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THE FIRST TRULY INDEPENDENT WATCHDOG FOR THOSE WORKING WITH NATURAL AROMATIC MATERIALS

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Fennel Oil Bibliography.

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Contents

Cropwatch notes. Fennel plants can be divided into a number of subspecies, and then further into a number of varieties of these subspecies. Due to the tendency to hybridise, the varieties can be difficult to properly identify. Garden Fennel *Foeniculum vulgare* ssp. *capillaceum* is a cultivated vegetable variety of Ass's Fennel *Foeniculum vulgare* ssp. *piperitum*. A commercial essential oil is prepared from the steam distillation of crushed seeds of bitter fennel *Foeniculum vulgare* (Mill.) ssp. *capillaceum* Gilib var. *vulgare* (Mill.) Thell., and it is this essential oil which is official in the European Pharmacopoeia. A second essential oil, fennel oil sweet is prepared by steam distillation from the crushed seeds of *Foeniculum vulgare* (Mill.) *ssp. capillaceum* Gilib var. *dulce*. The odour profile of bitter fennel oil includes a camphoraceous aspect, which makes the oil less commercially valuable, although in practice, the 'bitter' oil is frequently traded as the 'sweet' oil. The oil quality of bitter fennel oil is dependent on *trans*-anethole content, which can vary according to genotype and ontogenetic stage of the plant (Lawrence 1985). The bitter taste of bitter fennel is put down to the (+)-fenchone content. This can vary from 0 to 22%, but is usually in the range 4-12%, weighted more towards the lower figures (the above taken from T. Burfield (2000) *Natural aromatic Materials Odours & Origins*).

Biocidal activity of fennel oil.

Elgayyar M., Draughon F.A., Golden D.A.& Mount J.R. (2001) "Antimicrobial activity of essential oils from plants against selected pathogenic and saprophytic microorganisms." *J Food Prot.* **64**(7), 1019-24. Abstract. The beneficial health effects of extracts from many types of plants that are used as seasoning agents in foods and beverages have been claimed for centuries. The purpose of this study was to examine the effectiveness of selected herb and spice essential oils for control of growth and survival of microorganisms. Inhibition of growth was tested by the paper disc agar diffusion method. Antibiotic susceptibility discs were used as control. Minimum lethal concentration (MLC) was determined by the tube dilution method. Essential oils from anise,

angelica, basil, carrot, celery, cardamom, coriander, dill weed, fennel, oregano, parsley, and rosemary were evaluated. Inhibition ranged from complete with oregano to no inhibition with carrot oil for each of the test strains that included: *Listeria monocytogenes*, *Staphylococcus aureus*, *Escherichia coli* O:157:H7, *Yersinia enterocolitica*, *Pseudomonas aeruginosa*, *Lactobacillus plantarum*, *Aspergillus niger*, *Geotrichum*, and *Rhodotorula.* Oregano essential oil showed the greatest inhibition (zone, > or = 70 to 80 mm) (MLC, approximately 8 ppm). Coriander and basil were also highly inhibitory (MLC, approximately 25 to 50 ppm) to *E. coli* O:157:H7 and to the other bacteria and fungi tested. Anise oil was not particularly inhibitory to bacteria (inhibition zone, approximately 25 mm); however, anise oil was highly inhibitory to molds. Because some of the herbal and spice essential oils are highly inhibitory to selected pathogenic and spoilage microorganisms, they may provide alternatives and supplements to conventional antimicrobial additives in foods.

Khaldun A.O. (2006) "[Antibacterial action of ether oils of some plants]" *Zh Mikrobiol Epidemiol Immunobiol.* 2006 May-June (**3**), 92-3. Abstract. Inhibitory effect of clove oil on *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhimurium*, *Shigella dysenteriae* and *Candida albicans* was detected. Mint ether oil had the high antibacterial action on *S. aureus*, however against other microorganisms mint oil had a reliably low effect then clove oil. Fennel oil had high antibacterial effect on *C. albicans*, and bactericidal action on *S. typhimurium* and *S. dysenteriae*.

Kim D.H., Kim S.I., Chang K.S & Ahn Y.J. (2002) “Repellent activity of constituents identified in *Foeniculum vulgare* fruit against *Aedes aegypti* (Diptera: Culicidae).” *J Agric Food Chem* **50**, 6993-6996.

Kim S.I., Chang K.S., Yang Y.C., Kim B.S. & Ahn Y.J. (2004) "Repellency of aerosol and cream products containing fennel oil to mosquitoes under laboratory and field conditions." *Pest Manag Sci*. **60**(11),1125-30. Abstract. The repellency of fennel (*Foeniculum vulgare* Miller)-containing products (5% aerosol and 8% cream) against mosquitoes was compared with those of citronella oil, geranium oil and deet, as well as three commercial repellents, Baby Keeper cream containing IR3535, MeiMei cream containing citronella and geranium oils, and Repellan S aerosol containing 19% N,N-diethyl-m-toluamide (deet) under laboratory and field conditions. In a laboratory study with female *Aedes aegypti* (L), fennel oil exhibited good repellency in a release-in-cage test and repellency in skin and patch tests of the oil was comparable with those of citronella and geranium oils. In paddy field tests with five human volunteers, 5% and 8% fennel oil-containing aerosol and cream produced 84% and 70% repellency, respectively, at 90 min after exposure, whereas Baby Keeper cream and MeiMei cream gave 71% and 57% repellency at 90 min after exposure, respectively, and Repellan S aerosol gave 89% repellency at 210 min. The species and ratio of mosquitoes collected were the genera *Culex* (44.1%), *Anopheles* (42.2%), *Aedes* (7.8%) and *Armigeres* (5.9%). Fennel oil-containing products could be useful for protection from humans and domestic animals from vector-borne diseases and nuisance caused by mosquitoes.

Lee H-S. (2004) “Acaricidal activity of constituents identified in *Foeniculum vulgare* fruit oil against *Dermatophagoides* spp. (Acari: Pyroglyphidae). “ *J Agric Food Chem* **52**(10), 2887-2889. Abstract. Oil derived from *F. vulgare* fruit demonstrated acaricidal activity against *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* (house dust mites). The LD_{50} value for the oil was 119 and 103 mg/m^2 for *D. farinae* and *D. pteronyssinus*, respectively. Twelve volatile compounds were identified from the oil of *Foeniculum* fruits. The main constituents were t*rans*-anethole (53.2%), anisaldehyde (0.7%), β-asarone (0.9%), β-caryophyllene (1.1%), p -cymene (3.1%), estragole (12.7%), (+)– fenchone (14.2%), **d** -limonene (0.7%), 1,5,8- p-menthatriene (0.6%), α-pinene (0.8%), γ-terpinene (0.7%), and thymol (1.4%). The compound most toxic against both species was p -anisaldehyde. Further research is needed to determine any safety issues for the use of *F. vulgare* in humans.

Lee C-H., Sung B-K. & Lee H-S (2006) "Acaricidal activity of fennel seed oils and their main components against *Tyrophagus putrescentiae*, a stored-food mite " *Journal of Stored Products Research* **42**(1), 8-14. Abstract. The acaricidal activities of components derived from *Foeniculum*

vulgare (fennel) seed oils against *Tyrophagus putrescentiae* adults were examined using direct contact application and compared with those of the compounds benzyl benzoate, dibutyl phthalate and N,N-diethyl-m-toluamide. The biologically active constituent of the *F. vulgare* seeds was characterized as (+)-carvone by spectroscopic analyses. On the basis of LD50 values, the compound most toxic to *T. putrescentiae* was naphthalene (4.28 µg/cm2) followed by dihydrocarvone (4.32 µg/cm2), (+)-carvone (4.62 µg/cm2), (–)-carvone (5.23 µg/cm2), eugenol (10.62 µg/cm2), benzyl benzoate (11.24 µg/cm2), thymol (11.42 µg/cm2), dibutyl phthalate (13.11 µg/cm2), N,N-diethyl-m-toluamide (13.53 µg/cm2), methyl eugenol (39.52 µg/cm2), myrcene (39.88 µg/cm2) and acetyleugenol (72.24 µg/cm2). These results indicate that acaricidal activity of the *F. vulgare* seed oil could be caused by carvone and naphthalene of which the former is likely to be more important because it is 74.7 times more abundant than naphthalene. Carvone and naphthalene merit further study as potential stored-food mite control agents or as lead compounds.

Lo Cantore P., Iacobellis N.S., De Marco A., Capasso F. & Senatore F. (2004) "Antibacterial activity of *Coriandrum sativum* L. and *Foeniculum vulgare* Miller var. *vulgare* (Miller) essential oils." *J Agric Food Chem.* **52**(26), 7862-6. Abstract. Essential oils were extracted from the fruits of *Coriandrum sativum* L. and *Foeniculum vulgare* Miller var. *vulgare* (Miller) and assayed in vitro for antibacterial activity to *Escherichia coli* and *Bacillus megaterium,* bacteria routinely used for comparison in the antimicrobial assays, and 27 phytopathogenic bacterial species and two mycopathogenic ones responsible for cultivated mushroom diseases. A significant antibacterial activity, as determined with the agar diffusion method, was shown by *C. sativum* essential oil whereas a much reduced effect was observed for *F. vulgare* var. *vulgare* oil. *C. sativum* and *F. vulgare* var. *vulgare* essential oils may be useful natural bactericides for the control of bacterial diseases of plants and for seed treatment, in particular, in organic agriculture. The significant antibacterial activity of essential oils to the bacterial pathogens of mushrooms appears promising.

Mimica-Dukic N., Kujundi S., Sokovi N. & Couladis M. (2003) "Essential oil composition and antifungal activity of *Foeniculum vulgare* Mill. obtained by different distillation conditions." *Phytotherapy Research* **17**(4), 368 - 371. Abstract. The influence of different hydrodistillation conditions was evaluated from the standpoint of essential oil yield, chemical composition and antifungal activity from seeds of *Foeniculum vulgare* Mill. Three hydrodistillation conditions were considered. The main constituents of the oils were: (E)-anethole (72.27%-74.18%), fenchone (11.32%-16.35%) and methyl chavicol (3.78%-5.29%). The method of distillation significantly effected the essential oil yield and quantitative composition, although the antifungal activity of the oils against some fungi was only slightly altered.

