IJPSR (2014), Vol. 5, Issue 4 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 05 October, 2013; received in revised form, 16 February, 2014; accepted, 21 March, 2014; published 01 April, 2014

EVALUATION OF DIURETIC ACTIVITY FROM *TEUCRIUM POLIUM* L. CAPITATUM EXTRACTS (LAMIACEAE) IN RATS

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Keywords:

Teucrium polium L. *Capitatum*, Ethanolic extract, Electrolyte excretion, Diuretic activity, Urine output

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ABSTRACT: The present study was carried out to investigate the diuretic activity of the ethanolic extract of *Teucrium polium* L. Capitatum (Lamiaceae) in normal albino rats. The diuretic activity of extract was evaluated by determining the urine volume and electrolyte concentration in albino rats (n=4). Furosemide (20 mg/kg) was used as the reference diuretic drug while normal saline (0.9%) was used as control. Alcoholic extract of the drug (25 mg/kg and 50mg/kg) were used as tests. Urine output and electrolytes (Na^+, K^+ and Cl^-) excretion were estimated at the end of 8 hours. Ethanolic eextract has significantly increased the volume of urine (6.70±0.09ml/100g/8hr and 8.40 ±0.46ml/100gm/8hr), and has also increased the diuretic index to 1.09 and 1.37 for 25mg/kg and 50mg/kg dose ranges respectively ($P< 0.01$). The test drug, when compared to the control group, displayed a significant increase in the excretion of potassium and chloride. There was an increase in the saluretic index as reflected by the Na^+/K^+ ratio to 5.03 and 5.44 respectively for the two dosages studied when compared to furosemide which noted a saluretic index of 2.28. The extract (50 mg/kg) showed significant increase in urine volume as well as K+ and Cl- ion concentrations in albino rats. These findings support the traditional uses of *Teucrium polium* L. as diuretic agent in folk medicine.

INTRODUCTION: Diuretics are used in medicine to treat heart failure, liver cirrhosis, hypertension and some kidney disease [1, 2]. Proper electrolyte balance is essential for a good health and diuretics may cause electrolyte imbalance hypokalemia, hyponatremia, and hypernatremia.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.5(4).1259-62

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.5(4).1259-62

Plants medicines are commonly used for the treatment of some renal diseases and have also been reported to show significant diuretic activity [3].

Teucrium polium L. (Lamiaceae) is one of 300 species of the genus *Teucrium* and mainly it is found abundantly in south-western Asia, Europe and North Africa. It is widely distributed in Algeria.

In traditional medicaments, *Teucrium* species have been used as diuretic, anti-bacterial [4-6], anti-hypertensive [7], hypoglycaemic, hypolipidemic [8-9], anti-inflammatory [10] and it has also been reported

to have antitumour [10-11], hepatoprotective [12], neuro-protection [13] and antioxidant properties [14-15]. Chemical analysis of *T. polium* L. has shown that it contained various compounds such as flavonoids [16-17], terpenoids [18] and oils essentials [19-21].

There is no report on the diuretic studies of *Teucrium polium* L. Considering the various uses of folk medicine as a diuretic, the purpose of the current study was to evaluate the diuretic efficacy of ethanol extract of the plant in the rat.

MATERIALS AND METHODS:

Preparation of *T. polium* L. extract: The flowering tops and leaves of *T. polium* L. (200g); dried at room temperature and ground to a fine powder, and extracted with ethanol 95% under low pressure using a rotary vacuum evaporator with a yield of 47.76 %., were collected from Biskra, Algeria, in early summer 2010.

Experimental animals: Experiments were performed on male albino rats (*Rattus ratus*) obtained from Pasteur institute in Algeria and weighing 200-250g. They were maintained on standard light, temperature and feeding conditions for 10 days before the experiment. They were housed under standard conditions of temperature ($22 \pm 5^{o}C$), humidity ($65 \pm 5\%$) and dark light cycle (12h – 12h) and were allowed access to food and water *ad libitum*. All the experimental procedures and protocols used in this study were reviewed by the Institutional Animal Ethics Committee (IAEC).

Preliminary phytochemical screening: The extracts of *Teucrium polium* L. were subjected to the phytochemical tests for the presence of carbohydrates, flavonoids, tannins, phenolic compounds, saponins, and steroids [22].

Diuretic activity: The method of [23] was employed for the assessment of diuretic activity. The rats were divided into four groups of four rats each. Of these groups of animals, the first group served as a control and is feed with normal saline orally (25ml/kg), and the second group of animals received the same amount of normal saline in which Furosemide at a dose of 20mg/kg is dissolved. While the third and the fourth ones were treated with 20mg/kg and 50mg/kg of *T. polium* L. respectively. Immediately after administration, the animals were placed in metabolic cages (4 in each cage) specially designed to separate urine and faeces. Urine was collected in a graduated cylinder and its volume was measured at the end of 8 hours. Cumulative urine excretion was calculated in relation to body weight and expressed as ml/100 g bw. Electrolyte (Na^+, K^+, Cl^-) concentrations were estimated from the urine samples by flame photometric method and expressed as mequiv./100 g bw.

Statistical evaluation: Results are expressed as means ± SEM, significant differences among the groups were determined by one-way ANOVA using STATIT CF, with Newman and Keuils test, with the significant level set at $P<0.05$ and $P<0.01$.

