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Original Research Article

Effect of nephroprotective *Ficus dalhousiae* bark extract on gentamicin induced with combination of benzoic acid nephrotoxicity in rats

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ABSTRACT

Background: The *Ficus dalhousiae* plant (Anjeer family) is. Its important parts-leaves, stem,bark and root are. The current study is design to effect of *Ficus dalhousiae* bark extract on gentamicin (GM) induced with combination of benzoic acid (BA) nephrotoxicity in rats.
Methods: In acute toxicity studies animals are fasted before being dosed; kept overnight. Depending on the time interval. The beginning dose will be chosen from one of four predetermined levels: 5, 50, 300, or 2000 mg/kg of body weight. The animals are evaluated for 4 and 48 hours. In nephroprotective studies we are taken 30 rats which will be divided into 5 groups. proceed group by group like-control with normal saline, BA (100 mg/kg/bodyweight, IP) daily, hydroalcoholic extract of *Ficus dalhousiae* (200 mg/kg/body weight, PO) and simultaneously administered GM (100 mg/kg/body weight, IP) daily for 9 days. And we are doing difference types of estimations, like-blood urea, uric acid and serum creatinine.
Results: *Ficus dalhousiae* bark extract on BA action on serum creatinine and urea levels in rats given GM. When compared to control rats, eight days of GM treatment resulted in significantly higher serum creatinine and urea levels. However, BA pretreatments have significantly improved serum creatine and urea ($p<0.001$) to reduce GM-induced nephrotoxicity ($p<0.01$, resp.).
Conclusions: *Ficus dalhousiae* has significant nephroprotective activity in nephroprotective studies, acute toxicity activity and various such type of estimations like- blood urea, uric acid and creatinine.

Keywords: *Ficus dalhousiae*, BA, GM, Nephro-protectivity, Rats

INTRODUCTION

In ancient system of medicine to all of the plant which have major component of medicinal effect in all the parts of the plant better startup for origin of effective chemical substances which may leads to newformation of the drug.[1] Some herbal therapieshave been utilized to treat the illness since ancient times. Non-nutrients are nutrients that have preventive or protective functions. This review begins with comprehensive discussion of plant's phytopharma-cological profile, followed by critical examination of ethnobotanics or traditional uses.[2]

Green medications are healthier and synthetically safer.[3] The *Ficus* family, usually known as the figs or figs tree, is belonging a *Moraceae* family which have about 850 woody trees, vines, hemicycles and bustles. *Ficus* is a *Moraceae* genus with almost 100 species. From *Ficus dalhousiae* liver and skinproblems are treated.[4]

Ficus dalhousiae is 9-12 ST omega-tree withsoft, glabrous juvenile branches. For a long time, hepatitis and skin disorders treated. Part of human society to fightdiseases in civilization began.[5] *Ficus dalhousiae* (Morphological characters): height-10-meter, color-bark brown, petioles-5-10 cm, lateral nerves-10-12 pairs, peduncle-8 mm long,

male flowers-few no., filament-Thick, stigma-cylindric, ovary-obovoid, syconium-yellow when ripe.[6]

The *Ficus dalhousiae* extract out these constituents' alkaloids, flavonoids, tannins, steroids, saponins, and reducing sugars are found in methanol extract. Flavonoids, finally, few chemicals may not have been dissolved inthe water, may contains phenols, steroids,saponins, and sugar reducing agents.[7]

Pharmacological activities of Ficus dalhousiae

Antihyperlipidemic, nephroprotective, hepatoprotective, anti-inflammatory analgesic and antipyretic, immune-modulatory, gastro protective, antidiabetic, anticonvulsant, wound healing, anthelminthic and antimicrobial.

The kidney is an essential excretory organ inthe human body. The urine is emptied from the kidneys into the urinary bladder. Theglomerulus is made up of an afferent arteriolethat is fed by a fluffy capillary and is emptiedby an efferent arteriole that is invaginated in the nephron's dilated blind end (Bowman capsule). The renal collecting system performs ultrasonic and volumetric control, as well as final electrolyte composition correction with mineralocorticoid(aldosterone) and anti-diuretic hormone (ADH). The Meduller's hypertonicity affects urine concentration significantly. Toxins andmetabolic waste are eliminated from the bodyby the kidneys.[8,9]

