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Original Article

Preclinical evaluation of diuretic activity of aqueous extract of *Solanum xanthocarpum* leaves in experimental animals.

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Abstract

Diuretics are drugs that increase the rate of urine flow, sodium excretion and are used to adjust the volume and composition of body fluids in a variety of clinical situations. Drug-induced diuresis is beneficial in many life-threatening disease conditions such as congestive heart failure, nephritic syndrome, cirrhosis, renal failure, hypertension, and pregnancy toxaemia. A natural source serves as an additional source for the development of new diuretic agents because of their biological activity. Several plant sources used as diuetics in different systems of traditional medicine and Ayurveda. *Solanum xanthocarpum* is very commonly found throughout India in plains from seashore to hills up to 1000 m of height. It is used in Dhasamoolaristha and in combination with other expectorants, demulcents and aromatics, astringent and heart diseases. In Bengal the plant was used as diuretic in dropsy and root paste was utilized by the Mukundara tribals of Rajsthan for the treatment of hernia. The AESX leaves possess the acute diuretic activity, thus, validating the traditional uses of this plant as diuretic. However, further studies are necessary to isolate and characterize the phytoconstituents responsible for diuretic action and to explore exact underlying mechanism of action of *SolanumXanthocarpum.*

Keywords: *Diuretic, Solanum xanthocarpum.*

1. Introduction

Diuretics are drugs that increase the rate of urine flow, sodium excretion and are used to adjust the volume and composition of body fluids in a variety of clinical situations. Drug-induced diuresis is beneficial in many life-threatening disease conditions such as congestive heart failure, nephritic syndrome, cirrhosis, renal failure, hypertension, and pregnancy toxaemia (Agunu et al, 2005).Most diuretic drugs have the adverse effect on quality of life including impotence, fatigue, and weakness. Naturally occurring diuretics include caffeine in coffee, tea, and cola, which inhibit Na + reabsorption and alcohol in beer, wine inhibit secretion of ADH (Agus et al,1971 and Stookey J.D, 1999).Although most of the diuretics proved to be very effective in promoting sodium excretion, all cause potassium loss and prompted the search for potassium sparing diuretic. Hence search for a new diuretic agent that retains therapeutic efficacy and yet devoid of potassium loss is justified (Rang et al, 2004).A natural source serves as an additional source for the development of new diuretic agents because of their biological activity. Several plant sources used as diuetics in different systems of traditional medicine and ayurveda (Danamma et al, 2011).

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Solanum xanthocarpum is very commonly found throughout India in plains from seashore to hills up to 1000 m of height. It is used in Dhasamoolaristha and in combination with other expectorants, demulcents and aromatics, astringent and heart diseases. In Bengal the plant was used as diuretic in dropsy and root paste was utilized by the Mukundara tribals of Rajsthan for the treatment of hernia. Stem, flowers and fruits are bitter and carminative, employed as anthelmintic, in indigestion, cough, asthma and pains in chest, being used in the form of a decoction and also prescribed for relief in burning sensation in the feet accompanied by vesicular watery eruptions. Yet the diuretic activity of this plant is not scientifically reported, hence the present study was undertaken to evaluate the diuretic activity of aqueous extract of S *Solanum xanthocarpum* leaves (kumar et al, 2010).

2. Materials and Methods

2.1. Materials

2.1.1. Animals

Male Wistar rats (150-250 g) or female Swiss albino mice (18-25 g) obtained from the Yash Farm and National Toxicological Centre, Pune, were used for the study.

2.1.2. Housing conditions

Animals were housed in group of 5-6 in standard polypropylene cages with wiremesh top. Animals

were maintained at standard environmental conditions of temperature of 25±1°C and relative humidity of 45 to 55 % under 12-h light: 12-h dark cycle. The animals had free access to standard food pellets, procured from Pranav Agro Industries Ltd., Sangli, India and water *ad libitum*.

2.1.3. Chemicals and drugs
All the chemicals used in the study were of analytical grade. The chemicals and drugs used were procured from local vendors from Pune and Mumbai.

2.2. Methods
2.2.1. Collection and authentication of plant material
The leaves of *Solanum Xanthocrpum* (SX) were collected from Bhosari region of Maharashtra in the month of September-October 2010 and were authenticated by Department of Botany, Botanical Survey of India, Pune.

2.2.2. Preparation of aqueous extract of SX
The leaves were dried under shade and powdered by using grinder mixer. For the preparation of aqueous extract, powdered material (4000 g) was socked in cold distilled water for 72 h and filtered it. The filtrate obtained was evaporated on water bath (40-50^{0}C) to obtain solid reddish coloured dry mass of 1045 g (26.12%). The extract was then preserved in the dedicator and then used for phytochemical and fractionation studies (Khandelwal, 2001; Juvekar*et al*., 2008).

2.2.3. Effect of AESX on diuretic Activity in Rats (Vogel *et al*., 2002; Somova *et al*., 2003; Consolini *et al*., 1999). Male Wistar rats (200-250 g) were randomly divided in to six groups consist of six animals per group and treated as follows, Table 1.

