Journal of Ethnopharmacology 217 (2018) 7–10

Contents lists available at ScienceDirect

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Anti-inflammatory activity and gastroprotective effect of *Hertia cheirifolia* L. roots extract

Kaouther Majouli[a,*], Assia Hamdi[b], Amal Abdelhamid[b], Abderrahman Bouraoui[b], Adberraouf Kenani[a]

[a] Laboratory of Biochemistry, Research Unit: UR 12ES08 "Cell Signaling and Pathologies", Faculty of Medicine, University of Monastir, Tunisia
[b] Laboratory of Development of Drugs (LR12ES09), Marine Pharmacology Team, Faculty of Pharmacy of Monastir, University of Monastir, 5000 Monastir, Tunisia

ARTICLE INFO

Keywords:
Hertia cheirifolia
Anti-inflammatory
Gastroprotective
Liquid chromatography

ABSTRACT

Ethnopharmacological relevance: *Hertia cheirifolia* L. is used traditionally to treat rheumatic pains and known as a medicinal plant having several pharmaceutical and biological activities. The present study evaluated *in vivo* the anti-inflammatory and gastroprotective effects of the methanolic extract from *H. cheirifolia* L.
Materials and methods: Reverse phase high-performance liquid chromatography (RP-HPLC) was performed to identify various chemical components of the plant extract. Anti-inflammatory and gastroprotective activities were assessed on carrageenan-induced paw edema and HCl/ethanol-induced gastric lesions in rats, respectively.
Results: (RP-HPLC) analysis indicated that coumarin is the abundant component in the extract (53.80%). Intraperitoneal administration of the methanolic extract at different doses showed interesting activities in rats in a dose-dependent manner. At 100 mg/kg, this extract showed the highest acute anti-inflammatory activity and an important inhibition of gastric lesions with inhibition percentage of 79.41% and 88.53%, respectively.
Conclusion: Altogether, the results of this study reveal the anti-inflammatory and gastroprotective effects of *H. cheirifolia* extract and promote the traditional use of this plant in the treatment of different pain and inflammatory diseases.

1. Introduction

The inflammatory reaction is triggered as soon as the body is traumatized by endogenous and/or exogenous stimuli including extreme temperature, irritants, infectious pathogens, physical force and irradiation. The organism reacts by allowing immune cells to migrate through the cells of the endothelium (Nathan, 2002). This inflammatory response leads to the elimination of possible pathogens and to the return to the homeostasis of the damaged tissue (Lawrence and Gilroy, 2007). However, inadequately controlled, the inflammation can spread throughout the body and may cause various tissue damage including gastritis (Nathan, 2002; Barton, 2008; Coussens and Werb, 2002). There are many anti-inflammatory drugs, including steroidal or nonsteroidal drugs, can intervene through different mechanisms to regulate inflammatory responses (Vane, 2000). Non-steroidal anti-inflammatory drugs are the most used to modulate the adverse effects associated with inflammation; however, they have been reported to have a variety of side effects (Khan et al., 2017). On the other hand, plants are considered to be a good source of natural molecules to treat various diseases with a minimum of adverse effects (Battle et al., 2005).

Hertia cheirifolia L. is a species of a genus of flowering plants in the Asteraceae family. The leaves of this plant have been used in the traditional medicine to treat rheumatic pains and to reduce hyperglycemia (Majouli et al., 2016). In addition, the previous study suggests that the extracts of this plant may possess anti-inflammatory properties (Ammar et al., 2009). Collectively, these details prompted us to study the *in vivo* anti-inflammatory effects of *H. cheirifolia* roots extract. In the present study, we investigated the anti-inflammatory and gastroprotective effects of methanolic extract from *H. cheirifolia* L.

2. Materials and methods

2.1. Extraction

H. cheirifolia L. was collected from Thala in Tunisia. A voucher specimen (Hc 112) was deposited in the Laboratory of Medicinal Chemistry and Natural Products at the Faculty of Science, University of Monastir, Tunisia. The *H. cheirifolia* roots were air-dried at room

Abbreviations: V, Volume; NaCl, Sodium chloride; HCl, Hydrochloric acid; mm, millimeter; LD_{50}, median lethal dose

* Corresponding author.
E-mail address: kaouther.bio@gmail.com (K. Majouli).

https://doi.org/10.1016/j.jep.2018.02.010
Received 15 September 2017; Received in revised form 14 January 2018; Accepted 6 February 2018
Available online 08 February 2018
0378-8741/

temperature for 15 days and reduced to coarse powder. The powdered plant material was extracted by maceration in the methanol for 72 h at room temperature. The methanolic extraction was carried out in triplicate.

2.2. Animals

Wistar rats of either sex, weighing 150–200 g, and Swiss albinos mice weighing 18–30 g of both sex were obtained from Pasteur Institute (Tunis, Tunisia). Housing conditions and *in vivo* experiments were approved according to the guidelines established by the European Union on Animal Care (CCE Council 86/609).

2.3. Acute toxicity of H. cheirifolia L

Swiss mice were divided into three groups of ten animals each. The extract was injected *via* the intraperitoneal route at the dose of 50 mg/kg and 100 mg/kg, respectively. Mice were placed under observation for 48 h to determine the change in behavior and the percentage of mortality.