Ozcan MM, Sağdiç O, Ozkan G. (2006) "Inhibitory effects of spice essential oils on the growth of *Bacillus* species." *J Med Food.* **9**(3), 418-21. Abstract. A series of essential oils of 11 Turkish plant spices [black thyme, cumin, fennel (sweet), laurel, marjoram, mint, oregano, pickling herb, sage, savory, and thyme], used in foods mainly for their flavor, aromas, and preservation, in herbal tea, in alternative medicines, and in natural therapies, were screened for antibacterial effects at 1:50, 1:100, 1:250, and 1:500 dilutions by the paper disc diffusion method against six *Bacillus* species (*Bacillus amyloliquefaciens* ATCC 3842, *Bacillus brevis* FMC 3, *Bacillus cereus* FMC 19, *Bacillus megaterium* DSM 32, *Bacillus subtilis* IMG 22, and *B. subtilis* var. *niger* ATCC 10). All of the tested essential oils (except for cumin) showed antibacterial activity against one or more of the *Bacillus* species used in this study. Generally, the essential oils at 1:50 and 1:100 levels were more effective. Only one essential oil (laurel) was not found effective against the tested bacteria. The bacterium most sensitive to all of the spice essential oils was *B. amyloliquefaciens* ATCC 3842. Based on the results of this study, it is likely that essential oils of some spices may be used as antimicrobial agents to prevent the spoilage of food products.

Ozcan M.M., Chalchat J.C., Arslan D., Ateş A. & Unver A. (2006) "Comparative essential oil composition and antifungal effect of bitter fennel (*Foeniculum vulgare* ssp. *piperitum*) fruit oils obtained during different vegetation." *J Med Food.* **9**(4), 552-61. Abstract. The chemical composition of the flower and unripe and ripe fruits from fennel (bitter) (*Foeniculum vulgare* ssp.

piperitum) has been examined by gas chromatography and gas chromatography-mass spectrometry. The main identified components of the flower and unripe and ripe fruit oils were estragole (53.08%, 56.11%, and 61.08%), fenchone (13.53%, 19.18%, and 23.46%), and alpha-phellandrene (5.77%, 3.30%, and 0.72%), respectively. Minor qualitative and major quantitative variations for some compounds of essential oils were determined with respect to the different parts of *F. vulgare*. The oils exerted varying levels of antifungal effects on the experimental mycelial growth of *Alternaria alternata*, *Fusarium oxysporum*, and *Rhizoctonia solani*. The 40 ppm concentrations of fennel oils showed inhibitory effect against mycelial growth of *A. alternaria*, whereas 10 ppm levels were ineffective. The analyses show that fennel oils exhibited different degrees of fungistatic activity depending on the doses.

Ozkan G., O. Sadiç O. & Ozcan M. (2003) "Note: inhibition of pathogenic bacteria by essential oils at different concentrations." *Food Science and Technology International* **9**(2), 85-88. Abstract. The antimicrobial effect of 11 selected Turkish spice essential oils was investigated against seventeen pathogenic bacteria. The antimicrobial activity of the essential oils of six spices (cumin, fennel, laurel, mint, marjoram, oregano, pickling herb, sage, savory, thyme (black) and thyme) was tested at four concentrations (0.2, 0.4, 1 and 2%) on various microorganisms (*E. aerogenes*, *E. coli*, *E. coli O157:H7*, *K. pneumoniae*, *P. vulgaris*, *S. enteritidis*, S*. gallinarum*, *S. typhimurium*, *S. aureus*, *Y. enterocolitica*, *A. hydrophila*, *C. xerosis*, *M. luteus*, *M. smegmatis*, *E. feacalis*, *P. aeruginosa* and *P. fluorescens*). All preparations showed antibacterial activity against at least one or more bacteria. The inhibitory effect of the essential oils was evaluated through paper disc diffusion method. In general, the essential oils at 1 and 2% levels were effective. The most active essential oils were marjoram, thyme and oregano. According to the results, the studied essential oils potentially might be used as antibacterial agents to prevent the spoilage of food products, although further research is needed.

Pitasawat B., Champakaew D., Choochote W., Jitpakdi A., Chaithong U., Kanjanapothi D., Rattanachanpichai E., Tippawangkosol P., Riyong D., Tuetun B. & Chaiyasit D. (2007) "Aromatic plant-derived essential oil: an alternative larvicide for mosquito control." *Fitoterapia*. **78**(3), 205-10. Abstract. Five aromatic plants, *Carum carvi* (caraway), *Apium graveolens* (celery), *Foeniculum vulgare* (fennel), *Zanthoxylum limonella* (mullilam) and *Curcuma zedoaria* (zedoary) were selected for investigating larvicidal potential against mosquito vectors. Two laboratory-reared mosquito species, *Anopheles dirus*, the major malaria vector in Thailand, and *Aedes aegypti*, the main vector of dengue and dengue hemorrhagic fever in urban areas, were used. All of the volatile oils exerted significant larvicidal activity against the two mosquito species after 24-h exposure. Essential oil from mullilam was the most effective against the larvae of *A. aegypti,* while *A. dirus* larvae showed the highest susceptibility to zedoary oil.

Schelz Z, Molnar J, Hohmann J. (2006) "Antimicrobial and antiplasmid activities of essential oils." *Fitoterapia*. **77**(4), 279-85. Abstract. The antimicrobial and antiplasmid activities of essential oils (orange oil, eucalyptus oil, fennel oil, geranium oil, juniper oil, peppermint oil, rosemary oil, purified turpentine oil, thyme oil, Australian tea tree oil) and of menthol, the main component of peppermint oil, were investigated. The antimicrobial activities were determined on the Gram (+) *Staphylococcus epidermidis* and the Gram (-) *Escherichia coli* F'lac K12 LE140, and on two yeast *Saccharomyces cerevisiae* 0425 delta/1 and 0425 52C strains. The antiplasmid activities were investigated on *E. coli* F'lac bacterial strain. Each of the oils exhibited antimicrobial activity and three of them antiplasmid action. The interaction of peppermint oil and menthol with the antibiotics was studied on the same bacterial strain with the checkerboard method. Peppermint oil and menthol displayed additive synergy with oxytetracycline. A new mechanism of plasmid curing was established for one of the oil components.

Singh G, Kapoor IP, Pandey SK, Singh U.K. & Singh R.K. (2002) "Studies on essential oils: part 10; antibacterial activity of volatile oils of some spices." *Phytother Res*.**16**(7), 680-2. Abstract. The essential oils extracted from the seeds of seven spices, *Anethum graveolens*, *Carum capticum*, *Coriandrum sativum*, *Cuminum cyminum*, *Foeniculum vulgare*, *Pimpinella anisum* and *Seseli indicum* have been studied for antibacterial activity against eight pathogenic bacteria, causing

infections in the human body. It has been found that the oil of *C. capticum* is very effective against all tested bacteria. The oil of *C. cyminum* and A. graveolens also gave similar results. These oils are equally or more effective when compared with standard antibiotics, at a very low concentration.

Soylu E.M., Soylu S. & Kurt S. (2006) "Antimicrobial activities of the essential oils of various plants against tomato late blight disease agent *Phytophthora infestans*." *Mycopathologia*. **161**(2), 119-28. Abstract. The aim of this study was to find an alternative to synthetic fungicides currently used in the control of devastating oomycete pathogen *Phytophthora infestans*, causal agent of late blight disease of tomato. Antifungal activities of essential oils obtained from aerial parts of aromatic plants such as oregano (*Origanum syriacum* var. *bevanii*), thyme (*Thymbra spicata* subsp. *spicata*), lavender (*Lavandula stoechas* subsp. *stoechas*), rosemary (*Rosmarinus officinalis*), fennel (*Foeniculum vulgare*), and laurel (*Laurus nobilis*), were investigated against *P. infestans*. Both contact and volatile phase effects of different concentrations of the essential oils used were determined by using two in vitro methods. Chemical compositions of the essential oils were also determined by GC-MS analysis. Major compounds found in essential oils of thyme, oregano, rosemary, lavender, fennel and laurel were carvacrol (37.9%), carvacrol (79.8), borneol (20.4%), camphor (20.2%), anethole (82.8%) and 1,8-cineole (35.5%), respectively. All essential oils were found to inhibit the growth of *P. infestans* in a dose-dependent manner. Volatile phase effect of oregano and thyme oils at 0.3 microg/ml air was found to completely inhibit the growth of *P. infestans*. Complete growth inhibition of pathogen by essential oil of fennel, rosemary, lavender and laurel was, however, observed at 0.4-2.0 microg/ml air concentrations. For the determination of the contact phase effects of the tested essential oils, oregano, thyme and fennel oils at 6.4 microg/ml were found to inhibit the growth of *P. infestans* completely. Essential oils of rosemary, lavender and laurel were inhibitory at relatively higher concentrations (12.8, 25.6, 51.2 microg/ml respectively). Volatile phase effects of essential oils were consistently found to be more effective on fungal growth than contact phase effect. Sporangial production was also inhibited by the essential oil tested. Light and scanning electron microscopic (SEM) observation on pathogen hyphae, exposed to both volatile and contact phase of oil, revealed considerable morphological alterations in hyphae such as cytoplasmic coagulation, vacuolations, hyphal shrivelling and protoplast leakage.

Soylu S., Yigitbas H., Soylu E.M. & Kurt S. (2007) "Antifungal effects of essential oils from oregano and fennel on *Sclerotinia sclerotiorum*." *J Appl Microbiol*. **103**(4),1021-30. Abstract. AIMS: The antifungal effects of essential oils of oregano (*Origanum syriacum* var. *bevanii*) and fennel (*Foeniculum vulgare*) were evaluated against *Sclerotinia sclerotiorum*. Effects of the essential oils on morphological structures of hyphae and sclerotia were studied under light and scanning electron microscopes (SEM). METHODS AND RESULTS: Inhibitory effects of volatile and contact phases of the essential oils used were determined on hyphae and sclerotia. Both essential oils have a marked antifungal effect against *S. sclerotiorum*. Soil amendment with essential oils has significant effect on reducing sclerotial viability. Both essential oils significantly inhibited the fungal growth in soil, thereby increasing the number of surviving tomato seedling by 69.8% and 53.3%, respectively. Light and SEM observations on pathogen hyphae and sclerotia revealed considerable morphological alterations in hyphae and sclerotia. CONCLUSIONS: The significant reduction in the mycelial growth and germination of sclerotia would greatly reduce the pathogen inoculum source. This may influence the rate of disease development in soil. SIGNIFICANCE AND IMPACT OF THE STUDY: Considering the reduction in the number of diseased plants in infested soil amended with essential oils, we concluded that oregano and fennel essential oils could be used as possible bio fungicides alternative to synthetic fungicides against phytopathogenic fungi.

Traboulsi A.F., El-Haj S., Tueni M., Taoubi K., Nader N.A., Mrad A. (2005) "Repellency and toxicity of aromatic plant extracts against the mosquito *Culex pipiens molestus* (Diptera: Culicidae)." *Pest Manag Sci.* **61**(6), 597-604. Abstract. The insecticidal activities of essential oil extracts from leaves, flowers and roots of aromatic plants against fourth-instar larvae of the mosquito *Culex pipiens molestus* Forskal were determined. Extracts of *Foeniculum vulgare* Mill

were the most toxic, followed by those of *Ferula hermonis* Boiss, *Citrus sinensis* Osbeck, *Pinus pinea* L, *Laurus nobilis* L and *Eucalyptus* spp with LC50 values of 24.5, 44.0, 60.0, 75.0, 117.0 and 120.0 mg litre(-1), respectively. Combination tests between the LC50 and the maximum sub-lethal concentration (MSLC) were determined. Over 20 major components were identified in extracts from each plant species tested. Five essential oils and nine pure components were studied for their repellency against mosquito bites. Terpineol and 1,8-cineole were the most effective against *Culex pipiens molestus* bites offering complete protection for 1.6 and 2 h, respectively.

