

Medicinal Traits of the Phenolic Compound from *Foeniculum vulgare* for Oligomenorrhea [†]

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Abstract: A phenolic compound in *Foeniculum vulgare* can improve human health. *Foeniculum vulgare* contains flavonoids, glycosides, and other constituents that are used for medicinal ailments. Trans-anethole, fenchone, and estragole essential oils are the main ingredients in *F. vulgare* seeds. The principle component of fennel oil, anethole, has structural similarity with the synthetic oestrogen diethylstilbestrol, making it an active estrogenic agent. Women with PCOS may exhibit obesity, amenorrhea, oligomenorrhea, infertility, or androgenic features, which are characterized by the absence of ovulation and hyperandrogenism. Oligomenorrhea is a kind of irregular menstruation period. Treatment of oligomenorrhea depends on the causes; the main cause of oligomenorrhea is the presence of polycystic ovarian syndrome (PCOS), with 75–85% experiencing infrequent periods. This mini-review focuses on *F. vulgare* seeds as an advantageous addition to treat PCOS. Women with PCOS also have a lower level of the hormone progesterone due to the absence or reduction in ovulation. Numerous phytoestrogens can be found in *F. vulgare* seeds; with less insulin resistance and lower blood sugar level, fennel phytoestrogen content is beneficial. It is also thought to aid in reducing the cellular balance that causes PCOS's metabolic abnormalities.

Keywords: *Foeniculum vulgare*; phytoestrogen; anethole; oligomenorrhea; polycystic ovarian syndrome



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1. Introduction

Fennel, also known as *Foeniculum vulgare* (FV), is a popular medicinal herb that is indigenous to the Mediterranean region. It is grown in various parts of Europe and Asia, and much of it is imported from countries like Egypt, China, and India [1]. The biennial Apiaceae family member, *Foeniculum vulgare*, is a medicinal and aromatic fruit (Umbelliferaceae). With bright yellow flowers and delicately textured leaves, it is a hardy perennial plant having hollow stems that allow it to grow to a height of up to 2.5 m. The final section of each leaf is filiform (like a thread) and about 0.5 mm wide. Leaves grow to a height of 40 cm. Compound umbels are the structures that form flower terminals. Dry seeds that are 4–10 mm long make up the fruit [2]. FV fruit has a long history of use as a food and medicinal product. It has long been held that the plant increases the production of breast milk and functions as a carminative, which helps manage flatulence. Additionally, this herb has been said to increase libido, stimulate menstrual flow, lessen symptoms of the male climate, expedite delivery, ease indigestion, and relieve coughing [3].

Women of reproductive age who experience menstrual cycle problems may experience difficulties getting pregnant. One of the most typical menstrual bleeding disorders is oligomenorrhea, and in recent years, a rising number of individuals have sought medical

attention for this symptom. Women who have oligomenorrhea experience 5–7 cycles a year or menstrual intervals greater than 35 days and less than 90 days [4,5].

According to several studies conducted throughout the world, the prevalence of oligomenorrhea has significantly increased in recent years and now ranges from 12% to 15.3% [6], with 10–20% of cases occurring in infertile women [7]. Therefore, it is crucial to correctly diagnose and treat menstruation diseases [8,9].

Endocrine conditions such as polycystic ovary syndrome (PCOS), thyroid dysfunction, premature ovarian failure, hypothalamus dysfunction, and prolactinomas are frequently responsible for menstrual cycle disturbances [10]. Patients with PCOS, in particular, have expressed symptoms of irregular ovulation, and 75% to 85% of them are thought to suffer oligomenorrhea [11].

As a helpful supplement for managing PCOS, *Foeniculum vulgare* seeds are employed. Their phytoestrogen content is abundant. Therefore, *Foeniculum vulgare* seed extract and its impact on preventing conception were investigated. Due to its structural similarity to the synthetic oestrogen diethylstilbestrol, the main active ingredient in fennel oil, anol or anethole, is regarded as an active estrogenic agent. Phytoestrogen content in fennel helps in reducing insulin resistance and in bringing down the inflammation in PCOS. It is also believed that it helps in reducing cellular imbalance, which leads to metabolic disturbances in PCOS [12].

