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Open Access Research Paper

Nephroprotective Effect of Asgand Powder (*Withania somnifera Dunal)* on Cisplatin Induced Renal Injury in Rats

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Abstract

Background: The nephroprotective effect of crude powder of Asgand (*Withania samnifera Dunal)* was studied against cisplatin induced renal toxicity in wistar albino rats of either sex.

Results: The powder of *Withania somnifera Dunal* at dose level 700 and 1400 mg/kg body wt/day showed reduction in elevated blood urea, serum creatinine and uric acid. It was found to protect kidney damage by cisplatin induced nephrotoxicity as evidenced by oral administration of Asgand *(Withania samnifera* Dunal) (700 mg/kg) inhibited the rise in blood urea nitrogen (121.7%), Serum cratinine (76.64%), and uric acid (92.7%). There were 92.71% inhibition in the rise of BUN, 92% inhibition in the rise of serum creatinine and 106.6% inhibition in the rise of uric acid with 1400 mg.

Conclusion: The findings suggest that the famous Unani herb Asgand Powder possesses marked nephroprotective activity and could offer a promising role in the treatment of acute renal injury caused by nephrotoxins like cisplatin.

Keywords: *Withania somnifera* Dunal, Cisplatin, Asgand, Nephroprotection, Unani Medicine

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INTRODUCTION

Acute renal failure refers to the sudden and usually reversible loss of renal function, which develops over a period of days or weeks. Among the causes of acute renal failure acute tubular necrosis, which occurs due to ischemia or nephrotoxins like cisplatin and gentamicin (aminoglycoside) is most common, accounting for 85% of the incidences. Cisplatin is an important anticancer or antineoplastic drug and especially effective for the treatment of solid tumors of testes, ovaries, breast, lungs, bladder etc.[1-3] Its use is limited due to nephrotoxicity, which is a major clinical problem, seen in about 20% of patients despite the use of saline hydration and diuretics, and it is characterized by decreased glomerular filtration and tubular injury.[4-6]

Although the mechanism of cisplatin induced renal injury is not well understood. It may involve direct interference with tubular or mitochondrial transport processes[7] covalent modification of cellular constituents[8] or it has been suggested that oxygen free radicals play an important role.[9-11] But some hypotheses are given for explaining their mechanism. Experimental and clinical studies showed that after cisplatin injection, a marked decrease in renal blood flow and glomerular filtration rate was also observed.[12-13] Cisplatin increases lipid peroxidation in renal cortical slices.[9,14-15] It has been reported that the administration of free radical scavengers and antioxidants such as super oxide dismutase, sodium selenite[16] offered partial protection of the kidney against cisplatin toxicity. Although the mechanism of cisplatin renal toxicity is not clear, it has been suggested that oxygen free radicals play an important role.[9] The crude extract of *Ginkgo biloba* (Family: Ginkgoaceae) protects kidney slices against cisplatin induced lipid peroxidation and decreased uptake of *p*-aminohippuric acid.[9]

Search for nephroprotective agents has made man turn to alternative sources *viz* indigenous system of medicines especially Unani and Ayurveda. That has a rich literature from ancient time and provides a cheap, effective and safe medicine through it source of herbal, mineral and animal origin drugs.[17]

Asgand (*Withania somnifera*, Dunal) belongs to the family *Solanaceae*. It is very familiar name in Unani as well as in other traditional systems of medicine for its multifarious properties, due to the similarity between the restorative properties of Asgand root and Ginseng root it is also called 'Indian ginseng'. In Tibbe Unani, Asgand is well known for its therapeutic properties as rejuvenator, strengthen, immunomodulator, diuretics, adoptogenic etc.[18-19] The fresh roots are preferred for medicinal uses, two type of asgand mentioned in Unani literature. Our preliminary studies showed that Asgand (*Withania somnifera,* Dunal) protect the kidney damage against the cadmium chloride induced renal damage.[20] Rhubarb (*Rheum emodi*) against gentamicin, cadmium chloride, mercuric chloride and potassium dichromate,[21] Kulthi (*Dolichos biflorous*) against gentamicin and mercuric chloride induced nephrotoxicity,[22-23] Kundur (*Boswellia serrata* Roxb.)[24] Khar-e-Khasak Khurd (*Tribulus terrestris*)[25] Hilteet (*Refula foetida* Regal)[26] against gentamicin induced toxicity in experimental animals.

