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Phenolic content of *Solanum xanthocarpum* and their diuretic potential

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Abstract

Environmental factors have profound effect on quantity vis-a-vis quality of phytochemicals in medicinal plants. *Solanum xanthocarpum* Schrad. and Wendl. is among the 10 dashmool species which is utilized in more than hundreds of Ayurvedic preparations. Phenolics are the pharmacologically valuable compounds. Therefore, the present study was undertaken to assess the total phenolic (TP) in four different plant parts i.e., leaves, fruits, stem and roots of S. xanthocarpum sampled randomly from different locations of U.P. Plant samples were collected from 11 places of Jaunpur districts falling in 06 agroclimatic regions of Uttar Pradesh through random sampling. UV-VIS spectrophotometer and HPTLC were used to determine TP contents, respectively. Phytochemical screening was carried out using standard methods.

Preliminary phytochemical screening indicates the presence of alkaloids, cardiac glycosides, flavonoids, phenols, steroids and terpenoids in all plant parts. Quantification of TP contents revealed that it varied significantly between agroclimatic zones as well as within plant parts of *S. xanthocarpum*. Results revealed that among analysed plant parts, fruits and leaves had the highest TP content. Among agroclimatic regions, accessions of Trilochan Industrial area can be considered rich in TP contents for fruits (28.70 mg CE/g), leaves (27.90 mg CE/g) and roots (5.17 mg CE/g). For stem, highest TP (13.23 mg CE/g) contents were observed in samples of Sirkoni area mainly.

In traditional system of medicine *S. xanthocarpum* is used treating difficulty in urination and renal calculus. For diuretic study it was divided into two phases of evaluation (acute and sub-acute) with administration of aqueous extract of *S. xanthocarpum* roots. The animals were treated with either aqueous extract of *S. xanthocarpum* (AqSX; 200, 400 mg/kg, P.O.) or furosemide (25 mg/kg, P.O.) or hydrochlorthiazide (HCTZ; 25 mg/kg, P.O.). In acute study, the treated animals were observed for urine volume, urine pH, urine and serum electrolytes and creatinine after 6th and 24th h. While in sub-acute study observations for above mentioned parameters were done on day 1, day 7 and day 14. The results indicated strong diuretic potential with AqSX (400 mg/kg). The diuretic prospective of AqSX was similar to furosemide without any type of toxicity based on the observations of serum electrolytes, serum creatinine and urine creatinine measurement. The findings support ethnobotanical use of *S. xanthocarpum*.

Key words : *Solanum xanthocarpum*, Leaves, Fruits, Stem, Roots, Phytochemicals, Diuretic, Natriuretic, Saluretic

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Introduction

Solanum xanthocarpum Schrad. and Wendl., commonly known as Kantakari or Yellow Berried Night Shade, is a perennial herb of Solanaceae family. It is one of the dashmool species having an important place among medicinal herbs since ancient times. It is distributed to plains and lower hills of India and is abundantly available in Uttar Pradesh, a central Indian state[1]. All plant parts of this species are useful and reported to have medicinal properties[2]. Fruits of this herb are the source of solasodine, a valuable natural precursor of several commercial steroidal drugs such as corticosteroids, antifertility drugs, anabolic steroids and sex hormones[3, 4]. Fruits have also been reported to contain several medicinal properties like antihelmintic, antipyretic, anti-inflammatory, antitumor, cytotoxic, anti-asthmatic, antispasmodic, antidiabetic, hypotensive[5–7]. Flowers, fruits and stems are prescribed for relief during burning sensation in the feet[8]. Paste of leaves are used to relieve body or muscle pain; while its juice mixed with black pepper is advised for rheumatism[9]. Roots of the plant are used in formulation of "Dashmoolarishta", a well-established ayurvedic drug of Indian system of medicine utilized for treating general fatigue, oral sores and various gynecological disorders[10–13]. Due to various medicinal properties, annual demand of this herb is approximately 500–1000 MT per annum[14].

