ERURJ **2023**, 2, 4, 723 - 733

(Mini-Review)

Mini review: Anise (*Pimpinella anisum L.*): phytohemical and Pharmacological activities.

Mostafa B. Abouelela[1], Abdelrahman K. Abdelshakour[2], Mohamed K. Mohamed[2], Abdelrahman M. Elshobky[2], Ahmed S. Abdelmoneam[2], Felothaous E. Makeen[2], Eissa R. Elsheikh[2], Zakaria M. Eissa[2], Heba H. Hossny[2], Salma N. Elemam[2], Esraa N. Mahfouz[2], Yara H. Saber[2], Basant A. Abdelhameed[2], Thoria A. Abdullah[2], Manar O[2], Omayma Elgindi[1, *]

[1]*Department of Pharmacognosy, Faculty of Pharmacy, Egyptian Russian University, Badr City, Cairo-Suez Road, Cairo 11829, Egypt.*

[2]*Pharm D Program, Faculty of Pharmacy, Egyptian Russian University, Badr City, Cairo-Suez Road, Cairo11829, Egypt.*

*Corresponding author: Omayma Elgindi, E-mail addresses: Omaymaelgindi55@outlook.com.

Received 26th June 2023, Revised 21st August 2023, Accepted 27th October 2023

DOI: 10.21608/ERURJ.2023.215520.1039

ABSTRACT

Anise (*Pimpinella anisum* L.), which belongs to the family Umbelliferae, is an aromatic annual herb, native to the eastern Mediterranean region and western Asia. The fruit is incorrectly referred to be a seed. Nonetheless, the fruit is often known as aniseed, and when ripe and dried, it is a popular spice. In traditional medicine, anise seeds are used to treat migraines as well as a carminative, fragrance, disinfectant, and diuretic. Aniseed is traditionally used for milk production, menstruation, urine and sweat discharge, and skin health. In folk medicine, it is used to polish teeth, for treat nightmares, convulsions, and epilepsy. Also, anise tea has long been used to treat upper respiratory infections, and bronchial asthma in children. Along with, its usage as an expectorant, lozenge, and lactagogue. In addition to, utilization of the plant for helping with delivery and as a mild laxative. Anise is used in the culinary industry as a flavoring and aromatic ingredient in fish items, ice cream, sweets, and gums. Several chemical components, primarily anethole, were extracted as essential oils from aniseed. Several pharmacological studies on anise have been published, including antibacterial, antifungal, insecticidal, antiviral,

muscle relaxant, antispasmodic and relaxant of smooth muscle, anticonvulsant, antiulcer, antidiabetic, hypolipidemic, and pain relief in dysmenorrhea. This review aims to focus on phytochemical constituents, their structure elucidation, and the pharmacological activities of anise in the last five years.

Keywords: Anethole; Naringin; *Pimpinella anisum* L.; Cytotoxic activity; Antidepressant activity; wound healing activity.

1-Introduction

Anise (*Pimpinella anisum* L.), is an aromatic annual herb hardy, pubescent, 60 cm tall native to the eastern Mediterranean region and western Asia. It is a member of the Umbelliferae family, primarily its fruits (1). It is known by various names in different countries, such as Annesella in Italy; Anisa, Badian, Saunf, and Sop in Iran and India; and Boucage anis, in North Africa (2). It is grown in a variety of places, including China, Japan, South America, northern Africa, and southern Europe (3). The small fruit is wrongly called a seed. Nonetheless, the fruit is popularly known as aniseed, which is a popular spice when mature and dried (3). The plant grows from September to March, with blooming and fruits occurring between January and March (4). Since ancient times, anise seeds have been used for food and medicine, both of which play a clear part in preserving human health and enhancing the quality of life. Due to its diverse biological diversity and varied climatic circumstances, China has significant potential to produce fragrant and medicinal plants and herbs (5). It has been used in Chinese traditional medicine since the Fifth century (6) and other traditional Iranian and Indian medicine. Anise seeds are used traditionally as an analgesic for migraines, as well as a carminative, fragrant, disinfectant, and diuretic (7). In folk medicine, it is used to promote milk production, menstruation, urine, and perspiration secretion, as well as a healthy complexion (7). Moreover, in certain traditional literature, it is also useful for polishing teeth, treating nightmares, and the treatment of seizures and epilepsy (7). Anise tea has traditionally been used in children to treat upper respiratory infections, and bronchial asthma (8). It is also used as an expectorant and lozenge, and to assist women in making more milk. It is generally used to aid childbirth and as a mild laxative (8). Anise is used as a flavoring and aromatic agent in the culinary sector for fish products, ice cream, candies, and gums (9). Several chemical constituents were isolated from aniseed as