Objective of the study

The objective of this study was taken to evaluate the efficacy of the crude power of *Withania somnifera* Dunal, against cisplatin-induced nephropathy.

MATERIALS AND METHOD

Plant Material

The Asgand (*Withania somnifera* Dunal) was procured from Asian Traders, Kharibaoli, Delhi. The authenticity of Asgand (*Withania somnifera* Dunal) was established by the matching with authentic specimen available in Dept. of Ilmul Advia, F/o Medicine (U), Jamia Hamdard, New Delhi-110062. The root of Asgand (*Withania somnifera* Dunal) was dried and converted into fine powder (Asgand power=AP) and finally suspended in vehicle before its administration per orally.

Animals

Healthy albino rats of Wistar strain of either sex weighing 130-250 gms (aged 60-90days) were used for this study. Rats were obtained from Central Animal House Facilities, Jamia Hamdard, New Delhi. They were kept under standard laboratory conditions (Temperature and humidity controlled) and fed with standard diet. Water was allowed *ad libitum.* The study was conducted after obtaining Institutional animal ethical committee Clearance.

Research designed

Three days after acclimatization, the rats were assigned randomly to four equal experimental groups having six animals each. The group-I served as control and was injected with distilled water and orally administered gum acacia solution (2% w/v) for 7 days. The group-II was given cisplatin (1mg/kg/day, intra peritoneal) for four days and orally administered same as group-I,[27] group-III was treated with powder of *Withania somnifera* Dunal in the dose of 700 mg/kg body wt. orally suspended in acacia solution (2% w/v), group-IV was administered the test drug in the dose of 1400mg/kg body wt., orally. Group III and IV also received cisplatin 1g/kg/day intra peritoneal. On the next day the blood samples were collected, serum was separated by centrifuging at 3000 rpm for 10min. Serum were analyses for blood urea, serum creatinine and uric acid levels.[28]

Statistical Analysis:

Data were expressed as Mean+S.E.M and analyzed by one-way analysis of variance (ANOVA) followed by Dunnett's 't' test. The probability level less than 5% considered to be significant.

RESULTS

Table-1: Effects of Asgand (*Withania somnifera* Dunal) on BUN in Cisplatin induced nephrotoxicity in rat model (Oral treatment period –7 days)

Groups	Treatment	Dose	BUN Level (mg/dl) (Mean±SEM)	% of change	% of inhibition
I	Control (Vehicle)	10 ml/KG	20.19±0.68	-	-
II	Cisplatin (Toxicant)	1mg/Kg/day	29.8±1.15[a]*	100	-
III	AP + Toxicant	700+1mg/Kg/day	18.10±0.91[b]*	-21.7	121.7
IV	AP + Toxicant	1400+1mg/Kg/day	20.89±1.09[b] *	7.3	92.7

N=6, BUN = Blood urea nitrogen, *Statistically significant, [a]in comparison with control, [b]in comparison with toxicant, * P<0.01

