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Protective Effect of *Adiantum Capillus* Against Chemically Induced Oxidative Stress by Cisplatin

Kanchan Gaikwad*, Swati Dhande, Y M Joshi, Vilasrao Kadam.
Department of Pharmacology Bharati Vidyapeeth's College of Pharmacy, CBD Belapur, Navi Mumbai. Maharashtra, India.

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ABSTRACT

Damage to cells caused by free radicals has been implicated in the disease progression of at least 50 diseases that is cancer, cardiovascular disease, renal dysfunction and other. So many factors contribute to oxidative stress. Hence, the present study was designed to investigate the potential nephroprotective activity of 250mg/kg and 500mg/kg. Ethanolic extract of Adiantum capillus-veneris dried fronds against Cisplatin induced oxidative stress caused in male Wistar rats. Acute nephrotoxicity was induced by i.p. injection of Cisplatin (7 mg/kg of body weight (b.w.)). Administration of ethanol extract at dose level of 500 and 250 mg/kg (b.w.) to Cisplatin-intoxicated rats (toxic control) for 14 days attenuated the biochemical and histological signs of nephrotoxicity of Cisplatin in dose-dependent fashion. Ethanol extract at 500 mg/kg decreased the serum level of creatinine and urea as compared to the toxic control group. The ethanol extract of Adiantum capillus-veneris at 500 mg/kg (b.w.) exhibited significant and comparable nephroprotective potential. The statistically (one-way-ANOVA followed by Dunnet's test) processed results suggested the positive action of *Adiantum capillus-veneris* Cisplatin-induced nephropathy.

INTRODUCTION

The therapeutic value of some anticancer drugs is limited by their organ toxicity. It is susceptible by the anticancer drugs or by its metabolites, when taken at in therapeutic dose or in overdose. Nephropathy is widely encountered among the people of entire world irrespective of the age, racial, environment, and geographical variability. The etiology behind complication is broad ranging from substance-induced to metabolic and physiological disturbances, panelling nephropathy amongst the 10 leading causes of death across the world. Cisplatin (cis-diamine, dichloroplatinum II, CDDP) is extensively used for the treatment of several cancers like testicular and lung cancer. Unfortunately the gracious drug Cisplatin is conjoined with a brutal side effects since it induced nephrotoxicity (Zang *et al.,* 1993). The plant *Adiantum Capillus-veneris* locally known as Hansraj/ hanspadi belongs to the Adiantaceae family. *Adiantum capillus-veneris* is one the most widely distributed species.

* *Corresponding Author*
Ms. Kanchan Gaikwad
Masters of Pharmacy Second Year, Department of Pharmacology,
Bharati Vidyapeeth's College of Pharmacy, CBD Belapur,
Navi Mumbai, Maharashtra India.
Phone no: +91-8087039663/9975045430.

Ethno medicinally, the genus has been used as tonic and diuretic; in treatment of cold, fever, cough and bronchial disorders, as hyperglycaemic, as stimulant, emollient, purgative, demulcent, general tonic and hair tonic, in addition to skin diseases, tumours of spleen, liver and other viscera in treatment of jaundice and hepatitis and many other uses (Nadkarni *et al.,* 1976; Singh *et al.,* 2008).

MATERIAL AND METHODS

The dried plant fronds were collected from APMC market Vashi, and authenticated by Dr. Harshal Pandit HOD/Associate Professor in Botany at Guru Nanak Khalsa College Matunga, Mumbai. A voucher specimen no. KG/03212 was deposited. After authentication dried fronds were pulverized in a mechanical grinder to get coarse powder of dried fronds of *Adiantum capillus-veneris*. Healthy albino male rats of Wistar strain weighing between 150 and 200 g were selected for the investigation. The animals kept under maintained laboratory conditions with adequate supply of drinking water ad libitum and pallet diet.

The experimental protocol was approved by Institutional Animal Ethics Committee and the conditions in the animal house approved by committee for supervision on experiments on animals (Vide Registration No: 762/03/C/CPCSEA).

About 500g of coarse powder of Adiantum was taken and macerated successively with ethanol. The maceration for each solvent was carried out for 48 hrs. The ethanol extract was collected by evaporating the solvent by slow heat treatment. The dose limits were selected on the basis of previously performed oral acute toxicity studies in male Wistar rats, in accordance with the OECD guidelines no 425 (OECD. 2001). Total 30 male 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.

