Fructus Foeniculi

Definition

Fructus Foeniculi consists of the dried ripe fruits of *Foeniculum vulgare* Mill. (Apiaceae) (*1–8*).[1]

Synonyms

Anethum foeniculum Clairv., *A. foeniculum* L., *A. rupestre* Salisb., *Feniculum commune* Bubani, *Foeniculum azoricum* Mill., *F. capillaceum* Gilib., *F. dulce* DC., *F. foeniculum* (L.) H. Karst., *F. officinale* All., *F. panmorium* DC., *F. piperitum* DC., *F. sativum* Bertol, *Ligusticum divaricatum* Hoffmannsegg et Link, *L. foeniculum* Crantz, *Meum foeniculum* (L.) Spreng., *Ozodia foeniculacea* Wight et Arn., *Selinum foeniculum* (L.) E.H.L. Krause (*2, 3, 9, 10*). Apiaceae are also known as Umbelliferae.

Selected vernacular names

Aneth doux, arap saçi, besbes, bitter fennel, Bitterfenchel, brotanis, common fennel, dill, édeskömény, erva doce, fãnksal, fannel, Fencel, Fenchel, fenchul, Fennekel, fennel, Fennichl, fennikel, Fennkol, fenouil, fenucchiello, fenucchio, fenykl, finkel, Finkel, finichio, finocchio, finucco, fiolho, florence fennel, foenoli doux, funcho, gemeiner Fenchel, Gemüsefenchel, giant fennel, guvamuri, hierba de anis, hinojo, hui-hsiang, imboziso, insilal, koper wloski, lady's chewing tobacco, large fennel, madesi souf, madhurika, marathoron, maratrum, marui, misi, nafa, panmauri, razianeh, razianaj, sanuf, shamar, shomar, sladkij ukrop, sohoehyang, sopu, spingel, sup, thian khaao phlueak, thian klaep, venkel, sweet fennel, uikyo, uikyou, vegetable fennel, vinkel, wild fennel, xiao hui, xiaohuixiang, yi-ra (*2, 3, 6, 8, 9, 11–14*).

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[1] The *European pharmacopoeia* (*7*) recognizes *Foeniculum vulgare* Mill. ssp. *vulgare* var. *vulgare (*Foeniculi amari fructus, Bitter Fennel) and *F. vulgare* Mill. ssp. *vulgare* var. *dulce (*Foeniculum dulcis fructus, Sweet Fennel) as distinct entities for which separate monographs are provided. However, in the biological literature, a clear delineation at the variety level is generally not made. Therefore, this monograph has not made the distinction between the "bitter" and "sweet" varieties.

Geographical distribution

Indigenous to the Mediterranean region. Cultivated in Europe, Asia and temperate regions of Africa and South America (*2, 12, 15*).

Description

Perennial aromatic herb, 1–3 m high with green, glaucous, furrowed, branched stems bearing alternate leaves, 2–5 times pinnate with extremely narrow leaflets. Superior leaves with sheaths longer than the blade. Umbels compound, large, nearly regular, on long peduncles. Flowers yellow, no involucre; calyx with five very slight teeth; petals five, entire, tips involute; stamens five; ovary two-celled; stylopodium large, conical. Fruit an oblong cremocarp, 6–10 mm long, 1–4 mm in diameter, greenish; glabrous mericarp compressed dorsally, semicylindrical, with five prominent, nearly regular ribs. Seeds somewhat concave, with longitudinal furrows (*3, 15, 16*).

Plant material of interest: dried ripe fruits

General appearance

Cremocarp, oblong 3.5–10.0 mm long, 1–3 mm wide, externally greyish yellow-green to greyish yellow often with pedicel 2–10 mm long. Mericarps usually free, glabrous, each bearing five prominent slightly crenated ridges (*1–4, 7, 8*).

Organoleptic properties

Odour: characteristic, aromatic; taste: sweet to bitter (*1–4, 8*).