2. Botanical Description of *Foeniculum vulgare*

One of two fennel seeds can occasionally be found on the stem after splitting in two. They range in colour from light green to brown, are curved, and measure 4–8 mm (1/8–5/16 inch) in length (the green being superior). Fennel, which grows to a height of 1.5 to 2.5 m and is related to parsley but is hardly a perennial, is sometimes grown as an annual (5–8 ft.). It can cross-pollinate with dill because of its resemblance. As a result of the resulting seed's dulled flavour, it should be kept from dill. Before the seeds ripen, flower heads are harvested and then dried entirely before being thoroughly threshed. This plant, fennel, is quite lovely. It has a robust, perennial root system and a sturdy, cylindrical, erect, bright green, and heavily branched stem bearing leaves segments. Its height ranges from 4 to 5 feet. The bright golden flowers, produced in large, flat terminal umbels with thirteen to twenty rays, bloom in July and August [13]. The image of Fennel fruits is shown in Figure 1.



Figure 1. Fruits of *Foeniculum vulgare*.

2.1. Taxonomy

Kingdom—Plantae
Clade—Tracheophytes
Clade—Angiosperms
Clade—Eudicots
Clade—Asterids
Order—Apiales

Family—Apiaceae
 Genus—*Foeniculum*
 Species—*F. vulgare* [14]

2.2. Phytochemistry

Alkaloids, phytosterols, phenols, tannin, coumarin, flavonoids, and volatile oil are all present in *F. vulgare*. According to some estimates, *fennel* has 6.3% moisture, 9.5% protein, 10% fat, 13.4% minerals, 15.5% fibre, and 42.3% carbs. There are a number of vitamins and minerals in *F. vulgare*, including calcium, potassium, sodium, iron, phosphorus, thiamin, riboflavin, niacin, and vitamin C.

Essential Oils

The essential oil of *F. vulgare* is well known. Trans-anethole, fenchone, estragole (methyl chavicol), and alpha-phellandrene have been identified as the main components of *F. vulgare* seed essential oil. Their molecular structures are shown in Figure 2. The primary component, trans-anethole, had a content that ranged from 81.63% to 87.85%. According to a different study, the major phenylpropenes estragole and trans-anethole, which make up the oleoresin of the aerial part of *F. vulgare*, changed as the plant developed, with these two compounds peaking in the flowers and developing mericarps. The *F. vulgare* fruits' essential oil is typically responsible for their pharmacological effects. The primary acaricidal compounds against *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* were found to be fencholine and p-anisaldehyde. Anethole has been identified as an active oestrogenic agent in several studies. However, it has been demonstrated in several research that the real oestrogenic agents are dianethole and photoanethole polymers of anethole. Anethole's antiplatelet activity, clot-destabilizing effect, and vaso-relaxant action have been reported to make it a safe antithrombic drug [15]. The molecule structures of the major bioactive essential oil component of *F. vulgare* are shown in Figure 2.

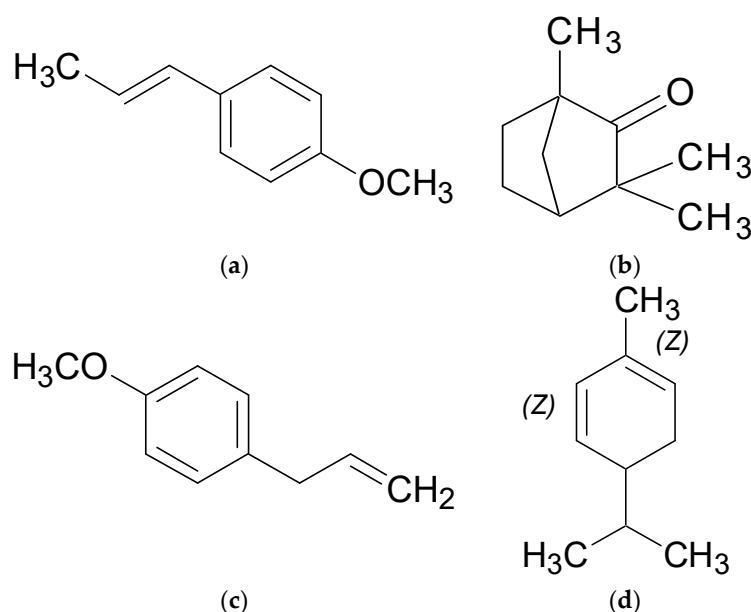


Figure 2. The molecule structures of the major bioactive essential oil component of *F. vulgare*. (a) Trans-anethole; (b) Fenchone; (c) p-anisaldehyde; (d) alpha-phellandrene.