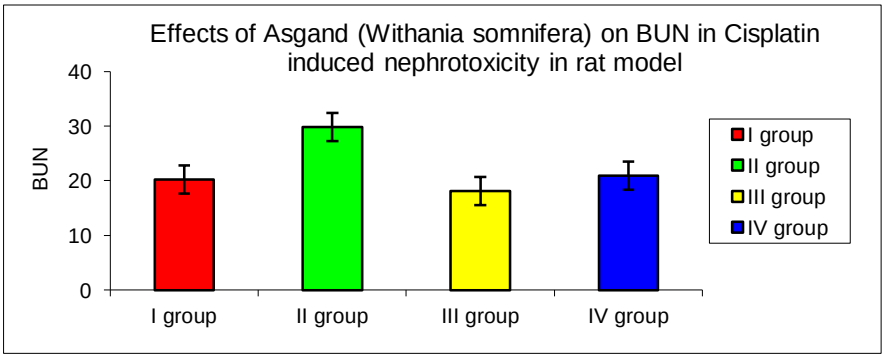

Figure-1: Effects of Asgand *(Withania somnifera Dunal*) on BUN in Cisplatin induced nephrotoxicity in rat model

Table-2: Effects of Asgand (*Withania somnifera Dunal*) on serum creatinine in Cisplatin induced nephrotoxicity in rat model (Oral treatment period –7 days

Groups	Treatment	Dose	S.Cr Level (mg/dl) (Mean±SEM)	% of change	% of inhibition
I	Control (Vehicle)	10 ml/KG	1.44±0.11	-	-
II	Cisplatin (Toxicant)	1mg/Kg/day	2.81±0.21[a]*	100	-
III	AP + Toxicant	700+1mg/Kg/day	1.76±0.13[b]*	23.40	76.6
IV	AP + Toxicant	1400+1mg/Kg/day	1.55±0.10[b] *	8.0	92

N=6, S.Cr = Serum Creatinine, *Statistically significant, [a]in comparison with control, [b]in comparison with toxicant, *P<0.01

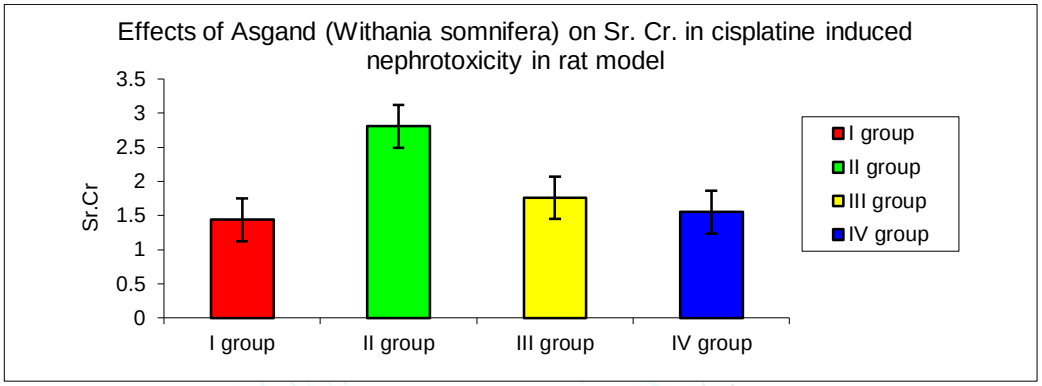

Figure-2: Effects of Asgand (*Withania somnifera Dunal*) on Sr. Cr. in cisplatine induced nephrotoxicity in rat model

Table-III: Effects of Asgand (*Withania somnifera Dunal*) on uric acid in Cisplatin induced nephrotoxicity in rat model (Oral treatment period –7 days)

Groups	Treatment	Dose	Uric Acid Level (mg/dl) (Mean±SEM)	% of change	% of inhibition
I	Control (Vehicle)	10 ml/KG	8.92±1.03	-	-
II	Cisplatin (Toxicant)	1mg/Kg/day	13.19±0.83[a]*	100	-
III	AP + Toxicant	700+1mg/Kg/day	9.23±0.62[b]*	7.3	92.7
IV	AP + Toxicant	1400+1mg/Kg/day	8.64±0.61[b] *	-6.6	106.6

N=6, UA= Uric Acid , *Statistically significant, [a]in comparison with control, [b]in comparison with toxicant, *P<0.01

