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Research Article

A Review on Pharmaceutical and Medicinal Importance of *Anethum graveolens* L.

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Abstract

Anethum graveolens is a well-acknowledged and widely used culinary annual herb belongs to the family Apiaceae, commonly known as "dill". The seeds of dill are stomachic, carminative, and diuretic. It comprises numerous bioactive compounds which are broadly exploited for different medicinal purposes. *A. graveolens* contain a specific odor due to the presence of essential oils. The plant extracts and oil have different activities such as antimicrobial, antioxidant, anti- hypercholesterolemic, anti-inflammatory, anti-diabetic, etc. The main aim of this review is to comprehend the importance, bioactivities and medicinal uses of *A. graveolens* and its secondary metabolites.

Keywords: *Anethum graveolens*; Bioactivates; Antinociceptive; Secondary Metabolites; Plant Extracts

Introduction

At the present time, researchers are focused on alternatives of synthetic drugs in the medical field due to their side effects. According to the world health organization (WHO), the trend of medicinal plants usage has been increasing globally day by day [1]. The *Anethum* is a Greek word that originates from aneeton or aneeson, which means strong-smelling. Many types of research have displayed various bioactivities of *A. graveolens* such as antimicrobial, anti-inflammatory, antidiabetic, anti-hypercholesteromic, and antispasmodic [2]. There have been records of the use of *A. graveolens* in the Greek and Egyptian before civilizations [3]. In Turkey, *A. graveolens* is consumed in salads and soups as carminative and in Ayurveda (Anatolian folk medicine) it is used to cure stomachache colic, indigestion, abdominal discomfort, and flatulence [4-6]. In Ayurveda, *A. graveolens* known as shatapushpa and is used in abdominal pains, eye diseases, ulcer, snigdha gunas, tiksna, laghu, vipaka, katu, usna virya, rasa, tikta, katu, vata, and kapha. Apart from this, *A. graveolens* is also used in the preparation of different ayurvedic medicines such as Dhanwantharam quatham, Maharasnadi kashayam, Gugguluthiktaquatham, Saraswatharishtam, Mrithasanjeevani, Dhanwanthararishtam, Dasmoolarishtam, etc. The paste of *A. graveolens* seed with milk helps in swellings of joints and rheumatic diseases. Different types of chemical compounds were found in essential oil, extracted from the leaves, flowers and seeds. The major compounds of essential oil are carvone and limonene (monoterpenes). The plant also contains α-phellandrene and myristicin which give a specific odor to the dill plant. Some reports suggested that this plant extract was used in Iranian folk medicine as an anti-hypercholesterolaemic [7-9]. In the following section, we are going to explore the different bioactivities and medicinal uses of *A. graveolens* (Figure 1).

Figure 1: Various types of pharmacological activities of *Anethum graveolens* L.

Botanical description

Anethum graveolens L. is a well-known culinary herb in the world [10]. It is believed to have originated from the region of Central Asia and Mediterranean and Southern USSR. *A. graveolens* has been cultivated in Malaysian archipelago, Indian subcontinent, and Japan including some other parts of Southern Asia as a cold-weather crop for its foliage. The botanical name of the genus *Anethum* has been originated from the Greek word aneson or aneton and, the species name *graveolens* derived from the grave from Latin gravis and olens the verb olere means strong odor [11]. *A. graveolens* L. is the only species of the genus *Anethum*, however, categorized as *Peucedanum graveolens* by some taxonomists in the related genus *Peucedanum* [12]. Worldwide, it is known by several names like Savaa in India, Soya in Pakistan, Shabat/Shabath in Arab world, Shevid in Iran, in European countries it is supposed to be related to Old Norse dilla which means calm/soothe, in Indonesia and Malaysia it is renowned as Adas manis, Adas sowa, Adas cina, Ender, and Adas pudus, in China it is more popular by Ou Zhou, Shi luo, Shi luo, and Tu hui xiang [13]. *A. graveolens* grows to a height of up to 90 cm with slender stems and the foliage is eventually divided into three to four pinnate segments slightly larger than similar leaves of fennel. The yellow flowers are produced into umbels. The seeds are not true seeds, which are halves of quite small dry fruits termed schizocarps. It is somewhat oval, compressed with three longitudinal ridges on the back alternate with three dark-colored oil cells between them. The taste and appearance of the dill seeds have resembled to that of "caraway" however they are smaller, flatter, and lighter than caraway with a nice fragrant. *Anethum* grows well in loose well-drained soil with a pH of 5.3 to 7.8 supported by hot summers with ample sunlight. Seed development takes place during dry weather. Propagation of *Anethum* occurs through seeds that are habitually self-sown when growing in a suitable environmental condition. Seeds show viability for up to 3–10 years [13].

