

Review article

Foniculum vulgare: review of pharmaceutical features

Hossein Zarei Amand¹, Zaman Vahidi Rad², Mahsa Vahidi Rad³, Marzieh Eneam⁴, Mehdi Vahidi Rad², Amir Hossein Vahidi Rad².

1-Coronary Care Unit, Department of Cardiology, Sari, Iran

2- General Hospital, Sari, Iran.

3- Clinical Psychologist, Sari, Iran

4- Marine Biotechnology, Sari, Iran

Corresponding author: Hossein Zarei Amand

Email: zareiamand.hossein@yahoo.com

Abstract

Human kind has used the herbal plants to treat lots of diseases since a long time ago and there was always a very close connection between people and plants due to the development of all the societies and they were used to treat different diseases in eastern Asia, India, China and Iran since a thousand years ago. This plant height is one to two meters and has some leaves with separated and narrow laminas. This plant has some estrogenic, anti-inflammatory and antioxidant effects and traditionally is used to treat infertile women. Its specific combinations are Anethole, limonene and fenchone. Its properties are: pharmaceutical effect on the treatment of the initial dysmenorrhea, testis growth, excretion channel and Prostate glands, mammary gland weight gain, fallopian tubes, ovaries, endometrium, myometrium protective effect on the liver by reducing Liver enzymes and bilirubin, have estrogenic effects in increasing the milk secretion, early periods, ease at birth and increased libido and anti hyper tension effects through the diuretic and natriuretic effects.

Keywords: : Herbal, Medicine, Foniculum Vulgare

Introduction

On one hand, herbal plants are considered as the potential sources of the creation and they could have specific positions in pharmaceutical and medicinal items, nutritional industry, cosmetic and hygienic industry and specially in the economical items without depending on oil (1). Now herbal plants have dedicated 20 percents of the pharmaceutical prescription in developed countries and 80 percents of developing countries (2). According to the analysis of the international exchange center, approximately 400 plant species are used in the western Europe. United States is the biggest market of world herbal plants and Japan is the biggest importer of them in Asia (3). Also there is a long antecedent of using this plant in Iran (4).
History: effects: increasing milk secretion, stomach empowering, period stimulator and diuretic and good for eyes and using it in foods which is mentioned by Dioscorid, Pelin and Galenus. In century 5th, attributed some lenitive effects and in

centuries 9 to 14 attributed various pharmaceutical properties to it and also considered it effective in the psychological diseases treatment (5). Its pharmaceutical usages entered a new level after century 18 and it has been analyzed till now. This plant has some positive effects and is able to treat some pains like liver or digestive ones in newborns.

In the traditional medicine, used this plant to empower the stomach, appetite, relaxation, stomachache, heart situation, milk secretion increasing and carminative (8). In investigations there are lots of properties mentioned for this plant. The emulsion effect of its oil is able to treat kidney or digestive pains for newborns (6), pharmaceutical effect on the treatment of the initial Dysmenorrhea (7), hypertension reduction (9), testis growth, excretion channel and Prostate glands, mammary gland weight gain, fallopian tubes, ovaries, endometrium,

myometrium ,ciproflaxecin absorption increase(10) and average life increase of it(11) ,low amount of death caused by the chronic and intense poisoning of it (12),protective effect on the liver by reducing Liver enzymes and bilirubin and AST,ALT ,ALKP(13), have estrogenic effects in increasing the milk secretion, early periods, ease at birth and increased libido (14)and anti hyper tension effects through the diuretic and natriuretic(15) effects which were mentioned before . .This plant height is one to two meters and has some leaves with separated and narrow laminas and it's leaves appearance are similar to dill ,but is so aromatic and it's flower is as the compound umbrella ,it's fruit height is 6 to 12 meters abs it's width is 2 to 4 Mm and is aromatic ,it's root is dense and white and is aromatic ,it's leaf is green and is separated from the plant after the complete grow and is used that way .It's seed is narrow and long and oval shape and it' s size is different depending on the plants grow .It's level is light green and in some samples yellow and lighter ,striate and without wool ,it's taste is sweet and it's odor is average and it's fresh one is inappropriate and(16) is planted vastly in Europe specially Mediterranean and warm places (16)and is observed in sea shores and humid places of England and Wiles and also it exists in northern places and different places close to Alborz .(17)

