



A Multidimensional Review of *Pimpinella anisum* and Recommendation for Future Research to Face Adverse Climatic Conditions

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Abstract

Anise, or *Pimpinella anisum*, has a long history of usage in traditional and alternative medicine, as well as in the pharmaceutical sector. The species is native to Southwest Asia, the Middle East, and the Mediterranean region. The current studies have revealed that wild and cultivated *P. anisum* are rich in bioactive compounds, such as phenols, tannins, carotenoids, and fatty acids. Different parts of *P. anisum* plant are used treatment of diseases, the treatment of pathogens for antiviral, antibacterial, and antifungal purposes, and cosmetics. In this paper, we reviewed the current knowledge on geographical distribution, cultivation, chemical compounds, extraction methods, and agronomic and medicinal uses of *Pimpinella anisum*. Equally, we suggested guidelines for future research to fill the gap in less investigated issues. Data for this paper was gathered via electronic literature search on Google, Google Scholar, and databases counting, Science Direct, Scopus, Springer, PubMed, and Hindawi, from 1930 to 2022. Analyzed data show that *Pimpinella anisum* is currently recorded from Portugal on the Atlantic Ocean in the west to China in the East. With new extraction methods, such as Ultrasound-Assisted Extraction, scientists have explored the higher quantities of polyphenols, flavonoids, and antioxidants, and revealed new constituents such as trans-anethole and estragole found in essential oil fruits by gas chromatography-mass spectrometry (GC-MS). These compounds showed significant therapeutic benefits against diseases, pathogens, and cosmetic roles. However, with the current impacts of climate change on natural vegetation cover, more investigations are needed to understand how these affect the geographical distribution, metabolic aspects, and chemical properties of *Pimpinella anisum*. These are suggested to increase the value of the species and ensure its conservation.

Keywords *Pimpinella anisum* · Chemical composition · Biological properties · Agronomic and pharmaceutical uses · Guidelines for future research

1 Introduction

Anise *Pimpinella anisum* is a Medicinal plant widely used in food and in both vernacular treatments and conventional medicine, as well as, currently in the modern pharmaceutical industry [1–4]. For thousands of years, this plant has been utilized for both culinary and medicinal uses, with clear benefits for preserving human health and enhancing the quality

of life [5]. Several traditional texts mention anise for treating nightmares, melancholy, seizures, and epilepsy [5, 6]. Generally, anise is a dominant spice and traditional medicinal plant used for both food and medicinal purposes due to its biochemical richness with bioactive molecules [5].

Around the Mediterranean basin, the flavor and aroma of *P. anisum* seeds have been used to flavor food, candy, and various alcoholic drinks [7, 8]. The most powerful flavor component of the anise is anethole (C₁₀H₁₂O) which is found in both seeds and leaves and has shown powerful inhibition against chronic diseases [9, 10]. Equally, the essential oil of *P. anisum* is rich in polyphenols, flavonoids, terpenes (C₅H₈) with noticeable therapeutic against diabetic, inflammatory, and gastric diseases. Further, different extracts from seeds and leaves have demonstrated powerful inhibitory effects

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against bacterial, fungal, and viral pathogens. These elements were widely studied and reviewed twice. Moreover, the review papers of 143 articles and most have focused on chemical constituents, and their roles in nutrition, medicine, and pharmacology in a specific area such as Iran. However, with the publication of new papers on new scientific features addressing *P. anisum* an integral review gathering data worldwide is required. However, the richness of chemical components in essential oils and extracts of *Pimpinella anisum* L. varies depending on the type of extract, used part of the plant, geographical location, climate conditions, and utilized extraction methods [11].

Anise is an herbaceous annual plant, cultivated in many areas in the Middle East and Asia, but native to the Mediterranean region [3, 12, 13]. The *Pimpinella anisum* belongs to Pimpinella Genus, the Apiaceae or Umbelliferae Family [14]. It has been reported, it is also cultivated for food, where seeds and fruits constitute the edible parts, as well as for extractions of bioactive compounds that are used in medicine and other industrial purposes [1]. Currently, many studies have addressed growth parameters to increase the productivity of this useful species. They addressed the germination of seeds, the growth of seedlings, and their impact on the quality, Content, and Chemical Composition [3, 5, 15]. The cultivation of this plant aims to respond to increasing agronomic and industrial uses.

In this paper, we highlighted previous reports on *P. anisum* including geographical range, cultivation, chemical composition, agronomic potential, as well as in vitro and in vivo pharmacological properties. Equally, we revealed the most promoting topics that need more advanced studies, and we suggested guidelines for future studies and conservation measures to ensure the conservation of wild varieties. This paper aimed to summarize the entire realized research on *P. anisum* from the early years of 19 century to the date.