Tuetun B, Choochote W., Kanjanapothi D., Rattanachanpichai E., Chaithong U., Chaiwong P., Jitpakdi A., Tippawangkosol P., Riyong D. & Pitasawat B. (2005) "Repellent properties of celery, *Apium graveolens* L., compared with commercial repellents, against mosquitoes under laboratory and field conditions." *Trop Med Int Health.* **10(**11), 1190-8. Abstract. In our search for new bioactive products against mosquito vectors, we reported the slightly larvicidal and adulticidal potency, but remarkable repellency of *Apium graveolens* both in laboratory and field conditions. Repellency of the ethanolic preparation of hexane-extracted *A. graveolens* was, therefore, investigated and compared with those of 15 commercial mosquito repellents including the most widely used, DEET. Hexane-extracted *A. graveolens* showed a significant degree of repellency in a dose-dependent manner with vanillin added. Ethanolic *A. graveolens* formulations (10-25% with and without vanillin) provided 2-5 h protection against female *Aedes aegypti.* Repellency that derived from the most effective repellent, 25% of hexane-extracted *A. graveolens* with the addition of 5% vanillin, was comparable to the value obtained from 25% of DEET with 5% vanillin added. Moreover, commercial repellents, except formulations of DEET, showed lower repellency than that of *A. graveolens* extract. When applied on human skin under field conditions, the hexane-extracted *A. graveolens* plus 5% vanillin showed a strong repellent action against a wide range of mosquito species belonging to various genera. It had a protective effect against *Aedes gardnerii*, *Aedes lineatopennis*, *Anopheles barbirostris*, *Armigeres subalbatus*, Culex t*ritaeniorhynchus*, Culex gelidus, *Culex vishnui* group and *Mansonia uniformis*. The hexane-extracted *A. graveolens* did not cause a burning sensation or dermal irritation when applied to human skin. No adverse effects were observed on the skin or other parts of the human volunteers' body during 6 months of the study period or in the following 3 months, after which time observations ceased. Therefore, *A. graveolens* can be a potential candidate for use in the development of commercial repellents that may be an alternative to conventional synthetic chemicals, particularly in community vector control applications.

Chemistry of fennel oil.

Akgul, A. (1986). Studies on the essential oils from Turkish fennel seeds (*Foeniculum vulgare* M. var. *dulce*). *Prog. in Essential Oil Res.* Walter de Gruyter & Co., Berlin. p. 487-489

Akgül A, Bayrak A: (1988) “Comparative volatile oil composition of various parts from Turkish bitter fennel (*Foeniculum vulgare* var. *vulgare*).” *Food Chem* **30**, 319-323.

Arslan N., Bayrak A., & Akgul A. (1989). “The yield and components of essential oil in fennels of different origin (*Foeniculum vulgare* Mill.) grown in Ankara conditions.” *Herba Hungarica* **28**(3):27-31.

Ashraf, M. & Bhatty M.K. (1975). “Studies on the essential oils of the Pakistani species of the family Umbelliferae, Part II. *Foeniculum vulgare* M. (Fennel) seed oil.” *Pakistan J. Sci. Ind. Res.* **18**, 236-240.

Baranska M., Schulz H., Rösch P., Strehle M.A. & Popp J. (2004). "Identification of secondary metabolites in medicinal and spice plants by NIR-FT-Raman microspectroscopic mapping." *Analyst* **129**, 926 - 930. Abstract. This paper demonstrates the special potential of vibrational NIR FT Raman microspectroscopy for the study of fennel fruits, chamomile inflorescence and curcuma roots to obtain detailed information about their microstructure and chemical composition. Microscopic Raman maps of fennel fruits demonstrate that anethole, which is the main essential

oil component, is present in the whole mericarp with highest concentration at the top of the fruit. In situ measurements obtained of the essential oil cells are dominated by two bands observed at 1657 cm–1 and 1609 cm–1 which are characteristic for anethole. Raman images of chamomile inflorescence show that spiroethers, identified by significant bands between 2150 and 2250 cm–1, are accumulated in the middle part of the flower head. Due to the intense curcumin bands in the Raman spectrum of curcuma root, the distribution of this dyeing substance can be clearly determined; highest concentration of curcumin was observed on the core of the root.

Bernath J., Nemeth E., Kataa A. & Hethelyi E. (1996). "Morphological and chemical evaluation of fennel (*Foeniculum vulagare* Mill.) populations of different origin." *J. Essent. Oil Res*. **8**,:247-253

Bilia A.R., G. Flamini G.R., Taglioli V., I. Morelli I. & Vincieri F.F. (2002) "GC–MS analysis of essential oil of some commercial Fennel teas." *Food Chemistry* **76**(3),307-310. Abstract. Fennel teas were prepared by classical infusion or microwave decoction of unbroken and crushed fruits, three pre-packaged teabags and two instant teas. Their volatile constituents were obtained by extraction with n-hexane and analysed by gas chromatography (GC) and gas chromatography/mass spectrometry (GC–MS), using two columns with stationary phases of different polarity. Of the constituents 85–95% were identified on the basis of their GC retention times and their mass spectra in relation to authentic compounds. No volatile constituents were detected in one sample of instant tea. Conventional teas from crushed fruits and teas prepared from the other instant tea showed the highest levels of volatile constituents. Anethole (30–90%) and/or anisaldehyde (0.7–51%) were the main constituents of all the samples. Methychavicol (0.8–4.1%), eugenol (1.5–11.3%) and fenchone (0.5–47%) were detected in most samples. Carvone (2.1–6.1%) was presenting only some teabags and camphor (2.3–2.6%) in others. The volatile constituents of only one instant tea included limonene (1.4%) and -terpineol (0.4%).

Charles, D.J. Morales M.R., & Simon J.E. (1993). "Essential oil content and chemical composition of finocchio fennel." p. 570-573. In: J. Janick & J.E. Simon (eds.), *New Crops*. Wiley, New York.

Coelho J.A.P., Pereira A.P., Mendes R.L. & Palavra A.M.F. (2003) "Supercritical carbon dioxide extraction of *Foeniculum vulgare* volatile oil." *Flav. & Frag. J.* **18**(4), 316-319. Abstract. Supercritical fluid extraction (SFE) with CO2 of the volatile oil from fennel (*Foeniculum vulgare* ssp. *piperitum* (Ucria) Coutinho) was carried out at temperatures of 40 and 50 °C and pressures of 90 and 100 bar in a flow apparatus using a two-stage fractional separation technique. The best conditions for extraction (pressure P = 90 bar, and temperature, T = 40 °C) and separation (P = 80 bar, T = -10 °C for the first separator and P = 20 bar, T = -10 °C for the second)were used to assess the effect of different mean particle size and flow rate of CO2. The yield of the extraction and composition of the volatile oil were compared with those obtained by hydrodistillation. The study showed that the particle size of the fruits does not practically affect either the yield or the composition of the oil, with the exception of the presence of a small amount of waxes in the volatile oil extracted by SFE from the fruits presenting the highest particle size. Further, increasing of the flow rate of CO2 does not seem to influence the composition, although it increases the rate of extraction, thus leading to a decrease of the extraction time. The fennel oil was analysed by gas chromatography (GC) and chromatography -mass spectrometry (GC -MS). The main compounds identified in the oils were fenchone (17%), estragol (21%) and (E)-anethole (43%).

Damjanovića B., Lepojevićb Z, Živkovićc V. & Aleksandar Tolić A. (2005) "Extraction of fennel (*Foeniculum vulgare* Mill.) seeds with supercritical CO2: Comparison with hydrodistillation." *Food Chemistry* **92**(1),143-149. Abstract. Ground fennel (*Foeniculum vulgare* Mill.) seeds, growing wild in Montenegro, were extracted with supercritical CO2 (SC-CO2) at a flow rate of 0.2 kg CO2/h under varying extraction conditions in order to determine yield, composition and organoleptic characteristics of extract. The extracts obtained were compared to fennel seed oil isolated by hydrodistillation. In the SC-CO2, extracts as well in the hydrodistilled oil, the major compounds were *trans*-anethole (68.6–75.0%) and (62.0%), methylchavicol (5.09–9.10%) and (4.90%), fenchone (8.40–14.7%) and (20.3%), respectively. With pressure varying from 80 to 150 bar and

temperature varying from 40 to 57 ℃, it was found that, for the selected herb material, the optimal conditions of SC-CO2 extraction (high percentage of trans-anethole, with significant content of fenchone and reduced content of methylchavicol and co-extracted cuticular waxes) are: pressure, 100 bar; temperature, 40 ℃; extraction time, 120 min. Organoleptic tests confirmed that hydrodistilled oil possessed a less intense fennel seed aroma than extracts obtained by SC-CO2.

Damjanovic B., Lepojevic Z Živkovic V. & Tolic A. (2005) "Isolation of essential oil and supercritical carbon dioxide extract of fennel seeds (*Foeniculum vulgare* Mill.) from Montenegro." *Paper presented at 36th International Symposium on Essential Oils, 4-7 September2005, Budapest, Hungary*

Díaz-Maroto M.C. Díaz-Maroto Hidalgo J., Sánchez-Palomo E. & Pérez-Coello M.S (2005) "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.,* **53** (13), 5385 -5389. Abstract. Volatile oil extracts of fennel seeds (*Foeniculum vulgare* Mill.) and thyme leaves (*Thymus vulgaris* L.) were obtained by simultaneous distillation-extraction (SDE) and supercritical fluid extraction (SFE) and analyzed by gas chromatography-mass spectrometry (GC-MS). In general, fennel oil extracted by SDE and SFE showed similar compositions, with *trans*-anethole, estragole, and fenchone as the main components. In contrast, thymol and p-cymene, the most abundant compounds in thyme leaves, showed big differences, with generally higher amounts of monoterpenes obtained by SDE. However, in this case, the differences between the extracts were higher. Key odorants of fennel seeds determined by gas chromatography-olfactometry (GC-O) showed similar patterns when applying SDE and SFE. *trans*-Anethole (anise, licorice), estragole (anise, licorice, sweet), fenchone (mint, camphor, warm), and 1-octen-3-ol (mushroom) were the most intense odor compounds detected in fennel extracts. Thymol and carvacrol, with oregano, thyme, and spicy notes, were identified as key compounds contributing to the aroma of thyme leaves.