essential oils mainly anethole, estragole, and limonene. Also, phenolic compounds were reported as gallic acid, naringin, and quercitin. Several pharmacological studies were reported in anise as; antibacterial, antifungal, insecticidal, antiviral, muscle relaxant, antispasmodic and relaxant of smooth muscle, anticonvulsant, antiulcer, antidiabetic, hypolipidemic, and reduction of pain in dysmenorrhea which assured its traditional uses (10). This review aims to focus on the pharmacological activities and phytochemical constituents of anise in the last five years.

2. Discussion

2.1. Chemical composition.

Several chemical compounds were identified and isolated from anise volatile oils, proteins, carbohydrates, and cellulose fibers. It includes 1.5-6.0 mass % of a volatile oil largely composed of anethole, limonene, estragole, apiole, and carvone which are responsible for activities, as well as up to 8-11 mass % of lipids rich in fatty acids such as palmitic and oleic acids, as well as around 4 mass % of carbs and 18 mass % of protein (11).

It was reported upon an investigation of four aniseed populations of volatile oils, and fatty acids composition using GC (12). Results showed Trans-anethole was the main essential oil (12), and the Other detected essential oils were anisole, *p*-anisaldehyde, and *γ*-himachalene as shown in figure 1 (12). Results showed the presence of palmitic acid, and petroselinic acid as main fatty acids, moreover capric acid, lauric acid, myristic acid, stearic acid, arachidic acid, oleic acid, linoleic acid, and linolenic acid in different concentrations at aniseed populations (12). Meanwhile, phenolic acids were investigated using RP-HPLC. Results showed the presence of gallic acid, chlorogenic acid, syringic acid, p-coumaric acid, rosmarinic acid, and ellagic acid (12). While flavonoid contents mainly were naringin, followed by quercetin, and other flavonoids epicatechin-3-Ɵ-gallate, coumarin, rutin, and apigenin as shown in Figure 2 (12).

Using GC-MS analysis, trans-anethole was discovered to be the primary ingredient of anise dry seed essential oil (13). Also, estragole, isopentyl N-butyrate, eugenyl acetate, linalool, propyl butyrate, and anethole were identified (13). This study discovered several new anise seed oil chemicals, including methyl butyrate, propyl butyrate, isopentyl Nbutyrate, myrtenal, p-anisaldehyde, methyl eugenol, cuparene, nuciferol, and eugenyl acetate (13).

Meanwhile, essential oil of leaves extracted using microwave-assisted hydrodistillation showed the presence of trans-anethole, E-Anethole, γ -himachalene, methyl chavicol, and apiole (14).

Elsewhere anise seeds using HPLC showed the presence of The most abundant compounds in the extract were p-coumaric acid and catechin, followed by oleuropein, gallic acid, caffeic acid, chlorogenic acid, trans-4-hydroxy-3-methoxycinnamic acid, quercetin, and myricetin (15).

In another study, Anise seeds were analyzed using GC-MS. Results showed the presence of anisole as a major compound, followed by estragole, 3,5,5-trimethyl-9-methylene 1H-Benzocycloheptene, 3,5,5,9-tetramethyl 1H-Benzocycloheptene, and Phenol, 2-methoxy-4-(1-propenyl)-, acetate (16).

The essential oils extracted from anise seed were identified using GC-MS. Results showed that the major components were Trans-Anethole followed by γ-Himachalene, Carvone, Estragole (Methyl chavicol), Trans-Pseudoisoeugenyl-2-methylbutyrate, α-Longipinene, β-Bisabolene, Sabinene Hydrate, p-Isopropyl benzaldehyde, Linalool, Humulene, Butanoic acid, 2-methyl-, 4-methoxy-2-(3-methyloxiranyl) phenyl ester, α-Curcumene, D-Limonene, γ-Terpinene, and γ-Muurolene (17).