Foniculum vulgare fruit

It's fruit has 10 to 12 percents of the oil substance ,little of sugar substance of mucilage and essence and also has some Phenol effects which is the main pharmaceutical property ,it's specific combinations are Anethole, limonene and Fenchone and it is the best source to extract trace anthole(18) ,also it has some phenol odors and trace anthole is the most important combination of this plant and the existence of these substances is more in the fruit of this plant in comparison with other parts and the best part to extract it ,is the fruit of that .(5)

Extract of Foniculum vulgare

According to past studies ,the extract of this plant decreases the hypertension through serotonergic receptors and histamine antagonist inhibition (19)and this system relieves pain .For example ,delicate and small stimulation in the brain stem in the pain relieving nuclear causes the Serotonin 5-hydroxy-tryptamine in the posterior horn of the spinal cord to increase .Also it is clear that serotonin exists in the Terminals of the posterior horn, and the horn cells Mediolateral column Anterior spinal cord. Serotonin exists combining with different peptides like leu- enkephalin, somatostatin depending on Calcitonin gene and GABA neurotransmitters and it can indirectly

relieve pain and it is proved that Serotonergic system can decrease the pain transformation through GBA neurotransmitters and there are at least three types of Serotonin the Posterior horn of the spinal cord ,though the role of these receptors in pain relief is not still clear but the Serotonin inner brain injection results in the pain relief in tail flick and hot plate tests and formalin test in rats (12).According to the results of previous studies regarding the hypertension decrease through serotonergic and histaminergic receptors and their role in pain relief ,it seems that this plant is able to relieve the pain through mentioned receptors but more investigation is needed .

There are two phases in Formalin test which is the most common test to analyze intense and chronic pain in laboratory and it's chronic phase regards norogenic pains and the pain of the chronic phase is due to the inflammation of Formalin injection and it empowers the assumption saying that the extract of this plant has the environmental neural system and analgesic effects . It's seed has 10 to 12 percents of the oil substance ,little of sugar substance of mucilage and 4 to 6 percents of essence(20) and also has some flavonids ,vitamins and mineral substances (21),it's specific combinations are Anethole, limonene and Fenchone and it is the best source to extract trace anthole .(22)

It's pharmaceutical properties are :initial dysmenorrhoea reduction (23),relief of norogenic and inflammatory pains(24) ,antioxidants (25)and antidiabetic activities (26),hypertension and blood cholesterol reduction(9) and antibacterial properties (27).Also the alcoholic extract of it's seed decreases the Epididymis weight and mature rat sperms(29) ,also according to the investigations regarding this plant , (25)Palmitic acid and systrole of it have some endrogonic properties .

Veterinary

The powder of this plant has some internal and external usages and it is included in appetizers ,digestive and milk increasing ones which is given to goats and horned animals .ranchers of Fars province added a little of Wheat flour, corn flour, fennel and cumin powder to the water in order to improve it's quality (taste and odor)and quality of their milks and combined it and fed them with this several times during the milking period of them .Another form to improve the quality and quantity of their milk in the mentioned region was feeding them with a combination of meatball fennels and cumin and sugar .Now a days the effect of cumin and this plants in the milk increase in proved and they are used in the nutritional industries in order to make milk increasing drops .(30)

Pain relief

According to studies of other investigators ,this plant includes some combinations like Velatyl oil (including Anatole, Astragal,Fenchun), flavonoids (rutin, quercetin, kaempferol glucoside) coumarin, sterols and sugar and some of them other effective in pain relief(13,31,32) .Some of the flavonoids like Kaempferol and quercetin avoid mRNA of Cox -2 to be translated and then they avoid the synthesis of prostaglandins E and inflammation .(33)

