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Review

A review of chemistry and bioactivities of a medicinal spice: *Foeniculum vulgare*

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***Foeniculum vulgare* Mill. with common name fennel, is a very popular spice as well as an important traditional Chinese medicine. The plant is native to Southern Europe and Mediterranean region. It has two important subspecies of *Capillaceum* and *Piperitum.* It mainly contains essential oil, fatty acids and phenolic compounds, etc. The most intense odor compounds of fennel are *trans*-anethole, estragole and fenchone. Fennel has many biological activities due to its volatile and nonvolatile compounds, and it has been used in traditional Chinese medicine for treating various conditions, particularly rheumatism, cold pain and stomach disorder. It is also used as a spice for its aromatic fruit. This review covers progresses on the chemistry, pharmacology and nutraceutical value of fennel, and aims to lay the foundation for further study and utilization of fennel.**

Key words: Chemistry, bioactivity, *Foeniculum vulgare*.

INTRODUCTION

Foeniculum vulgare Mill. (Apiaceae family) commonly known as fennel, is one of the widespread annual or perennial plants with aromatic odor. It was native to Southern Europe and Mediterranean region. Now it is widely cultivated throughout the temperate and tropical regions of the world. It is also a very popular medicinal and economic plant in China (Figure 1). The herb has many culinary and traditional medicine uses. The bulb, young shoots, leaves and fully ripened and dried fruits are commonly used for homemade remedies. Its aromatic fruits have been used as a culinary spice in many countries (Tanira et al., 1996). Fennel herbal tea including infusions and instant teas containing fennel seed extract, is a common household remedy traditionally used for the treatment of a variety of symptoms of the gastrointestinal and respiratory tract in some areas of Europe and Asia (Raffo et al., 2011). As an important economic crop, fennel has been used and traded internationally for centuries due to its therapeutic and culinary utilization.

In China, fennel fruit was used both as tradition Chinese medicine (TCM) and as common food with Chinese name 'Xiaohuixiang', which was recommended by Ministry of health of China. Fennel fruits have been used as TCM for the treatment of infants suffering from dyspeptic disorders in China for centuries. It was highly recommended for bronchitis and chronic coughs, kidney stones, dysmenorrhea, vomiting and diarrhea, and defection of sperm. It was considered to have diuretic, stomachic and galactogogue properties due to its volatile compounds.

F. vulgare has been intensively cultivated in China. It can be divided into different fennel subspecies or varieties by its chemicals or utilization. *Vulgare* and *Piperitum* were two important subspecies of *F. vulgare. Piperitum,* with bitter seeds, and is characterized by the presence of rotundifolone, while *vulgare*, with sweet seeds, varied with *e*stragole, *trans*-anethole, limonene and fenchone, by which different chemotypes can be divided (Muckensturm et al., 1997). *Vulgare* variety is usually used as flavorings in baked goods, meat and fish dishes, ice cream, and alcoholic beverages, due to its characteristic anise odor.

However, according to others botanists, *F. vulgare* has two varieties. One is sweet fennel (*F. vulgare* var*. dulce*), which is annuals or biennials with small sweet-tasting fruits. The other is bitter fennel (*F. vulgare* var*. vulgare*), which is a perennial with fruits having a bitter taste (Cosge et al., 2008; Miraldi, 1999). Different populations of *F. vulgare* contain 10-nonacosanone as a specific chemical marker, and *trans*-anethole is the major volatile

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Figure 1. The plant of *Foeniculum vulgare growing* in Shanghai.

constituent. This review aims to report the bioactive components of the fennel and their pharmacology, and to lay the foundation for further study and utilization of fennel.

CHEMICAL COMPOSITION

The chemical constituents from the fennel include essential oil, fatty acid, phenylpropanoids, monoterpenids, sesquiterpenes, coumarins. It also contains triterpenoids, tannins, flavonoids, cardiac glycosides, saponins, and other types of compounds.

