

Antiinflammatory and Antinociceptive of Hydro Alcoholic *Tanacetum balsamita* L. Extract

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Abstract—The use of herbs to treat disease is accompanied with the history of human life. This research is aimed to study the anti-inflammatory and antinociceptive effects of hydroalcoholic extract of aerial parts of "*Tanacetum balsamita balsamita*". In the experimental studies 144 male mice are used. In the inflammatory test, animals were divided into six groups: Control, positive control (receiving Dexamethason at dose of 15mg/kg), and four experimental groups receiving *Tanacetum balsamita balsamita* hydroalcoholic extract at doses of 25, 50, 100 and 200mg/kg. Xylene was used to induce inflammation. Formalin was used to study the nociceptive effects. Animals were divided into six groups: control group, positive control group (receiving morphine) and four experimental groups receiving *Tanacetum balsamita balsamita* (Tb.) hydroalcoholic extract at doses of 25, 50, 100 and 200mg/kg. I.p. injection of drugs or normal saline was performed 30 minutes before test. The data were analyzed by using one way Variance analysis and Tukey post test. Aerial parts of *Tanacetum balsamita balsamita* hydroalcoholic extract decreased significantly inflammatory at dose of 200mg/kg ($P<0/001$) and caused a significant decrease and alleviated the nociception in both first and second phases at doses of 200mg/kg ($p<0/001$) and 100mg/kg ($P<0/05$). *Tanacetum balsamita balsamita* extract has the anti-inflammatory and anti-nociceptive effects which seems to be related with flavonoids especially Quercetin.

Keywords— Inflammation, nociception, Hydroalcoholic extract, aerial parts of *Tanacetum balsamita balsamita* L.

I. INTRODUCTION

NOCICEPTION is an unpleasant feeling that indicates injury to the body and is aware of the source of pain [1].

Nociception may have different root causes, as: temperature, stroke, tension, electrical flow, necrosis, inflammation, spasm and even disruption of blood flow in a tissue [2].

Tanacetum balsamita balsamita is a pharmaceutical plant from *Compositae* family which has valuable remedial effects. It is a dynamic, fuzzy and fluffy plant [3].

This plant is a permanent gramineous which can grow, up to 80cm. Its top flowers are widely used as appetizer, booster of sexual, diuretic, germicide and migraine relieving [4].

Tanacetum balsamita balsamita traditionally called "basil" and it is one of aromatic species which widely grows in

Azarbaijan (Iran). In Iranian traditional medicine has used it as lenitive and heart reinforcement [5].

In Europe, the subfamily of *Balsamita* has been used as a medical plant and in cooking since middle centuries [6].

Its distillate is used to treat stomachache, and to make redolent tea and buttermilk for making them delicious. [7].

Many medicinal varieties of "*Tanacetum balsamita*" has been identified which are rich in flavonoids [8].

The most component in the essential oil of *Tanacetum balsamita balsamita* is carvone (%52) and camphor (%17 and %16) [9].

According to recent studies, the essence or volatile oil of *Tanacetum* species has showed anti-inflammatory [10], [11], anti-bacterial [12], antifungal [13], [14] and insecticide roles [15], [16].

It's interesting that the essences derived from *Tanacetum balsamita*, have anti-microbial effect. Also, this plant has been used to remove worms and increase appetite, strengthen the body, regulate menstruation, and treat migraine [17].

According to the analgesic properties of this plant in traditional medicine [5], this research has been studied the effects of hydroalcoholic extract of *Tanacetum balsamita balsamita* on inflammation and nociception.

II. MATERIAL AND METHOD

A. Extraction

Stems, leaves and flowers of *Tanacetum balsamita* were collected and dried in standard condition and then were ground and percolated (%80 alcohol). After extraction, the extract was concentrated with evaporator. Then, it was diluted by a solvent (normal saline) and was injected into peritoneum of mice. [18]

B. Animals

In this experimental study, 144 male mice (Pastor Institute of Iran) weighing 20 to 25gr. were used. The mice were kept in the animal's room and under controlled condition and free access of food and water. All experiments were according to rules of ethic committee of Payame Noor University.

