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Research Article

# EVALUATION OF THE DIURETIC EFFECT OF CONYZA DIOSCORIDES AND ALHAGI MAURORUM

ATTIA H. ATTA*[1], SOAD M. NASR [2], SAMAR M. MOUNEIR[3], NASER A. AL-WABEL[1], SOHA S. ESSAWY[4]

[1]Department of Veterinary Medicine, College of Agriculture and Veterinary medicine, Qassim University, Burydah, 51452, KSA, [2]Department of Parasitology and Animal Diseases, National Research center, Dokki, [3]Pharmacology Departments, Faculty of Veterinary Medicine, Cairo University, [4]Faculty of Medicine, Suez Canal University, Egypt. Email: attaattia52@yahoo.com

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**ABSTRACT**

The present study aimed to evaluate the diuretic effects of methanol extracts of *Conyza dioscorides* and *Alhagi maurorum* in a single or repeated (1 x 5 days) oral dose of 500 or 1000 mg $kg^{-1}$ and compared to furosemide 20 mg $kg^{-1}$, orally administered in albino rats. Oral administration of *Conyza dioscorides* significantly ($P < 0.05$) decreased serum and urine concentration of $Na^+$, $K^+$ and $Cl^-$ concentration when was given in single or repeated doses. The small and large doses increased the sodium and potassium excretion rate (FENa and FEK). *Alhagi maurorum* in a single oral dose of 500 mg $kg^{-1}$ significantly ($P < 0.05$) increased urine concentrations of $Na^+$, $K^+$ and $Cl^-$. Repeated oral administration of *Alhagi maurorum* in doses of 500 or 1000 mg$kg^{-1}$ significantly ($P < 0.05$) increased urine volume, FENa and FEK rate. It could be concluded that methanol extracts of *Alhagi maurorum* have a significant diuretic effect while the extract of *Conyza dioscoridis* requires further investigation.

**Keywords:** *Conyza dioscorides*, *Alhagi maurorum,* Diuretics, Medicinal plants

## INTRODUCTION

Medicinal plants are promising source of diuretic drugs[1,2,3]. Diuretics, either alone or in combination with other drugs, are valuable in the treatment of hypertension, congestive heart failure, ascites, and pulmonary edema, chronic renal failure, hypercalciuria and cirrhosis of liver[4,5,6,7,8,9]. *Conyza dioscoridis and Alhagi maurorum* are common perennial herbaceous plants grown in the Nile region (Delta, valley and Faiyum) and in the Oases of the desert. *Conyza dioscoridis* (Family Compositae) is a richly branched hairy shrub grown commonly in the Mediterranean region and tropical areas. Ibn El Bitar reported the use of *Conyza discoridis* in the treatment of epilepsy and as remedy for cold, diarrhea, colic and rheumatic pains[10]. *Alhagi maurorum* (Boiss), a member of Family Leguminosae, is used in folk medicine as a remedy for rheumatic pains, bilharzias, liver and urinary tract inflammation and for various types of gastrointestinal discomforts[11]. Recently these plants are proved to have antidiarrhoeal activity and induce relaxation of the smooth muscle[12] and antinociceptive effect[13]. Publics used to use the extracts of plants known to have sedative and/or diuretic effects without any scientific background. For this reason, we studied the diuretic effect of methanol extracts of *Conyza dioscoridis,* and *Alhagi maurorum* (Table 1).