Bioactivates

Antimicrobial activity

Chen., *et al*. [14] worked on dill seed essential oil to assess the antifungal activity using flow cytometric analysis against *Candida albicans* showing that propidium iodide enters into the plasma membrane of *C. albicans* and affects the ergosterol synthesis. Zeng., *et al.* [15] also worked on the anti-candida activity of *A. graveolens* using the dilution method and found positive results. The MIC was 0.312 µL/mL to 0.625 µL/mL obtained for *Candida tropicalis, Candida parapsilosis,* and *Candida krusei*. In a study, the antibacterial activity of dill was examined. Different bacterial strains were used as follows *Escherichia coli* ATCC 8739, *Klebsiella pneumoniae* ATCC 700603, *Salmonella typhimurium* ATCC 14028, *S. aureus* ATCC 29213, and *Staphylococcus aureus* ATCC 25923. The MIC was obtained at 10 mg/mL for the tested strains [16].

Hepatoprotective activity

In 2014, Rabeh., *et al*. [17] reported the hepatoprotective effect of *A. graveolens* essential oil against carbon tetrachloride (CCL_4) which is responsible for hepatotoxicity in rats. The result showed the mixture of dill oil with fennel oil has the capacity to inhibit hepatotoxicity of CCL_4 at $p < 0.05$ of significance level also decreased the level of aspartate transaminase (AST) and alanine transaminase (ALT) in blood serum.

Antinociceptive activity

Rezaee Asl., *et al*. [18] tested hydroalcoholic extracts of dill plant for their antinociceptive activity using the formalin test. The result found a positive reduction of inflammatory pain in mice and showed great analgesic effects in the late phase of the formalin test.

Insecticidal activity

Chaubey [19] evaluated the insecticidal activity of *A. graveolens*. The activity was assessed using the fumigation method. The lethal concentrations (LC_{50}) were obtained as follows 0.316 and 0.243 $\mu L.cm^{-3}$ air; *A. graveolens*. The reduction in progeny production was also observed after treatment.

Antioxidant activity

Al-Oqail and Farshori [20] reported antioxidant activity of *A. graveolens* using lung (A-549), human breast (MCF-7), and cervical (HeLa) carcinoma cell lines using H_2O_2 scavenging, DPPH radical scavenging, and ferrous reducing antioxidant assays. Antioxidant activity was found dose-dependent. The production of ROS also observed in treated cells.

Anticancer activity

Al-Oqail and Farshori [20] also reported the caspase-dependent effect of *A. graveolens*. It showed anticancer activity by increasing the activity of caspase-3 and caspase-9. Moreover, the antiproliferative activity was tested by Nehdia., *et al.* [21] on breast cancer cell lines.

Antiparasitic activity

Abas and Elagib [22] assessed antiparasitic activity *A. graveolens* against extraintestinal amebiasis causing *Entamoeba histolytica*. The *in vitro* testing of plant extract showed complete mortility of *E. histolytica* at 12.5 mg/mL of concentration. *In-vivo* screening also gave positive result.

Antidepressant and analgesic effects

El Mansouri., *et al.* [23] studied the antidepressant and analgesic effects in reference to sertraline and tramadol. *A. graveolens* aqueous extract was found to a good antidepressant and analgesic properties without showing any kind of side effects at the dose of 250 mg/kg body weight. Apart from all these activities, there are some more activities which showed in table 1.

Activity	Model	Chemical constituents	References
Antibacterial activity	*Lactococcus garvieae* GQ850376	D-carvacrol (36.09%)	[24]
	Escherichia coli ATCC 8739, *Klebsiella pneumoniae* ATCC 700603, *Salmonella typhimurium* ATCC 14028, *S. aureus* ATCC 29213 and *S. aureus* ATCC 25923	Dillapiole (19.98-48.9%), D-carvone (18.05-28.02%), and D-limonene (26.96-44.61%).	[16]
Antifungal activity	*Candida albicans*	-	[14]
	C. tropicalis, *C. parapsilosis*, and *C. krusei*	-	[15]
Anti-inflammatory	Lipopolysaccharide (LPS)-stimulated macrophages	Thymol (20.07 %), limonene (16.31%), and α-pinene (8.65%)	[25]
Antileishmanial activity	*Leishmania donovani* Dd8	-	[26]
Antinociceptive activity	Mice	-	[18]
Antioxidant activity	Human breast (MCF-7), lung (A-549), and cervical (HeLa) carcinoma cell lines	-	[20]
Antiparasitic activity	*Entamoeba histolytica*	-	[22]
Antiproliferative activity	Breast cancer cell lines	Oleic acid (52%), *cis*-vaccenic acid (6.2%), linoleic acid (5.5%), and palmitic acid (3.3%)	[21]
Anti-quorum sensing effects	*Pectobacterium carotovorum* and *Chromobacterium violaceum* CV026	Eugenol (49.62 %)	[27]
Cytotoxic activity	Hepatocellular carcinoma cell line cells	Carvone (53.13%), dillapole (25.42%), and dihydrocarvone 2 (11.35%)	[28]
Hepatoprotective activity	Rats	-	[17]
Insecticidal activity	*Callosobruchus maculates*	-	[29, 30]
	Sitophilus zeamais	Limonene	[19]