Phytochemical and pharmacological studies proved that *S. xanthocarpum* is rich in steroids, flavonoids, phenolics, coumarins and major one includes CA, lupeol, carpesterol, solanocarpine, solasonine, solamargine, and diosgenin[15]. CA (3, 4-dihydroxycinnamic acid) is one of the most commonly found phenolics in a wide range of medicinal plants and found effective in treatment of a number of chronic diseases[16, 17]. In *S. xanthocarpum*, CA was first identified in the berries[18] and in roots[19]. Other plant parts of this commercially important medicinal herb were not assessed for this valuable compound.Diuretics work by promoting the expulsion of urine (measured as the urine volume (UV) excreted) and uninary sodium (UNa) from the body and this helps to reduce the volume of blood circulating through the cardiovascular system[20-22]. To be clinically effective, however, such compounds must induce the loss of sodium[23]. This is achieved by compounds interfering with the reabsorption of ions, as well as water, through the walls of the kidney tubules[24-26] and this promote their excretion from the body. There is growing interest in the health benefits of herbs and botanicals, several plants or plant-derived products have been suggested to function as mild diuretic agents[27].

Methodology

*Collection and authentication of plant material***:** Different plant parts (fruits, leaves, roots and stem) of this species were collected from 11 locations of Jaunpur districts belonging to 06 agroclimatic regions by following random sampling. From each agroclimatic region 9 samples were collected on random basis. For confirmation of the species, herbarium of collected specimens was prepared and gets authenticated from the Department of Botany, BHU, Varanasi.

*Processing of plant materials***:** Plant parts were separated and brought to the laboratory. These were washed thoroughly in running water to remove soil and other foreign particles. Stem and roots were cut into small pieces. All samples were dried in shade and powdered. Equal amount of nine samples of all plant part collected from each agroclimatic region were pooled separately and was made for making extracts and chemical analysis.

Phytochemical screening: One hundred milligram of dried and powdered plant material, each of stem, leaves, fruits and roots of *S. xanthocarpum* was soaked overnight in 25 ml of different solvents namely water, methanol, ethanol, petroleum ether, chloroform, diethyl ether and ethyl acetate. Different extracts were filtered and filtrates were used for qualitative phytochemical screening following standard methods[28, 29].

*Determination of Total Phenolic (TP) content***:** TP content was determined by Folin-Ciocalteau method[30,31]. A quantity of 0.5 g of powdered sample was taken in a mortar and pestle and grinded in 10 times volume of 80% ethanol. The homogenate was then centrifuged at 10,000 rpm of 20 min. The supernatant was then evaporated to dryness. The residue was dissolved in a 20 ml of distilled water. Zero point two millilitre of sample was then taken in test tube and volume made up to 3 ml with distilled water. Zero point five millilitre of Folin-Ciocalteau reagent was then added. After 3 min, 2 ml of 20% sodium carbonate solution was added to each tube, mixed thoroughly, placed in boiling water for exactly 1 min, cooled and absorbance was taken at 650 nm against blank. TP content was determined from the linear equation of a standard curve of catechol and expressed as mg of catechol equivalent per g of dry extract weight.

Experimental Animals: Adult male Wistar rats (150-250 g) and female Albino mice (20-25 g) were purchased from Animal house, Institute of Medical Science, BHU, Varanasi. The animals were housed under 12h day and night conditions for 2-3 months. The animals had free access to

rat food pellet (Amrut laboratory, Pranav Agro Ltd., Sangli) and tap water *ad libitum*. The experimental protocol was approved by the Institutional Animal Ethics was approved by the Institutional Animal Ethics Committee (IAEC) of Poona & IMS BHU in accordance with the rules and guidelines of the Committee for the Purpose of Control and Supervision on Experimental Animals BHU, Varanasi.

Preparation of aqueous extract of roots of S. xanthocarpum: To obtain aqueous extract the roots were shade dried, powdered in grinder and extracted by cold maceration with distilled water (150 mL/100g powder) for 24h on mechanical shaker. The supernatant was removed, the mare dried and again macerated with 150 mL of distilled water for 24 h. The extract was filtered through Whatman filter paper no. 44 and dried at 50ºC to get a dark brown extract.