3. Oligomenorrhea

The prevalence of oligomenorrhea, defined as irregular menstrual periods occurring at intervals of 36 days to 6 months or 5–7 cycles per year, is 10.2% among women of reproductive age. The most prevalent endocrine condition in women, polycystic ovarian syndrome (PCOS), is frequently linked to oligomenorrhea. Hormone therapy is the primary

treatment for oligomenorrhea, although research on infertile women with PCOD found that only 25.6% of them adhered to the regimen well. Normal menstruation is considered a sign of healthy, normal reproductive organs in Iranian traditional medicine (also known as Humoral, Unani, or Persian traditional medicine) [16].

Different characters in living things are created by temperament, which is made up of the action and reactions of four key components (fire, air, water, and earth). Temperament can be broken down into four categories: hot, cold, wet, and dry. Diseases can be caused by any changes in the natural temperament of an organ (sometimes referred to as a mal-temperament). The goal of treatment is to alter temperament. In TPM, oligomenorrhea is modelled as “Ehtebas Tams”. According to TPM, the main causes of oligomenorrhea are structural and functional problems (mal-temperaments) in the uterus, ovaries, and other organs other than the genital system. Treatment for oligomenorrhea includes modifying one’s lifestyle (especially nutritional habits, diet, physical activities, and sleep). One of the main tenets of treatment is the use of herbal medicines, which can correct organ mal-temperaments [17].

Causes of Oligomenorrhea

- Polycystic ovarian disease: With PCOS, your body produces an excessive amount of androgens, which can prevent ovulation, the phase of your cycle when your ovaries release an egg.
- Androgen-secreting tumour: Your menstrual cycle may be messed up by androgens released by tumours on your ovary and adrenal glands. The symptoms of these tumours frequently resemble those of PCOS.
- Prolactinomas: A prolactinoma is a tumour that causes your pituitary gland to produce an excessive amount of the prolactin hormone and insufficient amounts of the sex hormones necessary for regular menstruation, such as oestrogen.
- Pelvic inflammatory disease: PID can result from untreated STIs (sexually transmitted diseases). The ensuing infection and inflammation may cause your menstrual cycle to become irregular.
- Asherman syndrome: Your natural menstrual flow is interrupted if you have scar tissue on your uterus or cervix, which most often results after gynecological surgery like dilatation and curettage.
- Uncontrolled diabetes mellitus: Diabetes types 1 and 2 have been connected to oligomenorrhea. Underweight (frequent in Type 1 diabetes) and overweight individuals are more likely to experience it (common in Type 2 diabetes).
- A side effect of oral contraceptive pills [18,19].

Oligomenorrhea often happens alongside polycystic ovary syndrome (PCOS). Of those with PCOS, 75% to 85% experience infrequent periods. PCOS and infrequent periods often happen together [19].

4. Polycystic Ovarian Syndrome

Hormonal levels in women are impacted by polycystic ovary syndrome (PCOS). The reproductive organs that produce progesterone and oestrogen, which control the menstrual cycle, are affected by PCOS in women. Additionally, the ovaries secrete a limited quantity of androgens, which are masculine hormones. A persistent ovulatory condition is polycystic ovarian syndrome (PCOS). The majority of women with PCOS have elevated levels of luteinizing hormone and reduced levels of follicle-stimulating hormone (FSH), along with elevated levels of androgens and insulin. Independent ultrasound and endocrine studies have suggested that PCOS is the cause in one-third of women with amenorrhea and 90% of women with oligomenorrhea [20]. These imbalances can manifest as oligomenorrhea or amenorrhea (infrequent or lack of menstruation). The under-production of estrogen and overproduction of androgens (testosterone, dehydroepiandrosterone, and androstenedione) by the ovaries can result in a number of additional clinical features, including tiny cysts on the surface of the ovaries (polycystic) and hair and skin symptoms [21].