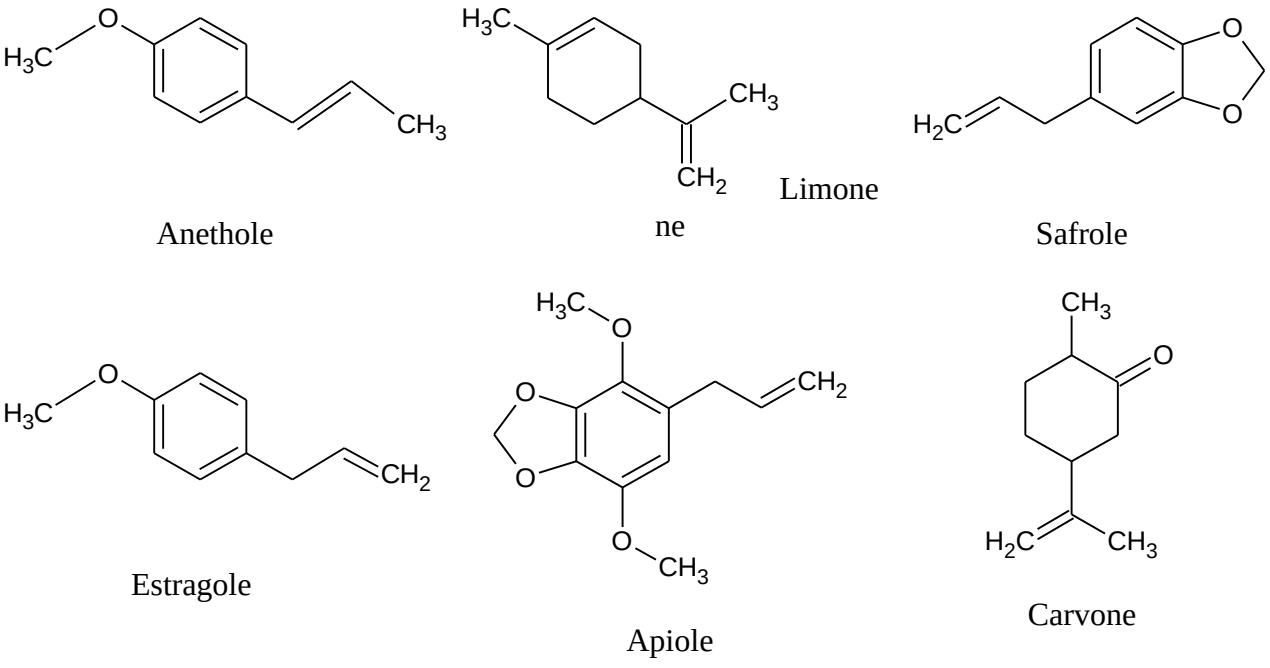


Figure 1. The main essential oil of anise.