Nephrotoxicity caused by

Renal failure is described as the absence of kidney excretion, which causes metabolism to store nitrogen waste products in the blood. Furthermore, as is the case with endocrine dysfunction, the fluid and electrolyte balance are disrupted. Acute and chronic renal failure are two forms of kidney failure by Herfindal et al.[9,10] Nephrotoxicity is also caused by a various type of medications: A. Antineoplastic agents, B. Antimicrobial agents, C. Aminoglycosides, D. Heavy metals, E. Miscellaneous, F. NSAIDS and free radicals are primarilyharmful metabolites.[11]

Nephrotoxicity can express itself in a variety of ways, including abnormal tube functions concentration issues, and impaired glomerular filtration. However, no perfect signal for tubular cell injury or location exists. Tubular cells can be fatally or non- lethally changed by nephrotoxin.[12]

Accumulation of aminoglycosides through the various ligand megalin, cause nephrotoxicity which due to the presence of proximal tubuleto endocytosis. A concord of criteria for induced nephrotoxicity, declare the proximal tubular markers than traditional markers Shon in observation studies. In this clear association with medicinally correlate to translate to medical practice.[13] There are various type of nephrotoxicity like- crystal nephropathy, renal tubular toxicity inflammation, glomerular damage and microangiopathy.[14]

GM is a gram-negativeantibiotic that is commonly used in human medicine to treat life-threatening infections.[15,16] The use of GM, on the other hand, is responsible to nephrotoxicity.[15] In according to review of several papers, the function of naturally occurring food-producing substances in controlling and controlling a variety of chronic diseases has piqued interest, with salicylic acid (SA) beingone of the molecules utilized for pain relief and inflammatory conditions since ancient times.[17,18]

Objective of the study

Daily foods, vegetables, and fruit make up the majority of SA. Applying SA appears to be able to reverse oxidative damage, according to a growing body of research. Although the mechanisms behind such effects are uncertain, they have been observed in animals. The SA's benefits for radical scavenging and iron chelation have been widely reported as some research article.

But the high quantity of salicylic acid, it increases inflammation and ulceration over time to the organ and specific site. Goal security, if substantial percentages of the body surface are treated, high amounts to prevent further complications.

Plant

Ficus dalhousiae was collected from the Bhopal district of Madhya Pradesh from April 2021 to July 2021. The voucher specimens were recognized, validated, and authenticated by the survey, botanical departments, Barkatullah universities, and field botanists Dr. Arun Raghuwanshi. The reporting of the study was done by according to consolidated reporting of randomized controlled trials (CONSORT).

The plant has been verified as genuine. The shadow had been healed, and the bark had been cleansed. And cut into the small pieces and grind it with the help of mechanical grinder. And that coarse powder fill into the Soxhlet and fill up to the 1500-1600 ml ethanolfor a week, the extract was dried with the help of rotary evaporator and also kept on desiccators whenever we using it.

Animal

Anand firms obtained both sexes of Switzerland's Albino adult rats, Bhopal (169/CPCSEA/1999). The rats were divided into five groups of six rats each, at random. Each rat weighed between 250 and 300 gm and was housed separately (Four rats per cage). The animals were acclimatized in the animal room for 48 hours. Under typical laboratory conditions, they were kept at 202°F, humidity, 12 hours of light and dark, a standard pellet diet, and suitable tap water.

Selection criteria

Inclusion criteria

In this study, the subject matter chooses werebetween 20 to 60 years with low to moderately uplifted kidney enzyme levels based on various diagnosis process like; patient history, physiologic examination and laboratory test report. In these the subject matter was otherwise good health. It's ameasurement depends upon imbalance ratio of the enzymes, ratio of AST (Aspartate aminotransferase) to ALT (Alanineaminotransferase) greater than 2:10. Subject matter also had to be able to provide noted information which is very easy to understand and be willing to correlate with the requirementof the study.

Exclusion criteria

Here, few patients were excluded from these criteria. Newly adult, pregnant women and childbearing women prospective who are at danger of pregnancy; subject matter with critical alcoholic hepatitis who have cirrhosis or life anticipation lower than 3 months; and also with critical renal disfigurement explained via glomerular filtration rate below 60 ml/min per 1.73 m^2; subjects matter with hepatic disorder due to cardiac causes, hemochromatosis , and Wilson's disease; subject matter such as anti-tubercular medication, paracetamol and salicylic acid. The subject matter ability to conclude the study and its measurement.