C. Inflammation test

In inflammation test, the animals were divided into six groups (each group contained 8 mice): control group received solvent (Normal Saline), positive control group received Dexamethason at dose of 15mg/kg and the experimental groups receiving hydroalcoholic extract of "*Tanacetum balsamita balsamita*", at doses of 25, 50, 100 and 200mg/kg. 15 minutes after extract injection at mentioned doses, the

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inflammation was induced by administrating 0/03ml of xylene (England Company of Romil) to the eanterior and posterior of the right ear and then animals were sacrificed after 2 hours [19], [20]. The left ear considered as control. The weight difference between right and left ears of mice showed inflammation [19].

D. Nociception test

In nociception test, animals were also divided into six groups (each group contained 8 mice): control group received normal saline, the positive control group received morphine at dose of 10mg/kg and the experimental groups receiving hydroalcoholic extract of *Tanacetum balsamita balsamita* at doses of 25, 50, 100 and 200mg/kg. Then nociception test was administered by using formalin test. All injections were performed 30 minutes before test intraperitoneally. The animal was immediately placed in a glass cylinder to formalin test on a flat glass floor and in order to better observing, a mirror with a 45° angle was placed under it and against the observer. After that, 0/02ml formalin (2/5%) (Romil Company) was injected subcutaneously into right hind paw of the mouse. The animal was returned to test box and licking or biting of the injected paw was considered as licking time. Data were considered in the first phase (0-5 minutes) and the second phase (15-30 minutes) of formalin test [21].

E. Statistic Analyses

Data was analyzed by using One Way ANOVA statistical test and "Tukey" post test.

III. FINDINGS

Results showed that hydro alcoholic extract of aerial parts of "*Tanacetum balsamita balsamita*" has anti-inflammatory effect and there was significant difference between Tb. and Sham group at doses of 200mg/kg ($P<0/001$) and 100mg/kg ($p<0/05$) (Fig. 1). The meaningful difference wasn't observed between Dexamethason group and Tb. group at dose of 200 mg/kg ($p>0/05$) (Fig. 1).

Also, this extract showed antinociceptive effect in the first and second phase of formalin test and there was significant difference between Tb. and Sham group at doses of 100 ($P<0/001$) and 200mg/kg ($P<0/01$) (Fig. 2). The significant difference wasn't observed between the group receiving morphine (positive control) and the group receiving 200 mg/kg and 100 mg/kg doses at the 2nd phase (Fig. 2).

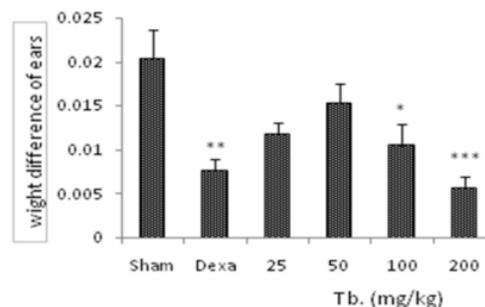


Fig. 1 The effect of hydroalcoholic extract of *Tanacetum balsamita* (Tb.) aerial parts on inflammation in the xylene test *($p<0/05$), **($p<0/01$), ***($p<0/001$) Difference with control group. There wasn't meaningful difference between the group receiving Dexamethason (Dexa) and the group receiving 200 mg/kg doses

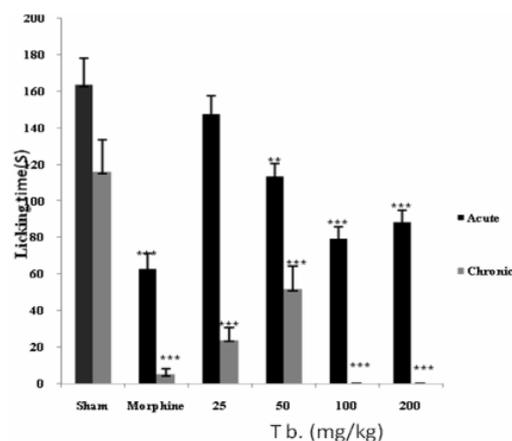


Fig. 2 The effect of hydroalcoholic extract of *Tanacetum balsamita* (Tb.) aerial parts on the 1st (0-5min) and 2nd (15-30min) phase of formalin test ** ($p<0/01$), ***($p<0/001$) Difference with control group. There wasn't meaningful difference between the group receiving morphine and the group receiving doses of 100mg and 200mg/kg *Tanacetum balsamita balsamita* extract in 2nd phase

