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Research Article

Nephroprotective Effect of Alcoholic Extracts of Fruits of *Solanum xanthocarpum* Against Cisplatin-Induced Nephropathy in Rats

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ABSTRACT

The objective was to conduct a Nephroprotective effect of alcoholic extracts of fruits of *Solanum xanthocarpum* against Cisplatin-induced nephropathy in rats. Wistar rats were divided randomly into five groups of six animals each (n=6) receiving different treatments, consisting of vehicle (distilled water), single dose of cisplatin (7 mg/kg of body weight; i.p), standard polyherbal drug cystone at a dose of 5ml/kg body weight, ethanolic extract of fruits of *Solanum xanthocarpum* at two different doses (viz., 200, 400 mg/kg body weight) respectively. The treatment duration was considered for 14 days. Nephroprotective activity was assessed by estimating various biochemical parameters related to urine and serum as parameters of assessment. The ethanolic extract 400 mg/kg treated rat group showed significant ($p<0.001$) elevation in body weight (7.13 ± 1.21) with a significant ($p<0.05$) increase in urine volume output (11.85 ± 0.75). However, the urine creatinine (01.75 ± 0.30) and albumin (0.30 ± 0.05) decreased significantly ($P<0.01$) as compared with the toxic control group. The serum creatinine (0.61 ± 0.08) and urea (31.30 ± 4.05) were found to be significantly ($P<0.001$) low when compared with the toxic control group. *Solanum xanthocarpum* showed Nephroprotective activity in a dose dependent manner compared to cystone.

Keywords: *Solanum xanthocarpum,* Nephroprotective.

INTRODUCTION

Nephropathy is widely encountered among the people of entire world irrespective of the age, racial, environmental, and geographical variability. The etiology behind this complication is broad ranging from substance-induced to various metabolic and physiological disturbances, paneling nephropathy among the 10 leading causes of death across the world. Cisplatin is extensively used for the treatment of several cancers like testicular and lungs cancer. Unfortunately, the gracious drug cisplatin is conjoined with a brutal side effect since it induces nephrotoxicity[1].

The mechanism by which cisplatin-induces renal injury is not well understood. It may involve direct interference with tubular or mitochondrial transport processes[2] (Zhang & Lindup1994), covalent modification of cellular constituents[3] (Mistry et al. 1991), or generation of free radicals[4] (Sadzuka et al. 1992). In addition, the changes in renal haemodynamics were found to play an important role in cisplatin induced nephrotoxicity[5] (Winston & Safirstein 1985). Experimental and clinical studies showed that after cisplatin injection, a marked decrease in renal blood flow and glomerular filtration rate were observed[6] (Offerman et al. 1984;Li et al. 1994). Accordingly, few studies tried to ameliorate the nephrotoxicity of cisplatin using the amino acid glycine.

Solanum xanthocarpum. (S. xanthocarpum) Schrad. & Wendl. (family: Solanaceae) commonly known as yellow berried nightshade (synonym: Kantakari), is a prickly diffuse bright green perennial herb, woody at the base, 2-3 m height found throughout India, mostly in dry places as a weed on road sides and waste lands. The fruits are of 1.3 cm diameter berry, yellow or white green veins, surrounded by enlarged calyx[7].

The fruits are known for several medicinal uses like anthelmentic, antipyretic, laxative, anti-inflammatory, anti-oxidant, anti-asthmatic and aphrodisiac activities. The stem, flowers and fruits

are prescribed for relief in burning sensation in the feet accompanied by vesicular eruptions. The hot aqueous extract of dried fruits is used for treating cough, fever and heart diseases. The fruit paste is applied externally to the affected area for treating pimples and swellings[8].

The flavanoids quercitrin and apigenin glycosides are the major chemical constituents which are present in the fruits of *S.xanthocarpum*[9]. To the best of our knowledge there was lack of scientific reports available in support of its traditional claim of renoprotective potential. Therefore, the present study was designed to demonstrate the renoprotective effect of *S.xanthocarpum* fruit extract against Cisplatin-induced nephropathy in rats.

MATERIALS AND METHODS

Fruits of *Solanum xanthocarpum* were collected from the field areas of Manjeshwar in the month of December and its identity was confirmed by Mrs. Noeline J.Pinto. H.O.D Dept of Botany, St Agnes College, Mangalore.