2 Methodology

All information and data sources used to formulate this review paper were collected and obtained using electronic search engines, principally Google Scholar, Science Direct, Springer, PubMed, MDPI, and Web of Science depending on the following keywords: *Pimpinella anisum*, *Pimpinella* genus, distribution range, germination and growth, Phytochemistry, chemical compounds, extraction methods, In vitro and in Vivo studies, inhibitory effects against bacterial, viral and fungal agents of *Pimpinella anisum*. A total of 340 peer-reviewed papers were read, while only 143 peer-reviewed papers have shown a significant relation to our study species and were selected for their scientific quality and relevance to prepare this paper. Non-peer-reviewed papers were eliminated to avoid any low-quality information

since this paper is aiming to integrate all addressed topics on *Pimpinella anisum*. We focused on recent research dating from 2015 to 2022, with regard to other dates for support.

3 Nomenclature and Classification

Since the species is worldwide, the *P. anisum* has local names depending on the geographical area and countries. The Mediterranean basin considered the origin of native species, it is named Anis vert (France), Annesella (Italy) Vigon's Anise (Spain) in the northern slope, while in North Africa (Morocco, Algeria, Tunisia, and Egypt) it is called Petit anise [16–18]. In Asia, it is named Anise seed in Japan and China, while in central zones of Iran and India, it is named Anisa, Kuppi, Badian, Saunf, Muhuri, and Sop. In North America, the species is named Anise and Star anise [5, 19, 20]. The Pimpinella's meaning could be derived from the Latin term “bipenne = bipenne,” which was changed to reflect the leaflets' 2 to 2 positioning. Other authors claim that it derives from the diminutive of “pampinus,” pampas, for the vine-like similarity of the leaves, or, ultimately, from the Italian name Sanguisorba for the rosacea, again based on the resemblance of the leaves. The word anisum, on the other hand, is of unknown foreign origin and is derived from the Greek word “anison.”

In terms of systematic, the *Pimpinella anisum* belongs to Pimpinella Genus, the Apiaceae or Umbelliferae Family, Order of Apiales, Rosidae Subclass, Magnoliopsida Class, Magnoliophyta Division, Tracheobionte Substitution, Kingdom of Plantae, and Eukaryota Domain [21].

4 Range, Cultivation, Growth, and Productivity

Anise (*Pimpinella anisum*) is recorded as a native plant in Mediterranean countries counting Morocco, Algeria, Tunisia, and Egypt in North Africa, Portugal, Spain, and Italy in the Northern slope of the Mediterranean basin. Equally, it has been reported as indigenous to central Asia regions from India, Iran, and Turkey [22, 23]. However, Anise is domesticated and is cultivated in many regions counting Southeast Asia (i.e. China and Japan), the Middle East (i.e. Iran and Emirates), and Africa (i.e. Sudan and Egypt) [24].

Anise is a slow growing annual plant that needs a sunny (Fig. 1), warm, and dry autumn to meet significant economical yield and high quality product for other uses such as extraction of essential oil [24]. In the nineteenth century, there were first attempts at cultivation. The field must be prepared in the fall for planting by being plowed and fertilized with manure or conventional compost. The planting period must be between March and April on well-prepared