**Table 1: Plants used for screening of the diuretic effect and the yield of methyl alcohol extraction**

| Plant species | Plant family | Parts used | Voucher No | Yield / 200 g dry plant |
|---|---|---|---|---|
| *Conyza dioscoridis. L. desf* | Compositae | Leaves | A2 | 48.5 |
| *Alhagi maurorum Medic* | Leguminosae | Aerial parts | A3 | 45.5 |

## MATERIALS AND METHODS

### Preparation of the methanol extract

The selected plants were collected and taxonomic identifications were established by the staff members of the Department of Flora, Ministry of Agriculture. A voucher sample was kept in the Department of Pharmacology, Faculty of Veterinary Medicine, Cairo University, Egypt. Each of the air-dried plant material (250 g) was pulverized, and stored for further use. Two hundred grams of the dried parts of each plant were extracted with methanol 95% for at least 24 h, followed by percolation for 5 to 7 times till complete exhaustion. The methanol extracts were concentrated under reduced pressure at temperature not more than 50 ˚C and kept at – 4˚C until used. The extracts were freshly suspended in sterile distilled water with few drops of Tween 80 to a final concentration of 200 mg/ml.

### Animals

A total of 72 albino rats (males and non-pregnant females) of body weight 130 to 150 g were used. Rats were allocated randomly into 12 equal groups. The first 6 groups were used to test the diuretic effect of single oral dose of the test plants. Each rat of each group was placed into a separate metabolic cage, with wire mesh floor provided with a conical-shaped bottom underneath designed to collect urine in a receptacle without fecal contamination. The test animal was fasted overnight (12-14 hr) but they had free access to fresh water. The first subgroup group was kept as normal control while rats of each of the 2nd groups were given an oral dose of furosemide of 20 mg kg b.$wt^{-1}$. The next 4 groups were used to test the diuretic effect of each of the previously prepared plant extracts in a single dose of 500 and 1000 mg.$kg^{-1}$ orally. In a separate experiment 6 groups of rats were used to test the diuretic effect of each of the tested plant extracts after repeated oral doses (500 and 1000 mg.$kg^{-1}$) for 5 consecutive days.

The urine output during 24 hours was collected and measured in graduated cylinder. Blood samples were collected 24 hours after the last dose by puncturing of retro-orbital plexus. Blood samples were placed in a plain centrifuge tube and clear serum was separated. Animals were handeled under the rules and regulations of Cairo University for the use of laboratory animal.

### Sample analysis

Sodium and potassium were estimated in serum and urine by flame photometer (Jenway, England Model, PFP7). Chloride concentration in serum and urine was estimated spectrophotometrically according to Skeggs and Hochstrasser[14] using kits (Quimico Clinica Applicada S. A., Spain). Serum urea[15], and creatinine in serum and urine[16] were estimated spectrophotometrically (spectrophotometer model 6105, Jenway, England) using test kits (bioMérieux – France). Creatinine clearance and fractional excretion of filtrated sodium or potassium rate were calculated by the following equations according to Coles [17], Mayer and Harvey [18] and Thrall-Mary et al. [19] ;

$$\text{Clearance of creatinine} = \frac{U_{Cr} \times UV\ (\mu l)}{S_{Cr} \times 24 \times 60 \times \text{b.wt./100g}}\ \mu l / \text{min} /100\ \text{g b.wt.}$$

Fractional excretion of filtrated sodium rate = ($U_{Na}$ X $S_{Cr}$ / $S_{Na}$ X $U_{Cr}$) X 100

Fractional excretion of filtrated potassium rate = ($U_K$ X $S_{Cr}$ /$S_K$ X $U_{Cr}$) X 100

Where; $U_{Cr}$ = Urine creatinine. $S_{Cr}$ = Serum creatinine. UV = Urine volume.

$U_{Na}$ = Urine sodium. $S_{Na}$ = Serum sodium.

$U_K$ = Urine potassium. $S_K$ = Serum potassium..

**Statistical analysis**

The data were expressed as mean ±Standard deviation (S.D.). Differences between means in different groups were tested for significance using a one-way analysis of variance (ANOVA) followed by Duncan's Multiple Range Test. Differences were considered significant at level $P<0.05$ according to Snedecor and Cochran[20] using SPSS version 10 computer program.

