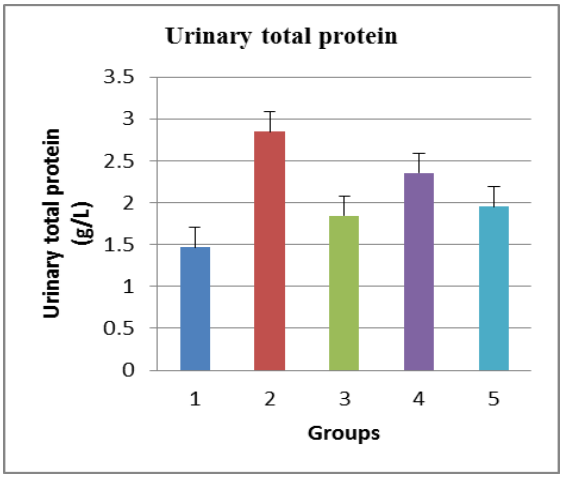


Figure No. 13.

The data are expressed as Mean ±S.E.M (n=6) rats in each group.

**P<0.05 when compared with Normal Control.

##P<0.05 when compared with Gentamicin (80mg/kg) control.

Effect of 10 days of oral administration of methanolic extract of Dalbergia latifolia on kidney anti-oxidants in gentamicin induced nephrotoxic rats

A significant decrease (P<0.05) in, Super oxide dismutase, Catalase, Glutathione peroxidase was seen in gentamicin treated group when compared with the control group and dose dependent increase (P<0.05) in Super oxide dismutase, Catalase, Glutathione peroxidase was observed on animals pretreated with MEDL along with gentamicin.

A significant increase (P<0.05) in MDA was seen in gentamicin treated group when compared with the control group and dose dependent decrease (P<0.05) in MDA was observed on animals pretreated with MEDL along with gentamicin.

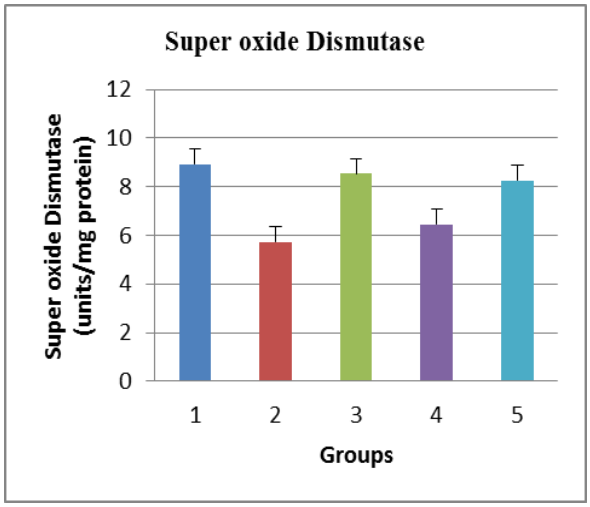
Table No: 7.

Sl. No.	Groups	Super oxide dismutase	Catalase	Lipid per oxidation	Glutathione peroxidase
1	Control (normal saline 10ml/kg)	8.920±0.006	0.693±0.0007	5.538±0.013	4.852±0.012
2	Gentamicin (80mg/kg)	5.720±0.005**	0.395±0.0007**	11.727±0.106**	2.552±0.013**
3	VitaminE (250mg/kg)+Gentamicin (80mg/kg)	8.523±0.005##	0.815±0.0013##	6.133±0.009##	3.942±0.008##
4	MEDL (250mg/kg)+Gentamicin (80mg/kg)	6.440±0.010##	0.484±0.0009##	8.738±0.009##	3.158±0.010##
5	MEDL (500mg/kg)+Gentamicin (80mg/kg)	8.252±0.009##	0.753±0.0010##	6.543±0.014##	3.658±0.014##

The data are expressed as Mean ±S.E.M (n=6) rats in each group.

**P<0.05 when compared with Normal Control.

##P<0.05 when compared with Gentamicin (80mg/kg) control.



