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RESEARCH ARTICLE

Nephroprotective activity of *Nelumbo nucifera* Gaertn. roots, leaves and flowers on gentamicin induced nephrotoxicity

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Abstract: The present study was designed to investigate the nephro-protective effect of ethanolic extract of *Nelumbo nucifera* Gaertn. leaves flowers and roots on gentamicin induced nephrotoxicity in wistar albino rats. Animals were divided in to five groups i.e. Group I Control, Group II Negative control: recived gentamicin 100mg/kg BW, i.p, O.D. for 12 days, Group III: received roots extract of *Nelumbo nucifera*, 100mg/kg BW, p.o. + gentamicin 100mg/kg, i.p, O.D. for 12 days, Group IV: received flowers extract of *Nelumbo nucifera*, 100mg/kg BW, p.o. + gentamicin 100mg/kg, i.p, O.D. for 12 days, Group V: received leaves extract of *Nelumbo nucifera*, 100mg/kg BW, p.o. + gentamicin 100mg/kg, i.p, O.D. for 12 days. As gentamicin associated nephrotoxicity involves the generation of free radicals via oxidative stress, *in vitro* antioxidant activity and free radical scavenging activity of different extracts was also performed. Effect of concurrent administration of various extracts of *Nelumbo nucifeara* was determined by assessing the change in body weight of animals, urine volume, analyzing the various biochemical parameters e.g. urine and serum creatinine, urea and uric acid as the marker of glomerular damage and histopathological findings. Overall results of this study suggested that roots extract of *Nelumbo nucifera* protects kidney damage caused by gentamicin induced Nephrotoxicity effectively by decreasing the biochemical urine and serum marker enzymes like creatinine, urea and uric acid. The histopathological studies of the kidney revealed a protective role of roots extract of *Nelumbo nucifera* in gentamicin treated animals. The results exhibited that the pretreatment with ethanolic extract of roots of *Nelumbo nucifera* may be useful in preventing the kidney damage induced by gentamicin in experimental animals.

Key Words: Nephrotoxicity, Antioxidant, Gentamicin, *Nelumbo nucifera*

INTRODUCTION:

Nephrotoxicity is a renal dysfunction arises from direct exposure to external agents such as drugs, toxins and environmental chemicals. Many therapeutic agents have been shown to induce clinically significant nephrotoxicity[1,2]. Aminoglycoside antibiotics have been extensively used for gram-negative infections. However, their nephrotoxicity and their ototoxicity are foremost limitations in clinical practice. Among numerous aminoglycosides, the ranking of nephrotoxicity has been reported to be in the following order, neomycin>gentamicin>tobramycin. Gentamicin is a central aminoglycoside antibiotic generally used in the treatment of dreaded gram-negative infections[3]. Gentamicin nephrotoxicity, occur in about 15-30% of gentamicin treated patients[4,5]. During the course of absorption, distribution, metabolism and excretion of gentamicin there are various interconnected pathways. Lipid peroxidation during gentamicin give rise to free radicals and reactive oxygen species, both are highly toxic to associated tissues and counted as main etiological factors in the pathogenesis of gentamicin induced Nephrotoxicity[6,7,8].

Gentamicin induced Nephrotoxicity and kidney damage is illustrated by tubular necrosis, principally restricted to the proximal tubule[9]. Precise mechanism of gentamicin nephrotoxicity is unknown; though, Gentamicin has been studied both *in vitro* and *in vivo* to enhance the generation of free radicals and reactive oxygen species. Elevated production of reactive oxygen species can damage a number of macromolecules, to provoke cellular injury and necrosis through numerous mechanisms together with peroxidation of membrane lipids, protein denaturation and DNA damage, and this is thought to be concerned in the etiology of several xenobiotics toxicity[10,11,12,13]. Gentamicin induced nephrotoxicity is a well established model to evaluate the effects of prospective renoprotective drugs. Nephrotoxicity induced by gentamicin is a multifarious phenomenon illustrated by increase in plasma Creatinine, uric acid and urea levels and rigorous proximal renal tubular necrosis, followed by acute and chronic renal failure[14].