Table 1.
Experimental design for Diuretic Activity in rats.

Group No.	Group title	Treatment
I	Normal control	Distilled water (10 ml/kg, p.o.)
II	Urea	Urea 1gm/kg, p.o.
III	HTZ	Hydrochlorhiazide 1mg/kg, p.o.
IV	AESX 100	AESX 100mg/kg, p.o.
V	AESX 200	AESX200mg/kg, p.o.
VI	AESX 400	AESX 400mg/kg, p.o.

After 15 h of fasting animals from different groups, receive the respective treatments in addition to the 0.9 % NaCl solution (5 ml/ kg, p.o.). Each animal was placed in metabolic cage provided with wire mesh bottom and a funnel to collect the urine. The volume of urine and electrolyte content of the urine were analyzed by using Autoanalyser at 5 h and 24 h after the treatment.

2.2.4. Evaluation parameters
2.2.4.1. Urine volume
2.2.4.2. Electrolyte contents in urine
a) Sodium b) Potassium c) Chloride
2.2.4.3. Lipschitz value for evaluation of mode of action

Results
Effect of AESX on urine volume and Lipschitz value
Urine volume at 5 h after administration of AESX
Administration of urea (1 g/kg, p.o.) and hydrochlorothiazide (10 mg/kg, p.o.) showed significant (p<0.001) increase in urine output as compared to normal control group. AESX (200 and 400 mg/kg) showed significant (p<0.01 and p<0.001 respectively) increase in urine output when compared with normal control group. AESX (100 mg/kg) showed insignificant effects in this regard.Lipschitz values were calculated with respect to the urea. Lipschitz values from urine volume for hydrochlorothiazide, AESX 100, 200 and 400 were 1.62, 0.37, 0.93 and 1.10 respectively (Table 2).

Table 2.
Effect of AESX on urine volume and Lipschitz value at 5 h.

Gr. No.	Groups	Urine volume (ml)	Lipschitz value (T/U)
I	Normal	1.527 ± 0.2268	-
II	Urea	4.7 ± 0.3718***	-
III	HTZ	7.637 ± 0.412***	1.62
IV	AESX 100	1.758 ± 0.4982	0.37
V	AESX 200	4.388 ± 0.2887**	0.93
VI	AESX 400	5.201 ± 0.9534***	1.10

Values are expressed as Mean±S.E.M (n=6). **p<0.01, ***p<0.001 as compared with normal control using one-way ANOVA followed by Dunnet'stest.

Effect of AESX on electrolyte contents of urine at 5 hr.

Sodium content

Administration of urea (1 g/kg, p.o.) and hydrochlorothiazide (10 mg/kg, p.o.) showed significant (p<0.001) increase in sodium content of urine as compared to normal control group. AESX (100, 200 and 400 mg/kg,p.o.) showed significant (p<0.05and p<0.01 respectively) increase in sodium content of urine as compared to normal control (Table 3).

Potassium content

Administration of urea (1 g/kg, p.o.) and hydrochlorothiazide (10 mg/kg, p.o.) showed significant (p<0.001) increase in potassium content of urine as compared to normal control group. AESX (200 and 400 mg/kg p.o.) showed significant (p<0.05 and p<0.01 respectively) increase in potassium content of urine as compared to normal control. AESX (100 mg/kg) showed insignificant effects in this regard (Table 3).

Chloride content

Administration of urea (1 g/kg, p.o.) and hydrochlorothiazide (10 mg/kg, p.o.) showed significant (p<0.01) increase in chloride content of urine as compared to normal control group. AESX (200 and 400 mg/kg,p.o.) showed significant (p<0.05) increase in chloride content of urine as compared to normal control. AESX (100 mg/kg) showed insignificant effects in this regard (Table 3).

Table 3.
Effect of AESX on electrolyte contents of urine at 5 h.

Gr. No.	Groups	Sodium content (mmol/L)	Potassium content (mmol/L)	Chloride content (mmol/L)
I	Normal	145.9 ±1.94	6.769 ± 0.57	113.1 ± 1.7
II	Urea	376.4±2.65***	13.02±1.00***	151±3.58**
III	HTZ	422± 2.73***	13.89±0.57***	146.9±2.62**
IV	AESX 100	146.2 ±1.13*	7.468± 0.75	114.5± 2.25
V	AESX 200	165.1 ±1.88*	9.76± 0.44*	134.8± 2.66*
VI	AESX 400	192.3 ± 2.26**	12.25± 0.78**	153.4± 3.4*

Values are expressed as Mean±S.E.M (n=6). *p<0.05, **p<0.01, ***p<0.001 as compared with normal control using one-way ANOVA followed by Dunnet's test.