Díaz-Maroto MC, Pérez-Coello MS, Esteban J & Sanz J. (2006) "Comparison of the volatile composition of wild fennel samples (*Foeniculum vulgare* Mill.) from central Spain." *J Agric Food Chem*. **54**(18), 6814-8. Abstract. Comparison of the volatile composition of fennel (*Foeniculum vulgare* Mill.) has been carried out using direct thermal desorption (DTD) coupled to gas chromatography-mass spectrometry. Forty-two wild fennel stem samples were collected in two different geographical areas of Central Spain. DTD allowed a high recovery of volatiles from small sample sizes without thermal decomposition. trans-Anethole was the main volatile compound for most cases, although a high variability was found among samples, showing clear phytochemical differences.

Embong M.B., Hadziyer D. & Molnar S. (1977). "Essential oils from spices grown in Alberta. Fennel oil (*Foeniculum vulgare* var. *dulce*)." *Can. J. Plant Sci.* **57,** 829-837.

Ercolan G.L. (1976) "Bacteriological quality assessment of fresh marketed lettuce and fennel." *Appl Environ Microbiol* .**31**(6), 847-852.

Gámiz-Gracia L. & Luque de Castro M.D. (2000) "Continuous subcritical water extraction of medicinal plant essential oil: comparison with conventional techniques." *Talanta* **51**(6), 1179-1185. Abstract. A subcritical extractor equipped with a three-way inlet valve and an on/off outlet valve has been used for performing subcritical water extractions (SWE) in a continuous manner for the isolation of the essential oil of fennel, a medicinal plant. The target compounds were removed from the aqueous extract by a single extraction with 5 ml hexane, determined by gas-chromatography-flame ionization (GC-FID) and identified by mass spectrometry (MS). The proposed extraction method has been compared with both hydrodistillation and dichloromethane manual extraction. Better results have been obtained with the proposed method in terms of rapidity, efficiency, cleanliness and possibility of manipulating the composition of the extract.

Guillén M.D & Manzanos M.J. (1996) "A study of several parts of the plant *Foeniculum vulgare* as a source of compounds with industrial interest ." *Food Research International* **29**(1), 85-88. Abstract. The yield and composition of the volatile fraction of the pentane extracts of leaves, stems and seeds of *Foeniculum vulgare* Mill, have been studied. The yield obtained from seeds was much higher than that obtained from leaves and stems. The volatile fraction of the pentane extract of the latter two has a higher concentration of terpene hydrocarbons and a smaller concentration of oxygenated terpene hydrocarbons than that of the seeds. Sesquiterpenes have been detected in the leaves, as has petroselinic acid in the seeds. Saturated aliphatic hydrocarbons with 25 or more carbon atoms have been found in all of the parts. The pentane extract of the leaves also contains the antioxidant vitamin E. These extracts from different parts of fennel show not only the proportion of their volatile flavour components, but also the concentration of fatty acids and antioxidant compounds (such as vitamin E), if any.

Guenther E. (1948). "Oil of Fennel." *The Essential Oils.* Robert E. Krieger Pub. Co., Inc.

Gupta K., Thakral K.K., Gupta V.K., Arora S.K. (1995) "Metabolic Changes of Biochemical Constituents in Developing Fennel Seeds (*Foeniculum vulgare*)." *J Sci Food Agric* **68**, 73-6.

Iten F, Saller R. (2004) ["Fennel tea: risk assessment of the phytogenic monosubstance estragole in comparison to the natural multicomponent mixture"] *Forsch Komplementarmed Klass Naturheilkd*. **11**(2), 104-8. Abstract. For centuries, fennel fruits have been used as traditional herbal medicine in Europe and China. For the treatment of infants and sucklings suffering from dyspeptic disorders, fennel tea is the drug of first choice. Its administration as a carminativum is practiced in infant care in private homes and in maternity clinics as well where it is highly appreciated for its mild flavor and good tolerance. The long standing positive experience is astonishingly contrasted by a recent statement of the German 'Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin' (BgVV, May 11, 2001), where consumers are advised to reduce their intake of foods containing estragole and methyleugenol, e.g. tarragon, basil, anis, star anis, jamaica pepper, nutmeg, lemon grass as well as bitter and sweet fennel fruits for reasons of health. These warnings are based on experiments with rats and mice where estragole, a natural ingredient of fennel fruits, proved to be carcinogenic. Meanwhile, criticism arose amongst experts concerning the interpretation of these studies. The crucial points of criticism concern the transfer of data obtained in animal models to the human situation as well as the high doses of the applied monosubstance, which do not at all represent the amounts humans are exposed to as consumers of estragole-containing foods and phytopharmaceuticals. Furthermore, studies on estragole metabolism revealed at least quantitative differences between the estragole metabolism of mice and men. In addition, it has been shown that an agent when administered in its isolated form may have significantly different effects and side effects than the same agent applied as a constituent in naturally occurring multicomponent mixtures. Thus, a multicomponent mixture such as fennel tea contains various antioxidants known to be protective against cancer. These differences were not considered in the risk assessment. A well done risk assessment should be based on appropriate data collected in humans. Considering the long traditional use of fennel tea and the total lack of epidemiological and clinical studies indicating a well founded cancerogenic potential, the probability of a serious risk connected with the consumption of fennel tea seems to be negligibly small

Kraus, A. & F.-J. Hammerschmidt F-J (1980). "An investigation of fennel oils." *Dragoco Report* **27**(2), 31.

Karlsen J., Baerheim Svendsen A., Chingova B. & Zolotovitch. G. (1969). "Studies on the fruits of *Foeniculum* species and their essential oil." *Planta Med.* **17**, 281-293.

Katsiotis, S.T. 1988. Study of different parameters influencing the composition of hydrodistilled sweet fennel oil. *Flavour Fragrance J.* **4**, 21-224. Abstract. Different parameters applied in the hydrodistillation of an essential oil not only influences the percentage yield of the oil but also the concentration of each of its constituents. In the present study the simultaneous influence of fennel

oil was investigated using the Latin square method for the experimental programme. The precentage cpmposition of the oil sample was determined by GLC. The results `showed for each oil constituent the mastrix sum combination of the parameters studied. The degree of comminution influenced the composition to a much greater extent than the other two parameters.

Lawrence B.M (1979) “Fennel Oil. Progress in essential oils.” *Perfumer & Flavorist* **4**, 49-55.

Merkes K. (1980) "Drogen mit ätherischem Öl (XVI) *Foeniculum vulgare* Miller-Fenchel." *PTA Repetitorium* **12**, 45-8.

Miraldi E. (2000) "Comparison of the essential oils from ten *Foeniculum vulgare* Miller samples of fruits of different origin." *Flavour & Frag J* **14**(6), 379-382. Abstract. The essential oil contents were determined of 10 samples of dry, ripe fruits of *Foeniculum vulgare* Miller of different origin; the fruits were collected from wild plants or commercial samples. The essential oils isolated by hydrodistillation were analysed by GC-MS; the 16 main constituents of each sample were identified, trans-anethole, estragole, limonene and fenchone being the most abundant. The amounts of trans-anethole and estragole were inversely proportional, so that clear phytochemical differences within the investigated samples were observed.

Misharina T.A. & Polshkov A.N. (2005) "Antioxidant properties of essential oils: autoxidation of essential oils from laurel and fennel and of their mixtures with essential oil from coriander" *Applied Biochemistry and Microbiology* **41**(6), 610-618. Abstract Changes in the composition of essential oils from the seeds of laurel (*Laurus nobilis* L.) and fennel (*Foeniculum vulgare* Mill., var. *dulce* Thelling) and their mixture with essential oil from coriander were studied by capillary gas-liquid chromatography during storage in the dark and in light. Under these conditions, essential oil of laurel retained its composition for 12 months. Essential oil of fennel was rapidly oxidized in light. However, the rate of its oxidation in the dark was lower. The major component of essential oil of fennel, *trans*-anethol, had a lower antioxidant activity than essential oil of coriander. The mixture of essential oils from laurel and coriander possessed antioxidant properties and strongly inhibited the oxidation of components of the fennel oil.

Miura Y, Ogawa K, Fukui H, Tabata M (1986) "Changes in the essential oil components during the development of fennel plants from somatic embryoids."*Planta Med.* 1986, **52**, 95-6.

Ostad S.N , Soodi M , Shariffzadeh M , Khorshidi N. & Marzban H. (2001) “The effect of fennel essential oil on uterine contraction as a model for dysmenorrhea, pharmacology and toxicology study.”. *J Ethnopharmacol .* **76(**3):299-304. Abstract. Increasing the ectopic uterine motility is the major reason for primary dysmenorrhea. This motility is the basis for several symptoms including for pain is the main complaints of patients with primary dismenorrhea. There are several mechanisms, which initiate dysmenorrhea. Therefore, different compounds can be employed to control its symptoms. In long-term therapy, combination of oestrogens and progestins may be useful. In short-term therapy, dysmenorrhea sometimes non-steroidal anti-inflammatory drugs (NSAIDs) are used. Most of NSAIDs in long-term therapy show severe adverse effects. In an attempt to find agents with less adverse effect the fennel essential oil (FEO) was chosen for this investigation. In this article, effects of FEO on the uterine contraction and estimation of LD50 in rat were described. For assessment of pharmacological effects on the isolated rat uterus, oxytocin (0.1, 1 and 10 mu/ml) and prostaglandin E2 (PGE2) (5×10−5 M) were employed to induce muscle contraction. Administration of different doses of FEO reduced the intensity of oxytocin and PGE2 induced contractions significantly (25 and 50 μg/ml for oxytocin and 10 and 20 μg/ml PGE2, respectively). FEO also reduced the frequency of contractions induced by PGE2 but not with oxytocin. LD50 of FEO was obtained in the female rats by using moving average method. The estimated LD50 was 1326 mg/kg. No obvious damage was observed in the vital organs of the dead animals.

Parejo I, Viladomat F, Bastida J. & Codina C. (2004) "Development and validation of a high-performance liquid chromatographic method for the analysis of antioxidative phenolic compounds

in fennel using a narrow bore reversed phase C18 column." *Analytica Chimica Acta*, **512**(2), 271-280. Abstract. A simple high-performance liquid chromatography (HPLC) method for the separation and quantitative determination of the main antioxidant phenolic compounds from bitter fennel, *Foeniculum vulgare*, was developed. The use of a narrow bore reversed phase (RP) C18 column and an acidic mobile phase enabled ten compounds (caffeoylquinic acids, dicaffeoylquinic acids, flavonoids and rosmarinic acid) to be separated within a 40 min time analysis. The method was validated to demonstrate its selectivity, linearity, precision, accuracy and robustness. In addition, some parameters were studied to optimize the complete extraction of the phenolic compounds. The method was applied to the evaluation of three different fennel materials: distilled and non-distilled aerial parts, as well as defatted fruits. Distilled fennel was found to contain a higher proportion of antioxidant phenolic compounds than the non-distilled plan material.