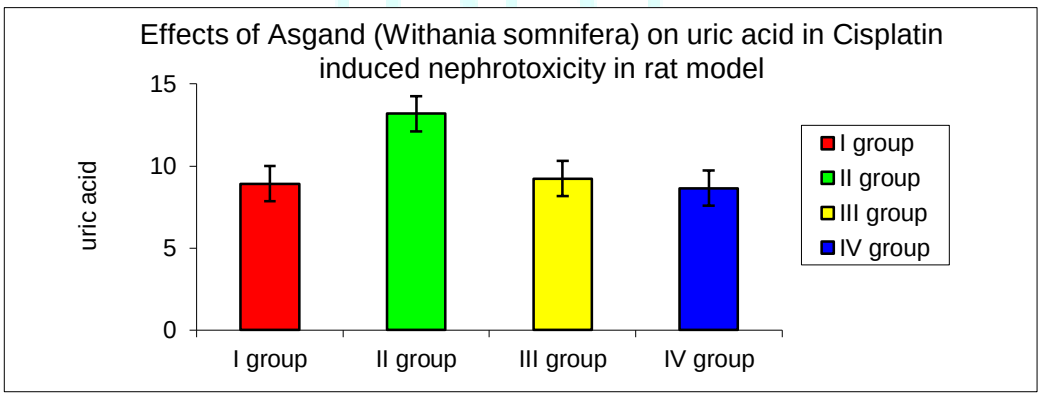

Figure-3: Effects of Asgand (*Withania somnifera Dunal*) on Uric acid. in cisplatine induced nephrotoxicity in rat model

Group I (Control) was compared Group II (Toxicant) for observation of change in the parameters. The Group III and Group IV were compared with Group II to observe the Inhibition. The inhibition was calculated in term of percentage of change in comparison to control. The level of the markers increased significantly in cisplatin treated (group-II) animals in comparison to Control (group-I). Cisplatin treatment caused nephrotoxicity as evidenced by marked elevation in blood urea nitrogen (BUN) 47.59%, serum creatinine (SC) 95.13% and uric acid (UA) 47.86% as shown in table I,II & III and table-1,2 & 3.

The elevation of serum markers were significantly reduced by the oral administration of Asgand powder (*Withania somnifera* Dunal) in the dose 700mg/kg, inhibited the rise in BUN 121.7%, SC 76.64% and UA 92.7%. There were 92.71% inhibition in the rise of BUN, 92% inhibition in the rise of SC

and 106.6% inhibition in the rise of UA with the dose 1400 mg/kg.

DISCUSSION

The study demonstrates renal injury due to cisplatin which was evidenced by the elevated blood urea and serum creatinine level. Crude powder of Asgand was found to reduce the elevated blood urea nitrogen, serum creatinine and uric acid. It has been evident from the data that the results are not significantly varying with respect to dose of 700mg/kg and 1400mg/kg. Therefore the dose 700mg/kg can be consider pharmacologically effective dose. Induction of nephrotoxicity by cisplatin is assumed to be a rapid process involving reaction with proteins in renal tubules. Evidence points out that cisplatin induce nephrotoxicity partly via oxidative stress. One mechanism proposed is that cisplatin induces renal damage by free radical generation, by altering arginine metabolism and by increasing the activity of calcium independent nitric oxide synthase.[29]

Hence the probable mechanism of nephroprotection by Asgand (*Withania somnifera)* could be due to its antioxidant property and free radical-scavenging property and thus this plant could play a promising role in the treatment of acute renal failure induced by nephrotoxin like cisplatin. Literature on Unani Advia Mufrada (Single drugs) is so rich and having many drugs mentioned for nephroprotection by great scholars in their treatises. Many of them have proved by scientists in experiments. These may be evaluated on the scientific parameters for the treatment of chronic kidney disease.[30-34]

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