IV. DISCUSSION

In traditional medicine, the extract of *Tanacetum balsamita balsamita* was used as a sedative and to treat stomachache and strengthen heart [5].

This research evaluated the anti-inflammatory and antinociceptive effects of hydro alcoholic extract of *Tanacetum balsamita balsamita* aerial parts for the first time. The most anti-inflammatory effect was observed at dose of 200mg/kg and the most antinociceptive effect was observed at dose of 100mg/kg.

The extract of aerial parts of this plant contains volatile oils and flavonoids [8]. Flavonoids are polyphenol compounds which are naturally available in plants, and have the antinociceptive and anti-inflammatory properties [22]. Quercetin is a major flavonoid in aerial parts of *Tanacetum balsamita balsamita* [23].

Quercetin is one of the most common flavonoids possess antinociceptive and anti-inflammatory property. Quercetin is a

therapeutic factor suitable to cure intestinal swelling and stomach lesions. Also, the external use of Quercetin eliminates the pain of oral lesions [24].

The root extract of *Arrabidaea* has anti-inflammatory effects. This plant relieves carrageenan-induced paw edema and decrease the leukocyte influence to enflamed peritoneal cavity in chronic inflammation. The anti-inflammatory and antinociceptive effects of this extract may be related to the presence of Quercetin and phenolic compounds [25].

Quercetin also inhibited the nociception via Glutamate and capsaicin [26].

Quercetin relieves inflammatory pain and decreases oxidative stress and cytokine production. This component reduces the inflammatory pain induced by acetic acid and phenyl-p-Benzoquinone and also controls the second phase of formalin and "Carrageenan" which create mechanical pains. This component also inhibits the severe pain generated by Cytokines (CXCL1, TNF α) but it doesn't affect on inflammatory mediators such as PGE2 and Dopamine [27].

An herbal complement called Glucosamine-condroitin-Quercetin- (GOQG)-Glycoside is used for osteoarthritis. After using this complement, an improvement was observed in the symptoms of daily nociception [28]. Quercetin has antinociceptive effect and its possible mechanism is related to L-Arginine, Nitric oxide, Serotonin, and GABAergic system [26].

The major component in the *Tanacetum balsamita* essential oil is Carvone [29]. This component has antinociceptive property associated with reduction of peripheral nerve excitation [30]. Also, Carvone has anti-inflammatory effects with potentiating of immune system and neutrophil activation [31].

V.CONCLUSION

With regard to present study, hydroalcoholic extract of aerial parts of *Tanacetum balsamita* possess anti-inflammatory and antinociceptive properties. Flavonoids, especially Quercetin in extract of "*Tanacetum balsamita*" seem to decrease inflammatory and neurologic pains by activating various neural paths. Also, essential oil of this plant specially Carvone is another probable agent for anti-inflammatory and antinociceptive effect of that. Using different fractions of extract and also interfering extract with neural carriers or their agonists and antagonists can determine neural paths affected by this extract.