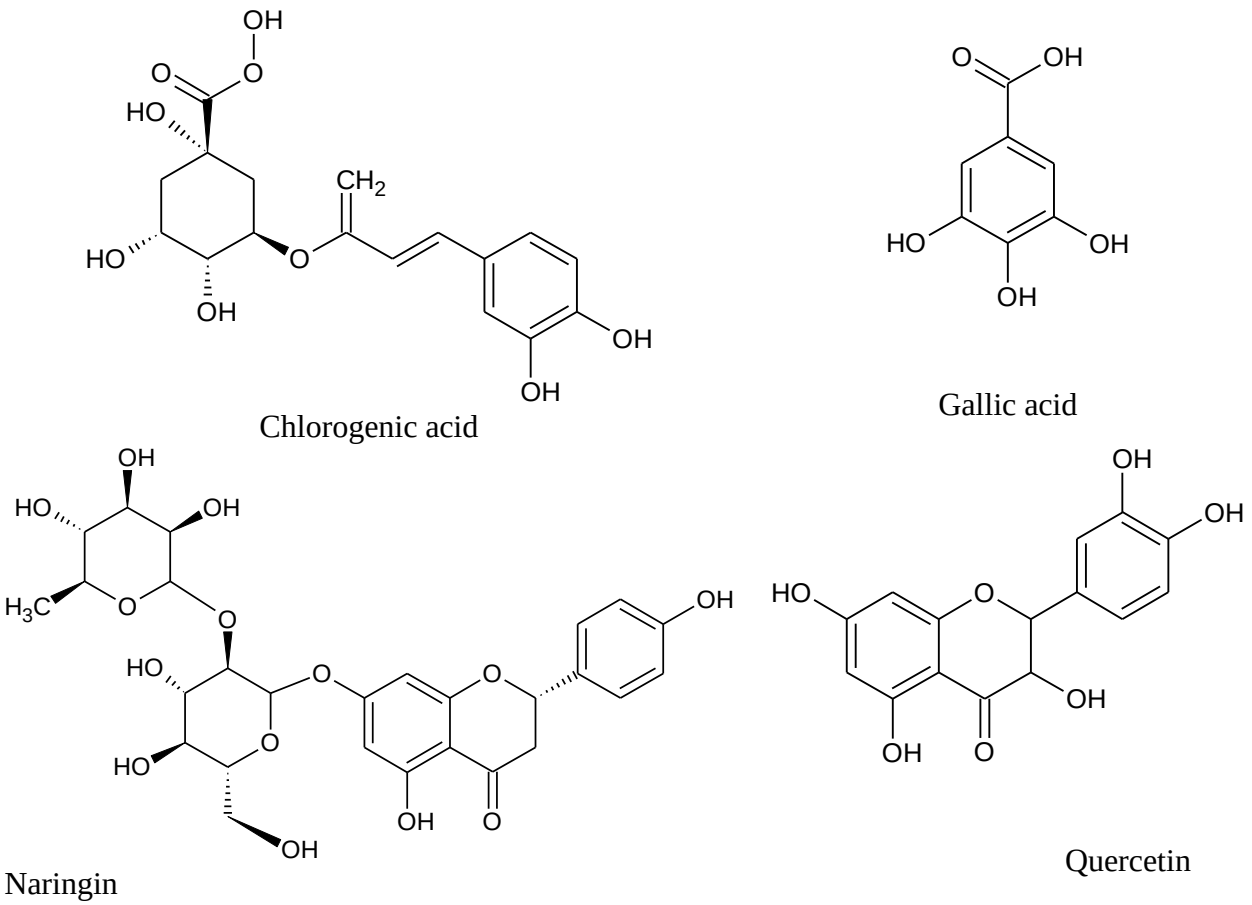


Figure 2. The main phenolic compounds reported from anise.

2.2. Biological activity

2.2.1. Antioxidant activities

The human body has a complex system of natural enzymatic and non-enzymatic antioxidant defenses that protect it against free radicals and other oxidants. A vast spectrum of diseases are caused by free radicals. (18). A strong antioxidant intake can help to fight against free radicals. Significant evidence suggests that antioxidant-rich diets, and maybe antioxidant foods in particular, may play an important role in disease prevention. (18). The antioxidant activity of aniseed essential oils was investigated using 2,2 diphenyl -1-picrylhydrazyl (DPPH) in a concentration-dependent manner. Results showed that it has a significant activity as the highest antioxidant (84.9±0.267%) was recorded at 10000 ppm compared to ascorbic acid as standard (16). Meanwhile, in another study in evaluation polysaccharides were isolated from *P. anisum* (PAP) with increased dose from 0.2 to 1.0 mg/mL using DPPH (19). Results showed that at the

high dose of 1.0 mg/mL, the scavenging activities of PAP against DPPH activity reached 69.4%, which was relatively lower than those of vitamin C at the same dose (90.5 %) (19). Moreover reducing power of PAP was found to be dependent on the concentration and displayed a maximum of 1.8 at 50 µg/ml (19).

