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Journal of Ethnopharmacology 79 (2002) 17–21

Journal of ETHNO-PHARMACOLOGY

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Biological effect of *Opuntia ficus indica* (L.) Mill. (Cactaceae) waste matter
Note I: diuretic activity

E.M. Galati [a,*], M.M. Tripodo [b], A. Trovato [a], N. Miceli [a], M.T. Monforte [a]

[a] *Pharmaco-Biological Department, School of Pharmacy, University of Messina, Vill. SS., Annunziata, 98168 Messina, Italy*
[b] *Department of Organic and Biological Chemistry, University of Messina, Salita, Sperone, S. Agata, 98166 Messina, Italy*

Received 22 September 2000; received in revised form 26 July 2001; accepted 9 August 2001

Abstract

In this work we studied in rat the diuretic activity of *Opuntia ficus indica* (L.) Mill. (Cactaceae) waste matter. The cladodes, flowers and non commerciable fruits were collected in S. Cono (CT, Sicily) cultivation. Acute and chronic diuretic activity of 15% infusion of cladodes, flowers and fruits were assayed. Natriuresis, kaliuresis and the activity on fructose-induced hyperuricemia was also studied. The results show that *O. ficus indica* cladode, fruit and flower infusions significantly increase diuresis. This effect is more marked with the fruit infusion and it is particularly significant during the chronic treatment. The fruit infusion shows also antiuric effect. In all experiments cladode, flower and fruit infusions showed a modest but not significant increase in natriuresis and kaliuresis.

Keywords: *Opuntia ficus indica* (L.) Mill.; Diuretic activity; Hypouricemic activity; Traditional use; Waste matter

1. Introduction

The *Opuntia ficus indica* (L.) Mill. species has gradually attained economic importance in Sicilian agriculture and the international scientific community, through FAO, also contributes to the diffusion of this cultivation. Besides, it is important to point out that the disposal of *O. ficus indica* wastes (non commerciable fruits and cladodes) constitutes a problem for environmental pollution due to fermentation phenomena.

A project of our group, financed by Regione Siciliana, has the aim of implementing the prickly pear culture through the study of biological properties and the valorization of the above mentioned wastes.

The use of prickly pear fruits is recommended for their beneficial and therapeutic properties (Barbera and Inglese, 1993). Literature data report that other parts of this plant are also used in folk medicine as: emollient, moisturizing, cicatrizant, hypocholesterolemic, hypoglycemic agent and in gastric mucosa diseases (Cruse, 1973; Meyer and Mc Laughlin, 1981; Harvala et al., 1982; Camacho-Ibanez et al., 1983; Brutsch, 1990; Frati et al., 1990; Hegwood, 1990; Pimienta, 1990; Fernandez et al., 1992, 1994; Rosado and Diaz, 1995).

In Sicilian folk medicine, a flower infusion has an effect generally defined as depurative and in particular it is used because of its diuretic and relaxant action on the renal excretory tract (Arcoleo et al., 1961, 1966; Sisini, 1969). Therefore, it is stipulated that a flower infusion may help the expulsion of renal calculus. The fruit also enhances renal function (Cacioppo, 1991).

In the present work, we studied the diuretic effects of cladode, fruit and flower infusions of *Opuntia ficus indica* in the rat, to explain the popular use and to compare the activity of flower infusion with the activity of cladode and fruit infusions.

Natriuresis, kaliuresis and the activity on fructose-induced hyperuricemia was also studied.

* Corresponding author.

0378-8741/02/$ - see front matter
PII: S0378-8741(01)00337-3

2. Materials and methods

2.1. Animals

Male Wistar rats (150–200 g) were placed in metabolic cages (temperature 22 ± 2 °C; humidity 60 ± 4%; natural light) and maintained on standard diet (S. Morini, Mil rat GLP).

2.2. Plant material

The plant material is the waste matter collected in a *O. ficus indica* cultivation located in S. Cono (CT-Sicily).

The cladodes, cleaned from epidermis and glochides, were homogenized in Ultra-Turrax for 5 min. The fruits, cut into pieces and homogenized in Ultra Turrax for 5 min, were centrifuged to remove the seeds. The flowers were air-dried.

The 15% infusions in tap water were prepared according to Farmacopea Ufficiale Italiana, 1998 and administered, by gavage, immediately after filtration, at a dose of 5 ml/100 g (body weight (b.w.)).

2.3. Acute diuretic activity

The diuretic activity was assessed as follows: each animal was placed in an individual metabolic cage 24 h prior to commencement of the experiment for adaptation. Rats were fasted overnight with free access to water. The animals were divided into five groups of 12 rats each and subjected to treatment in the morning.