Peterson, L. (1998). "Fennel Oil." In: *The New Rural Industries. A Handbook for Farmers and Investors.* Rural Industries Research & Development Corporation.

Piccaglia R, Marotti M. (2001) "Characterization of some Italian types of wild fennel (*Foeniculum vulgare* Mill.)." *J Agric Food Chem.* **49(**1), 239-44. Abstract. Wild samples of *Foeniculum vulgare* Mill. (fennel) were collected from thirteen Italian localities at different latitudes and grown in field trials to evaluate their morphological and agronomic characteristics and essential oil compositions. All the parameters were recorded at full bloom stage, and the essential oils (obtained by steam distillation) were characterized by gas chromatography (GC) and GC/mass spectrometry (GC/MS). The morphological characteristics showed positive relations among the number of umbels per plant, the plant weight, and the umbel weight percentage, and between these three parameters and the oil content. The essential oils evidenced five chemical groups characterized by (1) alpha-phellandrene, methyl chavicol, and trans-anethole; (2) alpha-pinene, limonene, and trans-anethole; (3) methyl chavicol and alpha-phellandrene; (4) methyl chavicol and alpha-pinene; and (5) alpha-phellandrene.

Poynter S.D. & Shellie R.A. (2008) "High-speed, low-pressure gas chromatography-mass spectrometry for essential oil analysis." *J Chromatogr A.* 2008 Mar 28. Abstract. Analysis of parsley and fennel essential oils was performed by using low-pressure gas chromatography-mass spectrometry (GC-MS). The low-pressure instrument configuration was achieved by fitting a GC-MS instrument with a 530mum I.D. capillary column and an appropriate capillary restrictor at the inlet of the column. Comparison of the performance of the low-pressure GC-MS setup was made with fast GC-MS using a narrow-bore capillary column. By comparing the two approaches side-by-side the benefits of low-pressure GC-MS for characterisation of moderately complex essential oils comprising less than 50 detectable components can be fully appreciated. Although efficiency is sacrificed, the improved sample capacity of the 530mum I.D. column leads to higher peak intensities and in-turn better mass spectral library matching thus providing highly satisfactory results.

Rothbächer H. & Kraus A. (1970) "[Terpene hydrocarbons in Rumanian fennel oil]" *Pharmazie*. **25**(9), 566-7.

Simándi B., Deák A., Rónyai E., Yanxiang G., Veress T., Lemberkovics E., Then M., Sass-Kiss A. & Vamos-Faiusi V. (1999) "Supercritical Carbon Dioxide Extraction and Fractionation of Fennel Oil" *J. Agric. Food Chem.* **47** (4), 1635 -1640. Abstract. Ground fennel seeds were extracted with supercritical carbon dioxide. Small-scale subsequent extractions of the same sample showed that the composition of volatile compounds was changed with the extension of extraction time and only principal volatile components (limonene, fenchone, methylchavicol, and anethole) were present in the last-extracted sample. Fennel oil was successfully fractionated into the essential oil rich and fatty oil rich products in pilot-scale apparatus using two separators in series. Designed experiments were carried out to map the effects of pressure and temperature in the first separator on the yields and compositions of the products. The minimum level of the total undesired components in both essential oil rich and fatty oil rich products appeared at a pressure of 80-84

bar and a temperature of 31-35 C in the first separator. Supercritical CO2 extraction of fennel seeds resulted in higher yield (10.0%) than steam distillation (3.0%), almost the same yield as hexane extraction (10.6%), and lower yield than alcohol extraction (15.4%). Analysis of the volatile compounds revealed the significant difference of the composition in distilled oil and oleoresins prepared by CO2 and solvent extractions. Sensory evaluation showed that the CO2 extraction product and distilled oil were more intense in odor and taste than alcohol and hexane extracts.

Strehle M.A., Rösch P., Baranska M., Schulz H. & Popp J. (2005) "On the way to a quality control of the essential oil of fennel by means of Raman spectroscopy." *Biopolymers*. **77**(1), 44-52. Abstract. Essential oils are one of the most valuable natural products. The price of special essential oils that can be purchased on the market strongly depends on the quality of the product. The quality, which depends on the quantitative and qualitative variation of different monoterpenes, varies with respect of the origin and the harvesting period. This contribution reports on a Raman spectroscopic study on the essential oil occurring in fennel. Cross-sections of fennel seed were investigated by use of Raman spectroscopy and Raman mapping to localize the essential oil and to analyze its chemical composition directly in the plant. Furthermore the practicability of a home-built mobile transportable Raman spectrometer to perform on-site measurements was successfully tested.

Taurin E., Rusli S. & Mapiliandari I. (1989) "Distillation of fennel oil." *Agris Centre record no ID93000194 CALTD (Indoneisa)*. Abstract Indonesia has produced few varieties of essential oil compared with its potential. Fennel oil is one of the essential oils that are potentially cultivated in Indonesia. Fennel seed which originates from Boyolali, Cipanas and Bintang has differences in oil contents. The highest oil content was produced by fennel seed from Bintang, that is 6.15 percent. Ground material and the fractination in the distillation kettle increased the oil content. However, those treatments had a little effect on characteristics of the oil. The highest yield of the oil produced was 4.21 percent with 26.17 percent of athenol content.

Toth L. (1967).”Untersuchungen uber das atherische Ol von *Foeniculum vulgare* II. Veranderungen der verschiedenen Fenchelole vor und nach der Ernte.” *Planta Med*. **15**, 371-389.

Trenkle, K. (1972) “Neuere Untersuchungen an Fenchel (*Foeniculum vulgare*, M.) II. Das atherische Ol von Frucht, Kraut und Wurzel fruktifizierenden Pflanzen.” *Pharmazie* **27**, 19-324.

Venskutonis P.R., Dapkevicius A., van Beek T.A. (1996) "Essential Oils of Fennel (*Foeniculum vulgare* Mill.) from Lithuania. *J Essent Oil Res* **8**, 211-3.

Verghese J: (1988) “Fennel.” *Indian Cocoa Arecanut Spices J*. 1988, 1**2,** 39-43.

Yamini Y., Sefidkon F. & Pourmortazavi S.M. (2002) "Comparison of essential oil composition of Iranian fennel (*Foeniculum vulgare*) obtained by supercritical carbon dioxide extraction and hydrodistillation methods." *Flav. & Frag J.* **17**(5) 345-348. Abstract. Essential oil of fennel cultivated in Iran was obtained by hydrodistillation and supercritical (CO2) extraction (SFE) methods. The oils were analysed by capillary gas chromatography using flame ionization and mass spectrometric detection. The compounds were identified according to their retention indices and mass spectra (EI, 70 eV). The effects of different parameters, such as pressure, temperature, modifier volume and extraction time, on the supercritical fluid extraction of fennel oil were investigated. The results showed that, under pressure of 350 atm, temperature 55 °C, methanol 5% and dynamic extraction time of 45 min, extraction was more selective for the extraction of (E)-anethol. Sixteen compounds were identified in the hydrodistilled oil. However, by using supercritical carbon dioxide in optimum conditions, only nine components represented more than 99% of the oil. The results showed that, in Iranian fennel oil, (E)-anethol is a major component.

Wang C, Gong NB, Zheng QT, Guo WS, Lu Y. (2003) "[Study on selective isolation of volatile oil in the seed of Fructus foeniculi]". *Zhongguo Zhong Yao Za Zhi* **28**(3), 240-2. Abstract.

OBJECTIVE: To study the selective isolation of a single chemical component from volatile oil of *Fructus foeniculi* by inclucion method. METHOD: The host molecule was selected and a single chemical component isolated from volatile oil by the host-guest recognition. RESULT: X-ray single crystal analysis showed that 1,1,6,6-tetraphenylhexa-2, 4-diyne-1, 6-diol could successfully include 4-[1-propenyl] benzaldehyde from volatile oil of Fructus foeniculi. CONCLUSION: The host-guest inclusion technology can be used to isolate a single component selectively from mixture.

Xia Z.H., Guo W.S., Tang X.D., Wang X.M., Tong J., You J, Cai Y.P. & Lu Y. (2001) "[Selective isolation of anethole from volatile oil of *Foeniculum vulgare* Mill by inclusion crystalline with chela-shape host]" *Yao Xue Xue Bao*. **(9),** 672-5. Abstract. AIM: To isolate the components from the volatile oil of *Foeniculum vulgare* Mill. METHODS: According to the function of molecular recognition of supramolecular chemistry, chela shape molecule, trans-1, 2-biphenyl-1, 2-acenaphthendiol was used as host molecule and the volatile oil of *Foeniculum vulgare* Mill as guest molecule. Trans-1, 2-biphenyl-1, 2-acenaphthendiol can recognize the components that endowed with interactional complementarity and form inclusion compound as crystals. RESULTS: The anethole in the volatile oil was selectively included as trans-1,2-biphenyl-1,2-acenaphthendiol which was obtained in pure state from the inclusion compound by Kugelrohr vacuum technology. The formation of inclusion compound was confirmed by means of IR and powder XRD. The structure of the selectively isolated component was elucidated as trans-anethole by means of IR, 1HMMR and MS. CONCLUSION: The experimental results showed that the method is simple, rapid and selective for isolation anethole from volatile oil of *Foeniculum vulgare* Mill.

Cultivation of fennel oil.

Abdallah N, El-Gengaihi S, Sedrak E. (1978) "The effect of fertilizer treatments on yield of seed and volatile oil of fennel (Foeniculum vulgare Mill.)." *Pharmazie* **33**(9), 607-8. Abstract. Nitrogen fertilization gave higher number of compound umbels and increased oil percentage, seed yield and oil yield with increase in dose. Phosphorus and potassium produced significant increase in the previous aspects with the second dose only.

Darzi M.T., Hadj Seyed Hadi M., Khodabandeh N., Yasa N. & Hadj Seyed Hadi Z. (2005) "Effect of sowing date and plant density on seed yield, quantity and quality of active substance in fennel (*Foeniculum vulgare* Mill.) Paper presented at *36th International Symposium on Essential Oils, 4-7 Septembe 2005r, Budapest, Hungary*

El-Gengaihi S, Abdallah N. (1978) "The effect of date of sowing and plant spacing on yield of seed and volatile oil of fennel (*Foeniculum vulgare* Mill.)." *Pharmazie* **33**(9), 605-6. Abstract. Wider spacing produced taller fennel plants. The compound umbels per plant increased as the distance between plants increased. The yield of seed per plant was greater in wider spacing. On the other hand, the medium space (30 cm) produced higher seed and oil contant per acre. Early sown plants produced taller plants, with higher compound umbels. The oil percentage was not affected while higher yield of seed and oil were significantly obtained.