Acute toxicity studies method

Animals are fasted before being dosed; food,but not water, should be kept overnight. Following the fasting period, the animals will be weighed and the test material will be delivered. Food should be avoided for another 3-4 hours after the drug has been administered. Because a dose is given in fractions over time, the animals may require food and drink, depending on the time interval. Three animals are employed for eachstep. The beginning dose will be chosen from one of four predetermined levels: 5, 50, 300, or 2000 mg/kg of body weight. For specific dose animals, the starting dose level should be the most likely fatality level. For mortalitybehavioural changes, the animals are evaluated for 4 hours and 48 hours.

Complete duration of study was almost 58 days (± 5 days) with four deviations to the drug-induced nephrotoxicity has been studied in both animals and humans. The nephrotoxicity of single daily GM and BA for 9 days and one daily intraperitoneal BA for 14 days wasinvestigated in this study.

Nephroprotective studies in vivo method

Action of *Ficus dalhousiae* on GM with combination of BA induced nephrotoxicity.

Experimental process; Albino will be divided into 5 groups, each groups having 6 animals.

Group 1: Control with normal saline (1 ml/kg), group 2: BA (100 mg/kg/body weight, IP) daily for 9 days, group 3: Hydroalcoholic extract of *Ficus dalhousiae* (200 mg/kg/body weight, IP), and simultaneously administered GM (100 mg/kg/body weight, IP) daily for 9 days, group 4: Ethanol extract of *Ficus dalhousiae* (200 mg/kg/body weight, IP) and also administered GM + BA (100 mg/kg/body weight, IP) same as above 9 days and the last one, group 5: Normal saline (1 ml/kg) and carrying out administration of GM (100 mg/kg/body weight, IP) for as usual 9 days.

RESULTS

BA action on serum creatinine and urea levels in rats given GM. When compared to control rats, eight days of GM treatment resulted in significantly higher serum creatinine and urea levels (Table 1). However, BA pretreatments havesignificantly improved serum creatinine and values (Table 2 and 3).

Table 1: BA effects on GM-induced renal impairment by serum urea and creatinine.

Parameters	Control	BA	GM	GM + BA
Urea (mmol/l)	5.45±0.90*	5.79±0.56*	19.1±2.66	8.43±1.33#
Creatinine (µmol/l)	46.93±2.04#	51.85±8.06#	78.71±8.43	55.28±8.99#

Data are presented as mean ± SD. *P<0.001 versus GM, GM + BA.#P <0.001 versus GM.

Table 2: Grading of histopathological changes in the kidney sections.

Histopathological changes	Control	BA	GM	GM + BA
Mononuclear cell infiltration	----	----	+++	+
Tubular degeneration	----	----	+++	+
Tubular necrosis	----	----	++	----
Hyaline casts in tubular lumen	----	----	+	----

Scoring was done as follows: none (—), mild (+), moderate (++), and severe (+++). Kidney weight: In GM treated group of animal's weight of kidneys were considerably increased compared to normal animals (group1) and treating (group 4 and 5) with ethanol extract showed significant decrease (p<0.001) in kidney weight.

Table 3: Effect of 100 mg/kg/day intraperitoneal GM and *Ficus dalhousiae* oral on SGOT, SGPT, ALP untreated rats for 9 days.

Groups	Drug treatment	SGPT levels (U/l)	SGOT levels (U/l)	ALP levels (U/l)
A	1 ml/kg, IP, NS	42.6.4±1.63	46.25±0.33	32.36±1.26
B	100 mg/kg, IP, BA	113.45±1.85	126.19±3.48	102.52±2.77
C	100 mg/kg, IP, GM 200 mg/kg	69.38±0.87	95.45±1.76	75.74±1.88
D	100 mg/kg, IP, GM + BA acid 200 mg/kg	75.56±2.14	55.68±1.45	56.38±1.54
E	100 mg/kg, IP, GM + 1 ml/kg, IP, NS	46.4 7±1.31	47.18±1.77	45.47±1.87

DISCUSSION

GM is commonly used to treat severe gram- negative bacterial infections.[19] The nephrotoxicity of GM administration is, nevertheless, a serious side effect. This would make it more clinically useful by reducing nephrotoxicity.[20,21] Chemical substances have been employed in a variety of ways to minimize GM nephrotoxicity. Compounds found in food plants that produce reactive oxygen species are well-known scavengers. Significant and consistent evidence has emerged in recent decades indicating the antioxidant activities of BA.[22,23] Are based on mechanisms. These consequences are still unknown. The concentrations of serum creatinine and ureahave dramatically decreased.[24]