Naturally occurring herbal remedies are the chief resource of primary healthcarefrom a long time. Since prehistoric times, plants have been serving as rich resource of efficient and safe medicines. *Nelumbo nucifera* Gaertn (Nymphaeceae) is perennial and rhizomatous aquatic herb with slender, elongated, branched with creeping stem. It has several commons names (e.g Indian lotus, Chinese water Lilly and sacred lotus) and synonyms (*Nelumbium nelumbo*, *N. speciosa*, *N. speciosum* and *Nymphaea Nelumbo*). It consist of model roots, flowers, leaves and membranous, peltate (60-90 cm and above), orbicular and concave to cup shaped; petioles are long rough with

small distinct prickles; flowers are white to rosy, sweet scented, solitary, hermophrodites 10-25 cm in diameter[15]. In traditional system of medicine *Nelumbo nucifera* is widely used in the management of tissue inflammation[16]. Rhizomes have nutritive, diuretic and cholagogue activities[17]. Stem is used in native ayurvedic medication as a diuretic; the leaves are used for the treatment of haematemesis, epistaxis, haemoptysis, haematuria, metrorrhagia and hyperlipidaemia[18]. The flowers are valuable to use as an antiemetic, poisoning antidote, diuretic and refrigerant[19,16]. Approximately all parts of the plant are eaten as vegetable and also used in the indigenous system of medicine. *Nelumbo nucifera* (*NN)* is reported to posses Anti-diarrheal, Psycho-pharmacological, Diuretic, Antipyretic, Antimicrobial, Hypoglycemic and Antioxidant activity of leaves, stamens and rhizomes[19,20,21,22,23]. Plant of *Nelumbo nucifera* contains a rich amount of phytoconstituents e.g. flavonoids, glycoside, tannins, alkaloids which have varieties of pharmacological applications in the effective treatment of various disorder[15, 24]

Aim of the present study to evaluate the Nephro-protective activity of *Nelumbo nucifera* root, flowers & leaves extract by gentamicin induced nephrotoxicity in experimental animals. However there are no established scientific reports of Nephro-protective activity on this plant, hence the plant *Nelumbo nucifera* has been choosen to established scientific data for its Nephro-protective activity.

2. MATERIAL AND METHODS

2.1. Collection and Authentication of Plant

Leaves flowers & roots of *Nelumbo nucifera* were collected locally in the month of January from Govindpura, Bhopal (M.P.). Herbarium file of individual plant parts was prepared and authenticated by Dr. Zia Ul Hasan (Professor, Department of Botany), Safia College Bhopal (M.P.).

2.2. Extraction of plant material

The leaves flowers & roots of *Nelumbo nucifera* dried separately under shade at room temperature in laboratory. After drying leaves flowers & roots were pulverized to coarse powder. The coarse powder of leaves flowers & roots was passed through sieve No.18 to maintain uniformity and stored in individual glass jars in cool and dry place for further physicochemical study & extraction. Coarsely dried powder of leaves flowers & roots (200 g) was first defatted separately with petroleum ether (50-60 ºC) for 72 hours to remove fatty materials and then extracted with ethanol using soxhlet apparatus for 36 hr., after complete

extraction, extract was collected, and concentrated in vacuum under reduced pressure using rotary flash evaporator[25], the percentage yield of corresponding extracts were calculated.and the dried crude extract was stored in air tight container at 2-8ºC for further study.

2.3. Physicochemical analysis of powder *Nelumbo nucifera* leaves flowers & roots

Coarsely dried powder of *Nelumbo nucifera* leaves flowers & roots was investigated for various physicochemical properties like Loss on drying, Total ash value, Acid insoluble ash value, Water soluble ash value and Foaming index using standard procedures[26,27].

2.4. Phytochemical screening of ethanolic extract of *Nelumbo nucifera* leaves flowers & roots

The ethanolic extract of leaves flowers & roots was subjected to qualitative chemical investigation for the identification of the phytoconstituents like flavonoids, alkaloids, glycosides carbohydrate, triterpenoids, phytosterols, and tannins using standard procedure[26,28].