Urine volume at 24 h. after administration of AESX:

Administration of urea (1 g/kg, p.o.) and hydrochlorothiazide (10 mg/kg, p.o.) showed significant (p<0.01 and p<0.001 respectively) increase in urine output as compared to normal control group. AESX (200 and 400 mg/kg) showed significant (p<0.01) increase in urine output when compared with normal control group. AESX (100 mg/kg) showed insignificant effects in this regard. Lipschitz values were calculated with respect to the urea.A Lipschitz value from urine volume for hydrochlorothiazide, AESX 100, 200 and 400 was 2.02, 0.79, 0.98 and 1.06 respectively (Table 4).

Table 4.
Effect of AESX on urine volume and Lipschitz value at 24 h.

Gr. No.	Groups	Urine volume (ml)	Lipschitz value (T/U)
I	Normal	6.932± 0.40	-
II	Urea	10 ± 0.42**	-
III	HTZ	19.47± 0.81***	2.82
IV	AESX 100	7.527± 0.54	1.09
V	AESX 200	9.589± 0.73**	1.38
VI	AESX 400	10.13± 0.46**	1.46

Values are expressed as Mean±S.E.M (n=6). **p<0.01, ***p<0.001 as compared with normal control using one-way ANOVA followed by Dunnet's test.

Effect of AESX on electrolyte contents of urine at 24 hr.

Sodium content

Administration of urea (1 g/kg, p.o.) and hydrochlorothiazide (10 mg/kg, p.o/) showed significant (p<0.01 and p<0.01 respectively) increase in sodium content of urine as compared to normal control group. AESX (200 and 400 mg/kg, p.o.) showed significant (p<0.01) increase in sodium content of urine as compared with normal control group. AESX100 mg/kg showed insignificant effects in this regard (Table 5).

Table 5.
Effect of AESXon electrolyte contents of urine at 24 h.

Sr. No.	Group	Sodium content (mmol/L)	Potassium content (mmol/L)	Chloride content (mmol/L)
1.	Normal	149.5±1.55	6.132±0.42	107.3± 0.72
2.	Urea	197.1±4.93**	8.8±0.36**	119.8±3.80*
3.	HTZ	365±10.08***	14.13±0.57***	147.8±1.14**
4.	AESX100	157.2±6.8	7.769±0.61	107.9 ± 2.48
5.	AESX200	191.3±5.25**	8.265±0.52*	117.6±2.81*
6.	AESX400	198±5.16**	8.253±0.45*	118.8±2.38*

Values are expressed as Mean±S.E.M (n=6). *p<0.05, **p<0.01, ***p<0.001 as compared with normal control using one-way ANOVA followed by Dunnet's test.

Potassium content
Administration of urea (1 g/kg, p.o.) and hydrochlorothiazide (10 mg/kg, p.o.) showed significant (p<0.01 and$p$<0.001 respectively) increase in potassium content of urine volume as compared to normal control group. AESX (200 and 400 mg/kg, p.o.) showed significant (p<0.05) increase in potassium content of urine volume when compared with normal control group. AESX (100 mg/kg) showed insignificant effects in this regard (Table 5).

Chloride content
Administration of urea (1 g/kg, p.o.) and hydrochlorothiazide (10 mg/kg, p.o.) showed significant (p<0.05 and$p$<0.01 respectively) increase in chloride content of urine volume as compared to normal control group. AESX (200 and 400 mg/kg, p.o.) showed significant (p<0.05) increase in chloride content of urine volume when compared with normal control group. AESX (100 mg/kg) showed insignificant effects in this regard (Table 5).

Discussion
Administration of AESX (200 and 400 mg/kg) showed significant increase in urine volume after 5 h and 24 h. Administration ofAESX (200 and 400 mg/kg) showed significant increase in urinary excretion of sodium, potassium and chloride and the effect was equipotent to that of hydrochlorthiazide (HTZ).The AESX exerted its diuretic activity possibly by inhibiting tubular reabsorption of water and accompanying anions, as such action has been hypothesized for some other plant species 10. As emphasized, diuretic properties of AESX could be due to other active principles such as flavonoids, saponins12. It is also possible that diuretic effect of the AESX could be due to other secondary active(s) metabolites(s) 13. The other possibility for the observed diuretic effect of AESX could be due to indirect changes of some physiological parameters before blood filtration step 14. On basis of the above results, we can conclude that AESX treatment produced a marked diuresis when rats were acutely treated. In our study, no lethality was observed at least for the dose and duration used. However, advanced toxicological studies remain to be performed in mice and rats. It remains necessary to study eventual adverse effect(s) of this plant such as alteration of some neural, metabolic and hormonal parameters, which are undetermined in this study, before its recommendation to clinical use. The precise site(s) and the molecular and cellular mechanism(s) of AESX action remain to be elucidated in further studies16. The preliminary phytochemical studies have confirmed the presence of carbohydrates, saponnins, tannins and flavonoids in AESX. Hence the diuretic effects of AESX leaves may be due to presence of saponnins, tannins and flavonoids which may act individually or in combination.

Conclusion
The AESX leaves possess the acute diuretic activity, thus, validating the traditional uses of this plant as diuretic. However, further studies are necessary to isolate and characterize the phytoconstituents responsible for diuretic action and to explore exact underlying mechanism of action of *SolanumXanthocarpum.*

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