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A review on *Anethum graveolens*: Its role in human life

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Abstract
Anethum graveolens L. (Dill), a member of the Umbelliferae family, is a significant herbal extract herb native to the Mediterranean and West Asia. It is a beneficial essential oil-bearing spice as well as a therapeutic herb. Dill is grown as a therapeutic herb all over the world. Dill seeds are used to flavour foods. Dill carvone, limonene, dill apiol, and -phellandrene are the main constituents of essential oil, which may be extracted from various sections of the plant. Dill essential oil and extracts have antibacterial, antifungal, antioxidant, insecticidal, anti-inflammatory, antidiabetic, antispasmodic, hypolipidemic, and other properties. *Anethum graveolens* elicited antibacterial, anti-inflammatory, analgesic, stomach mucosal protecting and antisecretory effects, smooth muscle relaxant action, hyperlipidemia, raised progesterone concentration, and many other effects in pharmacological tests.

Keywords: *Anethum graveolens*, Dill, pharmacology, limonene

Introduction
Anethum graveolens, belong to the family Umbelliferae, and is indigenous to southern Europe. an annual herb growing in the Mediterranean region, central and southern Asia and it is cultivated widely throughout the world. It is traditionally used as a popular aromatic herb and spice. It was used as a remedy for indigestion and flatulence and as milk secretion stimulant. Moreover, it is used as an anti-convulsion, anti-emetic, anti-cramp (in children), as a wound healer and to increase the appetite and strengthen the stomach. *Anethum graveolens* contained essential oils, fatty oil, moisture, proteins, carbohydrates, fibre, ash, furanocoumarin, polyphenols and mineral (Schiller and Schiller, 1994; Wildwood, 1996). Previous studies showed that *Anethum graveolens* induced antimicrobial, anti-inflammatory, analgesic, gastric mucosal protective and antisecretory effects, smooth muscle relaxant effect, hyperlipidemia, increased progesterone concentration, and many other effects. The aim of the review is to highlight the pharmacological effects of *Anethum graveolens* (Mahato & Sharma, 2018) [1].

Synonyms: *Pastinaca anethum* Spreng, *Peucedanum graveolens* Benth. and *Selinum anethum* Roth.

Common names: Unani: Soyaa, Siddha: Sadakuppai, Sanskrit: Sthatpushpi, Hindi: Sowa, Punjabi: Soya, English: Dill and Anet, Arabic: Shibth and Haba helwa (G. J. Kaur & Arora, 2010omrana).

Pharmacological properties
Antimicrobial effects
Anethum graveolens seed extracts have showed anti-ulcer activity, and also have shown modest activity against *Helicobacter pylori*. *Aqueous* and organic extracts of dill seeds have shown strong antibacterial activity. The essential oils also have shown active against three fungi (a yeast, *Candida albicans* and two molds, *Penicillium islandicum* and *Aspergillus flavus*). D-limonene and Dcarvone, have shown strong antifungal activity against *Aspergillus niger*, *Saccharomyces cerevisiae* and *Candida albicans*. Many authors mentioned that the antimicrobial activities could be attributed to furanocoumarin in *Anethum graveolens*. (Mohammed, G. J., Omran, A. M., & Hussein, H. M. (2016) [5].

Anti-inflammatory and analgesic effects
The hydro alcoholic extract of the *Anethum graveolens* seed caused significant decrease in the inflammation and pain in rats.

Anethum graveolens oil and diclofenac-gel showed a significant (p<0.001) decrease in the paw volume in rats compared to the blank group. *Anethum graveolens* oil showed even more decrease in the paw volume compared to the diclofenac. A single topical application of an ethanol extract of the fruits to the inner and outer surface of the ear of mice inhibited ear inflammation induced by 12-O-etradecanoylphorbol- 13 acetate by 60%. A 10% aqueous extract of the fruits and 5% aqueous solution of the essential oil had analgesic effects in mice pain induced by hot plate and acetic acid writhing models 20-22. The effect of the fruits (1.0 g/kg body weight) was comparable to 200 mg / Kg body weight of acetyl salicylic acid (G. J. Kaur & Arora, 2010b). [32]