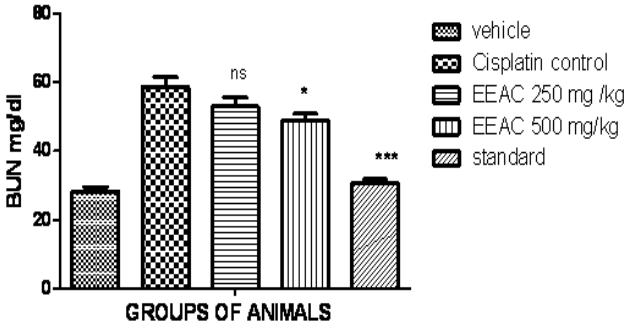
Group II (toxic control) received single dose of Cisplatin (Suzuki et al 1990) (7 mg/kg of body weight; i.p.) on day 14th.

Group III (Standard group) received standard polyherbal drug Cystone (250/kg; p.o.) (Cystone, Himalaya drug company, Bangalore, India) (Rao et al1998). for 14 days of single dose of Cisplatin (7mg/kg of body weight; i.p.) on day 14th.

Group IV (EEAC 250 mg/kg) and group V (EEAC 500mg/kg) received ethanol extract 250 and 500 mg/kg once in a day for 14 days respectively along with the dose of treatment of Cisplatin (7 mg/kg of the body weight; i.p.) on day 14th.

The treatment duration was considered for 14 days as documented (Yang *et al.,* 2006). Blood samples were collected from test animals under anaesthesia (phenobarbitone sodium; 40 mg/kg of body weight; i.p.) by cardiac puncture on 14th day before scarification and serum parameters including creatinine, urea, albumin, SGPT, SGOT and Uric acid(Cheesbrough *et al.,* 2003). The kidneys were removed from the rats organs were weighed and fixed using formosal solution (10% v/v of formaldehyde in normal saline), embedded with paraffin wax followed by preparation of tissue section using a microtome for histopathology study(Ogeturk *et al.,* 2005)

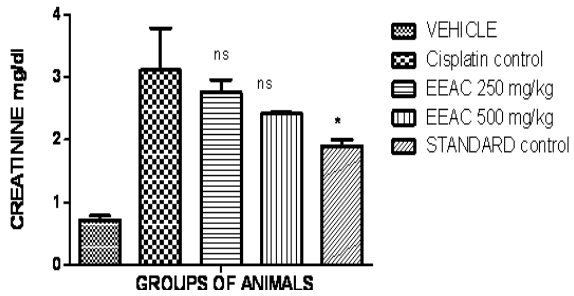
RESULTS



Sr No.	Treatment Group	Serum Bun (Mg/Dl)
1.	Vehicle control	28.26 ± 1.236
2.	Cisplatin control	58.58 ± 2.9
3.	EEAC 250 mg/kg	52.99 ± 2.57^{ns}
4.	EEAC 500 mg/kg	48.77 ± 2.09*
5.	Standard control	30.56 ± 1.23 ***

All values are expressed as mean ±SEM (n=6). *p<0.05,**p<0.01, ***p<0.001, ns nonsignificant as compared to Cisplatin control group using one way ANOVA followed by Dunnet's test.

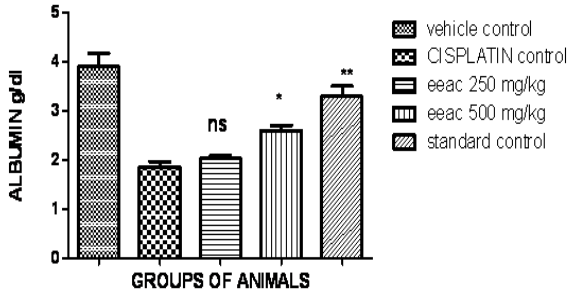
Serum Creatinine



Sr.No.	Treatment Groups	Serum Creatinine (Mg/Dl)
1.	Vehicle control	0.715 ± 0.070
2.	Cisplatin control	3.115 ± 0.670
3.	EEAC 250 mg/kg	2.760 ± 0.200 ^{ns}
4.	EEAC 500 mg/kg	2.420 ± 0.020 ^{ns}
5.	Standard control	1.9 ± 0.100 *

All values are expressed as mean ±SEM (n=6). *p<0.05,**p<0.01, ***p<0.001, ns nonsignificant as compared to Cisplatin control group using one way ANOVA followed by Dunnet's test.

