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Antinociceptive Activity of *Centaurea chilensis* Growing in Iran

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Abstract: A methanol/water (80:20) extract of aerial parts of *Centaurea chilensis* (Cc) (family: Asteraceae=copositea, Common Name: Cornflower & Knapweed) was investigated for its antinociceptive activity by Hot plate test in mice. The extract produced statistically significant inhibition of pain induced by hot plate latency at 400 mg kg^{-1} i.p. dose when compared to the control groups. On the contrary, Aqueous and methanolic extracts of leaves did not show any activity up to 400 mg kg^{-1} i.p. A significant increase in pain threshold was observed at both 30th and 60th min after ip injection of extract when compared with the control group ($P<0.001$). Administration of Aerial parts extracts *Centaurea chilensis* significantly attenuated effect and raised the pain threshold at observation time of 30 min in comparison with the control group ($P<0.05$) (58% for morphine at 30 mg kg^{-1} i.p.) The LD_{50} of this fraction after the 14 day acute toxicity calculated as 570 mg kg^{-1} i.p. No extracts exhibit toxicity when injected up to 0/4 g kg^{-1} intraperitoneally in mice.

Keywords: *Centaurea chilensis* · antinociceptive activity · Toxicity

INTRODUCTION

Pain is still one of the main health problems of the world's populations [1]. Many bioactive substances are involved in the modulation of pain sensation and eclectic physicians relied upon herbal medicines and natural remedies to treat disease [2, 3]. The pain relief composition is prepared from roots of the family of Burdock plants and in particular from at least one of the species Arctium lappa as Arctium minus (Asteraceae) in combination with roots of the Phytolacca family and in particular the species Phytolacca Americana [4]. *Centaurea* is a medical herb form Asteraceae. 74 species of dried flowers of *Centaurea*, which are available on western and northwestern of Iran, are used to relive pain and reduction of fever [5-7]. Another species *Centaurea* (There are approximately 1,544 species in this genus) is popular beverage in east Asia and Europe (Turkey and Spain) and also used as a herbal remedy in north America which are known for their astringent and antidiabetic, antidiarrhetic, antirheumatic, diuretic, antiinflammatory, hypotensive, antipyretic, cytotoxic and antibacterial effects by traditional medicines, and are used single or mixed [8-14]. In Chinese traditional medicines C. *chilensis* have been used as antipyretic and anti-rheumatics [15-17]. The purpose of this study is to report the analgesic effect of aqueous and methanolic extracts of aerial parts (flowered browes) of *Centaurea chilensis* grown in Iran by hot plate test. Although mechanism of plant action to inhibit or decrease antinociceptive activity in mice is unclear.

MATERIALS AND METHODS

Aerial parts (flowered browse) of *Centaurea chilensis* were collected from Mazandaran (a northern state in Iran) in April 2006 and identified by confirmed by department of Pharmacognosy (Dr. Gohari). A voucher specimen (No. 0506-17) has been deposited in Tehran school of pharmacy Herbarium. Aerial parts were dried at room temperature and powdered before extraction. One hundred grams of the powdered sample was extracted at room temperature by percolation with methanol/water (80:20, 400 ml × 3 times). The resulting

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extract was concentrated over a rotary vacuum evaporator until a solid extract sample was obtained. The resulting crude extract was freeze-dried. The extract was prepared in phosphate buffer (pH= 7.4) and tween 80 (4:1) for pharmacological studies.

Male swiss albino mice weighing 25-30 g were used for all experiments (n = 7). They were housed in groups of six under standard light (7.00 to 19.00) and temperature (22±1°C) with food and water *ad libitum*. The animals were transferred to the laboratory at least 1h before the start of the experiment. The experiments were performed during day (08:00-16:00 h). Each animal was used once only. Animal handling was performed as per *Good Laboratory Practice*. A research proposal was prepared according to the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA). The Institutional Animal Ethical Committee (IAEC) of Mazandaran University of medical sciences approved the proposal.

Morphine was injected intera peritoneal (ip) to mice a single dose of 30 mg kg^{-1} as positive control. Solvent was injected to the negative group (10 ml kg^{-1}, ip). Antinociceptive activity was assessed by measuring hotplate latency to heat as described by Eddy & Leimback [18]. A cut-off time of 55s was observed to prevent any injury to the paw. A minimum of three trials was recorded for each animal and toxicity studies carried out in mice according to the method of Reddy *et al.* [19].