The collected fruits were cleaned from adhering soil and other materials, and then it was dried under shade for two weeks. The dried fruits were chopped and pulverized in an electric grinder. The powdered plant material was subjected to Soxhlet extraction with about 80%w/v ethyl alcohol. The extract obtained was concentrated over a hot water bath. Percentage yield of thus obtained crude extract was calculated. Accordingly alcoholic extract of *Solanum xanthocarpum* was prepared in sufficient quantity and stored in the refrigerator for further use.

Healthy albino male rats of wistar strain weighing between 150 and 200 g were selected for the investigation. The animals were kept under maintained laboratory conditions with adequate supply of drinking water ad libitum and pallet diet. The experimental protocol was approved by the Institutional animal Ethics committee and the conditions in the animal house approved by Committee for Supervision on Experiments on Animals. The dose limits were selected on the basis of previously performed oral acute toxicity studies in mice, in accordance with the OECD guidelines[10]. Total 30 Wistar rats were divided randomly into five groups of six animals each.

Group I (normal control) received oral dose of distilled water (1 ml each) for 14 days.

Group II (toxic control) received single dose of cisplatin[11] (7 mg/kg of body weight; i.p) on day1.

Group III (standard group) received standard polyherbal drug cystone[12] (5ml/kg; p.o) (cystone Syrup, Himalya Drug Company., Bangalore, India) for 14 days with single dose of cisplatin (7mg/kg of body weight; i.p) on day 1,

Group IV (SX 200) received ethanolic extract 200 mg/kg b.w once in a day for 14 days respectively along with the single dose of cisplatin (7 mg/ kg of body weight; i.p) on day 1.

Group V (SX 400) received ethanolic extract 400 mg/kg b.w once in a day for 14 days respectively along with the single dose of cisplatin (7 mg/ kg of body weight; i.p) on day 1.

The treatment duration was considered for 14 days as documented by Yang et al[13].

Urine was collected over 24 h on 14 th day by keeping the test animals in individual metabolic cages. The volume of collected urine samples was measured followed by estimation of biochemical parameters, namely urine creatinine and urine albumin. Blood samples were collected from the test animals under anesthesia (phenobarbitone sodium; 40 mg/kg of body weight; i.p) by cardiac puncture before sacrifice and serum parameters including creatinine, urea, albumin and total protein were estimated[14, 15]. The biochemical estimations were done in a Biochemical-semi-auto analyzer by standard procedures using commercial Kits. The kidneys were removed from the rats before sacrifice and organs were fixed[16] using a formosal solution (10% v/v of formaldehyde in normal saline), embedded with paraffin wax followed by preparation of tissue sections using a microtome for histopathology study[17].

Statistics

Data obtained in the experiment were expressed in terms of mean + SEM. Statistical Significance of data was assessed by analysis of variance (one-way ANOVA) followed by a comparison between different groups using Tukey-Kramer multiple comparison test. The significance levels was set $P<0.05$. The toxic control group was compared with the normal control group and all other treatment groups were compared with the toxic control group.

RESULTS

The results as cited in Table 1 include change in body weight, Kidney weight, urine volume along with the urine, and serum biochemistry data. Cisplatin administration-induced renal injury was prominent as evidenced by significantly depressed renal functions, body weight, and urine volume as compared to the normal group.

The SX 400 (ethanolic extract 400mg/kg treated rat group) showed significant ($P<0.001$) elevation in body weight (7.13 ± 1.21) with a significant ($P<0.05$) increase in urine volume output (11.85 ± 0.75). However; the urine creatinine (01.75 ± 0.30) and albumin (0.30 ± 0.05) decreased significantly ($P<0.01$) as compared with the toxic control group. The serum creatinine (0.61 ± 0.08) and urea (31.30 ± 4.05) were found to be significantly ($P<0.001$) low when compared with the toxic control group.

The histological features found from the tissue sections of different groups are mentioned in table

2 and the photomicrographs of tissue sections are presented in figure 1a-d. The histopathology of tissue sections suggest that the toxic control group had encountered vast histological damages as evidenced by the glomerular and tubular congestion with abnormal Bowman's capsule, blood vessel congestion, epithelial cell desquamation, and presence of tubular cast with few inflammatory cells. The histological features of the SX 400 group showed minimal cellular damage in contrast to the toxic control group. The SX 400 group showed normal glomerular and tubular arrangements with normal Bowmen's capsule. Congestion of blood vessels was minimal and tubular cast were not present.