Table 1: Model/system used for the assessment of bioactivities of *Anethum graveolens* and chemical constituents.

Effects on disease

Diabetes

It's been investigated by several clinical trials that *Anethum* has significant antidiabetic activity by evaluating possible mechanisms like binding to bile acids in the intestine, increase in fecal excretion, inhibition of intestinal cholesterol absorption, and increased production of bile acids. Major components such as limonene, α-phellandrene and carvone of *Anethum* significantly participate in the hypolipidemic effects, via. 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase, reducing acyl CoA carboxylase and hence significantly affecting the cholesterol metabolism and fatty acid absorption [13,31].

Cardiovascular disease

Anethum graveolens is very impactful and beneficial for cardiovascular diseases. A meta-analysis of trials indicated that *A. graveolens* have effects on lipid profiles and glycemic indices in adults. The random-effects model was employed to demonstrate the weighted mean difference and integrated 95% confidence intervals (CI). The final analysis comprised a total of seven RCTs with a number of 330 subjects. Pooled results showed that *A. graveolens* supplementation remarkably reduced the concentration level of serum insulin (WMD: 2.28 lU/mL; 95% CI: 3.62 to 0.93; P ¼ 0.001) and LDL cholesterol (WMD: 15.64 mg/dL; 95% CI: 24.55 to 6.73; P ¼ 0.001) [32]. Nevertheless, it also demonstrated that *A. graveolens* have no effect on triglyceride, serum total cholesterol, fasting blood glucose, and high-density lipoprotein cholesterol. Thus, subgroup analysis was determined that the long-term supplementation of *A. graveolens* in higher doses has a significant beneficial impact on lipid profiles. A significant reduction in fasting blood glucose at doses of 1500 mg/d was also observed by using dose-response analysis. To uncover more about plant's clinical efficacy additional high-quality research in different ethnic clusters and cohorts is required [32].

Irritable bowel syndrome

Anethum graveolens is very impactful for irritable bowel syndrome patients. One study unveiled that *A. graveolens* have an analytically eloquent upshot on discrete irritable bowel syndrome (IBS) symptoms with P≤0.05 enhancement in total score percent 78.13%, than mebeverine 53.13%. This study unveiled that ingestion of a capsule comprising a powder of crude *A. graveolens* plant for two weeks may prove to be beneficial for patients with IBS without showing any side effects which determined the effectiveness and safety of *A. graveolens* in the treatment of IBS symptoms [33,34].

Conclusion and Future Perspective

Anethum graveolens is a very important herb that possesses several medicinal and ethno-medicinal uses. Numerous healing properties of *A. graveolens* are due to the presence of a variety of bioactive molecules and in *A. graveolens* major constituents are polyphenols, tannins terpenoids, polysaccharides, flavonoids, alkaloids, and saponins that have their individual remedial properties. *A. graveolens* unveil a significant efficacy because of its antihyperlipidemic, anticancer, antimicrobial, and antidiabetic characteristics. In conclusion, *A. graveolens* has a varied amount of remedial uses due to which it can be applied to treat several diseases as a single drug or compound drug. Further, high-quality studies are required to ascertain the key compounds of *A. graveolens* that play an active role in disease management through its significant characteristics.

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Author Contributions

Conceptualization, M.M., G.Y., P.R.S.; investigation, M.M.; resources, M.M., G.Y., P.R.S.; writing original draft— M.M., G.Y., P.R.S.; writing-review and editing, M.M., G.Y., P.R.S.; and visualization, M.M.; supervision, M.M. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

No associated data marked.

Conflicts of Interest

The authors declare no conflict of interest.

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