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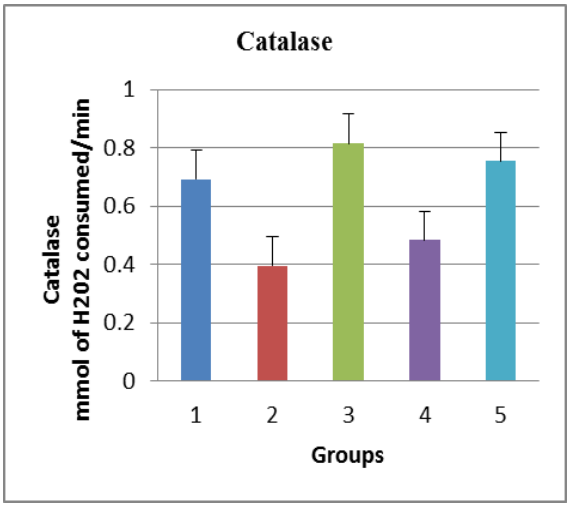


Figure No. 15.

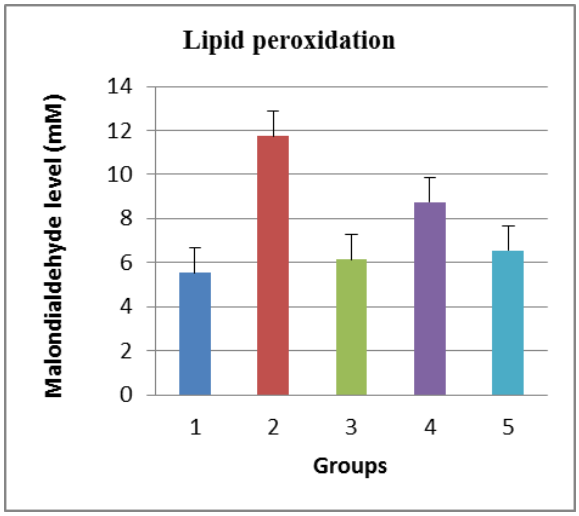


Figure No. 16.

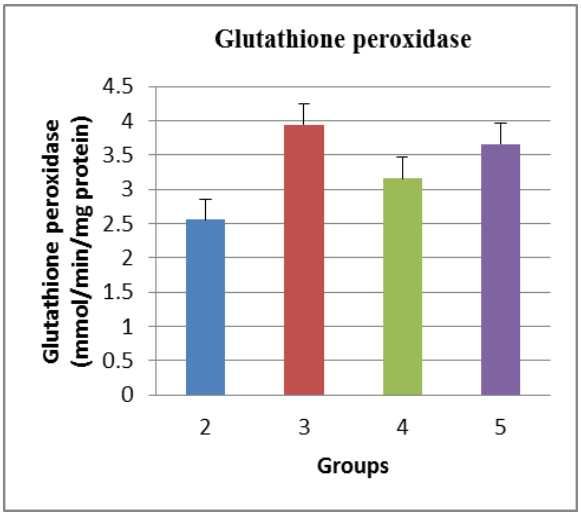


Figure No. 17.

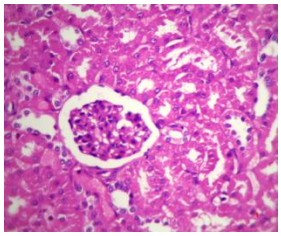
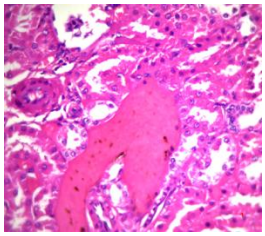
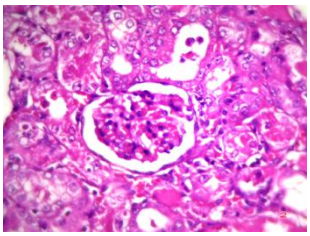
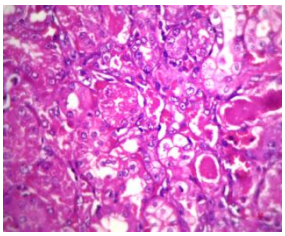
The data are expressed as Mean ±S.E.M (n=6) rats in each group

**P<0.05 when compared with Normal Control

##P<0.05 when compared with Gentamicin (80mg/kg) control

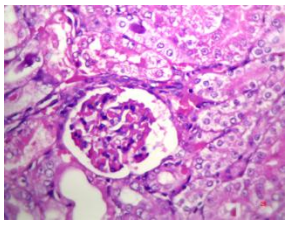
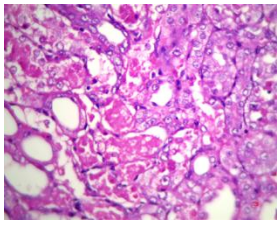
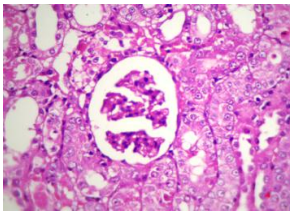
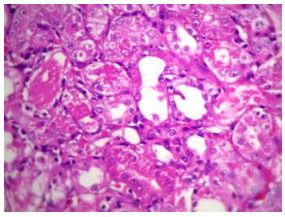
Histopathological analysis