Microscopic characteristics

Outer epidermis of the pericarp consists of thick-walled, rectangular, polygonal, colourless cells, with smooth cuticle, few stomata and no hairs. Mesocarp consists of brownish parenchyma; traversed longitudinally by six large schizogenous vittae, appearing elliptical in section and possessing brown epithelial cells; traversed in the ridges by vascular bundles, each having one inner xylem strand and two lateral phloem strands, and accompanied by strongly lignified fibres; some of the mesocarp cells, especially those about the vascular bundles, possess lignified, reticulate cells. Endocarp composed of one layer of flattened thin-walled cells varying in length, but mostly 4–6 µm thick, arranged parallel to one another in groups of five to seven. Endosperm, formed of somewhat thick-walled polygonal cellulosic parenchyma containing fixed oil, several aleurone grains (up to 6 µm in diameter) enclosing a globoid, and one or more microrosette crys-

tals of calcium oxalate, about 3 µm in diameter. Carpophore often not split, with thick-walled sclerenchyma in two strands (*2, 8*).

Powdered plant material

Greyish-brown to greyish-yellow. Yellowish-brown-walled polygonal secretory cells, frequently associated with a layer of thin-walled transversely elongated cells 2–9 µm wide, in a parquet arrangement; reticulate parenchyma of the mesocarp; numerous fibre bundles from the ridges, often accompanied by narrow spiral vessels; very numerous endosperm fragments containing aleurone grains, very small microrosette crystals of calcium oxalate, and fibre bundles from the carpophore (*7*).

General identity tests

Macroscopic and microscopic examinations (*1–4, 7, 8*), thin-layer chromatography for the presence of anethole and fenchone (*7*), and gas chromatography for the presence of anethole, fenchone and estragole (*7*).

Purity tests

Microbiological

Tests for specific microorganisms and microbial contamination limits are as described in the WHO guidelines on quality control methods for medicinal plants (*17*).

Foreign organic matter

Not more than 1.5% peduncles and not more than 1.5% other foreign matter (*4, 7*).

Total ash

Not more than 10% (*1, 4, 7, 8, 18*).

Acid-insoluble ash

Not more than 1.5% (*1, 2, 4*).

Water-soluble extractive

Not less than 20% (*3*).

Alcohol-soluble extractive

Not less than 11% (*3*).

Moisture

Not more than 8% (*7*).

Pesticide residues

The recommended maximum limit of aldrin and dieldrin is not more than 0.05 mg/kg (*19*). For other pesticides, see the *European pharmacopoeia* (*19*) and the WHO guidelines on quality control methods for medicinal plants (*17*) and pesticide residues (*20*).

Heavy metals

For maximum limits and analysis of heavy metals, consult the WHO guidelines on quality control methods for medicinal plants (*17*).

Radioactive residues

Where applicable, consult the WHO guidelines on quality control methods for medicinal plants (*17*) for the analysis of radioactive isotopes.

Other purity tests

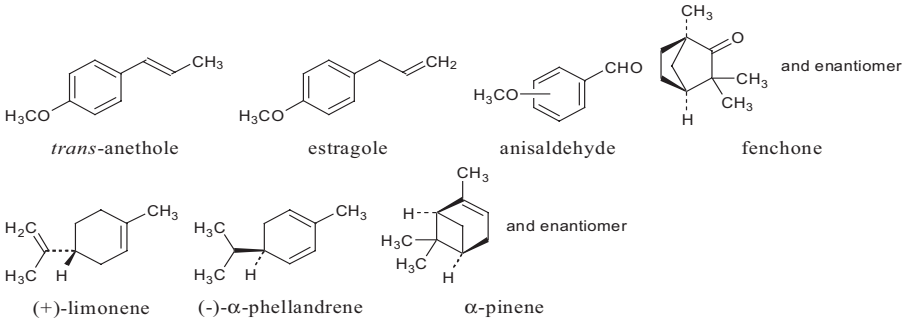
Chemical and sulfated ash tests to be established in accordance with national requirements.

Chemical assays

Contains not less than 1.4% v/w essential oil (*1, 2, 4, 6*).

Major chemical constituents

The major constituent is the essential oil (2–6%), which contains *trans*-anethole (50–82%), (+)-fenchone (6–27%), estragole (methylchavicol) (3–20%), limonene (2–13%), *p*-anisaldehyde (6–27%), α-pinene (1–5%) and α-phellandrene (0.1–19.8%) (*9, 12, 14, 21, 22*). Representative structures are presented below.



trans-anethole estragole anisaldehyde fenchone

Medicinal uses

Uses supported by clinical data

None.