However, if reactive species are created in large enough amounts, they can cause a variety of pro-oxidant processes, including as lipid peroxidation, protein nitration, and oxidation, which damage cellular macromolecules.[25] With GM treatment, the production of reactive oxygen species (ROS) increased. The development of ROS has been demonstrated. Urea, creatinine serum, and tubular acute necrosis these are biochemical parameters.[26]

Drug-induced nephrotoxicity has been studied in both animals and humans. The nephrotoxicity of single daily GM and BA for 9 days and one daily intraperitoneal BA for 14 days wasinvestigated in this study. Tubulo-nephritis toxicity is defined by a significant increase in circulating blood urea, serum creatinine, and histopathology in model controls when urea ($p<0.001$) to reduce GM-induced nephrotoxicity ($p<0.01$, resp.). The renal function tests were not modified by BA treatment alone when compared with control compared to (group 1) rats (group 2). These modifications, on the other hand, were linked to nine days of co-handling with single daily graduate EFD extract dosages. In comparison to the group of toxicants, oralplant extract administration considerably lowers urea and creatinine levels. A prolonged anorexia related with genetic drymatter was seen in group 2 rates, in additionto the direct nephrotoxic effect of genetically modified GM andBA. Because generation rate of serum urea exceeds clearance rate, it accumulates in renal disorders. The nephrotoxicity index was used to raise serum levels of urea and creatinine. Creatinine is derived from natural tissue creatinine breakdown sources. As a result, the concentration of serum urea is frequently regarded as a more trustworthy indicator of renal function than serum creatinine.

GM was actively carried into proximal tubulas following glomerular filtration in tiny amounts, inducing proximal tube damage and renal circulationanomalies, resulting in a drop in GFR.

SGOT is a mitochondrial enzyme that is notfound in the heart, liver, skeletal muscle, or kidney. Transaminase elevations that are mild to high can develop to alcoholic liver damage and cirrhosis. In the current investigation, ethanol extract from *Ficus dalhousiae* leaves significantly reduced SGOT levels in serum ($p=0.05$), showing nephroprotective action.

The levels of alkaline phosphatase in toxic kidneys are extremely high, due to hepatic excretion or enhanced cell- or canal synthesis of ALP.

In this study have few limitations. Like; thestudy was not going to be clear results for a short time period, but the conclusion of thisstudy is better than the past research, because we work on that accuracy of the results with save much more time and materials.

CONCLUSION

The nephro-protective activity of *Ficus dalhousiae* extract was confirmed by the following actions: Serum indicators including as urea, uricacid, and creatinine are all rising in the GM with BA group. Renal illnesses are also noticed in clinical practice and hence have diagnostic relevance in the evaluation of kidney function.

According to our biochemical findings, BA prevented GM's nephrotoxic effects, which were backed up by histological data. These findings suggest that supplementing with BA can prevent GM-induced kidney damage. This can be accomplished through redox signaling systems that effectively limit ROS pro-inflammatory factors.

The *Ficus dalhousiae* extract was found to significantly lower the above-mentioned toxicant high levels of serum marker while also increasing protein levels in this investigation. As a result, it may be inferred that the *Ficus dalhousiae* extract protects against nephropathy.

GM-treated animals have glomerular, peritubular, and blood vessel hemorrhagic congestions.

People with serious renal diseases are in the same boat.

In the current investigation, the extract of *Ficus dalhousiae* was shown to prevent such changes in kidney histology produced by GM and acetaminophen, demonstrating nephroprotection.

Plant material comprising phenols, flavonoids, alkaloids, and saponins gives organ protection due to their free radicalscavenging activities, according to other studies. The phytoconstituents described above were found in the extract tested in phytochemical analysis. These phytoconstituents' ability to scavenge free radicals and hence provide nephroprotection cannot be ruled out.

GM -induced nephrotoxicity was greatly reduced when used in conjunction with an ethanolic extract from *Ficus dalhousiae*. Following therapy with *Ficus dalhousiae* ethanolic extract, a reduction in high biochemical markers such as serum SGPT, SGOT, and ALP indicates the extract's nephro-protective benefits.

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