Aniseed

Species (Family)

Pimpinella anisum L. (Apiaceae/Umbelliferae)

Synonym(s)

Anise, Anisi Fructus, Anisum, *Anisum officinarum* Moench., *Anisum vulgare* Gaertn.

Part(s) Used

Fruit

Pharmacopoeial and Other Monographs

BHP 1996[G9]
BP 2001[G15]
Complete German Commission E[G3]
ESCOP 1997[G52]
Martindale 32nd edition[G43]
PDR for Herbal Medicines 2nd edition[G36]
Ph Eur 2002[G28]

Legal Category (Licensed Products)

GSL[G37]

Constituents[G2,G22,G41,G52,G58,G64]

Coumarins Scopoletin, umbelliferone, umbelliprenine; bergapten (furanocoumarin).

Flavonoids Flavonol (quercetin) and flavone (apigenin, luteolin) glycosides, e.g. quercetin-3-glucuronide, rutin, luteolin-7-glucoside, apigenin-7-glucoside; isoorientin and isovitexin (C-glucosides).

Volatile oils 2–6%. Major components are *trans*-anethole (80–95%), with smaller amounts of estragole (methyl chavicol),[G52] anise ketone (*p*-methoxyphenylacetone) and β-caryophyllene. Minor components include anisaldehyde and anisic acid (oxidation products of anethole), linalool, limonene, α-pinene, pseudoisoeugenol-2-methyl butyrate, acetaldehyde, *p*-cresol, cresol, hydroquinone, β-farnesene, α-, β- and γ-himachalene, bisabolene, *d*-elemene, *ar*-curcumene and myristicin.[1]

Other constituents Carbohydrate (50%), lipids 16% (saturated and unsaturated), β-amyrin (triterpene), stigmasterol (phytosterol) and its palmitate and stearate salts.

Food Use

Aniseed is used extensively as a spice and is listed by the Council of Europe as a natural source of food flavouring (category N2). This category allows small quantities of aniseed to be added to foodstuffs, with a possible limitation of an active principle (as yet unspecified) in the final product.[G16] In the USA, aniseed is listed as GRAS (Generally Recognised As Safe).[2,G41]

Herbal Use

Aniseed is stated to possess expectorant, antispasmodic, carminative and parasiticide properties. Traditionally, it has been used for bronchial catarrh, pertussis, spasmodic cough, flatulent colic; topically for pediculosis and scabies; its most specific use is for bronchitis, tracheitis with persistent cough, and as an aromatic adjuvant to prevent colic following the use of cathartics.[G2,G7,G64]

Aniseed has been used as an oestrogenic agent.[3] It has been reputed to increase milk secretion, promote menstruation, facilitate birth, alleviate symptoms of the male climacteric and increase libido.[3]

Dosage

Dried fruit Adults: 1.0–5.0 g crushed fruits in 150 mL water as an infusion several times daily.[G52] Children: 0–1 year old, 1.0 g of crushed fruits as an infusion; 1–4 years of age, 2.0 g; over 4 years, use adult dose.[G52]

Oil 0.05–0.2 mL three times daily.[G7]

Spirit of anise (BPC 1949) 0.3–1.0 mL three times daily.

Distilled anise water (BPC 1934) 15–30 mL three times daily.

Pharmacological Actions

The pharmacological effects of aniseed are largely due to the presence of anethole, which is structurally related to the catecholamines adrenaline, noradrena-

line and dopamine. Anethole dimers closely resemble the oestrogenic agents stilbene and stilboestrol.[3]

In vitro and animal studies

Antimicrobial, antifungal and insecticidal activities The volatile oil has antibacterial, antifungal and insecticidal activities.[G41,G52] Anethole, anisaldehyde and myristicin have exhibited mild insecticidal properties.[(G41,)]

Antispasmodic activity Anise oil (200 mg/L) was shown to antagonise carbachol-induced spasms in a guinea-pig tracheal muscle preparation.[G52]