REFERENCES

- [1] C. Guyton, J.E. Hall, "Text book of medical physiology", Translator by A. Haeri-Rohani. Tehran: AndisheRafea, 2006, pp. 595.
- [2] T. Saarto, Wiffen PJ, "Antidepressants for neuropathic pain : a Cochrane review", *Neurol Neurosurg Psychiatry*, 81(21),pp. 1372-3, 2010.
- [3] V. Mozaffarian, "A Dictionary of Iranian plants Names", Tehran: farhang Moaser, 1996, pp 534 .
- [4] M. Karaca, H. Ozbek, H.A. Akkan, M. Tutuncu, F. Ozgokce, A. Him, B. Bakir, "Antiinflammatory activities of Diethyl-Ether extracts of *Helichrysumplicatum* DC. And *Tanacetum balsamita* L. in rats", *Asian Jour of An& Vet Adv.*, 4(6),pp. 320-25, 2009.
- [5] Gh.Amin, "Popular Medicinal plants of Iran", 1st ed. Vol. 1, Tehran: Research center of Medical history and ethic and medical sciences of Tehran University, 1991, pp. 52.
- [6] P. H. Davis, R. Mill, "Flora of Turkey and the East Aegean Islands", vol. 5, Edinburgh: Edinburgh university press, 1975, pp. 256 – 294.
- [7] A.Karimi-Abdolmaleki, "Plants: *Tanacetum balsamita*", Available from <http://shabnamak.mihanblog.com/post/tag/Tanacetum>, 2011.
- [8] T. Fleming, "PDR for Herbal Medicines. 2nded Medical Economics company" NewJersey. 2000, 306 – 309.
- [9] K.H.C. Baser, B. Demirci, N. Tabanca, T. Ozek, N. Goren, "Composition of the essential oils of *Tanacetumarmenum* (DC.)", SchutzBip., T. balsamita L., T. chiliophyllum (Fisch&Mey) Schultz Bip. Var. chiliophyllum and T-hardjani(Rech. Fil.)Grieson and the enantiomeric distribution of camphor and carvon *flavifragr*J., 16 (3), pp. 195 – 200, 2001.
- [10] P. Mordujovich- Buschiazzo, E.M. Balsa, H.O. Buschiazzo, M. Mandrile, M. Rosella, G. Schinella, D. Fioravanti, "Anti – inflammatory activity of *Tanacetumvulgare*", *Fitoterapia LXVII*, 319-322, 1996.
- [11] A.Brown, C.M. Edwards, M.R. Davey, J.B. Power, K. C. Lowe, "Effects of extracts of *Tanacetum* species on human polymorphonuclear leucocyte activity *in vitro*", *PhytotherRes*, 11(7), pp. 479 – 484, 1997.
- [12] M. Stefavovic, N. Ristic, M.Vukmirovic, "Biological activities of sesquiterpene lactones. Investigations of microbial activities of Lactones isolated from the Yugoslav plant species of the genus *Tanacetum* L. [*Chrysanthemum* (Fam. Compositae)]", *Bull T XCV AcadSerbeSci Arts&classeSciNaturelles Math Sci Naturelles.*, 28 , pp. 23 – 43, 1998.
- [13] E. Hethelyi, P. Tetenyi, B. Danos, I. Koczka, "Phytochemical and antimicrobial studies on the essential oils of the *TanacetumVulgare* clones by gas chromatography / mass spectrometry", *Herba Hungarica.* , 30, pp. 82 – 90, 1991.
- [14] A. Nezmelyi, G. WA. Milne, E. Hethelyi, "Composition of essential oil of clone 409 of *Tanacetumvulgare* and 2 D NMR investigation of trans – chrysanthenyl acetate", *J Essent oil Res.*, 4 .pp. 243 – 250, 1992.
- [15] O.Panasiuk, "Response of Colorado potato beetles *Leptinotarsadecemlineata* (Say), to volatile components of tansy", *Tanacetum vulgare. chem J col E.*, 10(9), pp. 1325 -1333, 1984.
- [16] J. Hough-Golstein, SP. Hahn, "Antifeedant and oviposition deterrent activity of an aqueous extract of *Tanacetumvulgare*.on Two cabbage pests", *Environ Entomol.*, 21(4) .pp.837 – 844, 1992.
- [17] T. Baytop, "Therapy with medicinal plants in Turkey (past and present)", 2nd ed. Istanbul: Nobel Tip Kitabevleri Ltd, 1999, pp. 375.
- [18] V.Duraipandiyar, M. Ayyanar, S. Ignacimuthu, "Antimicrobial activity of some ethno medicinal plants used by player tribe from Tamil Nadu-India", *BMC ComplementAltern Med.*, 17(6),pp. 35, Oct. 2006.
- [19] S. Nasri, M. Ramezani, N. Yasa, "The effect of Antinociceptive and anti-inflammatory effects of hydroalcoholic extract of *Apium graveolens*", *Journal of Shahrekord University of Medical Sciences*, 2009, 10(4), pp. 25-31.
- [20] Sh. Oryan, S. Nasri, Gh.Amin, SMM. Kazemi-Mohammady, "Antinociceptive and anti-inflammatory effects of aerial parts of *Gundeliatournefortii* L. on NMRI male mic" *Journal of Shahrekord University of Medical Sciences*, 2011 Winter, 12 (4), pp.8-15 .
- [21] F. Hoodgar, S. Nasri, Gh.Amin, "Investigation of antinociceptive and anti-inflammatory effects of hydroalcoholic extract of *Securigera securidaca* L.", *Ofogh-e-Danesh Jour*, 2011, 17 (2), pp.12– 20.
- [22] S. Balasubramanian, L. Zhu, R. Eckert, "Apigenine inhibition of involucrin gene expression is associated with a specific reduction in phosphorylation of protein kinase C δ Tyr 311", *J Biol chem.* , 281 (47), pp. 361- 6, 2006 Nov.
- [23] B. Nickavar, Gh. Amin, N. Mehregan, "Quercetin Major flavonol Aglycon from *Tanacetum balsamita* L." *Iranian Jour of pharmaceut Res.*, pp. 246-250, 2003.
- [24] AA. Hamdy, MA. Ibrahem, "Management of aphthous ulceration with topical quercetin: a randomized clinical trial", *J Contemp Dent Pract.*, 11 (4), pp. E009 – 16, Jul 1 2010.
- [25] CQ. da Rocha, FC Vilela, GP. Cavalcante, L. Santos – e – Silva, MH dos Santos, A.Giusti – Paiva, "Anti – inflammatory and antinociceptive effects of *Arrabidaeabrachypoda* (DC) Bureau root", *J Ethnopharmacol.*, 133 (2) , pp. 396–401, 2011
- [26] AW. Filho, VC Filho, L.Olinger , MM. de Souza, "Quercetin : Further investigation of its antinociceptive properties and mechanisms of action", *Arc Pharm Res.* , 31 (6), 713-21, Jun. 2008.