2.5. Anti-oxidant activity of different extracts by DPPH method[29,30]

2.5.1. Preparation of standard solution

Required quantity of Ascorbic acid was dissolved in methanol to give the concentration of 100, 200, 300, 400 and 500 µg/ml

2.5.2. Preparation of test sample

Stock solutions of samples were prepared by dissolving 100 mg of all three dried extracts separately in 100 ml of methanol to give concentration of 1mg/ml. separately all the samples were diluted in 10 ml volumetric flask to give 100, 200, 300, 400 and 500 µg/ml concentration.

2.5.3. Preparation of DPPH solution

4.3mg of DPPH was dissolved in 3.3 ml methanol: it was protected from light by covering the test tubes with aluminium foil.

2.5.4. Protocol for estimation of DPPH scavenging activity

150µl DPPH solution was added to 3 ml methanol and absorbance was taken immediately at 516 nm for control reading. Diluted test sample with methanol up to 3 ml. 150µl DPPH solution was added to each test tube. Absorbance was taken at 516 nm in UV-visible spectrophotometer (Systronic) after 15 min using methanol as a blank.

The free radical scavenging activity (% antiradical activity) was calculated using the following equation:

$$\%Antiradical\ activity = \frac{Control\ Absorbance - Sample\ Absorbance}{Control\ Absorbane} X100$$

Each experiment was carried out in triplicate and results are expressed as mean % antiradical activity±SD.

2.6. Preparation of extracts formulation

A suspension formulation of ethanolic extract of *Nelumbo nucifera* leaves flowers & roots was prepared separately in 0.5% CMC solution for further *In-Vivo* studies.

2.7. *In Vivo* Pharmacological Study

2.7.1. Animal care and handling

The experiment was carried out on Wistar albino rats, of either sex, weighing 140-200gm. They were provided from Sapience Bioanalytical Research Lab., Bhopal, (M.P.). The animals were acclimatized to the standard laboratory conditions in cross ventilated animal house at temperature 25±2°C relative humidity 44-56% and light and dark cycles of 12:12 hours, fed with standard pallet diet and water *ad libitum* during experiment. The experiment was approved by the institutional ethics committee and as per CPCSEA guidelines and Approval Reference Number was SBRL/IAEC/June 2014/06.

2.7.2. Acute toxicity study of extracts (OECD guideline no. 425)

Acute oral toxicity study was evaluated as per OECD guidelines (425) on Wistar albino rats. Animals were provided by Sapience Bioanalytical Research Lab, Bhopal (M.P.) and experiment was done in the lab. Before experimentation rats were fasted overnight. Animals were divided in three groups containing three animals each. All three animals of first group received a dose of 2000mg/kg of ethanolic extract of *Nelumbo nucifera* leaves flowers & roots, all three animals of second group received a dose of 2000mg/kg of ethanolic extract of *Nelumbo nucifera* flowers, all three animals of third group received a dose of 2000mg/kg of ethanolic extract of *Nelumbo nucifera* leaves roots by gavage using oral canula. Animals of all groups was observed individually for any toxicity sign of gross changes like convulsion, tremor, circling, depression, and mortality after dosing for 24 hours, giving special attention during the first 4 hours, and thereafter 24 hours, No significant signs were noticed in animals of all groups after 24 hours. Hence administered dose was found tolerable as no death was found. Therefore, 2000mg/kg

dose of ethanolic extract of *Nelumbo nucifera* leaves flowers & roots was considered maximum safe dose.

2.7.3. *In-Vivo* nephroprotective activity in Gentamicin induced nephrotoxicity[31]

2.7.3.1. Grouping and treatment of animals

The animals were divided into 5 equal groups randomly including 6 rats each as follows:

Group I, Control: only vehicle treated

Group II, Negative control: Gentamicin 100 mg/kg BW, i.p, O.D. for 12 days

Group III, Test group I: received roots extract of *Nelumbo nucifera*, 100mg/kg BW, p.o. + gentamicin 100 mg/kg, i.p, O.D. for 12 days

Group IV, Test group II: received flowers extract of *Nelumbo nucifera*, 100mg/kg BW, p.o. + gentamicin 100mg/kg, i.p, O.D. for 12 days

Group V, Test group III: received leaves extract of *Nelumbo nucifera*, 100mg/kg BW, p.o. + gentamicin 100mg/kg, i.p, O.D. for 12 days

Gentamicin 100mg/kg/day, was injected intra-peritoneally for 12 days and extracts were administrated orally by gavage every day, 1 hour before gentamicin injection for 12 days.