Effect of sub acute administration of AqSX on diuretic activity in rats: The male Wistar rats were used for the study. The animals were divided into following 4 groups: Gr-I: (control) received saline only (10 mL/kg orally), Groups-II and III (test drug) received AqSX (200, 400 mg/kg), respectively. Gr-IV (standard): received a single oral dose of furosemide (10 mg/kg). All drugs were administered orally for 14 days. Urine was collected at day 1 (24h), day 7 and day 14. The parameters measured were urine volume, electrolyte content, pH and creatinine. Blood was withdrawn on day 1, day 7 and day 14 from retro orbital plexus. Blood samples were centrifuged at 7000 rpm for 10 min at 4ºC, the serum was recuperated and was used for estimation of sodium, potassium, blood urea nitrogen (BUN) and creatinine.

Results

Critical perusal of the results of phytochemical screening of fruits, leaves, roots and stem of *S. xanthocarpum* revealed the presence of alkaloids, cardiac glycosides, flavonoids, phenols, steroids and terpenoids in all the plant parts while saponins were present in fruits and leaves only. Tannins were not detected in any plant part. Analysis revealed significant variations for TP content within and between agroclimatic zones as well as among plant parts of *S. xanthocarpum* collected from 11 different places of Jaunpur, district, falling in 6 different agro-climatic regions. Estimates of TP contents in leaves, fruits, roots and stem of *S. xanthocarpum* are summarized in Table-1. TP content in fruits, leaves, roots and stem collected from 11 places

varied from 7.63–28.70, 7.02–27.90, 2.17–5.40 and 3.41–13.23 mg CE/g, respectively. Fruits, leaves, roots of Trilochan Industrial area and stem of Sirkoni were found to contain higher TP content i.e., 28.70, 27.90, 5.17 and 13.23 mg CE/g, respectively. Whereas, fruits and leaves of Jaunpur surrounding, roots of Kerakat and stem of Khetasarai were found to contain lower TP content i.e., 7.63, 7.02, 2.17 and 3.41 mg CE/g, respectively. On overall comparison, fruits of Trilochan Industrial region contained highest TP content (28.70 mg CE/g) whereas roots of Kerakat contained the lowest (2.17 mg CE/g).

Phytochemical screening helps in isolating and characterizing the chemical constituents present in the plant extracts and the knowledge of the chemical constituents of plants is desirable to understand herbal drugs, their preparations and finally in discovering the actual value of folkloric remedies. These phytochemicals (alkaloids, cardiac glycosides, flavonoids, phenols, steroids, terpenoids and saponins) were reported to have a number of biological activities and protect humans from most of the chronic diseases[32]. Our results of phytochemical screening are in agreement with the earlier findings[33-35]. Similar variations in TP content in different plant parts of *S. xanthocarpum* were also noticed in previous studies[35,36].

Table-1: TPC in fruits, leaves, roots and stem of *S. xanthocarpum*, Schrad and Wendl

S.No.	Agro climatic regions of Jaunpur District	Fruits	Leaves	Roots	Stem
		TPC (mg CE/g dry extract wt)	TPC (mg CE/g dry extract wt)	TPC (mg CE/g dry extract wt)	TPC (mg CE/g dry extract wt)
1	Mugarabadashpur	25.37±0.13	22.73±0.01	2.30±0.01	4.40±0.01
2	Machhalishahar	23.83±0.01	21.80±0.01	5.40±0.01	5.03±0.49
3	Sirkoni	24.20±0.01	23.63±0.01	2.93±0.01	13.23±0.01
4	Jallalpur	26.80±0.02	23.07±0.02	2.87±0.01	8.93±0.01
5	Trilochan Industrial Area	28.70±0.02	27.90±0.05	5.17±0.03	10.83±0.07
6	Kerakat	25.20±1.50	24.93±0.01	2.17±0.01	5.37±0.11
7	Shahganj	26.53±0.01	23.67±0.03	2.63±0.04	5.20±0.11
8	Khetasarai	8.61±0.07	14.29±0.23	2.96±0.03	3.41±0.02
9	Khutahan	9.44±0.06	18.29±0.11	3.50±0.03	3.50±0.03
10	Jaunpur Sadar	7.63±0.18	7.02±0.19	2.74±0.02	9.12±0.08
11	Mariyahu	9.39±0.05	20.45±0.03	4.15±0.02	3.50±0.07
C.D. at 5% (within the characters among the agroclimatic regions)		0.120	0.180	0.038	0.110