Antifungal activity

Deweer *et al*. 2013 [10] studied the IC_{50} (half maximum inhibitory concentration) values of dill seed essential oil and its two primary components carvone and limonene against two strains of *Zymoseptoria tritici*, S6 (sensitive strain) and R1187 (resistant strain). Dill seed essential oil crude, Tween 80 (5% v/v), and dimethyl sulfoxide (1% v/v) were all used in the experiments. The crude dill seed essential oil and dill seed oil with dimethyl sulfoxide (1%) were more effective on S6 (350 mg/L) than on R1187 (1000 mg/L), with the exception of oil used with Tween 80, which had the same impact on both strains (300 mg/L). Carvone, on the other hand, had the same impact on both strains across all preparations tested. Unless combined with Tween, limonene formulations were often less effective than carvone.

In both the contact and vapour phases, the antifungal activity of dill seeds essential oil and its two primary components, carvone and limonene, against mycelial development and influence on the viability of *Sclerotinia sclerotiorum* was evaluated. Dill seed essential oil, at 1.00 µl/ml under contact conditions and 0.125 µl/ml air under vapour conditions, effectively suppressed mycelial development and sclerotial germination. Carvone and limonene both suppressed fungal development in a synergistic manner, although carvone contributed more to the inhibition than limonene. *In vivo* tests revealed that the essential oil effectively reduced *S. sclerotiorum*, with significant morphological changes in the hyphae and sclerotia. The suppression of ergosterol synthesis, malate dehydrogenase, succinate dehydrogenase activity, and external medium acidification were all investigated to determine its mode of action (Ma *et al*. 2015).

The fungicidal effectiveness of dill seeds essential oil, its non-polar and polar components, and its two constituents (limonene and camphor) against *A. triticina* and *Bipolaris sorokiniana* was tested using spore germination inhibition at doses ranging from 0.25 to 3.0 mg/ml. With ED50 and ED90 values of less than 0.38 and 2.15 mg/ml, all of the components tested exhibited promising effectiveness against *A. triticina*.

All of the substances examined had ED50 and ED90 values of less than 0.78 and 2.1 mg/ml against B. sorokiniana, respectively (Chahal *et al*. 2016) [29].

Insecticidal activity

Continuos exposure bioassays and fumigant toxicity bioassays revealed that the dill seed essential oil is poisonous to *Periplanata americana* L., *Musca domestica* L., and *Tribolium castaneum*. During the first 3 hours of the contact toxicity bioassay and the first 12 hours of the fumigant toxicity bioassay, mortality against *P. americana* varied from 25 to 100 percent. For the *M. domestica* L., death varied from 33.3 to 70% in the first 3 hours, but for the *T. castaneum*, mortality ranged from 58.3 to 100% in the first 24 hours (Babri *et al*. 2012) [7].

(Khani and Basavand (2013) [8] used a fumigant toxicity experiment to determine the volatile toxicity of dill seed essential oil against two stored product insects, *T. confusum* and *C. maculates*. Based on LC_{50} results, *C. maculates* (LC_{50}=0.54 l/L air) was more vulnerable to the studied plant product than T. confusum (LC_{50}=143.8 l/L air).

Antioxidant activity

DPPH (1,1-diphenyl-2-picrylhydrazyl), reducing power, conjugated diene, and chelating impact experiments were used to investigate the antioxidant activity of dill essential oils and acetone extracts. At 5-25 l, the antioxidant activity was moderate to excellent (Singh *et al*. 2007) [9]. DPPH radical scavenging, trolox equivalent antioxidant capacity, reducing power, chelating power, and -carotene bleaching tests were used to investigate the antioxidant activity of hexane, ethyl acetate, and ethanolic extract of dill flowers, seeds, and leaves. The flower extract has stronger antioxidant activity than the leaf and seed extracts in all tests.