2.7.3.2. Evaluation of nephroprotective activity in Gentamicin induced Nephrotoxicity

The initial weight of the all animals was measured at the starting of the study (on starting day of study i.e. day 0) and final weight of all the animals were taken at the end of experiment (at the end of study i.e. 12 day). After the last injection of gentamicin, all the animals were immediately kept in a group of two animals in metabolic cages in order to collect 24 hour urine. Animals had free access to drinking water during the urine collection period. On next day collected urine was analyzed for volume (ml) of urine and pH using a digital pH meter. Before the storage a drop of concentrated hydrochloric acid was added to the urine then stored at 4^0C and further utilized for the estimation of various biochemical parameters e.g. Serum Creatinine, Urea and uric acid as the marker of glomerular damage.

Figure: Blood collection from animals

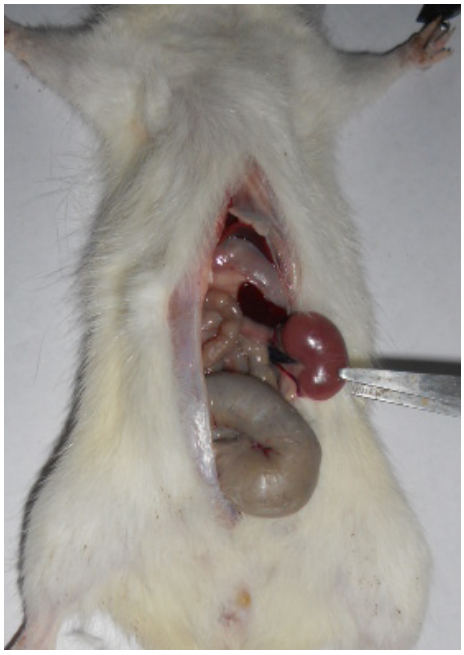

Figure: Removal of kidney after dissection of animals

After urine collection blood was obtained from animal of all groups by retro orbital puncture under light ether anesthesia. Blood samples were allowed to clot for 45 minutes at room temperature for serum analysis. Serum was separated by centrifugation at 3000 rpm at 4ºC for 15 min. using a cooling centrifuge and further utilized for the estimation of various biochemical parameters e.g. Serum Creatinine, Urea and uric acid as the marker of glomerular damage. At the end of study after urine and blood collection from all groups of animals, one animal from each group was sacrificed by cervical dislocation, the abdomen was opened and left kidneys were excised and fixed in 10% formaline solution. The fixed kidney was prepared by microtomy longitudinally to slices approximately 1mm thick, and after tissue processing, paraffin sections (5-µm thickness) were prepared and histological slides were stained with hematoxylin and eosin (H&E) for histopathological evaluation under light microscope.

2.7.3.3. Biochemical analysis on collected samples of urine and serum

Biochemical parameters was analyzed spectrophotometrically on collected samples of urine and serum parameters by using double beam UV Visible spectrophotometer (UV-Visible spectrophotometer). Estimation of Serum Creatinine, Urea and uric acid as the marker of

glomerular damage were carried out according to the methods described by Talke and Schubert *et al* 1965[32] and Tiffany *et al* 1972[33] using respective Autospan Diagnostic's kits.

2.8. Statistical analysis

All the values are expressed as mean±standard error of mean (S.E.M.) and analyzed for ANOVA and posthoc Tukey-Kramer Multiple Comparisons Test by employing statistical software, Graph Pad, In Stat 3. Differences between groups were considered significant at $P< 0.05$ levels.