Essential oil

In western countries, essential oil of fennel fruits (referred as fennel oil) was used for flavouring purpose, cosmetic and pharmaceutical products (Bilia et al., 2000). The volatile compounds of fennel fruits were well studied by hydrodistillation, extraction with classical solvents, supercritical fluid extraction (SFE), headspace solvent microextraction and solid-phase microextraction (SPME) (Damjanovic et al., 2005; Tschiggerl et al., 2010). The relative content of essential oil in fennel fruits was about 3.00% by weight.

The prominent component of oil was *trans*-anethole (70.1%) and the most intense odor compounds of fennel fruits were *trans*-anisole, estragole, fenchone and 1-octen-3-ol. (Diaz-Maroto et al., 2005; Mimica-Dukie´et al., 2003). Napoli et al. (2010) identified 78 compounds from fennel fruits by GC-FID-MS, representing more than 98% of the oils. They can be divided into monoterpene hydrocarbons, oxygenated monoterpenes and phenylpropanoids. The main compound estragole was ranging from 34 to 89%. The essential oil of bitter fennel fruits was characterized by relatively high concentrations of α-pentene and fenchone, and low concentrations of *trans*-anethole and estragole, unlike sweet fennel oils (Akgül and Bayrak, 1988).

Fatty acids

The fruits of fennel contain about 20% fatty acids and petroselinic acid is a characteristic fatty acid of fennel oil. The level of petroselinic acid could be as high as 70 to 80% (Reiter et al., 1998; Charvet et al., 1991). The sweet fennel and bitter fennel showed no obvious differences in oil content and fatty acid composition (Cosge et al., 2008). The chemical analysis of the acetone extract of fennel showed that linoleic acid (54.9%), palmitic acid (5.4%) and oleic acid (5.4%) were major components in acetone extract (Singh et al., 2006).

Phenolic compounds

There has been a growing interest in phenolic components of fruits and vegetables, which may promote human health or lowering the risk of disease. Aqueous extract of fennel fruits contains rich phenolic compounds. Many of them have antioxidant activities, such as 3-caffeoylquinic acid, 4-caffeoylquinic acid, 1.5-O-dicaffeoylquinicacid, rosmarinic acid, eriodictyol-7-O-rutinoside, quercetin-3-O-galactoside, kaempferol-3-O-rutinoside and kaempferol-3-O-glucoside. Besides, these compounds, fennel was reported containing hydroxyl-cinnamic acid derivatives, flavonoid glycosides and flavonoid aglycones (Parejo et al., 2004).

Flavonoids

Flavonoids were generally considered as an important category of antioxidants in the human diet. Flavonoids were rich in the plants of Apiaceae family. It was reported that the presence of flavonol glycosides in fennel species was related to their morphological heterogeneity and variation, and some flavonoids such as quercetin arabinoside were identified from *F. vulgare* (Harborne et al., 1971, 1972, 1984). Total flavonoid contents of the hydroalcoholic extracts were about 12.3 ± 0.18 mg/g. Flavonoids such as quercetin, rutin and isoquercitrin were reported to have the immunomodulatory activities

(Cherng et al., 2008).

Polyacetylenes

Polyacetylenes were chemosystematic marker compounds for Apiaceae and exhibited potential detrimental bioactivities for the human consumer. Falcarindiol and falcarinol are contained in fennel at trace amounts (less than 0.3 mg/g) (Christian et al., 2005). Fennel bulbs also contain polyacetylenes including falcarinol, falcarindiol and falcarindiol-3-acetate. Thermal processing had effect on these components. When compared to raw unprocessed fennel bulbs, boiling resulted in a significant decrease in the levels of polyacetylenes, and roasting resulted in a significant decrease in falcarindiol, falcarindiol-3-acetate, and falcarinol by 81, 78 and 66%, respectively (Rawson et al., 2011).

BIOLOGICAL ACTIVITY

Fennel has many biological activities due to its volatile and nonvolatile compounds. It is prescribed as an aromatic stomachic in TCM to treat various conditions, particularly rheumatism, cold pain and stomach. Fennel essential oil possessed carminative and stimulant activities as well as spasmolytic actions on the smooth muscles of experimental animals (Khan et al., 2009). Furthermore, it possessed analgesic, anti-inflammatory and antioxidant activities (Choi and Hwang, 2004). Oral administration of methanol extract of fennel exhibited inhibitory effect against acute and subacute inflammatory diseases and showed a central analgesic effect by inhibition of the Type IV allergic reactions.