Uses described in pharmacopoeias and well established documents

Symptomatic treatment of dyspepsia, bloating and flatulence (*9, 23–25*). As an expectorant for mild inflammation of the upper respiratory tract (*24, 26*). Treatment of pain in scrotal hernia, and dysmenorrhoea (*8*).

Uses described in traditional medicine

Treatment of blepharitis, bronchitis, constipation, conjunctivitis, diabetes, diarrhoea, dyspnoea, fever, gastritis, headache, pain, poor appetite and respiratory and urinary tract infections (*14*). As an aphrodisiac, anthelminthic, emmenagogue, galactagogue and vermicide (*14, 27, 28*).

Pharmacology

Experimental pharmacology

Analgesic and antipyretic activities

Intragastric administration of 500 mg/kg body weight (bw) of a 95% ethanol extract of Fructus Foeniculi to mice reduced the perception of pain as measured in the hot-plate test, and decreased yeast-induced pyrexia (*29*). Intragastric administration of 500.0 mg/kg bw of a 95% ethanol extract of the fruits to rats had significant ($P < 0.05$) analgesic activity in the hot-plate reaction test (*30*). In mice with yeast-induced pyrexia, treatment with 500.0 mg/kg bw of the same extract reduced rectal temperature from 36.5 °C to 34.7 °C 90 minutes after administration (*30*).

Antimicrobial activity

An essential oil from the fruits inhibited the growth of *Alternaria* species, *Aspergillus flavus, A. nidulans, A. niger, Cladosporium herbarum, Cunninghamella echinulata, Helminthosporium saccharii, Microsporum gypseum, Mucor mucedo, Penicillium digitatum, Rhizopus nigricans, Trichophyton roseum* and *T. rubrum* in vitro (*31, 32*). In another study, an essential oil was not active against *Aspergillus* species in vitro but a methanol extract of the fruits inhibited the growth of *Helicobacter pylori* (the bacterium associated with gastritis and peptic ulcer disease) in vitro, minimum inhibitory concentration 50.0 µg/ml (*33*). An essential oil from the fruits inhibited the growth of *Candida albicans, Escherichia coli, Lentinus lepideus, Lenzites trabea, Polyporus versicolor, Pseudomonas aeruginosa* and *Staphylococcus aureus* (*34*), and *Kloeckera apiculata, Rhodotorula rubra* and *Torulopsis glabrata* (*35*) in vitro. An ethyl acetate extract of the seeds inhibited the growth of *Shigella flexneri* (*36*), and an 80% ethanol extract of the seeds inhibited the growth of *Bacillus subtilis* and *Salmonella typhi* at concentrations of 250.0 µg/ml in vitro (*37*).

Antispasmodic activity

An ethanol extract of the fruits, 2.5–10.0 ml/l, 1 part fruits:3.5 parts 31% ethanol, inhibited acetylcholine- and histamine-induced guinea-pig ileal contractions in vitro (*23*). An essential oil from the fruits reduced intestinal spasms in mouse intestine, and was 26% as active as papaverine (*38*). Intragastric administration of 2.0–3.0 g/kg bw of an infusion of the fruits to cats inhibited acetylcholine- and histamine-induced ileum spasms by 50% (*39*). An essential oil from the fruits, 25.0 µg/ml and 10.0 µg/ml, respectively, inhibited oxytocin- and prostaglandin E_2-induced contractions of isolated rat uterus and reduced the frequency of the latter but not the former (*40*).

Cardiovascular effects

Intravenous administration of a 50% ethanol extract of the fruits (dose not specified) reduced blood pressure in dogs (*41*). An aqueous extract of the fruits, 10% in the diet, reduced blood pressure in rats. The effect was abolished by pretreatment of the animals with atropine (*42*). An unspecified extract of the seeds had diuretic effects in rabbits after intragastric administration. The effect was blocked by pretreatment of the animals with morphine (*43*).

Intragastric administration of 500.0 mg/kg bw of a 95% ethanol extract of the fruits to rats induced diuresis. The effect was comparable to that observed in animals treated with 960.0 mg/kg bw of urea, and was almost double that in controls (*30*).