Kaempferol has avoiding roles in the phospholipase A 2 (34)and also avoids the induction nitric oxide in macrophase (35).Since nitric acid could be a painful interface ,it's reduction results in analgesic activities .Flavonoids are analgesic and anti inflammation and they have direct effect on prostaglandin synthesis .(36)

According to some other studies ,Flavonoids decrease the calcium of cell inner receptors through the inhibition of D methyl N spartat and after that the activity of nitric oxide enzyme and phospholypaze A 2 dependent on calcium is decreased and shows it's analgesic properties by NO and Prostaglandin reduction (37,48,13).The inhibition of phospholipase A2 activity inhibits the oshopathic acid conversion into arachidonic acid and then the synthesis of prostaglandins is ceased .According to observations ,flanotoinds inhibits the production of prostaglandins from arachidonic acid responding to the inflammatory simulators through the inhibition of ycloxygenase .(43)

The secondary mechanism of this plant is related to the spasmolytic property of it which is due to the structural similarity of anthol and Dopamine which connects with dopamine receptors and relieves pain .(38,6)

Anti microbial effects

The scientific investigation procedure to the natural sources is very common in recent centuries due to the pharmaceutical resistance and side effects of chemical antibacterial drugs and the antibacterial effects of different plants is proved in different investigations .(49)

According to an investigation in Turkey ,the most antibacterial effect of this plant essence is observed on golden staphylococcus .In another investigation in Portugal ,there are just a few investigations regarding the essence of this plant (51).In another study about it's essence in Turkey ,the antimicrobial activity of it is not much (52).In another report on various plants ,the antibacterial effect of this plant was observed for bacillus cereus .(53)

There was a study regarding the effect of this plant on ten different bacteria and it's effect was positive on the growth inhibition of golden staphylococcus

and bacillus cereus and it's effect on Escherichia coli was negative(54) .In another study in India ,the blue extract of this plant could inhibit the growth of staphylococcus ,Escherichia coli and S ,typhi and among them the golden staphylococcus is effected the most (55).In another study regarding the blue extract of this plant with three different methods of extracting ,provided extracts with water and hot water showed the same results as before ,but there was no effect of the inhibition growth on MIC microorganism .According to the analysis of tube on the aquatic and Estonia of this plant was 60 ,30 and 60 MG for staphylococcus ,Escherichia coli and S,typhi (56).In another study regarding the effect of the extract of it's seed on 15 microorganisms like staphylococcus ,Escherichia coli and S,thypi ,there was no growth inhibition sign (57)and in another study the antibacterial effect of Estonia and methanol extracts was analyzed on various microorganisms and there was the growth inhibition in bacillus cereus (53).These results show the effect of the plant growth region and the extract type which causes the difference of extracts .

Some recent studies evaluated Chemical ingredientds, Antioxidant, antibacterial impacts and mechanism of action of essential oil from seeds of fennel (*Foeniculum vulgare* Mill.) (58,59,60)

Phytoestrogen

Lygnan is a plant rich of phytoestrogen (61)and it is used to treat pains of dysmenorrhea and digestive ones(7) ,also it effects testis and the weight of mammary glands (10)and treat osteoporosis (62)and hirsutism (63),which shows that this plant is used as the estrogenic factor .Also according to previous studies ,estrogens and phytoestrogens are anti-anxiety (64)and fennel has phytoestrogen too .(61)

Conclusion

Ethnobotanical studies reported the way of applications, where to prescribe and when for *Foeniculum vulgare*.(64-73) we concluded that it has antimicrobial, anti-inflammatory, antinociceptive, reducing dysmenorrhea, osteoporosis, hirsutism, antispasmodic, hypoglycemic, hypolipidemic, and memory enhancing characteristics. Therefore using *Foeniculum vulgare* as a supplementary agent is considerable.

References

1.Hassan Habibi . Study of new perspectives of the world's medicinal plants . Tehran : College of Agriculture , Tehran University, 1382, page 132 .