2.2.2. Antimicrobial activities.

Antibiotic usage against diseases has resulted in further antibiotic resistance, which has become a major public health problem (20). The medicinal potential of natural products is becoming increasingly important across the world (20). Nature has bestowed on us a plethora of medicinal antibacterial compounds derived from plants (20). Plants have an abundance of potentially beneficial bioactive compounds (20). With the current trend of a high percentage of microbe resistance to modern antibiotics, the importance of medications cannot be overstated (20). The antibacterial activities of anise seed essential oils against *Pseudomonas aeruginosa* planktonic forms were assessed using the agar-well diffusion method. The result showed significant activity against *P. aeruginosa* evaluated regarding the minimum inhibitory concentration of the range 4000-7000 ppm values of essential oils (16). It was reported that the oil extracted from anise seed showed antibacterial activity *Bacillus subtilis, and Staphylococcus aureus,* with inhibition zones (10, and 13). Meanwhile it showed potent antifungal activity against *Aspergillus flavus, Mucor racemosus, Rhizopus arrhizus, Candida albicans, Debaryomyces hansenii,* and *Pichia membranifaciens* with inhibition zones (10, 13, 24, 18, 26, 18, 12, and 26 mm) respectively compared to Clotrimazole (24, 18, 23, 24, 14, and 14) using agar diffusion method (17).

Moreover, the polysaccharide preparation from *P. anisum* seeds (50 mg/ml) was studied against gram-positive (*B. cereus* and *S. aureus*) and gram-negative bacteria (*P. aeruginosa* and *E. coli*) (24). Results showed that inhibition zones varied from 7.3 to 18.5 mm, as the largest inhibition zones were observed against *P. aeruginosa* and *B. cereus* at 18.5 ± 0.2 and 16.5 ± 0.7 mm, respectively (19).

2.2.3. Cytotoxic activity.

Cancer is a severe health issue that affects all human communities (21). Unfortunately, it is a tissue-level variety disease, and this variety is a big problem for its particular diagnosis, followed

by therapy efficacy (21). Nowadays, several cancer treatment guidelines are available and are being used as Chemotherapy, surgery, and radiotherapy with several side effects (22). These severe side effects led to the utilization of complementary and alternative medicine as alternative methods with fewer adverse effects (23).

The cytotoxic activity of *P. anisum* seeds aqueous extract was investigated using an MTT (Methyl Tetrazolium) assay against the KB cell lines (24). Results showed that concentrations of anise extract at 100 µg/ml showed a 32.19% Viability percentage of KB cell line compared to 14.96 % cisplastin at the same concentration (24). The current study found that anise seed extract has promising cytotoxic effects, encouraging more in vivo research for practical application (24).

2.2.4. Anti-inflammatory activities.

Inflammation is a multifaceted biological reaction of vascular tissues to aggressive agents such as infections, irritants, or damaged cells (25). It can be acute or chronic, and it includes a series of biochemical reactions involving the local vascular system, the immune system, and various cell types located in the wounded tissue (25). Nowadays, many herbal drugs are used as anti-inflammatories due to their wide range of safety and efficacy compared to synthetic ones (25).

The PAP was investigated for its anti-inflammatory activity against carrageenan-induced paw edema in mice (19). Results showed the PAP reduced edema volume by 0.68 ± 0.02 mm after 5 hours compared treated group with acetylsalicylic acid, and the non-treated group by 0.92 ± 0.04, and 1.59 ± 0.07 mm, respectively after 5 hours. Moreover, the edema improved with a reduction of the oxidative stress tissue damage produced by carrageenan, with an amelioration of the Malondialdehyde (MDA) non-treated group with 10.15 ± 1.25 nmol/mg protein to 5.73 ± 0.45, treated-group with PAP (19). Meanwhile superoxide dismutase (SOD) level increased from 7.52 ± 0.78 U/mg protein of the non-treated group to 16.40 ± 2.15 of treated PAP (19). The histological analysis revealed that the treated group with extract showed normal structure with only discrete signs of inflammation and slight intra-cellular edema in the intramuscular and adjacent sub-plantar tissue (24). An aqueous extract of *P. anisum L*. seeds was investigated for its anti-inflammatory on ovalbumin-induced asthma in a mouse model (26). Results showed that an aqueous extract of *P. anisum* seeds (0.16 mg/kg) reduced ovalbumin-stimulated asthmatic problems in mice by decreasing the count of eosinophils by (31±7) compared to budesonide-

treated group which decreased by (44.41±8.12). Moreover, it diminished the expression levels of IL-5, -13, and -33 in bronchoalveolar lavage fluid (26). It reduced mucus hypersecretion by (25±1 %) compared to the budesonide-treated group by (35±1 %). Also, it prevented goblet cell hyperplasia and inflammation in the peribronchial and perivascular regions, all of which were caused by ovalbumin exposure (26).