- [27] DA. Valerio, SR. Georgetti, DA Magro, R.Casagrande, TM.Cunha , FT. Vicentini , SM.Vieira, Mj. Fonseca, SH. Ferreira, FQ.Cunha, WA. Verri, "Quercetin reduces inflammatory pain: inhibition of oxidative stress and cytokine production", *J Nat Prod.* , 72 (11), 1975 – 9, Nov 2009.
- [28] H. Matsuno, H. Nakamura, K. Katayama, S. Hayashi, S. kano, K. Yudoh, Y.Kiso, "Effects of an oral administration of glucosamine – chondroitin – quercetinglucoside on the synovial fluid properties in patients with osteoarthritis and rheumatoid arthritis", *BiosciBiotechnolBiochem.*, 73 (2) , pp. 288 – 92 , Feb 2009.
- [29] K..H Can Baser, B. Demirci, N. Tabanca, T. Ozek, N. Goren, "Composition of the essential oil of *Tanacetum armenum* (DC.) Schultz Bip., var. *chiliophyllum* and *T. haradjani*(Rech. Fil.) Grierson and the enantiomeric distribution of camphor and carvone", *Flavour and Fragrance journal*, 16(3), pp. 195-200, 2001.
- [30] JC. Goncalves, F.S. Oliveira, RB. Benedito, DP. de Sousa, RN. de Almeida, DA.de Araujo, "Antinociceptive activity of (-)- carvone: evidence of association with decreased peripheral nerve excitability", *Biol Pharm Bull*, 31(5), pp. 1017-20, 2008.
- [31] R. de cassia da Silveira e Sa, L.N. Andrade, D.P. de Sousa, "A review on anti-inflammatory activity of monoterpenes", *Molecules*, 18, pp 1227-1254, 2013.