Estrogenic and antiandrogenic activities

Intragastric administration of 2.5 mg/kg bw of an acetone extract of the seeds daily for 15 days to male rats decreased the protein concentration in the testes and vas deferens, and increased it in the seminal vesicles and prostate gland (*44*). The same dose of the same extract administered to female rats daily for 10 days increased the weight of the mammary glands, while higher doses induced vaginal cornification, increased the weight of the oviduct, endometrium, myometrium, cervix and vagina, and induced estrus (*44*). A follow-up study demonstrated that the acetone extract induced cellular growth and proliferation of the endometrium, and stimulated metabolic changes in the myometrium of rats. These changes appeared to favour the survival of spermatocytes and the implantation of the zygote in the uterus (*45*). Conversely, intragastric administration of 2.0 g/kg bw of an aqueous extract of the seeds per day for 25 days significantly ($P < 0.025$) reduced female fertility in mice compared with controls. No effect was observed in male mice (*46*).

Intragastric administration of 0.5 mg/kg bw or 2.5 mg/kg bw of an acetone extract of the fruits per day for 10 days to ovariectomized female rats had estrogenic effects (*45*). Intragastric administration (dose not specified) of an essential oil from the fruits to goats increased the amount of milk produced and the fat content of the milk (*47*). Lactating mice fed the fruits in the diet (concentration not specified) produced pups that ate a larger quantity of fennel-containing foods, suggesting that the constituents of the fruits may be passed in breast milk (*48*). Intragastric administration of 250.0 mg/kg bw of unspecified extracts of the fruits induced estrus and increased the size of the mammary glands and oviducts in adult ovariectomized rats, and exerted an antiandrogenic effect in adult male mice. It also increased the weight of the cervix and vagina of ovariectomized rats, and increased the concentration of nucleic acids and protein in cervical and vaginal tissues. The hyperplasia and hypertrophy of the cervix and vagina were similar to changes seen during estrus in normal female rats (*45*).

Subcutaneous administration of anethole (dose not specified) to sexually immature female rats increased uterine weight and induced estrus. However, in ovariectomized mice the same treatment was not estrogenic (*49*). Intramuscular injection of 100.0 mg/kg bw or 500.0 mg/kg bw of anethole per day for 7 days to rats induced a significant decrease in dorsolateral prostate weight ($P < 0.05$) (*50*). Intragastric administration of 50.0 mg/kg bw, 70.0 mg/kg bw or 80.0 mg/kg bw of *trans*-anethole to rats had anti-implantation effects, with the maximum effect (100%) at the highest dose (*51*). The compound showed estrogenic effects, and did not demonstrate anti-estrogenic, progestational or androgenic effects (*51*).

Expectorant and secretolytic effects

Application of an infusion of Fructus Foeniculi, 9.14 mg/ml, to isolated ciliated frog oesophagus epithelium increased the transport velocity of fluid by 12%, suggesting an expectorant effect (*52*). Administration of 1.0–9.0 mg/kg bw anethole and 1.0–27.0 mg/kg bw fenchone by inhalation to urethanized rabbits produced a decrease in the specific gravity of the respiratory fluid and enhanced the volume output of respiratory tract fluid (*53*).

Gastrointestinal effects

Intragastric administration of 24.0 mg/kg bw of the fruits increased spontaneous gastric motility in unanaesthetized rabbits; at a dose of 25.0 mg/kg bw the fruits reversed the reduction of gastric motility induced by pentobarbital (*54*).

Sedative effects

Intragastric administration of an essential oil from the fruits (dose not specified) to mice reduced locomotor activity and induced sedation (*55*). A single intraperitoneal administration of 200.0 mg/kg bw of an ether extract of the seeds enhanced barbiturate induced sleeping time in mice. However, intragastric administration of 200.0 mg/kg bw of the extract per day for 7 days decreased barbiturate-induced sleeping time (*56*).

Toxicology

Intragastric administration of 3.0 g/kg bw of a 95% ethanol extract of the fruits induced piloerection and reduced locomotor activity in mice (*30*). Acute (24-hour) and chronic (90-day) oral toxicity studies with an ethanol extract of the fruits were performed in rodents. Acute doses were 0.5 g/kg, 1.0 g/kg and 3.0 g/kg per day; the chronic dose was 100.0 mg/kg per day. No acute or chronic toxic effects were observed (*57*). The acute median lethal dose (LD_{50}) of anethole in rats was 3.8 mg/kg bw after intragastric administration (*58, 59*). Intragastric or subcutaneous administration of 10.0–16.0 g/kg bw of a 50% ethanol extract of the fruits to mice had no toxic effects (*60*). The oral LD_{50} of an essential oil from the fruits in mice was 1326.0 mg/kg bw (*61*).