Parameters studied for the nephroprotective effect of the ethanol extract of *Solanum Xanthocarpum*

Groups	Change in body weight (g)	Urine volume(ml)	Kidney weight (g)	Urine creatinine (g/24h)	Urine albumin (g/24h)	Serum creatinine (mg/dl)	Serum urea (mg/dl)	Serum albumin (g/dl)	Serum total protein (g/dl)
Normal control	8.30± 1.25	13.80±1.23	1.413±0.059	1.61±0.14	0	0.57±0.07	22.21±3.06	3.15±0.07	5.17±0.13
Toxic control	22.33±5.21	6.76±0.65	1.563±0.023	3.98±0.33	0.81±0.12	1.85±0.27	74.6±5.47	2.12±0.21	8.19±0.49
Standard	4.73±1.18	11.56±1.05	1.513±0.035	1.80±0.15	0.30±0.02	0.65±0.11	29.4±3.06	3.12±0.30	5.45±0.41
SX- 200	2.81±2.25	09.11±0.79	1.530±0.036	2.44±0.23	0.54±0.11	0.89±0.13	43.08±4.79	2.75±0.39	5.90±0.79
SX-400	7.13±1.21	11.85±0.75	1.520±0.042	01.75±0.30	0.30±0.05	0.61±0.08	31.30±4.05	2.91±0.29	5.30±0.50
P value	<0.0001	0.0001	0.0889	0.0021	<0.0001	<0.0001	<0.0001	0.1910	0.0046
F value	21.284	8.127	2.265	5.312	15.436	13.253	21.324	1.556	3.856

P<0.05; P<0.01; P<0.001. For n=6; toxic control group was compared with the normal control group and all other groups were compared with the toxic control group. SX200; ethanolic extract of Solanum Xanthocarpum at 200 mg/kg; SX 400; ethanolic extract of *Solanum Xanthocarpum* at 400 mg/kg.

Histological features found from L.S of Kidneys of different groups

Groups	Normal control group	Toxic control group	Standard group	SX-400 group
Histological features				
Tubular congestion	–	++++	++	+
Tubular cast	–	+++	+	–
Epithelial Disquamation	–	+++	+	++
Glomerular congestion	–	++++	–	–
Blood vessel congestion	–	++	–	+
Inflammatory cells	–	+++	+	+

+++: presence of indicated histological abnormality. – : absence of indicated histological abnormality.

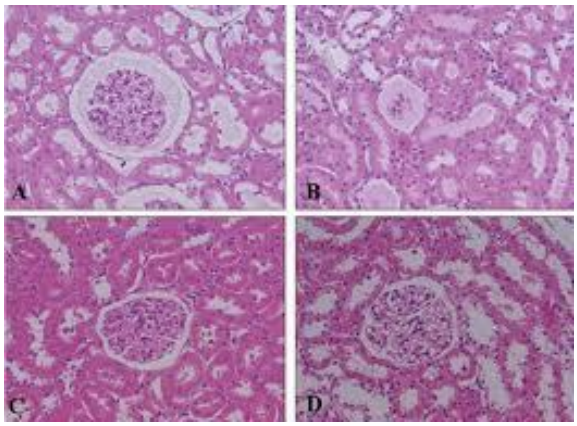

Fig. 1: Photomicrographs of L.S of kidney of different groups
(a) Normal Control Group, (b) Toxic Control Group, (c) Standard Group, (d) SX 400 group

DISCUSSION

The present study aimed to evaluate the Renoprotective effect of fruit extract (ethanol) of SX Linn. Plant against cisplatin-induced nephropathy in rats. Cisplatin-administered rats (toxic control group) had encountered acute kidney dysfunction as evidenced by elevation in serum urea and creatinine, decreased urine output and body weight with multiple histological damages. Treatment with the ethanol of SX at the dose level of 400 mg/kg b.w for 14 days (SX 400 group) significantly lowered the serum level of creatinine and urea, decreased urine creatinine and albumin with a significant weight gain, and increased urine output when compared with the toxic group. The histological damages in the SX extract-treated group were minimal in contrast to the toxic rats. The statistical significance of the nephroprotective activity of SX-treated group and the polyherbal drug cystone (standard group) treated group (both the groups were compared against toxic control) were found almost equal as both groups gained same levels of significance ($P<0.001$) against the toxic group in most of the parameters including serum urea and creatinine.

The results of our study suggest that the ethanolic extract of SX possesses nephroprotective potential depending on the dose levels. Extensive and multidimensional further research is nedded to elucidate the exact mechanism of nephroprotective action of this plant extract.

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