2.2.5. Antidepressant activity.

Depression is a complex, persistent, and sometimes fatal disorder with a global prevalence (27). Researchers are now looking for drugs that are both safer and less expensive (27). Medicinal plants have piqued the interest of scientists (27). Working in this sector because of the longevity of these plants has been used to treat certain disorders (27). The antidepressant activity of the total extract of *P. anisum* seeds was evaluated at the doses of 100 and 200 mg/kg, using *in vivo* tests; the Light–-Dark Box (LDB) Test, and Tail Suspension Test (TST), as an experimental paradigm of anxiety and depression, on Swiss albino mice (15). Results showed that a daily dose of total extract has a considerable anxiolytic and antidepressant-like effect by shortening immobility time by 17% with the dose of 100 mg/kg, 27% with the dose of 200 mg/kg, and decreasing downtime by 32% and 42% for the dose of 100 and 200, respectively in Tail Suspension Test (15). Meanwhile, in the LDB test, it was noted that using doses of 100 and 200 mg/kg increased the crossing time of mice in the lighted compartment by 172% and 228% respectively, compared to 96% noted for bromazepam compared to the normal control (15).

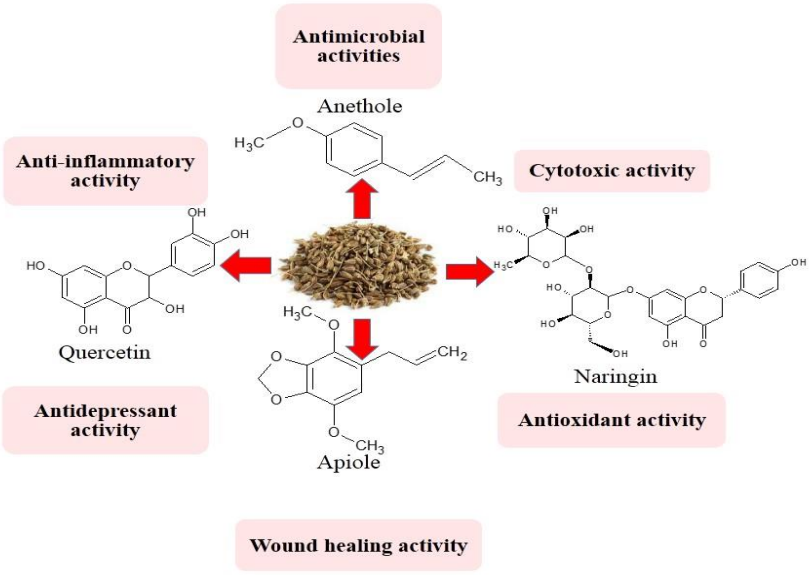
2.2.6. Wound healing activities.

Wound healing is a vital physiological process that involves the cooperation of several cell strains and their products (28). For thousands of years, nature has provided therapeutic remedies, and plant-based systems continue to play an important part in wound healing as a first line of treatment (29). However, increased knowledge of their activities, as well as prospective and likely safety issues, highlight the necessity for scientific standardization, validation, and rigorous safety review before their effective application to wound care (29).

Methanolic extract of anise was investigated for their potential wound healing activity using *in vivo* (10% cream) streptozotocin-induced diabetic rats (30). Results showed that the treated animals with *P. anisum* had a higher closure percentage of wounds than the other groups with

(94.07±1.215 %) compared to the group taking tetracycline with (83.24±2.53 %) at day 21 (30). Furthermore, *P. anisum* therapy reduced the number of lymphocytes while increasing the number of fibroblasts in the early phases of wound healing and decreasing the number of fibrocytes in the later stages (30). When compared to the control, other characteristics such as re-epithelialization, tissue alignment, better maturity of collagen fibers, and big capillary-sized blood vessels exhibited significant differences (30).