Estimates TP did not exhibit positive relationship because TP represents all types of phenolic compounds found in plants. Besides environmental factors such as temperature, altitude, soil, rainfall, humidity, drought, light intensity, high salinity, supply of water, minerals, freezing temperatures and CO_2 also affects concentrations of secondary metabolites[37-42]. Stressed conditions are well known to trigger the accumulation of secondary metabolites which help the plants to adapt and overcome stresses[43]. Analysis of variance revealed that estimates of TP varied significantly within the plant parts i.e., fruits, leaves, stem, roots samples and also among the agroclimatic regions. This indicates the importance of selection of plant parts used for commercial exploitation as well as revealed the environmental effect on yield of chemical constituents. However, trend is not consistent for TP contents in different plant parts across the agroclimatic regions. CA and its phenyl esters were reported to have strong biological activities such as antitumor activity in-vivo and in-vitro both, anti-platelet activity, acute pneumonitis, neuro protective, antioxidant, anti-microbial, antidepressant, anxiolytics, anti-inflammatory, analgesics, anti-cancer, potent collagen antagonist, anti-hypertensive, anti-ischemia reperfusion, anti-thrombosis, anti-hypertension, anti-fibrosis, anti-hyperglycemic etc.[44-50]

Effect of acute administration of AqSX on urine parameters

Effect on urine output and urine pH in rats: Extract of *S. xanthocarpum* alter urin discharge in albino rats. As shown in Table-2, saline administration (10 mL/kg) in the control group resulted in average output of 5.33±1.47 mL of urine after 6h. and 9.83±1.95 mL after 24 h. Administration of Aq. *S. xanthocarpum* (200 mg/kg) resulted non-significant increase in urine volume compared to control group after 6^{th} and 24^{th} h. Aq. *S. xanthocarpum* at 400 mg/kg showed significant urine output after 24 h only. Furosemide and HCTZ (25 mg/kg) treated group showed significant urine output after 6 h and 24 h. Urine pH was not altered at 6 h collection of urine in *S. xanthocarpum* treated group but changed in HCTZ group. At 24 h significant change in urine pH was observed for furosemide group only.

Effect on excretion of Na^+, K^+ and Cl^- in rat urine: Urine electrolyte alter after administration of *S. xanthocarpum* extract in albino rats. Table-3 shows effect of test drugs on electrolyte concentration in urine. Aq. *S. xanthocarpum* (400 mg/kg) resulted in significant increase in Na^+ excretion at 24 h but not at 6 h urine collection. Furosemide and HCTZ showed significant

increase in Na^+ concentration at both time intervals. Treatment with HCTZ showed significant increase in K^+ concentration in urine at both intervals, while AqSX (200 and 400 mg/kg) and furosemide treatment resulted in significant decrease in K^+ concentration in urine only at 6th h. Administration of AqSX (200 and 400 mg/kg) and furosemide resulted in significant increase in Cl^- excretion in urine at 24 h while HCTZ showed significant decrease in Cl^- concentration at 6 h but slight decrease at 24 h as compared to control.

Table-2: Effect of acute administration of AqSX on urine output and pH

[Values are mean±SE from 6 animals each]

Treatment	**Dose**	**Volume of urine output (mL)**		**Diuretic index[a]**		**Urine pH**	
		6h	**24h**	**6h**	**24h**	**6h**	**24h**
Control	10 mL/kg	5.33±1.47	9.83±1.95	- -	- -	6.15±0.16	6.38±0.15
AqSX	200 mg/kg	6.33±1.96	14.33±1.70	1.18	1.46	6.14±0.069	6.16±161
	400 mg/kg	7.66±1.72	18.25±1.16*	1.44	1.86	6.01±0.10	6.34±0.02
Furosemide	25 mg/kg	11.83±0.79*	20.67±1.74**	2.22	2.10	6.67±0.17	6.96±0.18*
Hydrochlorthiazide	25 mg/kg	12.50±1.23**	24.00±3.75***	2.35	2.44	6.94±0.31	6.36±0.16