2. Samsamshariat samsam . Extraction and exploration of medicinal plants and methods of identifying and evaluating them. Printing of Publication Mani , 1371 , pp : 54-14 .
3. Hans flock . Medicinal plants . Translator Reza Tavakkoli Saberi and the doctor Mohammad Reza integrity. Third Edition , Tehran: the day Behan , 1368, Pages: 10 8 .
- 4 MR Heidari , M. darban . To evaluate the analgesic effect of *Melissa officinalis* extract Tail-flick test in mice. *Journal of Physiology and Pharmacology* , Vol . 3, No. 1 , Winter 77 , Pages 87-81
- 5.zargari Ali . The second edition of Volume II of Medicinal Plants , Tehran, Tehran University Press . 1365, Pages: 115-113
6. Alexandrovich I, Rakovitskaya O, Kolmo E, Sidorova T, Shushunov S. The effect of fennel (*Foeniculum Vulgare*) seed oil emulsion in infantile colic: a randomized, placebo-controlled study. *Altern Ther Health Med* 2003; 9(4): 58-61.
7. Namavar Jahromi B, Tartifizadeh A, Khabnadideh S. Comparison of fennel and mefenamic acid for the treatment of primary dysmenorrhea. *Int J Gynaecol Obstet* 2003; 80(2): 153-7.
- 8.amyry ardekani , Muhammad . (1385). The use of medicinal plants in the health of livestock and poultry . Print Razavi
9. Abdul-Ghani AS, Amin R. The vascular action of aqueous extracts of *Foeniculum vulgare*. *J Ethnopharmacol* 1988; 24(2-3): 213-8.
10. Malini T, Vanithakumari G, Megala N, Anusya S, Devi K, Elango V. Effect of *Foeniculum vulgare* Mill: seed extract on the genital organs of male and female rats. *Indian J Physiol Pharmacol* 1985; 29(1): 21-6.
11. Zhu M, Wong PY, Li RC. Effect of oral administration of fennel (*Foeniculum vulgare*) on ciprofloxacin absorption and disposition in the rat. *J Pharm Pharmacol* 1999; 51(12): 1391-6.
12. Shah AH, Qureshi S, Ageel AM. Toxicity studies in mice of ethanol extracts of *Foeniculum vulgare* fruit and *Ruta chalepensis* aerial parts. *J Ethnopharmacol* 1991; 34(2-3): 167-72.
13. Ozbek H, Ugras S, Dulger H, Bayram I, Tuncer I, Ozturk G, and et al. Hepatoprotective effect of *Foeniculum vulgare* essential oil. *Fitoterapia* 2003; 74(3): 317-9.
14. Albert-Puleo M. Fennel and anise as estrogenic agents. *J Ethnopharmacol* 1980; 2(4): 337-44.
15. El Bardai S, Lyoussi B, Wibo M, Morel N. Pharmacological evidence of hypotensive activity of *Marrubium vulgare* and *Foeniculum vulgare* in spontaneously hypertensive rat. *Clin Exp Hypertens* 2001; 23(4): 329-43.
- 16.zargari Ali . The fifth edition of Volume II of Medicinal Plants , Tehran, Tehran University Press . 1370,
- 17.Fakuk Ah, M. Tavakkoli Saberi , sedaghat m . Medicinal Plants. Third edition. Roozbehan publications . 1368
- 18.Sefifkan f F . Quantitative and qualitative investigation of fennel *Foeniculum vulgar* in various stages of development , research of medicinal and aromatic plants , No. 10, Publication No. 270 , 1380 , pp : 104-85 .
- 19.Shahin Akhondzadeh . Encyclopedia of Medicinal Plants , Vol. 1 , Tehran: the almighty , 1379 , page 52
20. zargari Ali . The fifth edition of Volume II of Medicinal Plants , Tehran, Tehran University Press . 1370
- 21.Hadjiakhoondi AS , are eloquent . Practical Guideline medicinal plants . First Edition. Publication of Islamic Azad University . 1381
- 22Sefid kan f . Qualitative and quantitative study of fennel at different growth stages . *Foeniculum vulgare* medicinal plant research and - Aromatic Iran. # 10 . Publication No. 1380. 104 Page 85
- 23- Khorshidi .N.(2003)..Cilincal effects of essential oil on primary dysmenorhea , *Iranian J Pharmaceut Sci.*;2:82-93
- 24.Taherid AS , Dehghanian M, and Fayy A. Sadeghi H, Mila Georgian H.asr aqueous extract of fennel on neurogenic pain and inflammatory pain . *Journal of Medical Sciences* No. 2.1386
- 25 - Choi EM, Hwang JK (2004) ., Antiinflammatory, analgesic and antioxidant activities of the fruit of *foeniculum vulgare* ., *Fitoterapia.*,75(6): 557-65
- 26- Essway, G.S., Sobbhay,H.M., El- Banna,H.A . (1995)., The hypoglycemia effects of volatile oil of some Egyptian plants., *Vet. Med . J. Giza*, 43(2):167-172