Kapoor R, Giri B, Mukerji KG.(2004) "Improved growth and essential oil yield and quality in *Foeniculum vulgare* mill on mycorrhizal inoculation supplemented with P-fertilizer." *Bioresour Technol.* **93**(3), 307-11. Abstract. Two arbuscular mycorrhizal (AM) fungi *Glomus macrocarpum* and Glomus fasciculatum significantly improved growth and essential oil concentration of Foeniculum vulgare Mill. However, AM inoculation of plants along with phosphorus fertilization significantly enhanced growth, P-uptake and essential oil content of plants compared to either of the components applied separately. Among the two fungal inoculants, G. fasciculatum registered the highest growth at both levels of phosphorus used with up to 78% increase in essential oil concentration of fennel seeds over non-mycorrhizal control. The essential oil characterization by gas liquid chromatography revealed that the level of anethol was significantly enhanced on mycorrhization.

Pharmaceutical effects of fennel oil.

Albert-Puleo M (1980) “Fennel and anise as estrogenic agents.” *J Ethnopharmacol* **2**(4):337-344. Abstract. Fennel, *Foeniculum vulgare*, and anise, *Pimpinella anisum*, are plants which have been used as estrogenic agents for millennia. Specifically, they have been reputed to increase milk secretion, promote menstruation, facilitate birth, alleviate the symptoms of the male climacteric, and increase libido. In the 1930s, some interest was shown in these plants in the development of synthetic estrogens. The main constituent of the essential oils of fennel and anise, anethole, has been considered to be the active estrogenic agent. However, further research suggests that the actual pharmacologically active agents are polymers of anethole, such as dianethole and photoanethole.

Alexandrovich I, Rakovitskaya O, Kolmo E, Sidorova T, Shushunov S. (2003) "The effect of fennel (*Foeniculum vulgare*) seed oil emulsion in infantile colic: a randomized, placebo-controlled study." *Altern Ther Health Med.* **9**(4), 58-61. Abstract. CONTEXT: Despite its benign, natural course, colic is a significant problem in infants and imparts a psychological, emotional, and physical burden to parents. Dicyclomine hydrochloride is the only pharmacological treatment for infantile colic that has been consistently effective. Unfortunately, 5% of infants treated with dicyclomine hydrochloride develop serious side effects, including death. Fennel seed oil has been shown to reduce intestinal spasms and increase motility of the small intestine. However, there have not been any clinical studies of its effectiveness. OBJECTIVES: To determine the effectiveness of fennel seed oil emulsion in infantile colic. DESIGN: Randomized placebo-controlled trial. SETTINGS: Two large multi-specialty clinics. SUBJECTS: 125 infants, 2 to 12 weeks of age, who met definition of colic. INTERVENTION: Fennel seed oil emulsion compared with placebo. OUTCOME MEASURE: Relief of colic symptoms, which was defined as decrease of cumulative crying to less than 9 hours per week. RESULTS: The use of fennel oil emulsion eliminated colic, according to the Wessel criteria, in 65% (40/62) of infants in the treatment group, which was significantly better than 23.7% (14/59) of infants in the control group ($P < 0.01$). There was a significant improvement of colic in the treatment group compared with the control group [Absolute Risk Reduction (ARR) = 41% (95% CI 25 to 57), Number Needed to Treat (NNT) = 2 (95% CI 2 to 4)]. Side effects were not reported for infants in either group during the trial. CONCLUSION: Our study suggests that fennel seed oil emulsion is superior to placebo in decreasing intensity of infantile colic.

Boskabady MH, Khatami A, Nazari A. (2004) "Possible mechanism(s) for relaxant effects of Foeniculum vulgare on guinea pig tracheal chains." 1: Pharmazie. 2004 Jul;59(7):561-4. Abstract In a previous study the relaxant (bronchodilatory) effect of *Foeniculum vulgare* on isolated guinea pig tracheal chains was demonstrated. To study mechanisms responsible for this effect the present study evaluated the inhibitory effect of this plant on contracted tracheal chains of guinea pig. The relaxant effects of aqueous and ethanol extracts and an essential oil from *Foeniculum vulgare* were compared to negative controls (saline for aqueous extract and essential oil and ethanol for ethanol extract) and a positive control (diltiazem) using isolated tracheal chains of the guinea pig precontracted by 10 microM methacholine (group 1) and 60 mM KCl (group 2, $n = 7$ for each group). In the group 1, experiments diltiazem, ethanol extract, and essential oil from *Foeniculum vulgare* showed a significant relaxant effect on methacholine induced contraction of tracheal chains compared to those of negative controls ($p < 0.05$ to $p < 0.001$). In addition the effect of the ethanol extract was significantly greater than that of diltiazem ($p < 0.001$). However, the aqueous extract did not show any relaxant effect in group 1. In the group 2 experiments, only diltiazem showed a significant relaxant effect on KCl induced contraction of tracheal chains ($p < 0.001$). The relaxant effects of ethanol extracts and essential oil obtained in the group 2 experiments were significantly lower than those in group 1 ($p < 0.05$ to $p < 0.001$). These results confirm the bronchodilatory effects of ethanol extract and essential oil from *Foeniculum vulgare*. However with regard to the effect of KCl on calcium channels, the results indicated that the inhibitory effect of ethanol extracts and essential oil from *Foeniculum vulgare* on calcium channels is not contributing to their relaxant (bronchodilatory) effects on guinea pig tracheal chains. However the results suggest a potassium channel opening effect for this plant, which may contribute on its relaxant effect on guinea pig tracheal chains.

Capasso R., Savino F. & Capasso F. (2007) "Effects of the herbal formulation ColiMil on upper gastrointestinal transit in mice in vivo." *Phytother Res*. **21**(10), 999-1101. Abstract. Clinical evidence suggests that the herbal formulation ColiMil (which contains *Matricaria recutita* flowers extract, *Foeniculum vulgare* fruit extract and *Melissa officinalis* aerial parts extract) is effective in the treatment of breastfed colic in infants. Therefore the effect of this phytotherapeutic formulation and its herbal constituents on upper gastrointestinal transit was investigated in mice in vivo. Oral administration of the herbal formulation (0.4-0.8 mL/mice) dose-dependently delayed upper gastrointestinal transit. Among the herbal components, *Matricaria recutita* extract (0.89 and 1.78 mg/mouse) and *Melissa officinalis* extract (6.46 and 12.92 mg/mouse), but not *Foeniculum* vulgare (8.21 and 16.42 mg/mouse), reduced motility significantly. These results suggest that ColiMil reduces upper gastrointestinal motility in mice, with a major contribution by *Matricaria recutita* and *Melissa officinalis.* These experimental data may be important to better understand the observation that the herbal formulation ColiMil improves colic in breastfed infants.

Choi E.M. & Hwang J.K (2004) “Antiinflammatory, analgesic and antioxidant activities of the fruit of *Foeniculum vulgare* “. *Fitoterapia* **75**(6):557-565.

Faudale M., Viladomat F, Bastida J., Poli F. & Codina C. (2008) "Antioxidant activity and phenolic composition of wild, edible, and medicinal fennel from different Mediterranean countries." *J Agric Food Chem*. **56**(6), 1912-20. Abstract. Fennel (*Foeniculum vulgare* Mill.) is a typical aromatic plant of the Mediterranean area, long used as a medicinal and spice herb. Fennel is also well-known for its essential oil, which has been extensively studied for many years owing to its commercial importance. In this work, the antioxidant activity and the total phenolic and flavonoid contents, as well as the quantitative determination of individual flavonoids and phenolic acids of wild, edible, and medicinal fennel from different Mediterranean countries, have been determined. The antioxidant activity was measured as the free radical (DPPH), hydroxyl radical, and superoxide anion scavenging activities. Wild fennel was found to exhibit a radical scavenging activity, as well as a total phenolic and total flavonoid content, higher than those of both medicinal and edible fennels.

Hänsel R, Keller K, Rimpler H (1993) "Foeniculum 5". In *Hagers Hanbuch der Pharmazeutischen, Praxis 5*; Springer: New York, 1993, pp 156-81.

Haze S., Keiko Sakai K. & Gozu1 Y. (2002) "Effects of Fragrance Inhalation on Sympathetic Activity in Normal Adults." *Japanese Journal of Pharmacology* **90**(3), 247-253. Abstract. We investigated the effects of fragrance inhalation on sympathetic activity in normal adult subjects using both power spectral analysis of blood pressure fluctuations and measurement of plasma catecholamine levels. Fragrance inhalation of essential oils, such as pepper oil, estragon oil, fennel oil or grapefruit oil, resulted in 1.5- to 2.5-fold increase in relative sympathetic activity, representing low frequency amplitude of systolic blood pressure (SBP-LF amplitude), compared with inhalation of an odorless solvent, triethyl citrate ($P<0.05$, each). In contrast, fragrance inhalation of rose oil or patchouli oil caused a 40% decrease in relative sympathetic activity ($P<0.01$, each). Fragrance inhalation of pepper oil induced a 1.7-fold increase in plasma adrenaline concentration compared with the resting state ($P = 0.06$), while fragrance inhalation of rose oil caused a 30% decrease in adrenaline concentration ($P<0.01$). Our results indicate that fragrance inhalation of essential oils may modulate sympathetic activity in normal adults.

Javidnia K., Dastgheib L., Mohammadi Samani S. & Nasiri A. (2003) "Antihirsutism activity of Fennel (fruits of *Foeniculum vulgare*) extract. A double-blind placebo controlled study." *Phytomedicine*. **10**(6-7), 455-8. Abstract. Idiopathic hirsutism is defined as the occurrence of excessive male pattern hair growth in women who have a normal ovulatory menstrual cycle and normal levels of serum androgens. It may be a disorder of peripheral androgen metabolism. In this study we evaluated the clinical response of idiopathic hirsutism to topical Fennel extract. Fennel, *Foeniculum vulgare*, is a plant, which has been used as an estrogenic agent. The ethanolic extract of Fennel was obtained by using a soxhlete apparatus. In a double blind study,

38 patients were treated with creams containing 1%, 2% of Fennel extract and placebo. Hair diameter was measured and rate of growth was considered. The efficacy of treatment with the cream containing 2% Fennel is better than the cream containing 1% Fennel and these two were more potent than placebo. The mean values of hair diameter reduction was 7.8%, 18.3% and -0.5% for patients receiving the creams containing 1%, 2% and 0% (placebo) respectively.

