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Approach to pharmacological and clinical applications of Anisi aetheroleum

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PEER REVIEW

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Comments

This is a good, interesting and sufficient study about the Anisi aetheroleum which was obtained from *P. anisum*. This article included description of the plant (local names, distribution of the plant all over the world, morphology, medicinal uses). Except for overdose and precaution of the oil used, the author also discussed the preparation of the plant oil, toxicity, pharmacological uses and clinical application in details.

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ABSTRACT

Anisi aetheroleum is the oil obtained from *Pimpinella anisum* L. (*P. anisum*) by steam distillation. *P. anisum* seeds were air-dried, and then the dry seeds were crushed, pulverized, and weighed in sequence for anise oil preparation. *P. anisum* is one of the oldest medicinal plants that belong to family Apiaceae. The fruit of *P. anisum* is harvested in August and September. *P. anisum* is widespread in Asia, Africa and Europe. Local names of *P. anisum* include anise, anisoon, roomy, saunf, sweet cumin and yansoon. The anise oil odour is aromatic while the oil tastes sweet. The average daily dose of Anisi aetheroleum is 0.3 g. *trans*-Anethole is the major ingredient of the anise oil. Anisi aetheroleum also displays a protective action against neurotoxicity. In addition, Anisi aetheroleum increases glucose absorption and reduces urine output in the rat. The plant oil have pharmacological (antimicrobial, hepatoprotective, anticonvulsant, anti-inflammatory, antispasmodic, bronchodilator, estrogenic, expectorant and insecticidal) effects and clinical effects on nausea, constipation, menopausal period, virus, diabetes, obesity and sedative action. Owing to the wide application of Anisi aetheroleum in pharmacological and clinical fields, it is recommended for more clinical trails to discover a new medication from the active constituents of the plant oil in the future to treat human diseases especially chronic ones.

KEYWORDS

Anisi aetheroleum, *Pimpinella anisum*, Apiaceae, Pharmacology, Clinical effect

1. Introduction

Anisi aetheroleum is the oil prepared from *Pimpinella anisum* L. (*P. anisum*). *P. anisum* is one of the oldest medicinal plants that belong to family Apiaceae. It is an annual grassy herb with 30-50 cm high, white flowers, and small green to yellow seeds, which grows in the Mediterranean area, West Asia, Mexico, Egypt, and Europe[1]. The fruit of *P. anisum* is harvested in August and September. Anisi aetheroleum is used as flavouring, digestive, carminative, and for relief of gastrointestinal spasms. Consumption of the plant oil in lactating women increases milk and also relief their infants from gastrointestinal problems[2]. Local names of *P. anisum* include anise, anisoon, roomy, saunf, sweet cumin and yansoon. In the food industry, the anise oil is used as flavoring and aromatic agent for fish products, ice cream, sweets, and gums[1,3]. Anisi aetheroleum is used as analgesic in migraine and also as carminative, aromatic, disinfectant and diuretic in traditional medicine[4]. The anise oil has warm and dry nature. It can increase milk secretion, promote menstruation, facilitate birth, alleviate the symptoms of the male climacteric, and increase libido. It is also effective in polishing of teeth. In some traditional texts, anise oil is mentioned for melancholy, nightmare, and also in treatment of epilepsy and seizure[5,6]. Anisi aetheroleum was analyzed by gas chromatography. Gas chromatography-mass spectra showed the presence of *trans*-

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anethole (93.9%) and estragole (2.4%). Other compounds that were found with concentration higher than 0.06% were (E)-methyleugenol, α-cuparene, α-himachalene, β-bisabolene, *p*-anisaldehyde, and *cis*-anethole[3]. Some other compounds such as *trans*-pseudoisoeugenyl 2-methylbutyrate, *p*-anisaldehyde and methylchavicol were also identified in anise oil[7]. The other constituents of the plant oil, present in amounts of 1%-5% were *cis*-anethole, carvone, β-caryophyllene, dihydrocarvyl acetate, estragole and limonene[8]. Anisi aetheroleum is obtained from *P. anisum* grown in Spain, Germany, Italy and other European countries. The major constituents were anethole (>90%), γ-himachalene (2%-4%), *p*-anisaldehyde (<1%), methylchavicol (0.9%-1.5%), *cis*-pseudoisoeugenyl 2-methylbutyrate (3%), and *trans*-pseudoisoeugenyl 2-methylbutyrate (1.3%)[9]. Neophytadiene was isolated from the anise oil[10]. 4-(β-D-glucopyranosyloxy) benzoic acid, one of the phenolic glycosides, was also isolated from anise oil[11]. Four aromatic compound glucosides, an alkyl glucoside and a glucide were isolated from the anise oil as new compounds. The structures of the new compounds were clarified as (E)-3-hydroxy-anethole β-D-glucopyranoside, (E)-1'-(2-hydroxy-5-methoxyphenyl) propane β-d-glucopyranoside, 3-hydroxyestragole β-d-glucopyranoside, methyl syringate 4-*O*-β-D-glucopyranoside, hexane-1,5-diol 1-*O*-β-D-glucopyranoside and 1-deoxy-l-erythritol 3-*O*-β-dglucopyranoside[12]. Isolation and structure elucidation of flavonoid constituents from the anise oil by means of chromatography on cellulose columns lead to isolation of quercetin 3-glucuronide, rutin, luteolin 7-glucoside, isoorientin, and isovitexin as crystalline compounds, and apigenin 7-glucoside and a luteolin glycoside as noncrystalline compounds[13]. A silver ion high performance liquid chromatography procedure was used to determine the fatty acids composition of Anisi aetheroleum, and showed the positionally isomeric 18:1 fatty acids oleic acid (*cis* 9-18:1), petroselinic acid (*cis* 6-18:1), and *cis*-vaccenic acid (*cis* 11-18:1), in the plant oil by a single gradient run on a single cation exchange column laboratory converted to the silver ion form[14]. Also three lignin-carbohydrate-protein complexes were isolated from a hot water extract of the seeds of *P. anisum* by combination of anion exchange, gel filtration, and hydrophobic interaction column chromatography[15].