**RESULTS**

Oral administration of furosemide in a single or repeated oral dose of 20 mg $kg^{-1}$ significantly decreased serum $Na^+$, $K^+$ and $Cl^-$ concentrations, while it increased significantly the $Na^+$, $K^+$ and $Cl^-$ level in urine (Fig. 1 and 2). Oral administration of furosemide in a single or repeated oral dose of 20 mg $kg^{-1}$ significantly decreased creatinine clearance but significantly increased FENa and FEK. It also significantly increased urine volume (Table 2 and 3).

Oral administration of metha nol extracts of *Conyza dioscorides* in a single or repeated small or large dose (500 or 1000 mg $kg^{-1}$ ) significantly decreased serum and urine concentration of sodium, potassium and chloride. It decreased serum creatinine clearance but increased FENa and FEK rate and showed no effect on urine outflow (Fig. 1 and 2).

Oral administration of methanol extracts of *Alhagi maurorum* in a single oral dose of 500 mg $kg^{-1}$ significantly increased urine concentrations of sodium, potassium and chloride; however, it markedly decreased the levels of sodium, potassium but had no effect on chloride in serum (Fig. 1). Oral administration of methanol extracts of *Alhagi maurorum* in a single oral dose of 1000 mg $kg^{-1}$ significantly decreased serum and urine concentrations of sodium, potassium and chloride (Fig. 1). Its administration in a repeated oral dose of 500 mg $kg^{-1}$ significantly decreased serum and urine concentrations of sodium, had no effect on serum or urine potassium but significantly increased chloride concentration in urine (Fig. 2). Its administration in a repeated dose of 1000 mg/kg decreased sodium, potassium and chloride in serum and urine (Fig. 2).

Oral administration of methanol extracts of *Alhagi maurorum* in a single oral dose of 500 mg $kg^{-1}$ significantly decreased creatinine clearance and had no effect on FENa or FEK rate. It also significantly increased urine volume (Table 2). Its administration in a repeated oral dose of 500 or 1000 mg $kg^{-1}$ significantly decreased creatinine clearance but significantly increased FENa and FEK rate as well as urine volume (Table 3).

**Fig. 1: Effect of single oral administration of *Conyza dioscoridis* (CD) and *Alhagi maurorum* (AM) on serum and urine sodium, potassium and chloride (Mean ± SD, N = 6).**

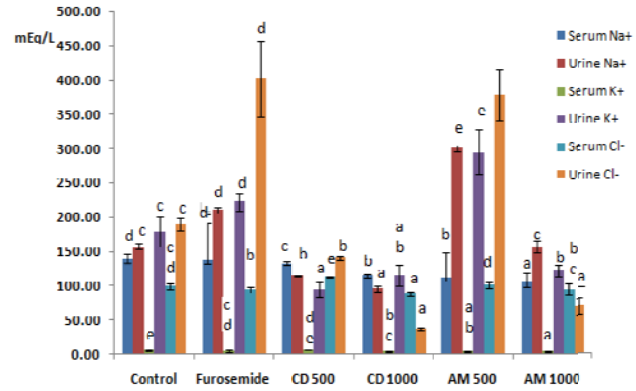
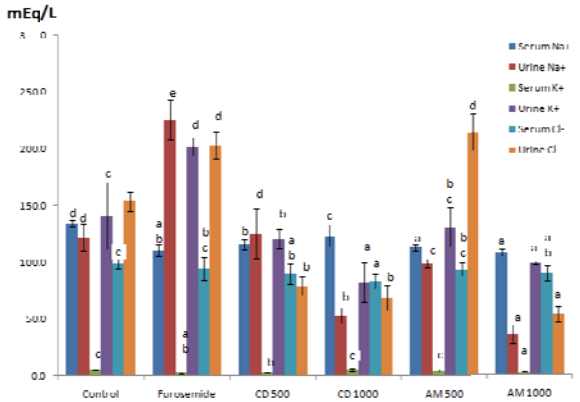



**Fig. 2: Effect of repeated (1 x 5) oral doses of *Conyza dioscoridis* (CD) and *Alhagi maurorum* (AM) on serum and urine sodium, potassium and chloride (Mean±SD,N= 6).**