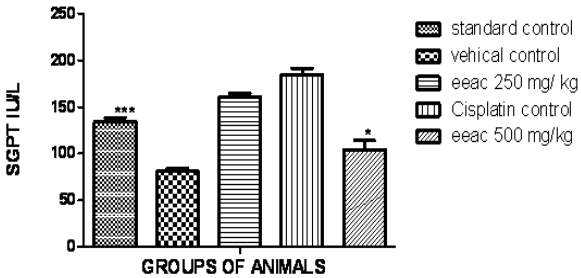
Serum Albumin



Sr. no	Treatment Groups	Serum Albumin (G/Dl)
1.	Vehicle control	3.9 ± 0.270
2.	Cisplatin control	1.86 ± 0.1
3.	EEAC 250 mg/kg	2.03 ± 0.07 ^{ns}
4.	EEAC 500 mg/kg	2.60 ± 0.101*
5.	Standard control	3.29 ± 0.210 **

All values are expressed as mean ±SEM (n=6). *p<0.05,**p<0.01, ***p<0.001, ns nonsignificant as compared to Cisplatin control group using one way ANOVA followed by Dunnet's test.

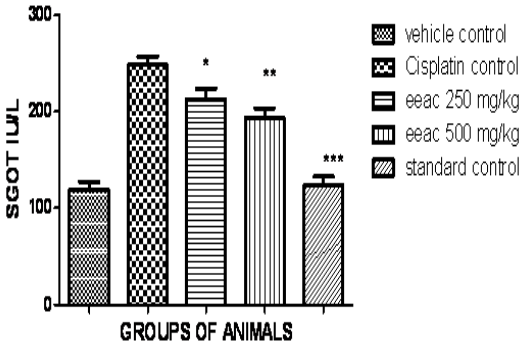
Serum SGPT



Sr. no	Treatment Groups	Sgpt (Iu/L)
1.	Vehicle control	41.97 ± 3.554
2.	Cisplatin control	75.87 ± 3.838
3.	EEAC 250 mg/kg	83.49 ± 2.001^{ns}
4.	EEAC 500 mg/kg	82.30 ± 3.113 ^{ns}
5.	Standard control	48.47 ± 3.41***

All values are expressed as mean ±SEM (n=6). *p<0.05,**p<0.01, ***p<0.001, ns nonsignificant as compared to Cisplatin control group using one way ANOVA followed by Dunnet's test.

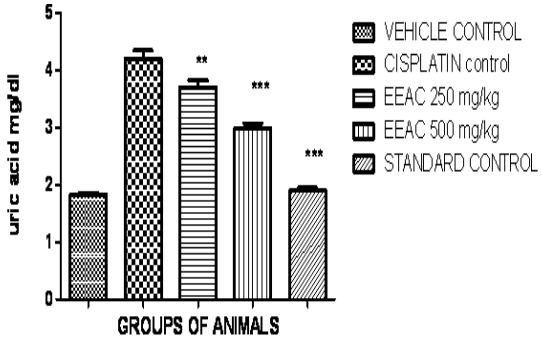
Serum SGOT



Sr.no	Treatment Groups	Sgot (Iu/L)
1.	Vehicle control	119.94 ± 7.840
2.	Cisplatin control	248.20 ± 9.19
3.	EEAC 250 mg/kg	212.80 ± 10.89*
4.	EEAC 500 mg/kg	193.13 ± 10.550**
5.	Standard control	123.80 ± 8.990***

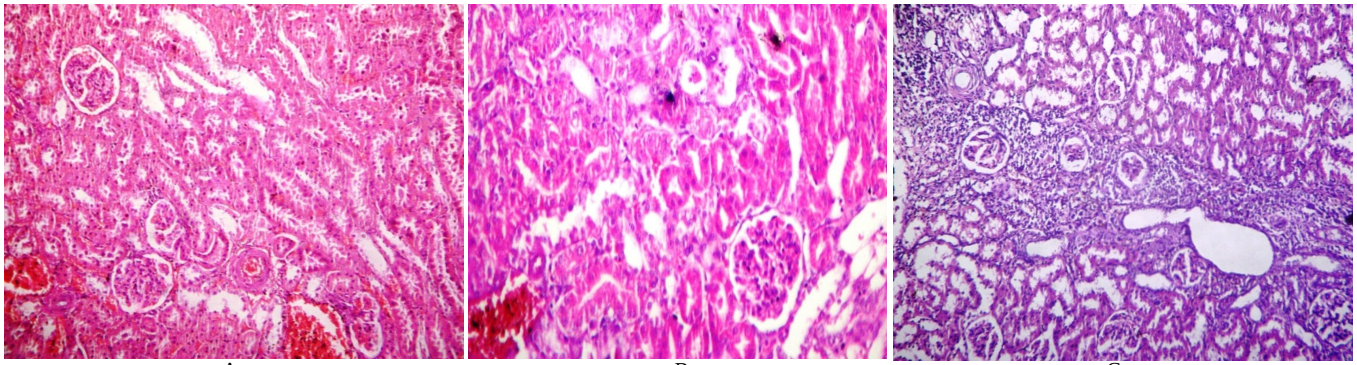
All values are expressed as mean ±SEM (n=6). *p<0.05,**p<0.01, ***p<0.001, ns nonsignificant as compared to Cisplatin control group using one way ANOVA followed by Dunnet's test.