- 27- Tanira,M., Shah,A.H., Mohsin, A.,Ageel,A.M.& Qureshi,S.(1996)., Pharmacological and toxicological investigation on *Foeniculum vulgare* dried fruit extract in experimental animals., *Phytother.Res.*,10(1):33-36
- 28- Joshi H, Parle M .(2006).,Cholinergic basis of memory – strengthening effect of *foeniculum vulgare* linn.,*J. Med Food.*,9(3):413-7
- 29.myrsyd S. F, Shiro AS , the Nosratabadi Heidari . Effect) intraperitoneal injection of alcoholic extract of fennel seed
- The hormones gonadotropins and testosterone (male Wistar rats . *Journal - Research Environment Animal studies* . 1. Autumn 87 .danshgah Islamic Azad .
- .30.Amin , Reza and parsley , Ahmed . (1387) . Cumin. Isfahan Province Agricultural Jihad Organization .
- 31- Mehmet O, Yagiz U, Mehmet G. Comparison of the effects of specific and nonspecific inhibition of nitric oxide synthase on morphine analgesia, tolerance and dependence in mice. *Life Sci*, 2003; 72: 1943- 57.
- 32- Diaz-Maroto MC, Diaz-Maroto Hidalgo IJ, Sanchez-Palomo E, Perez-Coello MS. Volatile components and key odorants of fennel (*Foeniculum vulgare* Mill.) and thyme (*Thymus vulgaris* L.) oil extracts obtained by simultaneous distillation extraction and supercritical fluid extraction. *J Agric Food Chem* 2005; **53**: 5385-5389.
- 33- OLeary KA, de Pascual-Tereasa S, Needs PW, Bao YP, OBrien NM, Williamson G. Effect of flavonoids and vitamin E on cyclooxygenase-2 (COX-2) transcription. *Mutat Res* 2004;551:245-54
- 34- Gil B, Sanz MJ, Terencio M, Ferrandiz ML, Bustos G, Paya M, et al. Effects of flavonoids on *Naja naja* and human recombinant synovial phospholipase A2 and inflammatory responses in mice. *Life Sci* 1994;54:333-38.
- 35- Liang YC, Huang YT, Tsai SH, Lin-Shiau SY, Chen CF, Lin JK. Suppression of inducible cyclooxygenase and inducible nitric oxide synthase by apigenin and related flavonoids in mouse macrophages. *Carcinogenesis* 1999;20:1945-52.
- 36- Alcaraz MG, Houli RS. Action of flavonoids and the novel anti-inflammatory flavone, Hyperlactin-8-Glucoside, on prostaglandin biosynthesis and inactivation. *Biochem pharmacol*, 1985; 34(14):2477-82.
- 37- Davidson EM, Coggeshal RE, Carlton SM. Peripheral NMDA and non-NMDA glutamate receptors contribute to nociceptive behaviors in the rat formalin test. *Neuroreport*. 1997; 8(4): 641-6.
- 38- Decherney A.H. Current obstetrics & gynecologic diagnosis & treatment. 9th Edition. New York. Mc Grow-Hill. 2003;pp:342.
- 39- Elisabetsky E, Amador TA, Albuquerque RR, Nunes DS, Carvalho Ado C. Analgesic activity of *Psychotria colorata*(Willd.ex R.& s.) Muell. Arg. Alkaloids. *J Ethnopharmacol*, 1995; 48(2): 77-83.
- 40- Goldman L, Bennett JC. *Cecil textbook of medicine*. Vol 1. 21th Ed. WB SaundersCo. 2000;p: 103.
- 41- Khotib J , Narita M, Suzuki M, Yajima Y, Suzuki T. Functional interaction among opioid receptor types: up regulation of mu and delta- opioid receptor functions after repeated stimulation of kappa-opioid receptors. *Neuro pharmacology*, 2004, 46(4): 531-40.
- 42- Koster R., Anderson M. and E. J. de Beer EJ De. Acetic acid for analgesic screening. *Fed Pro* 1959;18: 412.
- 43 - Kupeli E, tatli LL, Akdemir ZS, Yesilada E. Estimation of antinociceptive and anti-inflammatory activity on *Geranium pretense* subsp. *Finitinum* and its phenolic compounds.*J Ethno Pharmacology*, 2007; 114(2): 234-40.
- 44- Lanni C, Becker EL. Inhibition of neutrophil phospholipase A2 by p-bromophenylacetyl bromide, nordihydroguaiaretic acid, 5,8,11,14-eicosatetraenoic acid and quercetin. *Int Arch Allergy Appl Immunol* 1985;76:214-17.
- 45- Martino, E., Ramaiola, I., Urbano, M., Bracco, F., Collin, S.,. Microwave-Assisted