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Fig.1: Effects of acute administration of AqSX on urine output

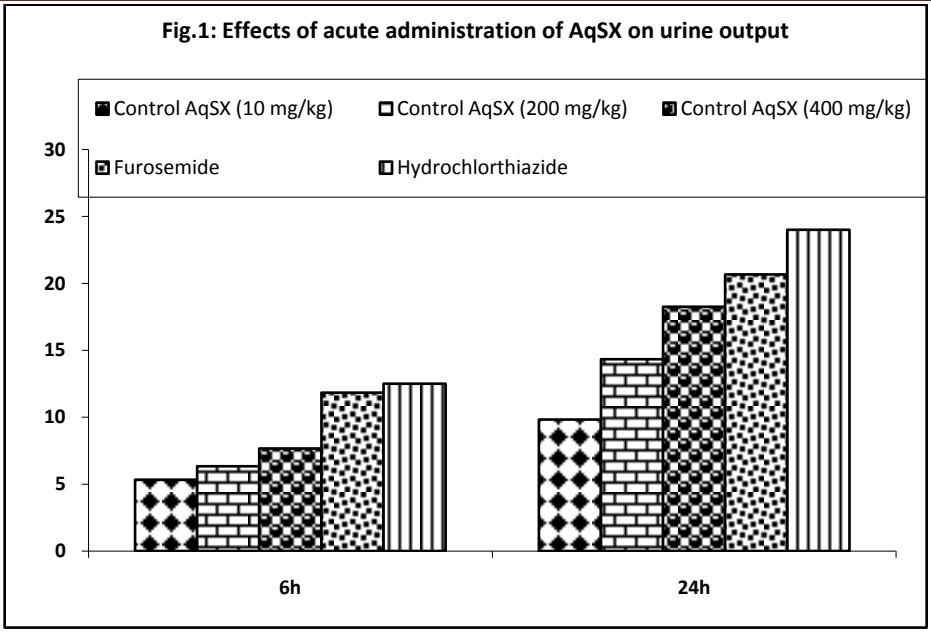
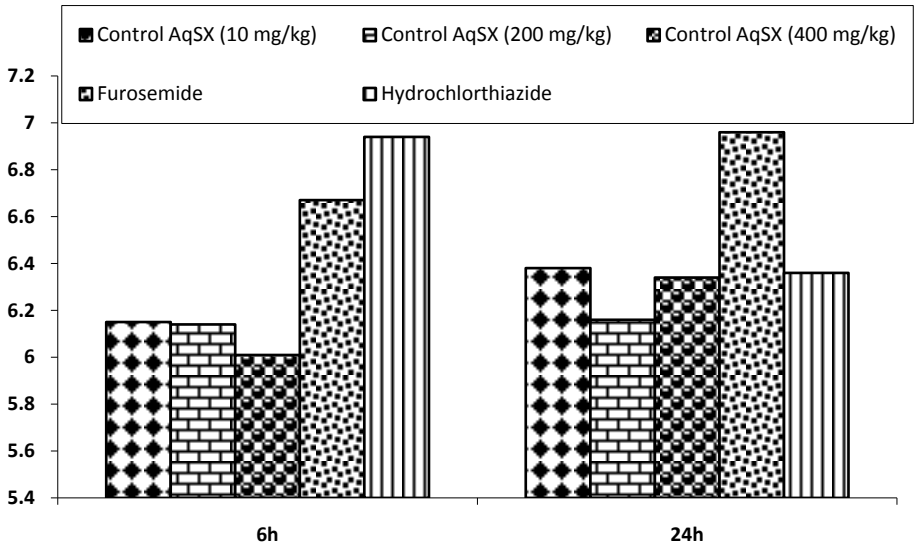


Fig.2: Effects of acute administration of AqSX on urine pH



Effect on excretion of creatinine in rat urine: Furosemide, HCTZ and test groups significantly increased urine creatinine at 6 h. At 24 h, there was non-significant increase in urine creatinine as shown in Table-3.