It significantly increased the specific activities of superoxide dismutase (SOD) and catalase, meanwhile significantly decreased the high density lipoprotein–cholesterol level, thus decreasing the peroxidative damage (Choi and Hwang 2004). The essential oil of fennel exhibited antibacterial and antiviral activities (Ruberto et al., 2000; Shukla et al., 1988). The aqueous and ethanol extracts of fennel exhibited potential antioxidant properties in vitro studies (Oktay et al., 2003). Methanol extracts of the whole plant of fennel administered for four successive days ameliorated the amnesic effect of scopolamine (0.4 mg/kg) and aging induced memory deficits in mice. It might be useful for the treatment of cognitive disorders such as dementia and Alzheimer's disease (Joshi, 2006).

Antioxidant activities

Naturally-occurring antioxidants can be used to protect human beings from oxidative stress damage (Scalbert et al., 2005). Fennel was known as excellent sources of nature antioxidants and contributed to the daily antioxidant diet (Shahat et al., 2011). Wild fennel was found to exhibit a radical scavenging activity with higher content phenolic and flavonoid than medicinal and edible fennel, and the aerial parts of the Italian populations showed the highest DPPH scavenging activity (Faudale et al., 2008). Phenolic compounds of fennel, including caffeoylquinicad, Rosmarinicacid, eriodictyol-7-O-rutinoside, quercetin-3-O-galactoside and kaempferol-3-O-glucoside, showed antioxidant activities (Parejo et al., 2004). The volatile oil showed strong antioxidant activity in comparison with butyrated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) (Singh, 2006). Ethanol and water extracts of fennel showed less antioxidant activity compared with essential oil (Diaz-Maroto et al., 2005).

Acaricidal and larvicidal activities

Since many natural products were largely free from adverse effects and have excellent biological activity, they may provide an alternative to currently use mite-control agents to control stored-food mites (Kim et al., 2004; Kim et al., 2001). Fennel oil show significant acaricidal activity against *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*.

The major bioactive component is fenchone. *P*-anisaldehyde was the most toxic compound to *D. farinae* and is much more effective compared with benzyl benzoate hymol and estragol (Lee, 2004). While carvone was characterized as bioactive constituent to *Tyrophagus putrescentiae*. They might be as potential house dust mite control agents or as potential stored-food mite control agents (Lee et al., 2006).

It was acknowledged that various plant oils or extracts can exert toxic activity against mosquito species. The fennel extracts was reported to have insecticidal activity against different mites and insects (Mimica-Dukić et al., 2003). Fennel essential oil at a concentration of 40 mg/L was sufficient to register 50% mortality for the second instars larvae after 2 h exposition time. Moreover, concentration at 60 mg/L after 4 h exposition time ensured 90% mortality for the fourth instars larvae (Zoubiri et al., 2011). *Trans*-anethole (72.27 to 74.18%), fenchone (11.32 to 16.35%) and methyl chavicol (3.78 to 5.29%) were main constituents of the fennel extracts. *Trans*-anethole was known to have effective larvicidal activity against mosquito species (Conti et al., 2010; Chantraine et al., 1998; Cheng et al., 2004).

Extracts of fennel were toxic against *Culex pipiens* larvae, and terpineol and 1,8-cineole were the most effective components against *Anopheles dirus* and *Aedes aegypti*, which suggested fennel was an alternative use of synthetic insecticides (Traboulsi et al., 2005; Kim et al., 2001; Lee et al., 2006).

Antimicrobial, antibacterial and antifungal activities

The antimicrobial activity of plant oils and extracts has been recognized for many years, and they have many applications, including raw and processed food preservation, pharmaceuticals, alternative medicine and natural therapies. The chloroform soluble fraction from the stems of fennel exhibited a potent antimicrobial activity against bacteria and fungi. Dillapional, scopoletin, dillapiol, bergapten, imperatorin, psolaren and dillapional were found to be antimicrobial principles against *Bacillus subtilis*, *Aspergillus niger* and *Cladosporium cladosporioides* (Kwon et al., 2002).