Lis-Balchin M. & Hart S. (1997) "A preliminary study of the effect of essential oils on skeletal and smooth muscle in vitro." *J Ethnopharmacol.* **58**(3), 183-7. Abstract. The pharmacological activity of nine commercial essential oils was studied on the rat isolated phrenic nerve diaphragm preparation and compared with activity on field-stimulated guinea-pig ileum preparations. The essential oils at final bath concentrations of 2 x 10(-5) and 2 x 10(-4) g/ml produced four different effects on skeletal muscle, whilst only a contracture with or without a decrease in response to field stimulation in smooth muscle. The first type of effect on skeletal muscle involved a contracture and inhibition of the twitch response to nerve stimulation shown by a sample of clary sage, dill, fennel, frankincense and nutmeg; a second, shown by thyme produced a contracture without a change in the twitch response; a third, shown by lavender reduced the twitch response alone and the fourth, shown by camphor, increased the size of the twitch response. Angelica root oil at the highest concentration studied showed no response on skeletal muscle.

Lods L.M., Dres C., Johnson C., Scholz D.B. & Brooks G.J.. (2000) "The future of enzymes in cosmetics." *Int J Cosmet Sci*. **22**(2), 85-94. Abstract. The skin employs a host of protective mechanisms to defend itself against the ravages of the environment. One of the most widely studied protective mechanisms is the system of free radical scavengers. Free radical scavengers help to protect the skin by neutralizing dangerous substances that can be generated by sun exposure and pollution. Two such protective substances - superoxide dismutase and peroxidase - were examined for their ability to reduce UV-induced erythema. The ability to reduce erythema is a measure of anti-irritant capabilities, which can also be thought of as free radical scavenging ability. There has been some research that shows that superoxide dismutase (SOD) and peroxidase work synergistically. The action of SOD, which neutralizes the superoxide anion, can sometimes produce hydrogen peroxide, which can have a detrimental effect on the lipid barriers of the skin. When peroxidase is present, it can work to neutralize the hydrogen peroxide, thus giving a full spectrum of free radical protection. The present study employs a superoxide dismutase extracted from yeast. The peroxidase is found in an aqueous extract of fennel (*Foeniculum vulgare*). Minimal erythemal dose (MED) was determined on the panellists. Test compounds were then applied and then they were exposed to solar simulators in doses equivalent to their respective MEDs. Development of erythema was then measured via chromameter, and reduction in the development of redness was determined.

Malini T , Vanithakumari G , Megala N , Anusya S , Devi K & Elango V (1985) “Effect of *Foeniculum vulgare* Mill. seed extract on the genital organs of male and female rats.” *Indian J Physiol Pharmacol* . 1985(1);**29**, 21-26.

Misharina T.A. & Polshkov A.N. (2005) "[Antioxidant properties of essential oils: autoxidation of essential oils from laurel and fennel and effects of mixing with essential oil from coriander]" *Prikl Biokhim Mikrobiol*. **41**(6), 693-702. Abstract. Changes in the composition of essential oils from the seeds of laurel (*Laurus nobilis* L.) and fennel (*Foeniculum vulgare* Mill., var. *dulce* Thelling) and their mixture with essential oil from coriander were studied by capillary gas-liquid chromatography during storage in the dark and in light. Under these conditions, essential oil of laurel retained its composition for 12 months. Essential oil of fennel was rapidly oxidized in light. However, the rate of its oxidation in the dark was lower. The major component of essential oil of fennel, transanethol, had a lower antioxidant activity than essential oil of coriander. The mixture of essential oils from laurel and coriander possessed antioxidant properties and strongly inhibited the oxidation of components of the fennel oil.

Modaress Nejad V, Asadipour M. (2006) "Comparison of the effectiveness of fennel and mefenamic acid on pain intensity in dysmenorrhoea." *East Mediterr Health J.* 1**2**(3-4), 423-7.

Abstract. A study in Kerman, Islamic Republic of Iran in 2002 compared the effectiveness of fennel and mefenamic acid on pain relief in primary dysmenorrhoea. Two groups of high-school girls (mean age 13 years) suffering dysmenorrhoea were randomized to receive fennel extract (n = 55) or mefenamic acid (n = 55) for 2 months. In the fennel group, 80% of girls and in the mefenamic acid group, 73% of girls showed complete pain relief or pain decrease, while 80% in the fennel group and 62% in the mefenamic acid group no longer needed to rest. There was no significant difference between the 2 groups in the level of pain relief.

Namavar Jahromi B., Tartifizadeh A & Khabnadideh S (2003) "Comparison of fennel and mefenamic acid for the treatment of primary dysmenorrhea." *Intern J Gynaecol Obstet* . **80**(2):153-157. Abstract. This study compares the effect and potency of mefenamic acid and an extract of fennel (2% concentration) for the treatment of primary dysmenorrhea in 30 women. Mefenamic acid was more potent than fennel on the second and third days of menstruation (**P** ≤ 0.05). However, on the other days, the difference was not significant. With the doses prescribed, no complications were reported in the mefenamic acid treatment cycles (250 mg every 6 hours). However, 5 cases (16.6%) withdrew from the study because of fennel's odor, and one subject reported a mild increase in the amount of her menstrual flow during the fennel treatment cycle

Ozbek H , Ugras S , Dulger H , *et al*. (2003) "Hepatoprotective effect of *Foeniculum vulgare* essential oil." . *Fitoterapia* . **74**(3):317-319. Abstract. Hepatoprotective activity of *Foeniculum vulgare* (fennel) essential oil (FEO) was studied using carbon tetrachloride (CCl(4)) induced liver injury model in rats. The hepatotoxicity produced by acute CCl(4) administration was found to be inhibited by FEO with evidence of decreased levels of serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and bilirubin. The results of this study indicate that FEO has a potent hepatoprotective action against CCl(4)-induced hepatic damage in rats.

Ozcan M.M., Chalchat J.C., Arslan D., Ate A. & Unver A. (2006) "Comparative essential oil composition and antifungal effect of bitter fennel (*Foeniculum vulgare* ssp. *piperitum*) fruit oils obtained during different vegetation." *J Med Food.* **9**(4), 552-61. Abstract. The chemical composition of the flower and unripe and ripe fruits from fennel (bitter) (*Foeniculum vulgare* ssp. *piperitum*) has been examined by gas chromatography and gas chromatography-mass spectrometry. The main identified components of the flower and unripe and ripe fruit oils were estragole (53.08%, 56.11%, and 61.08%), fenchone (13.53%, 19.18%, and 23.46%), and alpha-phellandrene (5.77%, 3.30%, and 0.72%), respectively. Minor qualitative and major quantitative variations for some compounds of essential oils were determined with respect to the different parts of *F. vulgare*. The oils exerted varying levels of antifungal effects on the experimental mycelial growth of *Alternaria alternata*, *Fusarium oxysporum*, and *Rhizoctonia solani*. The 40 ppm concentrations of fennel oils showed inhibitory effect against mycelial growth of *A. alternaria*, whereas 10 ppm levels were ineffective. The analyses show that fennel oils exhibited different degrees of fungistatic activity depending on the doses.

Reiter M. & Brandt W. (1985) "Relaxant effects on tracheal and ileal smooth muscles of the guinea pig." *Arzneimittelforschung* . **35**(1A):408-414. Abstract. The effects of volatile oils of 22 plants from 11 different families and of some of their constituents on tracheal and ileal smooth muscles were investigated. The results were compared with the relaxant effects of catecholamines and phosphodiesterase inhibitors. All of the oils had relaxant effects on the tracheal smooth muscle, the most potent were angelica root, clove, elecampane root, basil and balm leaves oil. 16 oils inhibited the phasic contractions of the ileal myenteric plexus-longitudinal muscle preparation, the most potent were elecampane root, clove, thyme, balm leaves and angelica root oil. 2 oils (anise and fennel) increased the phasic contractions, and 4 oils (bitter orange, caraway, mace, pepper) produced a marked increase in resting force (i.e. contracture). In regard to the relaxant effects, most of the 16 oils were more potent on the ileal than on the tracheal muscle. However, a small group of 4 oils (angelica root, clove, basil, black caraway) had a higher relaxant effect on the tracheal than on the ileal muscle. This was also found to be the

case with eugenol, eugenol acetate and cinnamic aldehyde as well as with isoprenaline and phosphodiesterase inhibitors.

Savino F., Cresi F., Castagno E., Silvestro L. & Oggero R. (2005) "A randomized double-blind placebo-controlled trial of a standardized extract of *Matricariae recutita*, *Foeniculum vulgare* and *Melissa officinalis* (ColiMil) in the treatment of breastfed colicky infants." *Phytother Res*. **19**(4):335-40. Abstract. OBJECTIVE: The aim of this randomized, double-blind, placebo-controlled trial was to investigate the effectiveness and side effects of a phytotherapeutic agent with *Matricariae recutita*, *Foeniculum vulgare* and *Melissa officinalis* in the treatment of infantile colic. METHODS: 93 breastfed colicky infants were enrolled, the diagnosis was made according to Wessel's criteria. After a 3 day observation period, the infants were randomly divided into two groups, one treated with phytotherapeutic agent (PA) and the other with placebo twice a day for 1 week. Crying time and side effects were recorded. RESULTS: 88 infants completed the trial: 41 in the PA group and 47 in the control. The daily average crying time for the PA was 201.2 min/day (SD 18.3) at the baseline and 76.9 min/day (SD 23.5) at the end of the study; for the placebo it was 198.7 min/day (SD 16.9) and 169.9 min/day (SD 23.1) ($p < 0.005$). Crying time reduction was observed in 85.4% subjects for the PA and in 48.9% subjects for the placebo ($p < 0.005$). No side effects were reported. CONCLUSION: The present study shows that colic in breastfed infant improves within 1 week of treatment with an extract based on *Matricariae recutita*, *Foeniculum vulgare* and *Melissa officinalis.*

Savino F., Capasso R., Palumeri E., Tarasco V., Locatelli E. & Capasso F. (2008) "Advances on the effects of the compounds of a phytotherapic agent (COLIMIL(R)) on upper gastrointestinal transit in mice." *Minerva Pediatr.* **60**(3):285-290 Abstract. AIM: Phytotherapic agents, such as herbal formulations containing *Matricariae recutita* flowers (chamomile) extract, *Foeniculum vulgare* fruit (fennel) extract and *Melissa officinalis* aerial parts (lemon balm) extract have beneficial effects on gastrointestinal tract in colicky infants. However, the mechanism is largely unexplored and, particularly, it is not clear if it affects intestinal motility. The aim of this experimental study was to evaluate the effect of different herbal formulations containing *Matricariae recutita* extract, *Foeniculum vulgare* extract and *Melissa officinalis* extract on upper gastrointestinal transit in mice in vivo. METHODS: Gastrointestinal transit was measured in male ICR mice and in croton oil-treated mice after the oral administration of herbal formulations containing chamomile, fennel and lemon balm (ColiMil(R)) and chamomile and lemon balm (ColiMil experimental). RESULTS: The herbal formulations tested (0.4-0.8 mL/mouse) dose-dependently and significantly inhibited gastrointestinal transit both in control and in croton oil-treated mice. Chamomile extract and lemon balm extract reduced significantly intestinal motility, but not fennel. At similar concentration ColiMil(R) evoked a more consistent response than ColiMil experimental. CONCLUSION: Our findings directly demonstrate in vivo the effect of a combination of herbal formulations on intestinal motility. The observed inhibitory effect might be studied with clinical studies to test the efficacy of these compounds in the treatment of colicky infants.