RESULTS AND DISCUSSION: The reference diuretic Furosemide significantly increased the urine volume when compared to control ($P<0.01$), which put the diuretic index at 1.57. The two doses of ethanolic extract of *Teucrium polium* L. 20mg/kg and 50mg/kg showed a marked increase in the urine output with a dose dependent increase in the diuretic index to 1.09 and 1.37as shown in **table 1**.

TABLE 1: EFFECT OF ORAL ADMINISTRATION OF ETHANOL EXTRACT OF *TEUCRIUM POLIUM* L. CAPITATUM ON URINARY VOLUME EXCRETION

Group	*n*	Urine volume (ml/100 g/8 h)	Diuretic index [a]	Lipschitz value [b]
Control	4	6.14±0.76	-	-
Furosemide 20 mg/kg	4	9.68±0.49*	1.57	-
Teucrium polium (Et OH) 20 mg/kg	4	6.70±0.09*	1.06	0.69
Teucrium polium (Et OH) 50 mg/kg	4	8.40 ±0.46*	1.37	0.87

The results show the mean values and standard errors; *n* = number of pairs used in each group. *$p < 0.05$ and **$p < 0.01$ compared with the control group (Newman and Keuils's unpaired *t*-test).

[a] Diuretic index = volume test group/volume control group.

[b] Lipschitz value = Mean urine volume of test/Mean urine volume of standard.

This study indicates that urinary Na^+ excretion tended to be lower in control rats compared with rats treated with *T. polium* L. extract, but the difference was not statistically significant (P<0.01). Further studies demonstrated that net losses of NaCl and fluid during regular diuretic administration are limited by post diuretic renal NaCl and fluid retention [24]. In contrast, *Teucrium polium* L. ethanol extract caused a significant increase in K^+ (P<0.05) and Cl^- (P<0.01) excretion.

Additional evidence indicates that potassium secretion is co-dependent on Cl^- secretion [25] and the β cell in cortical collecting duct shows a coupling operation of apical H^+-K^+-ATPase and apical Cl^- / HCO_3 exchange provides a new model for active KCL reabsorbtion [26]. Reduced potassium excretion was shown from the saluretic index at dose of 50mg/kg which has a value of 1.74 (1.83 for 20mg/kg dose and 3.55 for the furosemide group). The obtained observations are mentioned in **table 2**.

TABLE 2: EFFECTS OF ORAL ADMINISTRATION OF THE ETHANOL EXTRACT OF *TEUCRIUM POLIUM* L. CAPITATUM ON URINARY ELECTROLYTE EXCRETION

Group	Na+ (mequiv./100 g/8 h)	K+ (mequiv./100 g/ 8 h)	Cl− (mequiv./100 g/8 h)	Saluretic index [a]			Na/ K
				Na	K	Cl	
Control	246.26 ± 45.70	32.47± 2.17	248.13±27.98	-	-	-	7.58
Furosemide 20 mg/kg	262.56 ± 18.67	115.20± 38.41*	361.60±18.98**	1.06	3.55	1.46	2.28
Teucrium polium (Et OH) 20 mg/kg	300.30 ± 52.65	59.63± 15.82 *	332.45±69.40**	1.22	1.83	1.34	5.03
Teucrium polium (Et OH) 50 mg/kg	307.70 ± 55.08	56.50± 21.13 *	407.50 ±69.97**	1.25	1.74	1.64	5.44

The results show the mean values and standard errors; *n* = number of pairs used in each group. *$p < 0.05$ and **$p < 0.01$ compared with the control group (Newman and keuil's unpaired *t*-test).

[a] Saluretic index = mequiv. test group/mequiv. control group.

Na^+/K^+ ratio of 5.03 and 5.44 were obtained for ethanolic extract at doses of 20 and 50mg/kg respectively. The increase in the ratio of concentration of excreted sodium and potassium ions indicate that the extracts of *Teucrium polium* L. increase sodium ion excretion to a greater extent than potassium which indicates the interesting potassium-saving effect of the extract.

The concentration of aldosterone is found to be dependent on the Na+/K+ ratio. Adlosterone promotes potassium excretion through its effects on Na^+- K^+-ATPase and epithelial sodium and potassium channels in cortical collecting duct (CCD) [27].

The preliminary phytochemical screening showed the presence of flavonoids, glycosides, saponins, carbohydrates, tannins, terpenoids and the absence of alkaloids in all the extracts.

This promotes the hypothesis that these types of polar compounds may be responsible for the diuretic effects [28].

However, the effect may be produced by inhibition of tubular reabsorption of water and anions [29] or by producing stimulation of regional blood flow [30].

CONCLUSION: The present study shows that the ethanolic extract of *Teucrium polium* L. significantly increases the urine output and excretion of urinary potassium and chloride and has no effect on the urinary sodium excretion. Further studies elucidating the exact molecular and cellular mechanism(s) of action are desired.

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How to cite this article:
Malki S and Yahia AL: Evaluation of diuretic activity from *Teucrium polium* L. Capitatum extracts (Lamiaceae) in rats. *Int J Pharm Sci Res* 2014; 5(4): 1259-62.doi: 10.13040/IJPSR.0975-8232.5(4).1259-62