Means of different letters in the same column are significantly (P < 0.05) different

**Table 2: Diuretic effect of single oral dose of methanol extract of *Conyza dioscoridis* and *Alhagi maurorum* (mean ±SD, n = 6).**

| Groups | Doses mg/kg | Creatinine clearance µl/min/100g | Sodium fractional excretion rate (%) | Potassium fractional excretion rate (%) | Volume ml/100 g b.wt./24hr |
|---|---|---|---|---|---|
| Control | | 102.13±11.88$^{c}$ | 1.47±0.32$^{a}$ | 39.09±5.76$^{a}$ | 1.57±0.13$^{ab}$ |
| Furosemide | 20 | 80.07±12.64 $^{b}$ | 3.51±0.65 $^{b}$ | 128.39±33.02$^{c}$ | 2.52±0.73$^{d}$ |
| *Conyza* | 500 | 29.83±4.09$^{a}$ | 4.90±1.52 $^{c}$ | 82.00±16.82$^{c}$ | 1.68±0.19$^{ab}$ |
| *dioscoridis* | 1000 | 53.00±7.41 $^{b}$ | 2.06±0.63$^{a}$ | 79.29±16.51$^{c}$ | 1.85±0.5$^{bc}$ |
| *Alhagi* | 500 | 50.15±5.81$^{d}$ | 1.16±0.65$^{a}$ | 47.30±8.88$^{a}$ | 1.28±0.31$^{a}$ |
| *maurorum* | 1000 | 50.73±9.71$^{ab}$ | 4.63±1.76$^{bc}$ | 156.66±37.21$^{d}$ | 2.32±0.31$^{cd}$ |

**Table 3: Diuretic effect of repeated oral dose of methanol extract of *Conyza dioscoridis* and *Alhagi maurorum* (mean ±SD, n = 6).**

| Groups | Doses mg/kg | Creatinine clearance µl/min/100g | Sodium fractional excretion rate (%) | Potassium fractional excretion rate (%) | Volume ml/100 g b.wt/24 h |
|---|---|---|---|---|---|
| Control | | 107.02±11.5$^{d}$ | 0.98±0.26$^{a}$ | 30.57±2.93$^{a}$ | 1.60±0.2$^{ab}$ |
| Furosemide | 20 | 150.30±16.4$^{e}$ | 2.06±0.23$^{b}$ | 68.11±9. 36$^{b}$ | 2.67±0.45$^{d}$ |
| *Conyza* | 500 | 30.43±4.00$^{b}$ | 4.78±0.69$^{c}$ | 140.36±22.6d$^{de}$ | 1.65±0.40$^{ab}$ |
| *dioscoridis* | 1000 | 52.06±9.88$^{c}$ | 0.97±0.10$^{a}$ | 32.82±5.27$^{a}$ | 1.56±0.52$^{ab}$ |
| *Alhagi* | 500 | 48.23±9.32$^{c}$ | 2.78±0.36$^{b}$ | 95.60±16.06$^{c}$ | 2.20±0.37$^{cd}$ |
| *maurorum* | 1000 | 50.15±5.81$^{c}$ | 2.58±0.17$^{b}$ | 156.20±30.25$^{e}$ | 2.63±0.47$^{d}$ |

Means of different letters in the same column are significantly (P < 0.05) different

**DISCUSSION**

The rate of FENa is a measure of the percentage of sodium excreted in the urine versus the sodium reabsorbed by the kidney [21] (Bazari, 2007). The calculated FENa was 0.98 to 1.47. These values are nearly similar to those of most normal subjects[22] who reported that the FENa rate is usually less than 1 percent but may be raised with an increase in salt intake. The present data clearly demonstrated the diuretic effect of the tested plant extracts. Diuresis is achieved by increased urinary electrolyte concentration with significant increase in the urinary output[23,6,24]. These two processes are involved in the suppression of renal tubular reabsorption of electrolytes, water and low molecular weight organic compounds into blood stream and as a consequence, promoting the formation of urine[23, 25].