Secretolytic and expectorant effect Application of aniseed (6.4 g/140 mL) to isolated ciliated epithelium of frog trachea induces small increases in transport velocity.[G52] Dilutions of anise oil increased respiratory tract fluid in anaesthetised guinea-pigs, rats and cats. A similar action was observed in anaesthetised rabbits inhaling anise oil.[G52] The reputed lactogogic action of anise has been attributed to anethole, which exerts a competitive antagonism at dopamine receptor sites (dopamine inhibits prolactin secretion), and to the action of polymerised anethole, which is structurally related to the oestrogenic compounds stilbene and stilboestrol.[3]

CNS activities Whole plant aqueous infusions have been reported to delay (but not prevent) the onset of picrotoxin-induced seizures and to reduce the mortality rate in mice following intraperitoneal injection.[4] Aniseed has also been found to slightly elevate γ-aminobutyric acid (GABA) concentrations in brain tissue.[4] The anticonvulsant effect is much weaker with aniseed than with conventional drug treatment and therefore its use as an anticonvulsant in Arabic folklore is not supported.[4] Anise oil diluted in sesame oil (0.25–1.0 mL/kg) given intraperitoneally to mice increased in a dose-dependent manner the dose of pentylenetetrazole needed to induce clonic and tonic seizures.[5] Activity was also observed against tonic seizures induced by maximal electric shock. Motor impairment was observed at higher doses of anise oil. Pentobarbital-induced sleeping time was prolonged by intraperitoneal administration of anise oil (50 mg/kg) to mice.[G52]

Other activities Oral administration of anethole (250–1000 mg/kg) to Swiss albino mice with Ehrlich ascites tumour in the paws indicated antitumour activity.[6] The conclusions were based on biochemical changes (nucleic acids, proteins, malondialdehyde, glutathione), survival rate and tumour weight. Anise oil given to rats (100 mg/kg given subcutaneously) stimulated liver regeneration after partial hepatectomy.[G52]

Clinical studies

Aniseed is mainly used for the treatment of dyspeptic complaints and catarrh of the upper respiratory tract.[G2,G41,G52] There is a lack of documented clinical studies with aniseed.

Side-effects, Toxicity

Contact dermatitis reactions to aniseed and aniseed oil have been attributed to anethole.[7,G31,G51] Reactions have been reported with products, such as creams and toothpastes, flavoured with aniseed oil.[G51] The volatile oil and anethole have been stated to be both irritant and sensitising.[G31,G51] Two female workers in a cake factory developed severe dermatitis, and patch tests indicated sensitivity to anise oil and to anethole.[8] Soreness, dryness and cracking of lips and perioral skin occurred in an individual using a herbal (fennel) toothpaste; anethole was reported to be the sensitising agent.[9] Bergapten is known to cause photosensitivity reactions and concern has been expressed over the possible carcinogenic risk of bergapten.[G45]

Ingestion of as little as 1–5 mL of anise oil can result in nausea, vomiting, seizures, and pulmonary oedema.[7]

The LD_{50} values per kg body weight for anise oil and *trans*-anethole are 2.7 g and 2–3 g, respectively.[G52] Mild liver lesions were observed in rats fed repeated anethole doses (695 mg/kg) for an unspecified duration.[3] Hepatic changes have been described in rats fed anethole in their daily diet (1%) for 15 weeks,[G22] although at a level of 0.25% there were no changes after one year. Rats fed with 0.1% *trans*-anethole in their diet for 90 days showed no toxic effects, but higher concentrations (0.3%, 1.0% and 3.0%) resulted in liver oedema.[G52] In therapeutic doses, anethole is reported to cause minimal hepatotoxicity.[G22] *Trans*-anethole given orally to rats (50–80 mg/kg) resulted in dose-dependent antiimplantation activity.[10] Significant oestrogenic activity was observed, but no anti-oestrogenic, progestational, anti-progestational, androgenic or antiandrogenic activity.[10]