In another study, PAP was evaluated for its laser burn wound healing activity (19). Results showed that PAP induces a beneficial effect on cutaneous repair of laser burn wounds in mice and accelerates wound healing wound area by decreasing as compared to that of the untreated group at 3 ($P < 0.01$) and 7 ($P < 0.001$) days. (19). Moreover, It may have a pro-inflammatory impact, which might hasten wound healing (19). Histological observations of wound tissue on the 7th post-laser day revealed a full re - re-epithelialization with a well-structured layer without cell inflammation in PAP -the treated group (19).



Major pharmacological activities and main active constituents of *Pimpinella anisum* L.

3. Conclusion

In this review, *P. anisum*'s traditional applications, pharmacological activities, and phytochemical properties have all been studied in the last five years. It exhibits several biological activities as antibacterial, anti-inflammatory, antidepressant, and wound healing properties. The volatile constituents of *P. anisum* were primarily anethole, limonene, safrole, estragole, and

carvone. Furthermore, phenolic substances such as chlorogenic acid, gallic acid, naringin, and quercetin were the most abundantly discovered which may be responsible for its activities. Despite all of these investigations, given the increased demand for *P. anisum* in traditional medicine in recent years, we should pay attention to the necessity for new clinical studies on *P. anisum* to evaluate their efficacy, their characteristics for food and medicine, and to encourage future study. This review will add to the literature in this area and give insight into future research.

- **Conflict of Interest**

  The authors declare no conflict of interest.

4. References

1. Sungur I, Muluk NB, Sezer CV, Kutlu H, Cingi C. Efficacy and toxicity of anise oil as a potential topical wound healer: a cell culture study. Eur Rev Med Pharmacol Sci. 2023;27(2 Suppl):14-20.
2. Khare C. Carica papaya Linn. Indian Medicinal Plants (An Illustrated Dictionary) Springer, New York, NY, USA. 2007:122-3.
3. Singletary KW. Anise: Potential Health Benefits. Nutrition Today. 2022;57(2):96-109.
4. Asad M, Ashraf N, Rahman S, Ahmad K, Minhajuddin A, Zakir M. Traditional uses, phytochemistry and pharmacological activities of anisun (*Pimpinella anisum* l.): A comprehensive review. Ann For Res. 2022;65(1):5212-27.
5. Gülçın İ, Oktay M, Kıreçcı E, Küfrevıoğlu Öİ. Screening of antioxidant and antimicrobial activities of anise (Pimpinella anisum L.) seed extracts. Food chemistry. 2003;83(3):371-82.
6. Dargahi T, Ilkhani R, Ghiaee A, Arbabtafti R, Fahimi S, Jafari F, et al. Anti-inflammatory effect of Pimpinella anisum extract in a mouse model of allergic asthma. Research Journal of Pharmacognosy. 2021;8(3):41-9.
7. Amin G. Popular medicinal plants of Iran, vice chancellorship of research. Tehran University of Medical Science Press, Tehran, Iran. 2005.
8. Nasır A, Yabalak E. Investigation of antioxidant, antibacterial, antiviral, chemical composition, and traditional medicinal properties of the extracts and essential oils of the Pimpinella species from a broad perspective: a review. Journal of Essential Oil Research. 2021;33(5):411-26.
9. Salehi Surmaghi M. Medicinal plants and phytotherapy. Vol. 1. Donyay Taghziah Press, Tehran, Iran; 2010.
10. Shojaii A, Abdollahi Fard M. Review of pharmacological properties and chemical constituents of Pimpinella anisum. International Scholarly Research Notices. 2012;2012.
11. Besharati-Seidani A, Jabbari A, Yamini Y. Headspace solvent microextraction: a very rapid method for identification of volatile components of Iranian Pimpinella anisum seed. Analytica Chimica Acta. 2005;530(1):155-61.
12. Rebey IB, Wannes WA, Kaab SB, Bourgou S, Tounsi MS, Ksouri R, et al. Bioactive compounds and antioxidant activity of Pimpinella anisum L. accessions at different ripening stages. Scientia horticulturae. 2019;246:453-61.