Group(1) **Group(2)**

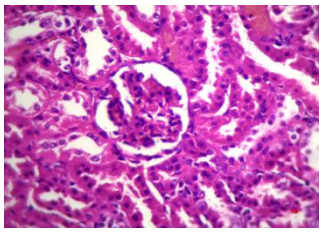
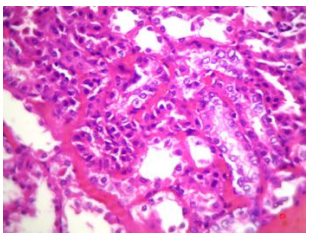
(18) [Fig. A, H&E x400] (18) [Fig.B, H&E x400] (19)[Fig.A, H&E x400] (19) [Fig.B, H&E x400]

Group(3) **Group(4)**

(20) [Fig.A, H&E x400] (20) [Fig.B, H&E x400] (21) [Fig.A, H&E x400] (21) [Fig.B, H&E x400]

Group (5)

(22) [Fig.A, H&E x400] (22) [Fig.B, H&E x400]

Group (1) Control (normal saline 10ml/kg)

Architecture of kidney is Intact, Glomerulus have Normal cellularity [Fig.A, Arrow],Tubules are Intact, Blood Vessels are appearing congested [Fig.B, Arrow], Interstitium is to be Unremarkable.

Group (2) Gentamicin (80mg/kg)

Architecture of kidney is intact, Glomerulus is with Normal cellularity [Fig.A, Arrow], Tubules have marked Necrosis with tubular casts [Fig.B, Arrow],Blood Vessels are intact, Interstitium is with mild mononuclear inflammatory infiltration.

Group (3) Vitamin E (250mg/kg)+Gentamicin(80mg/kg)

Architecture of kidney was Intact, Glomerulus have Normal cellularity [Fig.A, Arrow], Tubules are found with moderate Necrosis [Fig.B, Arrow], Blood Vessels are Intact. Interstitium is intact.

Group (4) MEDL (250mg/kg)+Gentamicin(80mg/kg)

Architecture of kidney was Intact, Glomerulus had Normal cellularity [Fig.A, Arrow], Tubules had Moderate Necrosis [Fig.B, Arrow],Blood Vessels are Intact, Interstitium is Intact.

Group (5) MEDL (500mg/kg)+Gentamicin(80mg/kg)

Architecture of kidney was Intact, Glomerulus had normal cellularity [Fig.A, Arrow],Tubules were Intact, Blood Vessels appeared congested [Fig.B Arrow], Interstitium is Unremarkable.

IV. DISCUSSION

Different physiological and chemicals changes play a significant role in renal damage. Gentamicin a potent bactericidal agent has been used in limited manner due to its nephrotoxicity .Since, it is cationic in nature it has strong affinity towards brush border membrane of proximal tubule and forms drug receptor complex with megalin, further due to pinocytosis drug is transferred drug is translocated to lysosomes , where phosopholipidosis is interpreted to cause renal injury leading Nephrotoxicity.[22] In this study we have found that methanolic extract of Dalbergia latifolia have showed significant nephroprotective activity by decreasing the levels of serum creatinine, blood urea nitrogen, serum uric, serum total protein, urinary creatinine, urinary urea, urinary uric acid, urinary total protein.

V. CONCLUSION

The results of the study indicated that administration of methanolic extract of Dalbergia latifolia at the dose of 250 and 500mg/kg b.w. possess nephroprotective activity in GM induced nephrotoxicity in rats. The acute toxicity study revealed that the extract was devoid of major toxic effect. The nephroprotective effect of MEDL was confirmed by its prevention over the GM induced toxicity. This MEDL reduced elevated kidney weight, serum creatinine, blood urea nitrogen, serum uric, serum total protein, urinary creatinine, urinary urea, urinary uric acid, urinary total protein in GM treated rats. Histopathological studies concluded that animal pre-treated with MEDL decreased the GM induced renal damage. MEDL also possess

the protective effect against the oxidative induced stress which may be due anti-oxidant property of the drug.

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