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Table-3: Effect of acute administration of AqSX on Urinary Parameters

[Values are mean±SE from 6 animals each]

Treatment	Dose	Sodium excretion (mEq/L)		Potassium excretion (mEq/L)		Chloride excretion (mEq/L)		Creatinine excretion (mg/dL)		Na/K		Na/Cl	
		6h	24h	6h	24h	6h	24h	6h	24h	6h	24h	6h	24h
Control AqSX	10 mL/kg	93.13± 12.66	127.6± 22.40	122.7± 11.91	147.0± 3.18	326.7± 15.85	313.3± 22.01	3.70± 0.29	4.46± 0.50	0.75	2.71	344.83	440.9
	200 mg/kg	118.3± 13.97	286.9± 25.03	34.66± 6.522***	160.5± 32.64	345.0± 12.32	541.7± 27.01**	4.82± 0.21*	2.86± 0.57*	3.41	1.37	463.3	761.9
	400 mg/kg	118.3± 0.2459	899.4± 89.62***	34.42± 5.207***	136.2± 17.94	363.3± 22.01	781.7± 75.91***	4.90± 0.27*	3.73± 0.09	3.43	6.60	481.6	1681.1
Furosemide	25 mg/kg	974.0± 19.56***	1072± 99.95***	31.24± 1.42***	158.8± 16.18	360.0± 29.44	575.0± 28.61***	4.93± 0.36*	4.40± 0.10	31.16	6.75	1334	1647
Hydrochlorthiazide	25 mg/kg	519.9± 17.23***	468.3± 37.99**	274.6± 22.07***	325.2± 22.78	176.7± 18.01***	296.7± 13.58	3.68± 0.29	3.29± 0.16	1.78	1.60	696.6	765

Natriuretic and saluretic effect AqSX: At 6th h natriuretic activity of AqSX (200 and 400 mg/kg) was lesser than furosemide but more than HCTZ. At 24 h natriuretic effect of AqSX (400) was similar to furosemide. AqSX (200 mg/kg) and HCTZ showed less natriuretic effect (Table-3). AqSX (200 and 400 mg/kg, po) showed less saluretic activity as compared to furosemide and HCTZ at 6th h. However at 24th h, AqSX (400 mg/kg) showed high saluretic effect than furosemide and HCTZ. While on the other hand AqSX (200 mg/kg) and HCTZ had less saluretic activity (Table-3).

Effect of acute administration of AqSX on blood parameters

Effect on Na^+/K^+ and Na^+/Cl^- concentration in rat serum: Administration of AqSX (200 and 400 mg/kg) and furosemide resulted significant change in serum Na^+/K^+ concentration as compared with control group where as HCTZ showed significant decrease in Na^+ concentration in comparison to treated group. Administration of AqSX (400 mg/kg) and furosemide resulted

decrease in K^+ concentration in serum where as HCTZ increase the K^+ concentration as compared to control group. Administration of AqSX (400 mg/kg) and furosemide resulted in significant decrease in serum Cl^- concentration as compared with control group.

Effect on creatinine concentration in rat serum: Administration of AqSX (200 and 400 mg/kg) and furosemide resulted slight increase in serum creatinine concentration as compared to control group. HCTZ showed decrease in serum creatinine concentration as compared to control group.

Discussion

Diuresis has two components: increase in urine volume and a net loss of solutes (i.e. electrolytes) in the urine. These processes result from suppression of renal tubular reabsorption of water and electrolytes into the blood stream. The reference drug, furosemide, increases urine output and urinary excretion of sodium by inhibiting Na/K/Cl symporter in the thick ascending limb of the Henley, while the thiazide diuretics inhibit the Na/Cl symporter in the distal convoluted tubule, by competing for the Cl^- binding site, and increasing the excretion of Na^+ and Cl^-.

In acute diuretic study, AqSX (400 mg/kg) showed marked increase in urine volume at 24th hour as compared to control group, while 200 mg/kg dose
failed to do so. The plausible mode of action might be similar to furosemide which has brisk diuretic activity.

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