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DIURETIC AND NEPHROPROTECTIVE ACTIVITY OF FRUITS OF *FRAGARIA VESCA* LINN.

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ABSTRACT

Diuretic activity and nephroprotective activity of different extracts of fruits of *fragaria vesca* in rat was studied. The study suggested that the extracts have good diuretic property. Diuretic study was carried out as per Lipschitz method. Where successive aqueous, ethonolic and petroleum extracts were studied for diuretic activity. The 6 hrs acute study of successive aqueous, ethonolic extracts showed increase in urine volume and K^+ ion excretion as compared to control. However, advanced toxicological studies remain to be performed in rodents. Fruit extracts have shown moderate nephroprotective effect against gentamicin induced nephrotoxicity.

INTRODUCTION: Drugs that induce a state of increased urine flow are called diuretics. These are most often in congestion of heart, hypertension, oedematous problems. *Fragaria vesca* [1] is a widely growing plat has been reported to possess number of medicinal properties. In the traditional system of medicine, the plant is said to be possess diuretic and liver tonic property. The present study is to investigate the diuretic activity of different extracts of the fruits of *fragaria vesca*.

Fragaria vesca is commonly called as wild strawberries, is a plant that grows naturally throughout the northen hemisphere. It propagates via runners; viable seeds are also found in soil seed banks and seem to germinate when the soil is disturbed [3]. It has been consumed by humans since the Stone Age. *Fragaria vesca* is an effective remedy for various ailments, and this natural holistic approach to health is becoming more and more popular but should not replace conventional medicine or prescription drugs [2].

It has certain therapeutic properties such as astringent, arthritis, diuretic, GI disturbances and liver tonic etc. It contains flavonoids, phenolic acids, tannins, anthocyanins, as well as anti oxidants [4]. The following study was undertaken for evaluation of diuretic and nephroprotective activity in normal healthy rats.

MATERIALS AND METHODS:

Plant Material: *Fragaria vesca* fruits were collected from local market from Hyderabad during January and taxonomical identification and authentication was done through Department of pharmacognosy. The fresh fruits were washed and cleaned with water to remove dirt, chopped shade dried and pulverized.

Preparation of Extracts: Pulverized fruits were extracted in Soxhlet apparatus with petroleum ether, alcohol. Aqueous extract is prepared by decoction. The extracts are filtered and the filtrates obtained were evaporated to dryness by vacuum evaporator.

Animals: The male Wister albino rats weighing 160gm-200gm were used to study the diuretic activity. Animals were housed in standard environmental conditions and fed with standard diet and water *ad libitum*. Protocol is approved by institutional animal ethical committee.

Drugs: Urea was bought from Hychem laboratories, Hyderabad. *Fragaria vesca* fruits were purchased from market. All other reagents were analytical grade.

Acute Toxicity Studies: The male Wister albino rats weighing 160gm-200gm were used divided into different groups comprising of five animals each. The control group received normal saline 25ml/kg i.p. The other groups received 100,200, 400, 600, 800, 1000, 2000, 4000mg/kg of test extracts. The animals were observed continuously for the behavioral changes for the first 5 hours and then observed for mortality if any for 24 hours. The acute oral toxicity study was carried out as per the guidelines set by Organization for Economic Co-operation and Development [5] (OECD), revised draft guide lines no. 423, received from Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

Evaluation of Diuretic Activity: Diuretic activity determined by Lipschitz method [6]. In brief, animals were divided in five groups containing 6 in each group. The control group received normal saline. Group two received urea (100 mg/kg). The other groups received petroleum ether, alcohol and aqueous extracts respectively. All extracts were administered by oral route. Animals were kept fasting for overnight before testing [8].

After the dosing animals were placed in metabolic cages and urine was collected in regular intervals of time. Room temperature was maintained up to 25^{o}C.The urine volume during 24 hrs and urine electrolyte estimation was carried out for sodium, potassium, using flame photometer and chloride was estimated by titrations [7].

Evaluation of Nephroprotective Activity: Animals were divided in 5 groups containing six in each group. Control group received normal saline. The second group received only Gentamicin 40 mg/kg twice a day for 10 days. Other groups received petroleum ether, alcohol, aqueous extracts along with Gentamicin 40 mg/kg in the dose of 400 mg/kg twice a day for 10 days. Gentamicin is administered through i.p. after the period all the animals were sacrificed by over dosing of anesthetic ether and blood was collected by cervical decapitation.

Serum was separated from the blood and the level of urea and creatinine was estimated. Elevation of urea and creatinine level in the serum was taken as the index of nephrotoxicity [9].

Statistical Analysis: All results are expressed as mean ± standard error. The data was analyzed statistically using ANOVA followed by student't' test.

RESULTS: The results of the preliminary phytochemical screening of petroleum ether, alcoholic and aqueous extracts revealed the presence of carbohydrates, saponins, triterpenoids, and steroids. In acute toxicity study, it was found that the extracts of petroleum ether, alcoholic and aqueous extracts showed no morbidity even at 4000 mg/kg. In the evaluation of diuretic activity, Urea treated rats showed a significant increase in volume of urine and urinary excretion of sodium, potassium, chloride ($P<0.01$) as compared to control [8].