Statistical analysis was performed using SPSS for Windows (Ver.10, SPSS, Inc., Chicago, USA). Data were analyzed by one-way analysis of variance (ANOVA) and presented as mean ± Standard error in the mean (S.E.M). Student-Newman-Keuls test was used for statistical analysis and P<0.05 was considered to be significant [20].

RESULTS AND DISCUSSION

The results of present study showed that the aqueous methanolic extract of aerial parts (flowered browse) of *Centaurea chilensis* produced statistically significant rasised the pain threshold at 30th min in comparison with control at 400 mg kg^{-1} (Figure 1). The effect was dose dependent but the activity was low in lower doses. This activity was comparable to that of morphine (30 mg kg^{-1} i.p). The antinociceptive activity of *C. chilensis* increased until 60th min. P value was less than 0.05 respect to morphine (Figure 2). The LD_{50} of this fraction after the 14- day acute toxicity calculated as 570 $mgkg^{-1}$ i.p. The result of this study support the extensive use of this plant in East Asia and Europe [8, 21-24]. Some

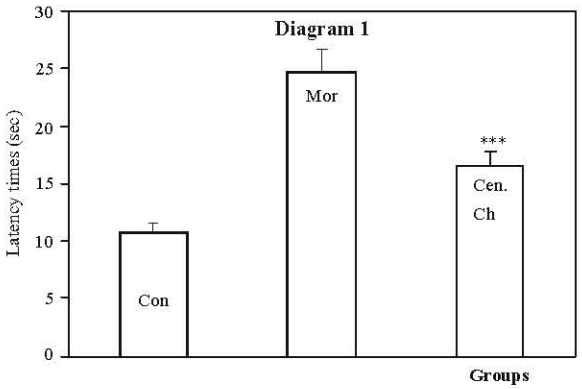

Fig. 1: Antinociceptive activity of methanolic and aqueous extracts of *C. chilensis* aerial parts at 30th min. Values are presented as mean ± SEM ($N = 7$), ***$P < 0.001$ with respect to control, (ANOVA followed by Newman–Keuls multiple comparisons test)

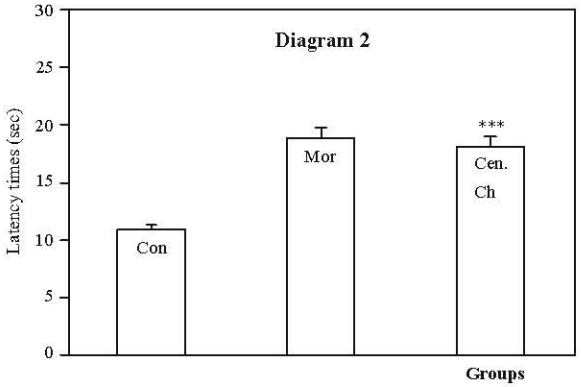

Fig. 2: Antinociceptive activity of methanolic and aqueous extracts of *C. chilensis* aerial parts at 60th min. Values are presented as mean ± SEM ($N = 7$), ***$P < 0.001$ with respect to control, (ANOVA followed by Newman–Keuls multiple comparisons test).

antiinflammatory components has been reported from *C. chilensis* [25, 13]. The presence of bitter substances in centaury would account for most of the gastrointestinal effects reported, including the choleretic or cholagogue properties. In the British Pharmacopoeia, centaury is listed as a bitter, aromatic and stomachic, and used to treat anorexia and dyspepsia [26]. Leaves used medicinally by Indians of the of the southwestern US. Also a modern source of steroids [27]. Some plants secrete bioflavonoids that inhibit the growth and seed germination of nearby plants of a different species. This

phenomenon, called allelopathy, One potent allelopathic flavonoid called catechin is produced by the roots of spotted knapweed (*Centaurea* biebersteinii syn. *C. maculosa*). The positive (+) form catechin is an antibiotic and antioxidant that prevents the formation of free radicals. It is present in a number of plants, including green tea (*Camellia sinensis*). The -catechin induces oxidation and cellular death in root cells of neighboring plants. Although the mechanism is complex, -catechin is a potent phytotoxin that causes plants to self destruct by producing free radicals as well as triggering genes that kill the cells. Cellular death may occur within an hour of exposure to catechin [28]. May be the same components lead to antinociceptive activity in our extract. This needs more studies. Based on our result, *C. chilensis* can be candidate as an anti analgesics, too.

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