3. RESULT

Table 1: Physiochemical analysis of powder of *Nelumbo nucifera* roots, leaves & flowers

S. No.	Parameters	Observation (%)		
		Roots	Leaves	Flowers
1	Loss on drying	08	0.6	0.3
2	Total ash value	8	8.5	7
3	Acid insoluble ash value	2.8	3.1	2.7
4	Water soluble ash value	1.28	2.02	1.78
5	Foaming index	21ml	18ml	14ml

Table 2: Phytochemical screening of ethanolic extract of *Nelumbo nucifera* roots, leaves & flowers

S. No.	Chemical constituents	Ethanolic extract of *NN* roots	Ethanolic extract of *NN* flowers	Ethanolic extract of *NN* leaves
1	Carbohydrates	+	+	+
2	Tannins	–	+	+
3	Alkaloids	+	+	+
4	Glycosides	+	–	–
5	Flavonoids	+	+	–
6	Steroids	–	–	–
7	Proteins and Amino Acids	+	–	+

(+) = Present, (–) = Absent

Table 3: Anti-oxidant activity by DPPH method

S. No.	Concentration (µg/ml)	% Inhibition			
		Roots extract	Flowers extract	Leaves extract	Ascorbic acid
1	100	21.5±2.21	10.35±0.65	15.76±2.32	41.65±1.01
2	200	48.23±1.56	25.76±1.76	27.06±1.07	58.65±1.29
3	300	65.6±1.76	36.56±2.98	39.05±0.75	70.69±0.92
4	400	74.58±1.54	44.28±1.04	49.43±1.76	82.5±1.16
5	500	78.76±1.63	58.98±0.85	64.38±1.45	89.39±0.62

Table 4: Change in Body Weight

Groups	Treatment	Body weight (gm)		% Change in BW
		Initial	Day 12	
I	Vehicle	157.46±4.09	158.5±3.34	-
II	Gentamicin	169.6±1.52	160.42±3.25	5.41
III	RENN + GTN	148.38±3.06	145.14±2.75	2.18
IV	FENN + GTN	190.43±3.5	184.2±2.02	3.27
V	LENN + GTN	153.4±3.09	147.5±3.92	3.84

Where

GTN - Gentamicin

RENN – Root extract of *Nelumbo nucifera*

FENN - Flower extract of *Nelumbo nucifera*

LENN N - Leaves extract of *Nelumbo nucifera*

Table 5: Urine Analysis

Groups	Treatment	Volume of urine
I	Vehicle	2.85 ± 0.76
II	Gentamicin	1.64 ± 0.46
III	RENN + GTN	3.83±0.69b**
IV	FENN + GTN	2.63 ± 0.57
V	LENN + GTN	2.83±0.65

All values are mean ± SEM, n = 6. $^{**}p<0.01$

a- Significance difference as compared to group-I (Vehicle)

b- Significance difference as compared to group-II (GTN)

Table 6: Urine Analysis for Kidney Function Test

Groups	Treatment	Creatinine mg/day/ml	Urea mg/day/ml	Uric acid mg/day/ml
I	Vehicle	1.14 ± 0.076	2.25 ± 0.26	36.48±3.53
II	Gentamicin	4.06 ± 0.065a***	5.34 ± 0.76a***	55.65±2.09 a***
III	RENN + GTN	2.32± 0.068a*,b*	3.03±0.29b**	44.59±1.38a**,b**
IV	FENN + GTN	3.78 ± 0.095a**	4.6 ± 1.52a**	48.39±2.76 a***,b*
V	LENN + GTN	3.69 ± 0.083a**	4.53±1.45a**	50.28±3.43a***

All values are mean ± SEM, n = 6. $^{*}p<0.05$, $^{**}p<0.01$

a- Significance difference as compared to group-I (Vehicle)
b- Significance difference as compared to group-II (GTN)

Table 7: Serum Analysis for Kidney Function Test

Groups	Treatment	Creatinine mg/dl	Urea mg/dl	Uric acid mg/dl
I	Vehicle	0.64 ± 0.031	17.5 ± 1.46	3.8±0.23
II	Gentamicin	0.96 ± 0.045a***	24.54 ± 1.16a***	7.65±0.49 a***
III	RENN + GTN	0.74 ± 0.028a*,b**	20.3± 1.63a*,b*	4.79±0.78
IV	FENN + GTN	0.82 ± 0.025a***	22.36±1.82a***	6.79±0.26 a***
V	LENN + GTN	0.89 ± 0.033a***	22.3 ± 2.05a***	6.38±0.63a***

All values are mean ± SEM, n = 6. $^{*}p<0.05$, $^{**}p<0.01$

a- Significance difference as compared to group-I (Vehicle)
b- Significance difference as compared to group-II (GTN)