Serum Uric acid



Sr.no.	Treatment Groups	Serum Uric Acid (Mg/Dl)
1.	Vehicle control	1.830 ± 0.034
2.	Cisplatin Control	4.190 ± 0.1600
3.	EEAC 250 mg/kg	3.700 ±0.1200 **
4.	EEAC 500 mg/kg	2.980 ± 0.0680***
5.	Standard control	1.893 ± 0.056 ***

All values are expressed as mean ±SEM (n=6). *p<0.05,**p<0.01, ***p<0.001, ns nonsignificant as compared to Cisplatin control group using one way ANOVA followed by Dunnet's test.



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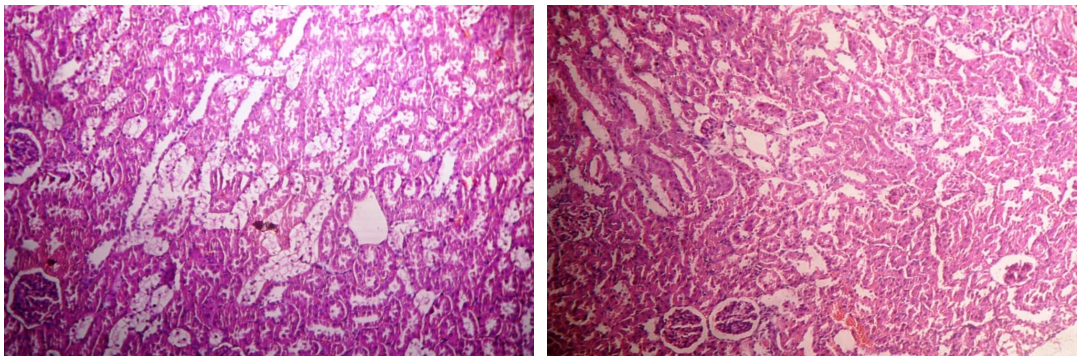

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Fig. 2: Photomicrographs of Kidney Section showing changes in Kidneys of various treatment groups.

A) Vehicle control
B) Disease control (Cisplatin Control)
C) 250 mg of EEAC + Cisplatin
D) 500 mg of EEAC + Cisplatin
E) Standard Drug + Cisplatin

Table : Histological features of kidney in different groups of animals.

Histopathological features	Vehicle control	Cisplatin treated	250 mg EEAC + Cisplatin	500 mg EEAC+ Cisplatin	Standard control
Tubular dilatations	_	+++	++	+	_
Interstitial fibrosis	_	+++	++	+	_
Atrophy of tubular Epithelium	_	+++	++	+	+
Necrosis	_	+++	++	+	_
Vacuolar degeneration	_	+++	+	+	+

Statistics

Data obtained in the experiments 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 Dunnet's test. The significance level was compared with the normal control group and all other treatment groups were compared with the toxic control groups.

DISCUSSION

The present study aimed to evaluate the protective effects of dried fronds extract (ethanol) of AC plant against Cisplatin-induced nephropathy in rats. Cisplatin-administered rats (toxic control group) had encountered acute kidney dysfunction as evidenced in serum urea and creatinine and body with multiple histological damages. Treatment with the ethanol extract of AC the dose level of 500mg/kg b.w. for 14 days (EEAC 500 group) significantly lowered the serum level of creatinine and urea with a significant weight gain. The histological damages in AC extract-treated group were minimal in contrast with the toxic rats. The statistical significance of the nephroprotective activity of AC-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 group same level of significance ($P<0.001$) against the toxic group in most of the parameter including serum urea and creatinine.

The results of our studies suggest that the ethanol extract of *Adiantum capillus-veneris* possess nephroprotective potential depending on dose levels. Extensive and multidimensional further research is needed to elucidate the extact mechanism of nephroprotective action of the plant extract.

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