13. El-Rokiek KG, Ibrahim ME, El-Din SAS, El-Sawi SA. Using anise (Pimpinella anisum L.) essential oils as natural herbicide. J Mater Environ Sci. 2020;11:1689-98.
14. Boumahdi Y, Moghrani H, Nasrallah N, Ouarek S, Maachi R. Microwave-assisted hydrodistillation of the essential oil from Algerian Pimpinella anisum seeds. Flavour and Fragrance Journal. 2021;36(1):34-46.
15. Es-Safi I, Mechchate H, Amaghnouje A, Elbouzidi A, Bouhrim M, Bencheikh N, et al. Assessment of antidepressant-like, anxiolytic effects and impact on memory of Pimpinella anisum L. total extract on swiss albino mice. Plants. 2021;10(8):1573.
16. Al-Wendawi SA, Gharb L. Antioxidant, antibacterial and antibiofilm potentials of anise (Pimpinella anisum) seeds extracted essential oils. Iraqi Journal of Agricultural Sciences. 2021;52(2):348-58.
17. Abd-Elhafeez E, Ramadan BR, Abou-El-Hawa SH, Rashwan MR. Chemical Composition and Antimicrobial Activity of Anise and Fennel Essential Oils. Assiut Journal of Agricultural Sciences. 2023;54(2):127-40.
18. Alam MN, Bristi NJ, Rafiquzzaman M. Review on in vivo and in vitro methods evaluation of antioxidant activity. Saudi pharmaceutical journal. 2013;21(2):143-52.
19. Ghlissi Z, Kallel R, Krichen F, Hakim A, Zeghal K, Boudawara T, et al. Polysaccharide from Pimpinella anisum seeds: Structural characterization, anti-inflammatory and laser burn wound healing in mice. International journal of biological macromolecules. 2020;156:1530-8.
20. Bajpai VK, Baek K-H, Kang SC. Control of Salmonella in foods by using essential oils: A review. Food Research International. 2012;45(2):722-34.
21. Hassanpour SH, Dehghani M. Review of cancer from perspective of molecular. Journal of cancer research and practice. 2017;4(4):127-9.
22. Arruebo M, Vilaboa N, Sáez-Gutierrez B, Lambea J, Tres A, Valladares M, et al. Assessment of the evolution of cancer treatment therapies. Cancers. 2011;3(3):3279-330.
23. Olaku O, White JD. Herbal therapy use by cancer patients: a literature review on case reports. European journal of cancer. 2011;47(4):508-14.
24. Mukunda A, Pynadath MK, Kadar N, Mohan A. Cytotoxic effect of anise seed (Pimpinella anisum) extract on KB cell line-a comparative study with CISPLATIN. Oral & Maxillofacial Pathology Journal. 2020;11(1).
25. de Cássia da Silveira e Sá R, Andrade LN, de Sousa DP. A review on anti-inflammatory activity of monoterpenes. Molecules. 2013;18(1):1227-54.
26. Dargahi T, Ilkhani R, Ghiaee A, Arbabtafti R, Fahimi S, Athari SS, et al. Anti-inflammatory effect of Pimpinella anisum extract in a mouse model of allergic asthma. Res J Pharmacogn. 2021;8(3):41-9.
27. Rabiei Z, Rabiei S. A review on antidepressant effect of medicinal plants. Bangladesh Journal of Pharmacology. 2017;12(1):1-11.
28. Gonzalez ACdO, Costa TF, Andrade ZdA, Medrado ARAP. Wound healing-A literature review. Anais brasileiros de dermatologia. 2016;91:614-20.
29. Maver T, Maver U, Stana Kleinschek K, Smrke DM, Kreft S. A review of herbal medicines in wound healing. International journal of dermatology. 2015;54(7):740-51.
30. Hashemnia M, Nikousefat Z, Mohammadalipour A, Zangeneh M-M, Zangeneh A. Wound healing activity of Pimpinella anisum methanolic extract in streptozotocin-induced diabetic rats. Journal of Wound Care. 2019;28(Sup10):S26-S36.