Table 8: Histopathological analysis

Groups	Treatment	Vacuolization in proximal tubular epithelial cells	Tubular Necrosis in proximal tubular epithelial cells
I	Vehicle	---	---
II	Gentamicin	+++	+++
III	RENN + GTN	+++	++
IV	FENN + GTN	++	++
V	LENN + GTN	+	+

Figure: Histological examination of different groups of animals in Nephroprotective activity

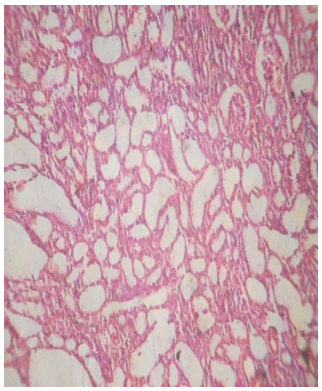

Figure (A): Histopathological slide of group I (Vehicle group)

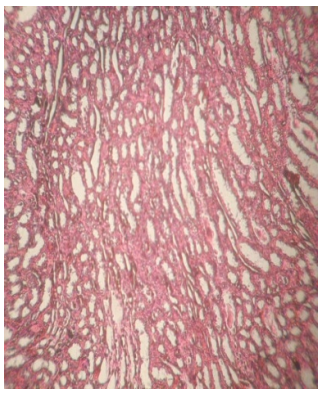

Figure (B): Histopathological slide of group II (Gentamicin treated group)

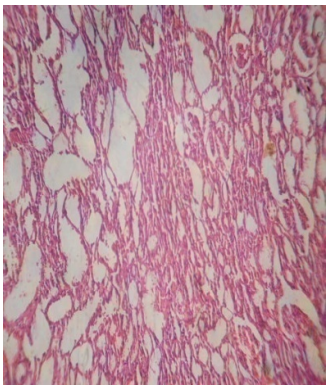

Figure (C): Histopathological slide of group III (RENN + GTN treated group)

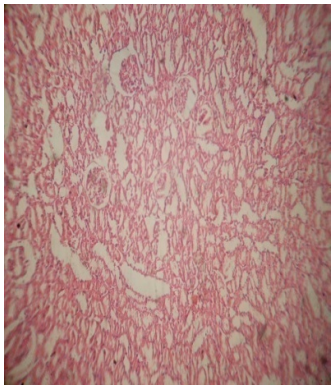

Figure (D): Histopathological slide of group IV (FENN + GTN treated group)

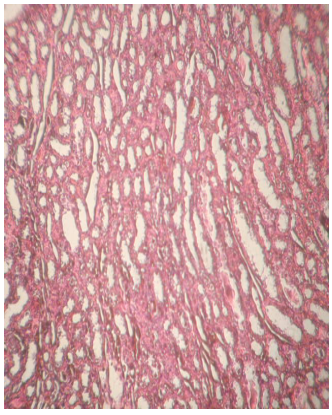

Figure (E): Histopathological slide of group V (LENN + GTN treated group)

4. DISCUSSION

Gentamicin induced nephrotoxicity has been extensively used as an animal model to study acute kidney failure in investigational research[34], In the pathogenesis of gentamicin induced nephrotoxicity, oxidative stress has been anticipated to have a say to nephrotoxicity, and it has been suggested that reactive oxygen species are the fundamental key in the mechanisms that straight to tubular necrosis and decline of glomerular filtration rate. It may be assumed that the fundamental role of gentamicin induced nephrotoxicity is generation of oxidative stress and inflammation; a loop of damage amplification and a connection between mechanisms of tubular and glomerular Changes[35]. Marked elevations of serum creatinine and urea concentration were suggested as a important purposeful destruction of kidney in gentamicin induced

nephrotoxicity[36]. Serum Creatinine concentration is a strong marker than the urea in the initial pathogenesis of kidney disease. Additionally, urea concentrations commence to augment just after parenchymal injury[37].

Numerous studies have reported that oxygen free radicals are considered to be significant peacekeepers of gentamicin induced acute renal failure (ARF). Consequently, among the major approaches used to improve gentamicin induced nephrotoxicity is the make use of of formulations with antioxidant properties[38].