5. Effect of *Foeniculum vulgare* on PCOS

To manage PCOS, *Foeniculum vulgare* seeds are a useful complement and source of abundant phytoestrogens. The anti-fertility impact of the seed extract of *Foeniculum vulgare* was studied. Due to its structural similarity to the synthetic oestrogen diethylstilbesterol, the molecule anole, also known as anethole, which constitutes the majority of *fennel* oil's active ingredient, is thought to be an active estrogenic agent. It was discovered that the extract increased nucleic acids, and both tissues' organ weights and protein concentrations were measured. Fennel's phytoestrogen concentration aids in lowering inflammation in PCOS and improving insulin resistance. It is also thought to aid in reducing the cellular imbalance that causes PCOS's metabolic abnormalities. The estrogenic effects of oral fennel extract for 10 days on the weight of female genital organs (the mammary glands, oviduct, endometrium, myometrium, cervix, and vagina) have been shown [22]. Fennel has the ability to manage polycystic ovary (PCO) treatment due to its phytoestrogen components and traditional beliefs. In PCOS, fennel extract enhanced serum progesterone levels and endometrial thickness while decreasing serum oestrogen levels and uterine epithelial cell thickness [23].

6. Conclusions

Women of reproductive age who experience menstrual cycle problems may experience difficulties getting pregnant. One of the most typical menstrual bleeding disorders is oligomenorrhea (irregular periods). Treatment of oligomenorrhea depends on the causes; the main cause of oligomenorrhea is polycystic ovarian syndrome (PCOS) present, with 75–85% experiencing infrequent periods. The mini-review focuses on *F. vulgare* seeds as an advantageous addition to treat PCOS. Oligomenorrhea and polycystic ovary syndrome (PCOS) happen together. PCOS and infrequent periods often happen together. *Foeniculum vulgare* seed is a helpful supplement for managing PCOS; its phytoestrogen content is abundant. The main active ingredient in *fennel* oil, anole or anethole, is regarded as an active estrogenic agent. Fennel's phytoestrogen concentration aids in lowering inflammation in PCOS and improving insulin resistance. It is also believed that it helps in reducing cellular imbalance, which leads to metabolic disturbances in PCOS.

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References

1. Sodeghpour, N.; Khaki, A.A.; Najafpour, A.; Dolatkah, H.; Montaseri, A. Study of *Foeniculum vulgare* (Fennel seed) Extract on Serum Level of Estrogen, Progesterone, and Prolactin in Mouse, Crescent. *J. Med. Biol. Sci.* **2015**, *2*, 59–63.
2. Badgujar, S.B.; Patel, V.V.; Bandivdekar, A.H. *Foeniculum vulgare* Mill: A Review of Its Botany, Phytochemistry, Pharmacology, Contemporary Application, and Toxicology. *BioMed Res. Int.* **2014**, *2014*, 842674. [[CrossRef](#)] [[PubMed](#)]
3. Khazaei, M.; Montasari, A.; Khazaei, M.R.; Khanahmadi, M. Study of *Foeniculum vulgare* Effect on Folliculogenesis in female Mice. *Int. J. Fertil. Steril.* **2011**, *5*, 122–125. [[PubMed](#)]
4. Deligeoroglou, E.; Tsimaris, P. Menstrual disturbances in puberty. *Best Pract. Res. Clin. Obstet. Gynaecol.* **2010**, *24*, 157–171. [[CrossRef](#)] [[PubMed](#)]