2.4. Anti-inflammatory activity

The anti-inflammatory activity of the methanolic extract on carrageenan-induced paw edema was determined according to Salem et al. (2017). Wistar rats were divided into five groups of six rats each. The control group received an intraperitoneal dose of saline solution (NaCl 9‰, 2.5 mL/kg), the reference group received Diclofenac (25 mg/kg) and the test groups received the methanolic extract of *H. cheirifolia* (50 and 100 mg/kg). Thirty minutes later, 0.05 mL of a 1% carrageenan suspension was administered by subplantar injection into the left hind paw. The paw volume was measured using a plethysmometer (Ugo Basile no. 7140) immediately before carrageenan injection (basal volume V_0) and then 1, 2, 3, 4 and 5 h later (V_T) after carrageenan injection. The percentage of inhibition in increase of paw volume for each group was calculated by the following formula:

$$\% \text{ inhibition} = [(V_T - V_0)_{control} - (V_T - V_0)_{treated\ group}/(V_T - V_0)_{control}] \times 100$$

2.5. Gastroprotective activity

The gastroprotective activity of *H. cheirifolia* roots extract was studied in HCl/EtOH induced gastric ulcer model (Salem et al., 2017). Animals were divided into three groups of six rats each and fasted 24 h prior the test. The control group received an intraperitoneal dose of vehicle (NaCl 9‰, 2.5 mL/kg), the reference group received Omeprazole (30 mg/kg) and the test groups received the methanolic extract of *H. cheirifolia* at different doses (50 and 100 mg/kg). After 30 min, all groups were orally treated with HCl/ethanol (40:60, v/v) solution for gastric ulcer induction. Animals were killed after 1 h later and their stomachs were excised, opened along the great curvature, washed and stretched on cork plates. The surface was examined for the presence of lesions and the extent of the lesions was measured. The summative length of the lesions along the stomach was recorded (mm) as lesion index.

2.6. Analysis of phenolic compounds by analytical RP-HPLC /UV

Separation of phenolic compounds was performed with an Agilent 1100 series HPLC system equipped with on-line degasser (G1322A), a quaternary pump (G 1311A), a thermostatic autosampler (G 1313A), a column heater (G 1316A) and a diode array detector (G 1315A). Instrument control and data analysis were carried out using Agilent HPLC Chemstation 10.1 edition through windows 2000. The separation was carried out on a reverse phase ODS C18 (5 µm, 250 mm × 4.6 mm, hypersil) column used as a stationary phase at ambient temperature. The mobile phase consisted of acetonitrile (solvent A) and water with 0.2% formic acid (solvent B). The flow rate was kept at 0.7 mL/min. The gradient program was as follows: 35% A/65% B (0–6 min), 60% A/40% B (6–9 min), 80% A/20% B (9–14 min), 100% A (14–25 min), 35% A/65% B (25–30 min). The injection volume was 20 µL and peaks were monitored at 280 nm. Peaks were identified by congruent retention times compared with standards.

2.7. Statistical analysis

Results were given as mean ± SEM. Data were subjected to one-way ANOVA, and Duncan's multiple range tests was used to compare means. Statistical analyses were performed with the SPSS statistical software program (SPSS v.16). Statistical significance was set at $p < 0.05$.

3. Results and discussion

3.1. Acute toxicity

According to the findings, 48 h after, pretreatment of the animals with the methanolic extract from *H. cheirifolia* roots had no severe signs of toxicity or mortality in any group. This result indicates that the median lethal dose (LD_{50}) of the methanolic extract is more than 100 mg/kg.

Considering substances possessing LD_{50} greater than 50 mg/kg are classified as non-toxic materials (Osweiler et al., 1985), the tested methanolic extract can be categorized as a benign one. Although, the treatment of the animals by the extract caused hyperactivity in almost all the mice, these reactions were transitory (some seconds) and not observed thereafter until the end of the experimental period.

3.2. Anti-inflammatory activity

The study of the anti-inflammatory activity of the methanolic extract from *H. cheirifolia* roots was performed by measuring the change in paw volume in the absence (control group) and in presence of an anti-inflammatory treatment.

Intraperitoneal administration of 50 mg/kg of methanolic extract

Table 1
Anti-inflammatory effect of *H. cheirifolia* L. methanolic extract in carrageenan-induced rat paw edema model.

Sample	Dose mg/kg	Volume of plantar edema (10^{-2}/mL)					Edema inhibition (%)				
		1 h	2 h	3 h	4 h	5 h	1 h	2 h	3 h	4 h	5 h
Control	–	34.60 ± 0.55	63.16 ± 0,99	78.80 ± 0.44	87.50 ± 0.84	97.17 ± 0.98	–	–	–	–	–
Diclofenac (Reference drug)	25	18.83^{a} ± 0.41	31.50^{c} ± 1.22	32.33^{d} ± 1.21	31.16^{c} ± 0.41	30.33^{b} ± 0.82	45.57	50.13	58.97	64.38	68.78
Methanolic extract	50	18.75^{a} ± 0.96	29^{b} ± 1.41	32^{c} ± 0.81	34.75^{d} ± 0.50	33^{c} ± 0.82	45.81	54.10	59.40	60.28	66.04
	100	10^{a} ± 1.73	17^{b} ± 2.50	20^{c} ± 2.06	19.5^{c} ± 1.41	20^{c} ± 2.87	71.88	73.09	74.61	77.71	79.41

Values were expressed as mean ± SEM (n = 6).
The different letters indicate a significant difference between the extracts ($p < 0.05$).