Schöne F., Vetter A., Hartung H., Bergmann H., Biertümpfel A., Richter G., Müller S. & Breitschuh G.(2006) "Effects of essential oils from fennel (*Foeniculi aetheroleum*) and caraway (*Carvi aetheroleum*) in pigs." *J Anim Physiol Anim Nutr* **90**(11-12), 500-10. Abstract. The ban of antibiotics as a feed additive requires alternatives to stabilize the health and performance particularly of the young animals. Essential oils obtained from fennel seed (*Foeniculi aetheroleum*) and caraway seed (*Carvi aetheroleum*) were tested in diets for weaned piglets in comparison with either a diet without feed additive or with a combination of formic acid and copper (positive control). Four groups of sixteen piglets (live weight 7 kg, age 26 days) received diets without (1) or with supplements of 7.5 g formic acid + 160 mg Cu/kg (2), 100 mg fennel oil/kg (3) or 100 mg caraway oil/kg (4) during 3 weeks after weaning. In the subsequent 4 weeks, all piglets were fed a diet without these additions. Fennel oil contained almost 2/3 anethol, approximately 1/5 fenchon and the remaining part consisting of alpha + beta-pinen, limonen (p-mentha-1,8-dien) and estragol. In the caraway oil, half of the contents was represented by limonen and the other half by carvon. There were no piglet losses and only few cases of

diarrhoea. The combination of formic acid and copper increased feed consumption by 27% and daily weight gain by 25%. There were no differences in the performance between the group fed fennel oil and the control without additives. Piglets fed caraway oil tended to consume less feed and to gain approximately 10% less. In feed choice experiments, pigs consumed the same two diets from two troughs with 50% of total feed amount, as expected. The diets containing fennel or caraway oils were consumed at less than 50%. If the diet contained 100 mg fennel oil/kg, the decrease of percentual feed intake was significant. The results of the feeding experiment and of the feed choice experiment question the classification of fennel and caraway oils as flavour additives or as 'appetite promoters' in diets for weaned piglets.

Stashenko E.E., Puertas M.A. & Martínez J.R. (2003) " SPME determination of volatile aldehydes for evaluation of in-vitro antioxidant activity." *Chemistry & Materials Science* **373** (1-2), 70-74. Abstract. The in-vitro antioxidant activity of natural (essential oils, vitamin E) or synthetic substances (tert-butyl hydroxy anisole (BHA), Trolox) has been evaluated by monitoring volatile carbonyl compounds released in model lipid systems subjected to peroxidation. The procedure employed methodology previously developed for the determination of carbonyl compounds as their pentafluorophenylhydrazine derivatives which were quantified, with high sensitivity, by means of capillary gas chromatography with electron-capture detection. Linoleic acid and sunflower oil were used as model lipid systems. Lipid peroxidation was induced in linoleic acid by the Fe2+ ion (1 mmol L-1, 37 °C, 12 h) and in sunflower oil by heating in the presence of O2 (220 °C, 2 h). The change in hexanal (the main lipoxidation product) concentration found in the lipid matrix subjected to oxidation with and without the substance being tested was used to calculate the antioxidant protection effect. These procedures were employed to evaluate the antioxidant activity of the essential oils of cilantro (*Coriander sativum* L.), fennel (*Foeniculum vulgare* Mill.), rosemary (*Rosmarinus officinalis* L.), "salvia negra" (*Lepechinia schiedeana*), and oregano (*Origanum vulgare* L.), and the well-known antioxidants BHA, vitamin E, and Trolox, its water-soluble analog. In the sunflower oil system, the essential oils had a stronger protective effect against lipid peroxidation than BHA, vitamin E, and Trolox within the range of concentrations examined (1-20 g L-1). The highest protecting effect, corresponding to a 90% drop in hexanal release, was observed for cilantro oil at 10 g L-1.

Subehan , Zaidi SF, Kadota S, Tezuka Y. (2007) "Inhibition on human liver cytochrome P450 3A4 by constituents of fennel (*Foeniculum vulgare*): identification and characterization of a mechanism-based inactivator." *J Agric Food Chem.* **55**(25),10162-7. Abstract. Fennel, a seed of *Foeniculum vulgare*, is used as a culinary spice and traditional medicine. The methanolic extract of fennel showed a characteristic of mechanism-based inactivation on erythromycin N-demethylation mediated by human liver microsomal cytochrome P450 3A4 (CYP3A4). The present study was conducted to identify the fennel constituent having the inhibition. Thirteen compounds have been isolated from a methanol extract of fennel and tested for their inhibition on CYP3A4. Among them, 5-methoxypsoralen (5-MOP) showed the strongest inhibition with an IC50 value of 18.3 microM and a mixed type of inhibition. In addition, with the preincubation time of 20 min only 5-MOP showed preincubation time dependency; the IC50 value decreased from 18.3 microM with a preincubation time of 0 min to 4.6 microM with a preincubation time of 20 min. Further investigation on 5-MOP showed the characteristics of time-dependent inhibition, requirement of NADPH, lack of protecting effect of nucleophiles, and recovery of CYP3A4 activity by the competitive inhibitor. This result suggests that the inhibitory activity of CYP3A4 by 5-MOP was a mechanism-based inactivation. The kinetic parameter for mechanism-based inactivation was characterized by a KI value of 15.0 microM and a kinact value of 0.098 min(-1).

Tognolini M., Ballabeni V., Bertoni S., Bruni R., Impicciatore M. & Barocelli E. (2007) "Protective effect of *Foeniculum vulgare* essential oil and anethole in an experimental model of thrombosis." *Pharmacol Res*. **6**(3):254-60. Abstract. In a previous screening work, *Foeniculum vulgare* essential oil emerged from a pool of 24 essential oils for its antiplatelet properties and its ability to destabilize the retraction of the coagulum. In the present work the main component of the oil, anethole, tested in guinea pig plasma was as potent as fennel oil in inhibiting arachidonic acid-, collagen-, ADP- and U46619-induced aggregation (IC(50) from 4 to 147 microg ml(-1)). It also

prevented thrombin-induced clot retraction at concentrations similar to fennel oil. The essential oil and anethole, tested in rat aorta with or without endothelium, displayed comparable NO-independent vasorelaxant activity at antiplatelet concentrations which have been proved to be free from cytotoxic effects in vitro. In vivo, both *F. vulgare* essential oil and anethole orally administered in a subacute treatment to mice (30 mg kg(-1)day(-1) for 5 days) showed significant antithrombotic activity preventing the paralysis induced by collagen-epinephrine intravenous injection (70% and 83% protection, respectively). At the antithrombotic dosage they were free from prohemorrhagic side effect at variance with acetylsalicylic acid used as reference drug. Furthermore, both F. vulgare essential oil and anethole (100 mg kg(-1) oral administration) provided significant protection toward ethanol induced gastric lesions in rats. In conclusion, these results demonstrate for *F. vulgare* essential oil, and its main component anethole, a safe antithrombotic activity that seems due to their broad spectrum antiplatelet activity, clot destabilizing effect and vasorelaxant action.

Warrier PK, Nambiar VPK, Ramankutty C. Foeniculum vulgare. In: *Indian Medical Plants*.Volume 3. Chennai. Orient

Toxicology of fennel oil

Blumenthal M , Goldberg A , Brinckmann J. eds. (2000) *Herbal Medicine: Expanded Commission E Monographs* . Newton, MA: Integrative Medicine Communications. ***Cropwqtch comments***: LD_{50} given as 1326mg/Kg.

Opdyke D.L.J. (1974) “Monographs on Fragrance Raw Materials. Fennel oil.” *FCT* **12**, 879-80. ***Cropwatch comments:*** Undilutef fennel oil found severely irritating to mouse skin, moderately irritating to rabbit skin. Not irritation to humans at 4%. Not sensitizing in a maximization test at 4%.

Opdyke D.L.J. (1976) “Monographs on Fragrance Raw Materials. Fennel oil bitter.” *FCT* **14**, 309.

Ostad S.N , Khakinegad B & Sabzevari O. (2004) “Evaluation of the teratogenicity of fennel essential oil (FEO) on the rat embryo limb buds culture.” *Toxicol In Vitro* **18**(5);623-627. Abstract. The use of FEO as a remedy for control of primary dysmenorrhea increases concern about its potential teratogenicity due to its estrogen-like activity. Limb bud mesenchymal cells, when grown in high-density cultures, can be differentiated into a number of cell types including cartilage and muscle. These cells have been used extensively for in vitro studies of chondrogenesis. Therefore, we used limb bud cells and Alcian blue staining method that is specific for staining cartilage proteoglycan, to determine the teratogenic effect of FEO. Limb bud cells obtained from day 13 rat embryo were cultivated and exposed to various concentrations of FEO for 5 days at 37 ℃ and the number of differentiated foci were counted. Retinoic acid (90 µg/ml) was chosen as positive standard control. The differentiation was also evaluated using limb bud micromass culture using immunocytochemical techniques and BMP-4 antibody. The results showed that FEO at concentration as low as 0.93 mg/ml produced a significant reduction in the number of stained differentiated foci. However, this reduction was due to cell loss, determined by neutral red cell viability assay, rather than to be related to decrease in cell differentiation. These findings suggest that the FEO at the studied concentrations may have toxic effect on fetal cells, but there was no evidence of teratogenicity.

Özbek H (2002) "Investigation of the level of the lethal dose 50 and the hypoglycemic effect of *Foeniculum vulgare* Mill. Fruit essential oil extract in healthy and diabetic mice." *Van Tip Dergisi* **9**(4), 98-103.

De Vincenzi M., Silano M., Maialettia F. & Scazzocchio (2000) "Constituents of aromatic plants: II. Estragole." *Fitoterapia* **71**(6}, 725-729. Abstract. Estragole (ES) is a natural constituent of a number of plants (e.g. tarragon, sweet basil and sweet fennel) and their essential oils have been widely used in foodstuffs as flavouring agents. Several studies with oral, i.p. or s.c. administration to CD-1 and B6C3F1 mice have shown the carcinogenicity of ES. The 1-hydroxy metabolites are

stronger hepatocarcinogens than the parent compound. Controversial results are reported for the mutagenicity of ES. However, the formation of hepatic DNA adducts in vivo and in vitro by metabolites of ES has been demonstrated.

Schelz Z , Molnar J & Hohmann J. (2006) . “Antimicrobial and antiplasmid activities of essential oils” . *Fitoterapia* . 2006;77(4):279-285. ***Cropwatch Comments***: Fennel oil found genotoxic in *B. subtilis* DNA-repair test. :