The most active floral extract was ethyl acetate, which was followed by ethanol and hexane extracts (Shyu *et al*. 2009) [10]. In albino rats, the antioxidant effectiveness of ethanolic extract of dill was tested in carbon tetrachloride-induced hepatotoxicity. The results demonstrated that 100 mg/kg of ethanolic dill extract restored serum enzyme activity and antioxidant enzyme activity in experimental rats (Tamilarasi *et al*. 2012).

Anti-inflammatory activity

Inflammation is a complex series of biological processes that occurs when tissues are exposed to physical damage, toxic chemicals, or infections. In rats, a hydro ethanol extract of the dill seed reduced inflammation and discomfort significantly (Valadi *et al*. 2010) [12]. When rats were given dill oil or diclofenac-gel, their paw volume decreased significantly (p0.001) compared to the control group. When compared to diclofenac, dill oil demonstrated a greater reduction in paw volume (Naseri *et al*., 2012) [11]. Rezaee-Asl *et al*. (2013) [13] used formalin test and hot plate test to examine hydro alcoholic extracts of dill seed and aerial parts for usage as an analgesic medication on mice. Seed and crop extracts considerably reduced pain indicators in a formalin test. Crop and seed extracts demonstrated hyperalgesic characteristics in a hot plate test. Animals given crop extracts had a stronger impact than those given seed extracts.

Table 1: Pharmacological activities of *Anethum graveolens* L

Activity	Target Cell	Model Used	Extract Type	Dosage	Result	Reference
antifungal	*A niger*, *A oryzae*, *A flavus* and *A. alternata*	*In vitro* and *in vivo* poisoned technique	Essential oil	0.25-2.0µL/mL for 9 days	MIC value for the tested fungi was 2.0 0µL/mL. degenerative changes were observed in conidial heads and hyphal morphology	(Tian *et al*., 2011) [14]
	Sensitive (S6) and resistant (R1187)	Microplate assay	Essential oil	---	Dill seed oil with DMSO had a greater impact on the sensitive strain (350 mg/L) than the resistant strain (1000 mg/L), however dill oil with tween 80 had the same effect on both strains (300 mg/L).	Deweer, C., *et al*. 2013 [15]
	Trichoderma spp., *C albicans* and *A. niger*	*In vitro*, disc diffusion assay test	Essential oil	0.5-5.0 µL/mL	At 2.5, 1.0, and 3.5 L/mL, complete suppression of the tested fungi was recorded.	Karimi *et al*., 2016) [17]
	Colletotrichum nymphaea	*In vitro* and *in vivo* contact and volatile fungicide activity bioassay and spore germination assay	Essential oil	50-1000 ppm	Conidia germination was severely suppressed at 250-1000 ppm dill seed oil.	(Karimi *et al*., 2016) [17]
Antibacterial	*E. coli*	Spectrophotometric methods	Essential oil/dill powder	10µl/L and 20µl/L	MIC value of dill oil and powder was 0.73mg/mL	(Isopencu & Ferdeş, 2012) [18]
	S. aureus and *E. coli*	Agar well diffusion, agar dilution and broth-micro dilution techniques	Essential oil	In agar well diffusion test: 100µL.in agar dilution test:0.01-0.20mg/mL. in broth-micro dilution test: 0.50mg/mL	The diameters of the inhibition zones were 20 and 16 mm, respectively. Oil has a MIC value of 5.99 g/mL against both bacterial strains.	(Madandoust & Fooladchang, 2018) [19]
	P. aeruginosa, *E. coli*, *K. pneumonia*, *Entero coccus* sp and *S. aureus*	Agarwell diffusion method	Essential oil	50µL	Enterococcus sp. had the greatest *in vitro* inhibitory efficacy, with an inhibition zone of 15 0.11 mm.	(Khanday *et al*., 2016)
	E. coli, *S. typhi*, *S. dysenteriae*, *B. cereus*, *S. aureus* and *S. facium*	Disc diffusion agar method	Essential oils	10-20µL	With increasing oil content, activity increased. The inhibitory impact of chloramphenicol was greater than that of tetracyclin.	(Hojjati, 2017) [21]
	S. aureus, *B. cereues*, *B. subtilis*, *E. coli* and *S. typhimurium* mice	Organoleptic evaluation	Essential oil	1-3mL	Dill seed oil proved efficient against both Gram-positive and Gram-negative bacteria.	(Ferreira & Moura, 2014)
Analgesic		Formalin test and hot plate test	Crop and seed extract in ethanol	0.5mL (300mg/kg)	When mice were given seed extracts instead of crop extracts, the effects were less.	(Ramezani *et al*., 2009)
	Raw 264.7 macrophages	TLC bioautography screening and fractionation	Essential oil	------	At 45.0 g/mL, NO release was inhibited by 82.0 0.0 percent. Sabinene had the greatest action, inhibiting NO generation by 84.12 0.1 percent at 45.0 mol/L.	(Kazemi, 2015)
	rats	Formalin test	Dill oil and aerial pert extract essential oil	2g dill oil, 100mg dill extract	The combination of dill oil and Diclofenic-gel reduces paw volume (P.001).	(Nguyen *et al*., 2020)
	mice	BALB/c mice model	Essential oil	2% and 4%	Bacterial growth and wound area were decreased in comparison to the control (P.05).	(Manzuoerh *et al*., 2019) [26]
Antioxidant	β-Carotene bleaching test and Reducing power	Dot-blot DPPH staining method, TLC- bioautography test and fractionation	Essential oil	-----	Sabinene was active first, followed by oil, and then limonene. IC_{50} = 15.3 0.0 g/mL was found to inhibit -carotene bleaching.	(Kazemi, 2015) [24]
	Lipid peroxidation and DPPH scavenging	DPPH radical scavenging assay and thiocyanate method	Essential oil fraction, deodorized hot	For DPPH scavenging: 2.0 mL. For	Hot water extract inhibits lipid peroxidation the most, with an IC_{50} of 4.7 g/mL, but methanol extract	(Ruangamnart *et al*., n.d.) [28]