In this study, furosemide increased the excretion of $Na^+$, $K^+$ and $Cl^-$. Furosemide acts by inhibiting electrolytes re-absorption in the thick, ascending limp of the loop of Henle by inhibiting Na+/K+/2Cl− symporter (co-transporter system) in the thick ascending limb of the Loop of Henley[26, 6].

Oral administration of methanol extracts of *Conyza dioscorides* in a single or repeated small or large dose (500 or 1000 mg kg-1 ) significantly decreased serum and urine concentration of sodium, potassium and chloride. It decreased serum creatinine clearance but increased FENa or FEK rate and showed no effect on urine outflow. The FENa is measured in terms of plasma and urine sodium, rather than by the interpretation of urinary $Na^+$ concentration alone, as urinary sodium concentration can vary with water resorption. The increased values of FENa or FEK rate by methanol extract of *Conyza dioscorides* may be due a high salt content of this extract. Similar conclusion have been postulated for other plant extracts[27].

Alhagi *maurorum* methanol extract produced a diuretic, kaluretic and saluretic effect. This was indicated by the increased urine output, urine concentration of $Na^+$, $K^+$ and $Cl^-$ increased FENa and FEK. It was observed that the increased urine concentration of sodium, potassium and chloride was clear after administration of the small dose (500 mg. kg-1), however small repeated and large dose single or repeated did not affect urine concentration of sodium or potassium concentration. This indicates that the saluretic effect of *Alhagi maurorum* was achieved by the small single dose only. The small dose also has increased significantly the $Cl^-$ concentration in urine but not in the serum.

Small or large dose of *Alhagi maurorum* either single or repeated significantly increased urine volume, FENa and FEK rate. However repeated administration for 5 days appeared more effective in increasing urine outflow. This indicates either a delayed diuretic effect or due to variation in the dose which may overcome a compensation mehanisms as it has been suggested for other plant extracts[28]. This delayed effect may be due to the slow release of the active principle, or due to slow changing the active component of the plant into active material or due to accumulation effect. The delayed diuretic effect was recognized for a number of other plant extracts[29]. However the difference in the dose could not be ruled out particularly in relation to the effect on the hydrostatic filtration pressure. Although there is no study on the effect of *Alhgi maurorum* on vascular smooth muscle, it has been found that methanol extract of *Alhagi maurorum* induced complete relaxation of gastrointestinal smooth muscle at low concentration and spasm at higher concentration[12]. Similar effect of *Alhagi maurorum* on the afferent arterioles may increase renal blood flow. The diuresis was apparent when the small dose was used. The diuretic effect of other plants was clear by small but not large doses[30].

It was noted that methanol extract of *Alhagi maurorum* caused increase in both urine and electrolytes excretion qualitatively similar to furosemide which is known by its potential saluretic and diuretic effects[31,32]. In a previous work in our laboratory[12], the preliminary phytochemical analysis of the tested plants revealed the presence of flavonoids, tannins, unsaturated sterols/triterpenes, carbohydrates, lactones and proteins/amino acids in addition to traces of saponins. At present, it is not known which compounds are responsible for the diuretic, natriuretic and kaliuretic activities of *Conyza dioscoridis* and *Alhagi maurorum*. In previous work, the diuretic properties of methanol extract of other plant extracts were attributed to their content of flavonoids[34,9]. Therefore, the diuretic effect could be attributed to their content of flavonoids.

The repeated administration of *Conyza dioscoridis* and *Alhagi maurorum* showed little effect on potassium excretion which is essential quality of a good diuretic with lesser hyperkalaemic side effect[34,9].

**CONCLUSION**

In conclusion, our results demonstrated that methanol extracts of *Alhagi maurorum* have a significant diuretic effect probably because of increased urinary electrolyte excretion with significant increase in the urinary output while the extract of *Conyza dioscoridis* requires further investigation.

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