Oral administration (1% of diet) of *trans*-anethole to rats resulted in induction of parathion-degrading drug enzymes.[G52] Male Wistar rats were treated with *trans*-anethole (125 or 250 mg/kg) by gavage for 10 days and the activities of liver microsome and cytosol phase I and II biotransformation enzymes were determined.[11] There was no effect on cyto-

chrome P450, but UDP-glucuronyltransferase activity in the cytosol towards the substrates 4-chlorophenol and 4-hydroxyphenol was significantly increased for both doses. It was concluded that *trans*-anethole preferentially induces phase II biotransformation in rat liver *in vivo*.[11]

The safety of *trans*-anethole (4-methoxy propenylbenzene) has been reviewed by the Expert Panel of the Flavour and Extract Manufacturer Association (FEMA).[2] The evaluation was based on whether the hepatotoxic metabolite anethole epoxide is produced. At low levels of exposure, *trans*-anethole is efficiently detoxicated in rodents and humans, primarily by O-demethylation and ω-oxidation, respectively, while epoxidation is only a minor pathway. At higher doses in rats, a metabolic shift occurs resulting in epoxidation and formation of anethole epoxide. The continuous intake of high doses of *trans*-anethole induces a continuum of cytotoxicity, cell necrosis and cell proliferation. In chronic dietary studies in rats, hepatotoxicity resulted when the daily production of anethole epoxide exceeded 30 mg anethole epoxide per kg body weight. Neither *trans*-anethole nor anethole epoxide showed any evidence of genotoxicity. The Expert Panel concluded that the hepatocarcinogenic effects in female rats occur via a non-genotoxic mechanism and are secondary to hepatotoxicity caused by continuous exposures to high hepatocellular concentrations of anethole epoxide. *Trans*-anethole was reaffirmed as GRAS, based on a thorough study of the scientific literature.[2] Because *trans*-anethole undergoes efficient metabolic detoxication in humans at low levels of exposure, the neoplastic effects in rats associated with dose-dependent hepatotoxicity are not indicators of any significant risk to human health from the use of *trans*-anethole as a flavouring substance.[2]

Contra-indications, Warnings

Aniseed may cause an allergic reaction. It is recommended that the use of aniseed oil should be avoided in dermatitis, and inflammatory or allergic skin conditions.[G31,G58] Aniseed should be avoided by persons with known sensitivity to anethole.[G52] Bergapten may cause photosensitivity in sensitive individuals. The documented oestrogenic activity of anethole and its dimers may affect existing hormone therapy, including the oral contraceptive pill and hormone replacement therapy, if excessive doses are ingested. In view of the structural similarity reported between anethole and myristicin, consumption of large amounts of aniseed may cause neurological effects similar to those documented for nutmeg.

Pregnancy and lactation Traditionally, aniseed is reputed to be an abortifacient[G22] and also to promote lactation. The safety of aniseed taken during pregnancy and lactation has not been established; however, there are no known problems provided that doses taken do not greatly exceed the amounts used in foods. It has been proposed that aniseed and preparations used at recommended dosages may be used during pregnancy and lactation.[G52]

Pharmaceutical Comment

The chemistry of aniseed is well studied and documented pharmacological activities support some of the herbal uses. Aniseed is used extensively as a spice and is widely used in conventional pharmaceuticals for its carminative, expectorant and flavouring properties. Aniseed contains anethole and estragole which are structurally related to safrole, a known hepatotoxin and carcinogen. Although both anethole and estragole have been shown to cause hepatotoxicity in rodents, aniseed is not thought to represent a risk to human health when it is consumed in amounts normally encountered in foods. Anethole was reaffirmed as GRAS in 1997 on the basis of the recognised metabolic detoxication of *trans*-anethole in humans at low levels of exposure (1 mg/kg body weight).[2] For medicinal use, it is recommended that treatment should not be continued for extended periods.

References

See also General References G2, G3, G9, G15, G16, G22, G25, G29, G31, G36, G37, G41, G43, G51, G52, G58 and G64.

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5 Pourgholami MH *et al.* The fruit essential oil of *Pimpinella anisum* exerts anticonvulsant effects in mice. *J Ethnopharmacol* 1999; 66: 211–215.
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