5. Cardigno, P. Homeopathy for the treatment of menstrual irregularities: A case series. *Homeopathy* **2009**, *98*, 97–106. [CrossRef] [PubMed]
6. Yavari, M.; Khodabandeh, F.; Tansaz, M.; Rouholamin, S. A neuropsychiatric complication of oligomenorrhea according to Iranian traditional medicine. *Iran. J. Reprod. Med.* **2014**, *12*, 453–458. [PubMed]
7. Shayan, A.; Masoumi, S.Z.; Shobeiri, F.; Tohidi, S.; Khalili, A. Comparing the effects of agnugol and metformin on oligomenorrhea in patients with polycystic ovary syndrome: A randomized clinical trial. *J. Clin. Diagn. Res.* **2016**, *10*, 13–16. [CrossRef] [PubMed]
8. Panidis, D.; Tziomalos, K.; Chatzis, P.; Papadakis, E.; Delkos, D.; Tsourdi, E.A.; Kandaraki, E.A.; Katsikis, I. Association between menstrual cycle irregularities and endocrine and metabolic characteristics of the polycystic ovary syndrome. *Eur. J. Endocrinol.* **2013**, *168*, 145–152. [CrossRef] [PubMed]
9. Jenabi, E.; Shobeiri, F.; Hazavehei, S.M.; Roshanaei, G. Assessment of Questionnaire Measuring Quality of Life in Menopausal Women: A Systematic Review. *Oman Med. J.* **2015**, *30*, 151–156. [CrossRef] [PubMed]
10. Diaz, A.M.R.L.; Laufer, M.R.; Breech, L.L. Menstruation in girls and adolescents: Using the menstrual cycle as a vital sign. *Pediatrics* **2006**, *118*, 2245–2250. [PubMed]
11. Harris, H.R.; Babic, A.; Webb, P.M.; Nagle, C.M.; Jordan, S.J.; Risch, H.A.; Rossing, M.A.; Doherty, J.A.; Goodman, M.T.; Modugno, F.; et al. Polycystic Ovary Syndrome, Oligomenorrhea, and Risk of Ovarian Cancer Histotypes: Evidence from the Ovarian Cancer Association Consortium. *Cancer Epidemiol. Biomark. Prev.* **2018**, *27*, 174–182. [CrossRef] [PubMed]
12. Meena, D.M.; Sharma, D.M.; Dhakar, A.; Singh, C.; Sharma, L.; Purvia, R.P. Role of *Foeniculum vulgare* in PCOS—A Review Article. *World J. Pharm. Res.* **2019**, *8*, 344–350.
13. Yadav, N.; Yadav, P.; Maurya, P.; Maurya, P.; Yadav, S.K. Fennel: *Foeniculum (vulgare mill)*. *IJCRT* **2021**, *9*, 2003–2011.
14. Fennel-Wikipedia. Available online: <https://en.m.wikipedia.org/T1/textgreater{}wiki> (accessed on 9 October 2022).
15. Rather, M.A.; Dar, B.A.; Sofi, S.N.; Bhat, B.A.; Qurishi, M.A. *Foeniculum vulgare*: A comprehensive review of its traditional use, Phytochemistry, pharmacology, and safety. *Arab. J. Chem.* **2012**, *9*, S1574–S1583. [CrossRef]
16. Yavari, M.; Rouholamin, S.; Tansaz, M.; Esmaeili, S. Herbal Treatment of Oligomenorrhea with *Sesamum indicum* L.: A Randomized Controlled Trial. *Galen Med. J.* **2016**, *5*, 114–121. [CrossRef]
17. Jazani, A.M.; Hamdi, K.; Tansaz, M.; Nazemiyeh, H.; Bazargani, H.S.; Fazljou, S.M.B.; Azgomi, R.N.D. Herbal Medicine for Oligomenorrhea and Amenorrhea: A Systematic Review of Ancient and Conventional Medicine. *BioMed Res. Int.* **2018**, *2018*, 3052768. [CrossRef] [PubMed]
18. Oligomenorrhea. Available online: <https://my.clevelandclinic.org/health/diseases/22834> (accessed on 20 October 2022).
19. Riaz, Y.; Parekh, U. Oligomenorrhea. In *StatPearls [Internet]*; Updated 2021 December 28; StatPearls Publishing: Treasure Island, FL, USA, 2022.
20. Haqq, L.; McFarlane, J.R.; Dieberg, G.; Smart, N.A. Effect of lifestyle intervention on the reproductive endocrine profile in women with polycystic ovarian syndrome: A systematic review and meta-analysis. *Endocr. Connect.* **2014**, *3*, 36–46. [CrossRef] [PubMed]
21. Salley, K.E.S.; Wickham, E.P.; Cheang, K.I.; Essah, P.A.; Kargane, N.W.; Nestler, J.E. Glucose Intolerance in polycystic ovary syndrome: A position statement of the Androgen Excess Society. *J. Clin. Endocrinol. Metab.* **2007**, *92*, 4546–4556. [CrossRef] [PubMed]
22. Elizabeth, A.A.; Josephine, G.; Muthiah, N.S.; Muniappan, M. Evaluation of analgesic and Anti-inflammatory effect of *Foeniculum vulgare*. *Res. J. Pharm. Biol. Chem. Sci.* **2014**, *5*, 658–668.
23. Malini, T.; Vanithakumari, G.; Megala, N.; Anusya, S.; Devi, K.; Elango, V. Effect of *Foeniculum vulgare* Mill. seed extract on the genital organs of male and female rats. *Indian J. Physiol. Pharmacol.* **1985**, *29*, 21–26. [PubMed]