Chronic use of high doses of *trans*-anethole in rodent dietary studies has been shown to induce cytotoxicity, cell necrosis and cell proliferation. In rats, hepatotoxicity was observed when dietary intake exceeded 30.0 mg/kg bw per day (*62*). In female rats, chronic hepatotoxicity and a low incidence of liver tumours were reported with a dietary intake of trans-anethole of 550.0 mg/kg bw per day, a dose about 100 times higher than the normal human intake (*62*). In chronic feeding studies, administration of *trans*-anethole, 0.25%, 0.5% or 1% in the diet, for 117–121 weeks had no effect on mortality or haematology, but produced a slight increase in hepatic lesions in the treated groups compared with controls (*63*).

Unscheduled DNA synthesis was not induced in vitro by anethole, but was induced by estragole, an effect that was positively correlated with rodent hepatocarcinogenicity (*64*). However, the dose of estragole used (dose not specified) in the rodent studies was much higher than the dose normally administered to humans. Low doses of estragole are primarily metabolized by *O*-demethylation, whereas higher doses are metabolized primarily by 1'-hydroxylation, and the synthesis of 1'-hydroxyestragole, a carcinogenic metabolite of estragole (*65, 66*).

Clinical pharmacology

No information available.

Adverse reactions

In rare cases, allergic reactions such as asthma, contact dermatitis and rhinoconjunctivitis have been reported in sensitive patients (*67, 68*).

Contraindications

The fruits are contraindicated in cases of known sensitivity to plants in the Apiacaeae (*69, 70*). Owing to the potential estrogenic effects of the essential oil from the seeds and anethole (*44, 45, 50*), its traditional use as an emmenagogue, and the lack of human studies demonstrating efficacy, Fructus Foeniculi should not be used in pregnancy. Pure essential oils should not be given to infants and young children owing to the danger of laryngeal spasm, dyspnoea and central nervous system excitation (*12*).

Warnings

The pure essential oil from the fruits may cause inflammation, and has an irritant action on the gastrointestinal tract.

Precautions

Carcinogenesis, mutagenesis, impairment of fertility

An aqueous extract of the fruits, up to 100.0 mg/ml, was not mutagenic in the *Salmonella*/microsome assay using *S. typhimurium* strains TA98 and TA100 with or without metabolic activation with homogenized rat liver microsomes (*71, 72*). Aqueous and methanol extracts of the fruits, up to 100.0 mg/ml, were not mutagenic in the *Bacillus subtilis* recombination assay (*71*). However, a 95% ethanol extract, 10.0 mg/plate, was mutagenic in the *Salmonella*/microsome assay using *S. typhimurium* strains TA98 and TA102 (*73*). An essential oil from the fruits, 2.5 mg/plate, had mutagenic effects in the *Salmonella*/microsome assay in *Salmonella typhimurium* strain TA100 with metabolic activation (*74*), and in the *Bacillus subtilis* recombination assay (*75*). A similar essential oil had no effects in the chromosomal aberration test using Chinese hamster fibroblast cell lines (*76*).

Pregnancy: teratogenic effects

An essential oil from the fruits, up to 500.0 µg/ml, had no teratogenic effects in cultured rat limb bud cells (*61*).

Pregnancy: non-teratogenic effects

See Contraindications.

Nursing mothers

No restrictions on the use of infusions prepared from Fructus Foeniculi or the seeds.

Paediatric use
No restrictions on the use of infusions prepared from Fructus Foeniculi or the seeds. See also Contraindications.

Other precautions
No information available on general precautions or precautions concerning drug interactions; or drug and laboratory test reactions.

Dosage forms
Dried fruits, syrup and tinctures. Store the dried fruits in a well-closed container, protected from light and moisture (*7*).

Posology
(Unless otherwise indicated)
Daily dose: fruits 5–7 g as an infusion or similar preparations, higher daily doses (> 7 g fruits) should not be taken for more than several weeks without medical advice (*25*); fennel syrup or honey 10–20 g; compound fennel tincture 5–7.5 g (5–7.5 ml).

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