Physicochemical analysis of powder of *Nelumbo nucifera* leaves flowers & roots

Physicochemical analysis of powder of *Nelumbo nucifera* leaves flowers & roots was done by standard reported methods. Results of Physicochemical analysis are displayed in Table 1.

Phytochemical screening of ethanolic extract of *Nelumbo nucifera* roots, leaves & flowers

Phytochemical screening of ethanolic extract of *Nelumbo nucifera* roots, leaves & flowers revealed the presence of a rich amount of phytoconstituents e.g. flavonoids, glycosides, alkaloids, carbohydrates etc. Results of Phytochemical screening of ethanolic extract of *Nelumbo nucifera* roots, leaves & flowersare displayed in Table 2.

***In vitro* antioxidant activity of ethanolic extract of *Nelumbo nucifera* leaves flowers & roots DPPH method**

The percentage scavenging activity of ascorbic acid was found to be 41.65%, 58.65%, 70.69%, 82.5% and 89.39% at defined concentration of 100µg/ml, 200µg/ml, 300µg/ml, 400µg/ml and 500µg/ml respectively. All three ethanolic extract of *Nelumbo nucifera* leaves flowers & roots showed a concentration dependent free radical scavenging activity in comparison to standard ascorbic acid. In the present study we evaluated the anti-oxidant effect of Root, flower & leaf extract of *Nelumbo nucifera* through DPPH method and found root extract more potent antioxidant as compared to other two extract (Table 3)

Effect of ethanolic extract of *Nelumbo nucifera* leaves flowers & roots on body weight and urinary volume on

Body weight among different treated groups changes significantly in comparison to control group the control group. Body weight of control group animals decrease significantly on repeated intraperitoneal injection of gentamicin (Table 4). Urinary volume increased significantly in the III (RENN+GTN treated group) group as compared to control group. In IV (FENN + GTN treated group) and V (LENN + GTN treated group) groups, urine volume was

significantly reduced as compared to III (RENN+GTN treated group) group. In fact, IV (FENN + GTN treated group) and V (LENN + GTN treated group) group's animals showed decrease in the urine volume to the level of the control. (Table 5)

Effect of ethanolic extract of *Nelumbo nucifera* leaves flowers & roots on urine and serum biochemical analysis for kidney function test

After this study, effects of above extract of *Nelumbo nucifera* were evaluated against gentamicin induced renal injury. Group III manifested a significant decrease in urine and serum Creatinine, urea and uric acid levels when compared with the GTM group on the 12^{th} day of experiment. Also, urine and serum Creatinine, urea and uric acid concentrations in group IV & V did not demonstrate a significant change in comparison with GTM group on day 12 (Table 6 and 7)

Effect of ethanolic extract of *Nelumbo nucifera* leaves flowers & roots on histopathological analysis:

Group I (Vehicle treated) animals showed common glomerular and proximal tubular histology. Animals of group II (Gentamicin) showed sever glomerular congestion, tubular necrosis, blood vessel congestion and occurrence of inflammatory cells in the kidney histology. Treatment with only repeated intraperitoneal injection of gentamicin caused a marked vacuolization in proximal tubular epithelial cells and necrosis (+++) in proximal tubular epithelial cells. Animals of group III (RENN+GTN treated group) showed less vacuolization in proximal tubular epithelial cells and necrosis in proximal tubular epithelial cells as compare to control group. In IV (FENN + GTN treated group) and V (LENN + GTN treated group) groups, there is significantly less vacuolization and less tubular necrosis in comparison to group III (RENN+GTN treated group) and also in comparison to control group. The histopathology results also confirmed that the Root extract of *Nelumbo nucifera* protection against gentamicin induced nephrotoxicity. Renal tissue necrosis was significantly higher in gentamicin group but not in root extract of *Nelumbo nucifera* treated group (Table 8)

5. CONCLUSION

In conclusion, the present study demonstrates that gentamicin increases nephrotoxicity indices including serum and urine Creatinine, uric acid and urea concentrations as well as renal tissue toxicity. It seems that Root extract of *Nelumbo nucifera* are able to improve kidney function against gentamicin induced nephrotoxicity. Further investigations with different

phytoconstituents of this extract are advised to evaluate the probable molecular mechanism of action on gentamicin induced nephrotoxicity.

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