Essential oils from the fruits of fennel showed significant antibacterial activity to *Escherichia coli* and *Bacillus megaterium* (Araque et al., 2007; El-Adly et al., 2007). Fennel essential oils may be useful natural bactericides for the control of bacterial diseases of plants. Chloroform soluble fraction from *F. vulgare* exhibited potent antimicrobial activity against bacteria and fungi. Dillapional, scopoletin, dillapiol, bergapten, imperatorin and psolaren were found to be antimicrobial principle of fennel against *B. subtilis*, *A. niger* and *C. cladosporioides* (Kwon et al., 2002).

Essential oils of *F. vulgare*, anethole, fenchone and camphor showed antifungal activities against *C. cladosporioides*, *Penicillium helianthi* and *Trichophyton mentagrophytes*, compared with a standard mycotoxic bifonazol, *Penicillium ochrochloron, Penicillium funiculosum and Trichoderma viride* were the most resistant species (Mimica-Duki et al., 2003; Singh et al., 2006).

Dichloromethane extracts and essential oils from *F. vulgare* showed antifungal activity against *Candida albicans*. It could be the candidate for a new antifungal agent for candidiasis and other fungal diseases (Park et al., 2010).

Hepatoprotective activity

Fennel essential oil could inhibit the CCl_4 induced acute hepatotoxicity by decreasing levels of serum aspirate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and bilirubin. D-limonene and β-myrcene of the oil might be the potential candidates (Ozbek et al., 2003).

Estrogenic activity

Since the discovery of the estrus inducing effects of some plant products in 1926, considerable effort has been devoted to the isolation and structural and pharmacological characterization of phytoestrogens, including flavonoids, isoflavonoids, chalcons, coumestans, stilbenes, lignans, saponins, and essential oils,etc. (Lóránd et al., 2010; Shaaya et al., 1997). Fennel oil was reported to exhibit estrogenic activity, promote menstruation, alleviate the symptoms of female climacteric, and increase libido (Albert-Puleo, 1980). The mechanism was probably different from that of oxytocin and PGE2. It may be used for alleviation of dysmenorrhea sequalee (Albert-Puleo, 1980; Ostad et al., 2001).

Flavor and nutraceutical properties

The Mediterranean diet was currently attracting considerable interest because of its likely health benefits (Willett, 1994). Due to unique and preferred flavour and aroma, dried seeds of sweet fennel were commonly used in cooking as kitchen vegetable. Fennel seeds are used for savory formulations, sauces, liqueurs, confectionery, cookies, cheeses, sauces, pickles and beverages, etc. Medicinal diet, also called ‘yaoshan’ in Chinese, was very popular in china, such as ‘sausages fried fennel leaves’, ‘shredded pork fennel’. The swollen bases of fennel were freshly consumed in salad, cooked fish for grilling, preserve food, and bread bouillons.

In addition, fennel provided an excellent source of potassium, calcium, magnesium, iron, phosphorous and zinc (Trichopoulou et al, 2000). Different parts of fennel all have nutritional values. They contained rich carbohydrates, sugars, fatty acid, mucilage and vitamin A. Fennel is a health food which can be used to reduce the potential of lung cancer, asthma and prevent thrombosis and atherosclerosis (Vardavas et al., 2006). However, this herb or preparations containing fennel are not suggested for small children or pregnant women and should not be used for a prolonged period of time, though it was highly appreciated as a carminative for its mild flavor and good tolerance in infant care (Raffo et al., 2011).

CONCLUSIONS

Fennel has been used as food and medicine with long history in central Europe and Mediterranean region as well as in China. It is also a flavor food with health value. Numerous compounds including *trans*-anethole, estragole, fenchone, sesquiterpenoids, coumarins and polyphenolics were isolated from this plant, most of which exhibited significant bioactivities. The fennel has potential beneficial therapeutic actions in the management of bacterial and fungal infections and colic pain. Both the fruit and whole plant of this plant might be the source of chemical and biological materials in future. For further utilization of this plant, systematic phytochemical and biological mechanic studies are needed.

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