The I, II and III groups of rats received 15% infusion of *O. ficus indica* cladodes, flowers and fruits, respectively (5 ml/100 g b.w.). The IV group (control) received only the tap water (5 ml/100 g b.w.). The V group received the diuretic compound: hydrochlorothiazide (SIGMA, Milano) (10 mg/kg in 5 ml/100 g b.w.).

The experiment was repeated three times at weekly intervals.

The urine was collected and measured at 1, 2, 4, 6, 8 and 24 h after administration. Natriuresis and kaliuresis were measured by flame spectrophotometry.

The results were expressed as average value ± S.E. The significance between the averages was evaluated with Student's *t*-test for unpaired data.

2.4. Chronic diuretic activity

A low dose (1.5 ml/100 g b.w.) of 15% infusions was used to study the effects of repeated administrations.

The animals were placed individually in metabolic cages. Five groups, each consisting of 12 male rats, were used. Three groups were administered every morning 1.5 ml/100 g of 15% cladode, flower and fruit infusions respectively, for 7 days. The IV group received only water and served as control. The V group received the diuretic compound: hydrochlorothiazide (SIGMA, Milano) (10 mg/kg in 1.5 ml/100 g b.w.).

The urine excreted in 24 h was collected daily and measured for every single rat.

The results were expressed as average per rat per day. The average was calculated using the values obtained, as well as standard error (S.E.).

The significance between the averages was evaluated with Student's *t*-test for unpaired data.

2.5. Antiuric activity

In order to assess the antiuric activity, the rats, placed individually in metabolic cages, were divided into five groups of six each.

The first group was treated only with water and used as control.

The rats of the second, third, fourth and fifth group were made to become hyperuricemic through the administration by gavage of 4 g/kg b.w. of fructose (20% solution), that, as known, stimulates nucleotide degradation (Brosh et al., 1982; Itoh, 1983). The rats in the second group did not receive any other treatment.

The rats of the third, fourth and fifth group received by gavage 5 ml/100 g 15% infusion of cladodes, flowers and fruits, respectively (5 ml/100 g b.w.).

The treatment was always undertaken 15 min after fructose administration. Urine was collected 2, 5 and 8 h after treatment with the infusions. At the same time a blood sample was taken to measure uricemia. Plasmatic and urinary uric acid was measured with the colorimetric enzyme method (Trinder, 1969; Fossati et al., 1980).

The results were expressed as average ± S.E. The significance between the averages was evaluated with Student's *t*-test for unpaired data.

3. Results

3.1. Results of acute diuretic activity

The treatment with cladode infusion gives a slight increase in diuresis at the second hour after administration of infusion (controls 3.1 ml ± 0.9; treated 4.8 ± 1.2). After 4, 6 and 8 h of treatment, the urine volume was equal to the controls. The increase in urinary volume in 24 h is statistically significant with respect to controls (Fig. 1) (controls 24.2 ml ± 1.0; treated 38.2 ml ± 1.1).

In the acute experiment, we did not observe significant variations of diuresis up to the eighth hour after infusion of flowers. In fact, the urinary volume at 1, 2, 4, 6 and 8 h is analogous to that of controls. The total volume of urine in 24 h instead presented statistically significant variations (controls 24.2 ml ± 1 0; 32.4 ml ± 1.7) (Fig. 1).

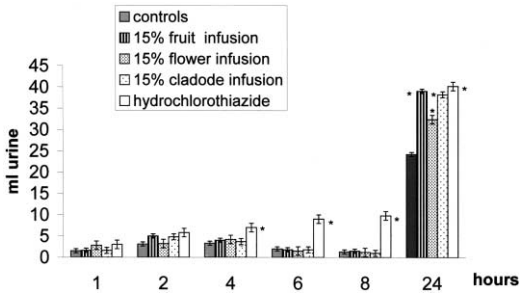

Fig. 1. Acute diuretic activity of *Opuntia ficus indica* (L.) Mill. 15% cladode, flower and fruit infusions (5 ml/100 g b.w.) in rat. The volume of excreted urine was measured 1, 2, 4, 6 and 8 h after treatment. The 24 h value corresponding to cumulative results (mean ± S.E.). $^*P < 0.05$ compared with controls; Student's *t*-test.

The diuretic activity of the fruit infusion is evident after 2 h from administration (controls 3.1 ml ± 0 9; treated 5.0 ml ± 0.8). The rate of diuresis of treated rats is similar to that of controls at 4, 6, and 8 h after treatment. The 24 h urinary volume is markedly higher in treated rats (controls 24.2 ml ± 1.0; treated 39.0 ml ± 0.7) (Fig. 1).