Comparatively the petroleum ether extract not showed significant change urine excretion but effective in increasing the sodium ions and much less effect as diuresis whereas, alcohol and aqueous extracts showed significant change. Evaluated study is listed in **table 1**. And aqueous and alcoholic extracts showed significant Lipschitz values listed in **table 2**.

Rats showed a significant increase in volume of urine and urinary excretion of Na^{+}, K^{+} and Cl^{-} as compared to control is listed in **table 3**.

In the evaluation of nephroprotective activity the alcoholic and aqueous extracts were found to produce moderate significant nephroprotective effect against gentamicin induced nephrotoxicity. Aqueous, alcohol and petroleum extracts were showed considerable low nephrotoxicity and serum urea and creatinine levels were found to be significantly low. Evaluated study is shown in **table 4.**

TABLE 1: DIURETIC ACTIVITY OF DIFFERENT EXTRACTS OF *FRAGARIA VESCA*

Treatment	Dose(mg/kg)	Volume of urine (ml /100 gm)				
		After 5 hr	After 10 hr	After 15 hr	After 20 hr	After 24 hr
Vehicle	-	2.15±0.05	3.10±0.08	3.75±0.04	4.90±0.05	4.96±0.05
Urea	1000	3.96±0.09	4.37±0.05	4.66±0.08	5.42±0.08*	5.96±0.10
Pet. ether	400	2.54±0.06	4.05±0.08*	4.41±0.06	5.10±0.06	5.28±0.12
Alcohol	400	3.89±0.04	4.20±0.03	4.58±0.03	5.62±0.04	6.06±0.04*
Aqueous	400	4.12±0.06	4.43±0.06	4.86±0.05	5.70±0.07	6.15±0.06*

All values are mean ±SEM (n=6); *p< 0.01 when compared to control

TABLE: 2 LIPSCHITZ VALUE OF DIFFERENT EXTRACTS OF *FRAGARIA VESCA*

Treatment	Dose(mg/kg)	Lipschitz value T/U value				
		After 5 hr	After 10 hr	After 15 hr	After 20 hr	After 24 hr
Pet. ether	400	0.64	0.93	0.95	0.94	0.89
Alcohol	400	0.98	0.96	0.98	1.04	1.02
Aqueous	400	1.04	1.01	1.04	1.05	1.03

All values are mean ±SEM (n=6); *p< 0.01 when compared to control

TABLE: 3 PARAMETERS OF DIURETIC ACTIVITY OF DIFFERENT EXTRACTS OF *FRAGARIA VESCA*

Treatment	Dose(mg/kg)	Concentration of ions (meq./L) at 24 h			
		Na^+	K^+	Cl^-	Na^+/K^+
Vehicle	-	67.23±0.09	61.33±0.08	66.78±0.08	1.09
Urea	1000	95.47±0.07	88.49±0.07	92.63±0.07	1.07
Pet. ether	400	73.48±0.08	67.11±0.06	69.92±0.08	1.09
Alcohol	400	83.64±0.05	78.25±0.06	79.30±0.06	1.06*
Aqueous	400	89.05±0.07	81.05±0.08	86.89±0.08	1.09*

All values are mean ±SEM (n=6); *p< 0.1 when compared to control.

TABLE 4: NEPHRO PROTECTIVE ACTIVITY THE ALCOHOLIC AND AQUEOUS EXTRACTS OF *FRAGARIA VESCA*

Treatment	Dose (mg/kg)	Body weight (gm)	Serum urea	Serum creatinine
Control	-	135.5±4.0	52.00±1.5	0.68±0.06
Gentamicin	40	135.0±4.0	98.66±2.4	1.98±0.08
Gentamicin + petroleum ether	40+400	120.0±3.0	85.4±1.9	1.53±0.82
Gentamicin + alcohol	40+400	125.0±2.5*	83.2±2.0	1.33±0.01
Gentamicin + aqueous	40+400	125.5±2.5*	77.5±2.0	1.08±0.03

All values are mean ±SEM (n=6); *p< 0.1 when compared to control

DISCUSSION: Diuretic agents are useful in reducing the syndrome of volume overload, pulmonary congestion including orthopnea and paroxysmal nocturnal dysponea. They decrease plasma volume and venous return. This decreases cardiac overload, oxygen demand and plasma volume, thus decreasing blood pressure. In the present study, we demonstrated that aqueous, alcohol and petroleum extracts may produce diuretic effect by increasing the excretion of Na^+, K^+ and Cl^-.

The elevation of serum Urea and serum creatinine levels have been considered important parameter in gentamicin induced nephrotoxicity. But, concomitant administration with extracts did not produce considerable nephrotoxicity. Thus, the study indicated that the alcoholic and aqueous extracts of *Fragaria vesca* fruits protect the kidney from the toxic effect of gentamicin. Both extracts have shown an increase in total urine production over a period of 5hrs. They also increased the excretion of Na^+, K^+ and Cl^- significantly.

CONCLUSION: On the basis of the results, it could be concluded that *fragaria vesca* used as a diuretic agent [10, 11]. Acute toxicity studies showed that no mortality was observed even at 2000mg/kg. However, advanced toxicological studies remain to be performed in rodents. Fruit extracts have shown moderate nephro-protective effect against gentamicin induced nephro-toxicity.

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