Extraction of Coumarin and Related Compounds from *Melilotus Officinalis* (L) Pallas as an Alternative to Soxhlet and Ultrasound-Assisted Extraction. *J Chromatography A* 2006; 1125,147–151.

46- Mimica-Dukic N, Kujundzic S, Sokovic M, Couladis M. Essential oil composition and

antifungal activity of *Foeniculum vulgare* Mill obtained by different distillation

conditions. *Phytother Res* 2003; 17: 368-371.

47- Piccaglia R, Marotti M. Characterization of some Italian types of wild fennel (*Foeniculum vulgare* Mill.). *J Agric Food Chem* 2001; 49: 239-244.

48- Rang HO, Date MM, Ritter JM. Text book of Pharmacology. 3d ed, New York, Churchill, Livingstone. 1999; 148-76, 609-33.

49. Morteza-Semnani K, Saeedi M, Mahdavi MR, Rahimi F. Antibacterial studies on extracts of three species of *Phlomis*, *Pharm Biol* 2006; 44 (6): 426-429.

50. Soyulu S, Soyulu EM, Evrendilek GA. Chemical composition and antibacterial activity of essential oils of bitter fennel (*Foeniculum vulgare*) and dill (*Anethum graveolens*) against the growth of food-borne and seed-born pathogenic bacteria. *Italian J Food Sci* 2009; 21(3): 347-355.

51. Miguel MG, Cruz C, Faleiro L, Simoes MT, Figueiredo AC, Barroso JG, et al. *Foeniculum vulgare* essential oils: chemical composition, antioxidant and antimicrobial activities. *Natur Prod Commun* 2010; 5(1): 319-328.

52. Sagdic O, Yasar S, Kisioglu AN. Antibacterial effects of single or combined plant extracts. *Annal Microbiol* 2005; 55(1): 67-71.

53. Alzoreky NS, Nakahara K. Antibacterial activity of extracts from some edible plants commonly consumed in Asia. *Int J Food Microbiol* 2003; 80: 223-230.

54. Shahidi Bonjar GH. Antibacterial screening of plants used in Iranian folkloric medicine. *Fitoterapia* 2004; 75(2): 231-235.

55. Arora DS, Kaur GJ. Antibacterial activity of some Indian medicinal plants. *J Nat Med* 2007; 61(3): 313-317.

56. Kaur GJ, Arora DS. Antibacterial and phytochemical screening of *Anethum graveolens*,

Foeniculum vulgare and *Trachyspermum ammi*. *BMC Complement Alternat Med* 2009; 9(30): 1-10.