At the same time, the urine volume of the rats treated with hydrochlorothiazide exceeded the values of the control group from the beginning, but also the values of the groups treated with *O. ficus indica* infusions. At 24 h, as Fig. 1 shows the difference between the urine volume of the animals treated with fruit and cladode infusions (respectively, 39.0 ml ± 0.7 and 38.2 ml ± 1.1) and those treated with hydrochlorothiazide (40.2 ml ± 1.8) is similar.

The cladode, flower and fruit infusions show a modest but not significant increase in natriuresis and kaliuresis (Figs. 2 and 3).

3.2. Chronic diuretic activity

In the chronic experiment (Fig. 4), the cladode infusion from the first day of treatment, gives an increase in diuresis with respect to controls. This increase reaches its peak on the third day but remains statistically significant up to the sixth day.

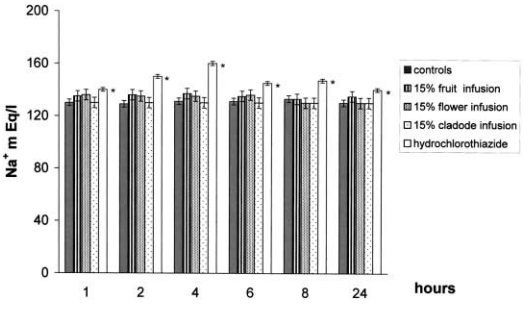

Fig. 2. Effect of oral administration of *Opuntia ficus indica* (L.) Mill. 15% cladode, flower and fruit infusions (5 ml/100 g b.w.) on the urinary concentrations of sodium and potassium in rat (mean ± S.E.). $^*P < 0.05$ compared with controls; Student's *t*-test.

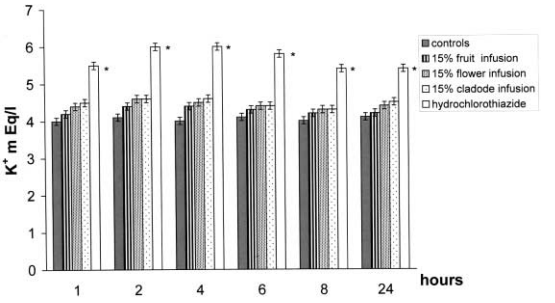

Fig. 3. Effect of oral administration of *Opuntia ficus indica* (L.) Mill. 15% cladode, flower and fruit infusions (5 ml/100 g b.w.) on the urinary concentrations of sodium and potassium in rat (mean ± S.E.). $^*P < 0.05$ compared with controls; Student's *t*-test.

The flower infusion has a minor diuretic activity. The increase in diuresis is significant from 3 to 7 days of treatment.

Fruit infusion possesses important diuretic action. The increase in diuresis is significant from the first day of treatment, reaches its peak value on the third day and maintains this value up to the seventh day of treatment. This effect is quantitatively similar to hydrochlorothiazide (Fig. 4).

3.3. Antiuric activity

The level of plasmic uric acid in normal rats is about 1.3 mg/dl and the urinary one about 1.2 mg/dl. Two hours after treatment with fructose, plasmic uric acid reaches an average value of 4.2 mg/dl, and the urinary one of 4.15 mg/dl. After treatment with cladode and flower infusions, blood and urine variations of uric acid were not statistically significant.

After treatment with fruit infusion the blood levels of uric acid decreases after 2 h from administration. The decrease is statistically significant also at the fifth and eighth hour. The urinary values of uric acid show an opposite course. Maximum elimination is obtained at the second hour and the increase in uric acid is statisti-

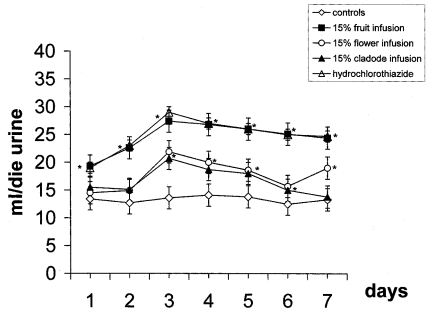

Fig. 4. Chronic diuretic activity of *Opuntia ficus indica* (L.) Mill. 15% cladode, flower and fruit infusions (1.5 ml/100 g b.w.) in rat. The volume of excreted urine was measured after 1, 2, 3, 4, 5, 6, 7 days of treatment (mean ± S.E.). $^*P < 0.05$ compared with controls; Student's *t*-test.