This review should act to stimulate a thought process on importance of the pharmacological and clinical applications of the Anisi aetheroleum and the usefulness of this plant oil in pharmaceutical industry process.

2. Preparation of Anisi aetheroleum

P. anisum seeds were air-dried in an oven at 40 ℃ for 4 d and then the dry seeds were crushed, pulverized and weighed in sequence for oil preparation. Distilled water was placed in the steam generator, and then the steam generator started heating to produce steam. The seed powder was placed in the round bottom flask. A vigorous current of steam from steam generator passed through the round bottom flask. A part of the steam condensed in the round bottom flask. As more and more steam passed, the steam volatile components of the seed powder passed through the condenser along with steam. These contents on condensation were collected in the receiver. The contents in the round bottom flask were heated by a Bunsen burner to prevent excessive condensation of steam. The process of steam distillation was continued for about half an hour. The distillate was transferred to a separating funnel and extracted with petroleum ether 3 times. Then, the petroleum ether extract was dried with anhydrous sodium sulphate. The solvent was removed from the dried filtrate by careful distillation in a water bath and the essential oil was left behind in the distillation flask.

3. Toxicology of Anisi aetheroleum

El-Wahab and Moram investigated the effect of *trans*-anethole of Anisi aetheroleum[16]. The anethole induced a significant decrease in body weight, hemoglobin concentration and red blood cell count. Also there was a significant decrease in reduced glutathione content, glutathione-S-transferase (GST) and superoxide dismutase activities in both blood and liver of rats in test groups compared to control group. On the other hand, a significant increase in serum alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase activities, bilirubin, urea, creatinine, total protein and albumin were observed in all test groups when compared with control group. In a study, combinations of two cytotoxic phytochemicals (anethole and curcumin) from Anisi aetheroleum were applied in binary combination with platinum drugs (cisplatin and oxaliplatin) against three epithelial ovarian cancer cell lines: parental A2780, $A2780^{cisR}$ (cisplatin-resistant) and $A2780^{ZD0473R}$ (ZD0473-resistant). Cell viability was quantified using the 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide reduction assay and the combined drug action was analyzed. Greatest synergism was observed when the phytochemical Anisi aetheroleum anethole was added first followed by the platinum drug 2 h later, and additiveness to antagonism in combined drug action was observed when the two compounds were administered as a bolus[17]. The essential oils from four Apiaceae species including anise oil were evaluated for their antifeedant, growth inhibitory, and insecticidal activities against *Pseudaletia unipuncta* (Lepidoptera: Noctuidae) fourth instar larvae. Essential oils were characterized by gas chromatography and mass spectrometry. The results showed that anti-insect activity the essential oils varied according to plant specie/composition, type, and exposure period. The plant oils containing *trans*-anethole exerted acute effects on larvae feeding and growth. For the most active essential oils/compounds, dose-dependent toxicity was determined and inverse relationships of LC_{50} with time were established[18]. Natsch and Haupt examined the suspected prohaptens such as *trans*-anethole as well as methyl isoeugenol and eugenol as skin-sensitizing prohaptens in a modified KeratinoSens assay. The result obtained showed no, or only weak, gene induction in absence of S9 fractions, and a significantly enhanced luciferase induction in presence of S9, proving their prohapten status[19]. On another study, Chang *et al*. studied the toxicity of 12 insecticides and 3 essential oils which contained anethole as a major constituent[20]. Based on the results, mixture of *Bacillus thuringiensis* var. *israelensis* and anethole were significantly more toxic against *Aedes albopictus* larvae (0.023 7 mg/L) and *Anopheles sinensis* larvae (0.054 1 mg/L) than either *Bacillus thuringiensis* var. *israelensis* (1.788 4 and 2.168 1 mg/L) or anethole (16.660 0 and 25.110 0 mg/L) alone.

4. Pharmacological effects

4.1. Antimicrobial effect

Gülçin *et al*. examined the antimicrobial effect of Anisi aetheroleum against 10 bacterial species and *Candida albicans* (*C. albicans*) with disc diffusion method[21]. In this study, the plant oil showed significant inhibitory activity against all tested bacteria. However, the antimicrobial effect of Anisi aetheroleum was effective against *C. albicans*. Anisi aetheroleum also showed antibacterial activity against *Micrococcus luteus* and *Mycobacterium smegmatis*[22]. Synergic antibacterial activity of *Thymus vulgaris* and *P. anisum* essential oils was evaluated against 9 pathogenic bacteria. Essential oils of these plants exhibited antibacterial activity against most tested pathogens, and the maximum effect was