57. Sagdic O, Ozcan M. Antibacterial activity of Turkish spice hydrosols. *Food Contr* 2003; 14(3): 141-143.

58. Diao W, Hu Q, Zhang H, Xu J. Chemical composition, antibacterial activity and mechanism of action of essential oil from seeds of fennel (*Foeniculum vulgare* Mill.) *Food Control*. 2014;35(1):109–116.

59. Roby MHH, Sarhan MA, Selim KA, Khalel KI. Antioxidant and antimicrobial activities of essential oil and extracts of fennel (*Foeniculum vulgare* L.) and chamomile (*Matricaria chamomilla* L.) *Industrial Crops and Products*. 2013;44:437–445.

60. Senatore F, Oliviero F, Scandolera E, et al. Chemical composition, antimicrobial and antioxidant activities of anethole-rich oil from leaves of selected varieties of fennel [*Foeniculum vulgare* Mill. ssp. *vulgare* var. *azoricum* (Mill.) Thell] *Fitoterapia*. 2013;90:214–219.

[61] Thompson L U, Robb P, Serraino M, Mammalian lignin production from various foods. *Nutr Cancer* 16 (1991) 43-52.

[62] Jaffary F, Ghannadi A, Najafzadeh H, Evaluation of the Prophylactic Effect of Fennel Essential Oil on

Experimental Osteoporosis Model in Rats. *Int J Pharmacol* 2 (2006) 588-592.

[63] Javidnia K, Dastgheib L, Mohammadi Samani S, Nasiri A, Antihirsutism activity of Fennel (*Fruits of Foeniculum vulgare*) extract, A double – blind placebo controlled study. *Phytomedicine* 10 (2003) 455-8.

[64] Lund T D, Lephart E D, Dietary soy phytoestrogens produce anxiolytic effect in the elevated plus-maze. *Brain Res* 913 (2001) 180-184.

65. Ghorbani A. Studies on pharmaceutical ethnobotany in the region of Turkmen Sahra, north of Iran (part 1): general results. *Journal of Ethnopharmacology*. 2005;102(1):58–68. [PubMed]

66. Jabbar A, Raza MA, Iqbal Z, Khan MN. An inventory of the ethnobotanicals used as anthelmintics in the Southern Punjab (Pakistan) *Journal of Ethnopharmacology*. 2006;108(1):152–154. [PubMed]

67. Jain A, Katewa SS, Galav PK, Nag A. Unrecorded ethnomedicinal uses of biodiversity from Tadgarh-Raoli wildlife sanctuary. *Acta Botanica Yunnanica*. 2007;29(3):337–344.
68. Wyk VBE. A review of Khoi-San and Cape Dutch medical ethnobotany. *Journal of Ethnopharmacology*. 2008;119(3):331–341. [[PubMed](#)]
69. Neves JM, Matos C, Moutinho C, Queiroz G, Gomes LR. Ethnopharmacological notes about ancient uses of medicinal plants in Trás-os-Montes (northern of Portugal) *Journal of Ethnopharmacology*. 2009;124(2):270–283. [[PubMed](#)]
70. Benítez G, González-Tejero MR, Molero-Mesa J. Pharmaceutical ethnobotany in the western part of Granada province (southern Spain): ethnopharmacological synthesis. *Journal of Ethnopharmacology*. 2010;129(1):87–105. [[PubMed](#)]
71. Savo V, Giulia C, Maria GP, David R. Folk phytotherapy of the Amalfi Coast (Campania, Southern Italy) *Journal of Ethnopharmacology*. 2011;135(2):376–392. [[PubMed](#)]
72. Oliveira SGD, de Moura FRR, Demarco FF, Nascente PDS, Pino FABD, Lund RG. An ethnomedicinal survey on phytotherapy with professionals and patients from Basic Care Units in the Brazilian Unified Health System. *Journal of Ethnopharmacology*. 2012;140(2):428–437. [[PubMed](#)]
73. Guarrera PM, Savo V. Perceived health properties of wild and cultivated food plants in local and popular traditions of Italy: a review. *Journal of Ethnopharmacology*. 2013;146(3):659–680. [[PubMed](#)]