			water extract and methanol extract	lipid peroxidation: 0.5 mL	inhibits DPPH the most.	
	Free radicals	DPPH, hydroxyl, nitric oxide, superoxide radical scavenging methods and FRAP assay	Essential oil, hexane and DCM extract	1.0-0.05mg/mL	Carveol and perilly alcohol were the most effective (IC_{50} 0.16 mg/mL), whereas camphor was the least effective (IC_{50} > 10 mg/mL). Polar fractions were more active than non-polar fractions and essential oil.	(N. Kaur *et al*., 2019) [29]
Effect on reproductive system	Wistar female rats	Hormonal assay and transmission electron microscopy	Ethanolic and aqueous dill extract	0.045 g/kg and 0.45 g/kg of aqueous extract and 0.5 g/ kg and 5.0 g/kg of ethanol extract for 10 d	The oestrus cycle was affected by alterations in vaginal smears. The duration of the oestrus cycle, the dioestrus phase, and the concentration of progesterone all increased.	(Monsefi *et al*., 2006) [30]
	women	Electronic foetal monitoring	Dill seed infusion	One tablespoon of dill extraction	The rate of uterine contraction was higher in treated women and fell: In comparison to the control, the increase ratio was lower.	(Zagami *et al*., 2012) [31]

Conclusion and Future Perspective

Herbal medicine has been used to treat patients since ancient times. Herbal medications, namely *A. graveolens*, have anticancer, antihyperlipidemic, antibacterial, and anti-diabetic effects. According to epidemiological studies, A. graveolens consumption and the risk of cardiovascular disease are inversely associated.

A. graveolens has several beneficial components such as polyphenols, tannins, terpenoids, polysaccharides, flavonoids, alkaloids, and saponins. The results of in silico molecular docking support carvone, an active ingredient of A. graveolens, as a possible anticancer agent. Nonetheless, the interaction of other medications with these active substances must be normalised, and the dose and duration of intake must be standardised through additional clinical studies in other populations. More research is needed to determine the essential ingredients of A. graveolens that actively contribute to illness therapy through its useful qualities.

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