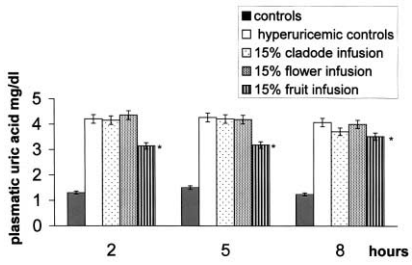

Fig. 5. Antiuric activity of *Opuntia ficus indica* (L.) Mill. 15% cladode, flower and fruit infusions (5 ml/100 g b.w.) in rat with fructose-induced hyperuricemia. Plasmatic and urinary uric acid was measured 2, 5 and 8 h after treatment (mean ± S.E.). $*P < 0.05$ compared with controls; Student's *t*-test.

cally significant up to 8 h after the treatment (Figs. 5 and 6).

4. Conclusions

Perfumi and Tacconi (1996) reported that flower infusion shows a modest increase in diuresis and natriuresis. In our experimental conditions, treatment with cladode and flower infusions increases diuresis but does not significantly influence the uric acid pattern.

The fruit infusion instead had diuretic and antiuric activity. Cladode, flower and fruit infusions do not give significant alteration of urinary levels of sodium and potassium (Figs. 2 and 3).

The diuretic action observed may depend on stimulation of the urinary tract and is linked to the activation of neurohumoral mechanism, mediators of stimuli acting on glomerules, tone acid on the pyelo-uretral peristaltis. These effects might be due to the influence that the electrolytes, present in considerable quantities on the plant, exert on renal epithelium. In particular, *O. ficus indica* is rich in K^+ ions, which, in our samples, are present in concentration of 548 mg/kg in the cladodes, 21.7 mg/kg in the flowers and 18 mg/kg in the fruit (d'Aquino, 1998).

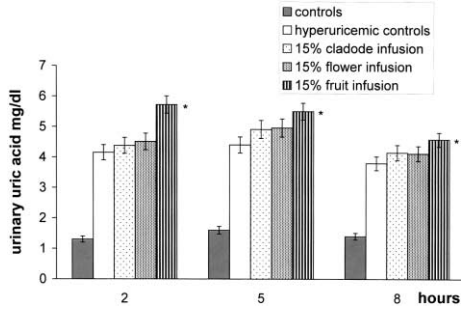

Fig. 6. Antiuric activity of *Opuntia ficus indica* (L.) Mill. 15% cladode, flower and fruit infusions (5 ml/100 g b.w.) in rat with fructose-induced hyperuricemia. Plasmatic and urinary uric acid was measured 2, 5 and 8 h after treatment (mean ± S.E.). $*P < 0.05$ compared with controls; Student's *t*-test.

Reference data report that K^+ concentration in the fruit is about 100 mg/100 ml (Duro and Condorelli, 1971; Wills et al., 1986).

Other monovalent and bivalent cations are present in this plant and might have a diuretic activity synergetically with K^+ (Kanias et al., 1979).

The theory that the majority of the medicinal plants have a diuretic effect only due to the presence of the potassium seems somewhat doubtful (Ribeiro et al., 1988). In fact pharmacodynamic studies performed on medicinal plants emphasized that frequently no correlation exists between the diuretic effect observed and the K^+ content of the extract (Abed and Benmerabet, 1981; Jouad et al., 2001).

In the present study, the diuretic effect observed does not exclude the possibility that changes in the diuresis may occur as a consequence of the presence of polar drug compounds (Szentmihályi et al., 1998; Chodera et al., 1991), e.g. flavonoid glycosides (Piattelli and Minale, 1964; Piattelli and Imperato, 1969; Duro and Condorelli, 1971, Alard et al., 1985, Forni et al., 1992) and ascorbic acid (Pinto and Acevedo, 1983; Sawaya et al., 1983; Kuti, 1992; Teles et al., 1994).

Preliminary phytochemical analysis revealed that these compounds are the main constituents of OFI infusions (d'Aquino, 1998). These natural compounds might be acting synergetically or individually promoting an initial vasodilatation (Stanic and Samaržija, 1993). It is also possible that OFI infusions might manifest cumulative effect of several substances in the extract and/or due to secondary active metabolite (Tanira et al., 1988). The other possibility for the observed diuretic effect could be due to indirect changes of some physiological parameters before blood filtration step.

The antiuric effect of fruit infusion cannot be explained only by the increase of diuresis or by an increased urinary excretion of urates. Probably, it could be bound to an influence on the uric acid metabolism due to an alteration of some enzymatic activity.

Acknowledgements

Financial support for this research was provided by Regione Siciliana (Italy).

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