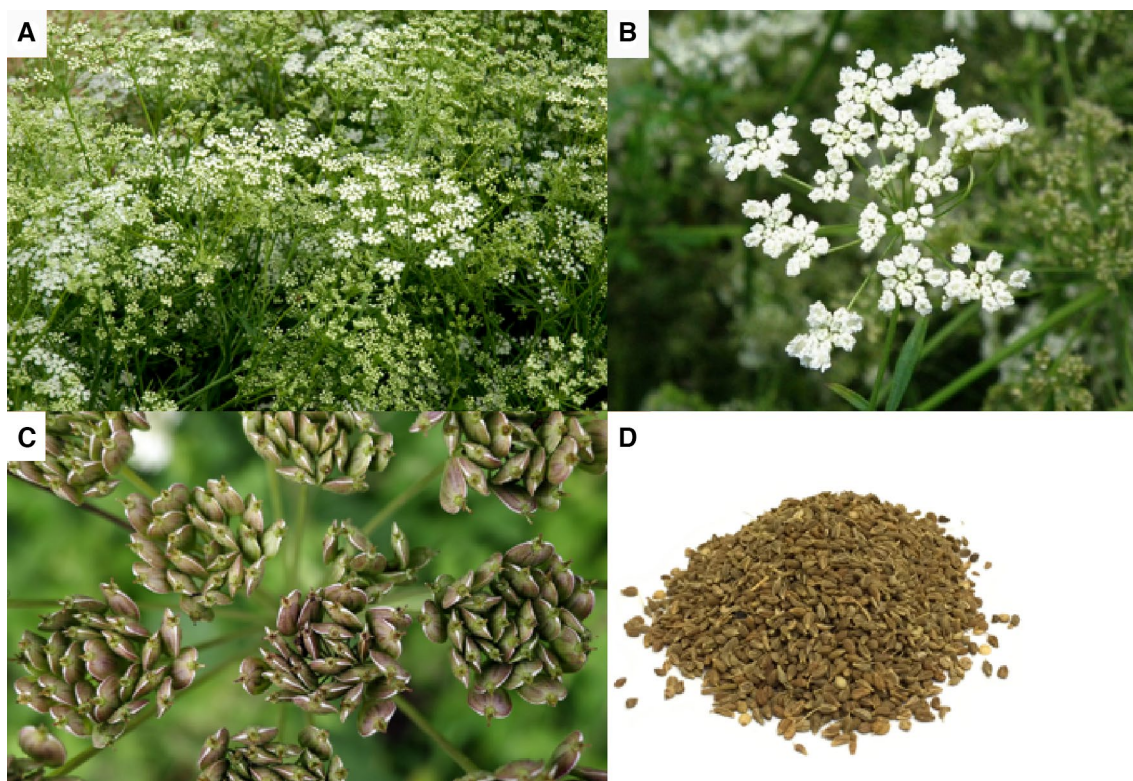


Fig. 1 Plant (A), flower (B), and seeds of *Pimpinella anisum* (C the form of seeds on the plant; D dried seeds)

soil. Because aniseed crops are sensitive to late frost, sowing should take place in warm climates [25]. After then, it takes the seeds about a month to germinate, although vegetative growth starts to increase extremely quickly as soon as the first leaves show. Until the blossoming phase, which lasts between June and July, watering must be provided concurrently. Additionally, it is frequently necessary to manually eradicate wildflower competitors along growth phases. Plants are harvested in traditional bundles between August and September, usually when their umbels are only partially dried and dark in color. They are then dried in airy locations for 7–8 days in the shade and 1–2 h in the sun. Then, by shaking the plants, aniseeds may be sorted from the entire batch [22, 25].

Anise often thrives in dry, rocky terrain, pastures in mountains, fields, meadows, and grasslands, but seed germination is extremely weak in nature due to dormancy [26]. The impacts of pretreatment elements, fertilization, seeding, and agronomic procedures have, however, been the subject of numerous studies recently in an effort to increase anise germination rates, growth, production, and quality. The germination traits (mean time germination, germination percentage, germination rate, and seed vigor index) and growth parameters (coleoptile length, seedling length, and radicle length) were significantly improved with the use of Gibberellic Acid, Benzyladenine, and Kinetin as hormone treatments

(0, 15, 30 and 45 days), according to Shahrajabian et al. [3]. Combining these hormones produced the highest germination. The authors also pointed out that the use of endogenous Benzyladenine + Kinetin and Gibberellic Acid + Kinetin is the most efficient method for releasing seeds from dormancy. Water stress also inhibits anise germination, although the use of polyethylene glycol (PEG) 6000 and ascorbate (1.4 mM) considerably enhances anise germination percentage (89% and 93%) and, in turn, the tolerance to water stress by lowering osmotic potential [27]. Darzi et al. [13] considerably increased the umbel quantity per plant, biological yield, and seed production of anise cultivated in vermicompost (0.5 and 10 ton/ha) by using the Phosphate Solubilizing *Bacillus Circulans* (inoculation of seeds and inoculation + spray on base at stem elongation stage). The effects of sowing dates and row spacing on yield-related features, seed yield, growing degree days (GDD), essential oil content, and chemical composition of anise have been studied by Kara [28] in a study that is intended to promote the crop. The use of delayed sowing treatments (15/April and 1/May) with sowing dates of 1/April, 15/April, and 1/May with row spacings of 15, 20, and 25 cm revealed that seed yield and its components (plant height, the number of umbels, and number of branches per plant) reduced in these treatments. The 15 April planting date produced the best essential oil content values, and row spacing of 20 and 25 cm produced the maximum yield

components and essential oil content [28]. Elevated CO₂ (eCO₂) in seeds has an effect on anise seeds' nutritional and biological value, but the effectiveness depends on the seed's maturity and provenance [29]. While essential oil metabolism declines, the decrease can be mitigated by the application of eCO₂, seed maturation increased the antioxidant metabolites and nutrients in eCO₂-treated accessions [29].

5 Diversity and Variation of Chemical Components

When the chemical components of anise were studied in the second half of the twentieth century, anethole was the first identified element [30–32]. El Sissi and El Sherbeiny [33] via a micro-screening survey of 600 sampled plants in Egypt, revealed a considerable amount of tannins in 56 plants including *P. anisum*. Further, with the development of chemical techniques and screening materials, scientists have described qualitatively and quality of Anise chemicals. However, the chemical composition varies depending on the provenance area, climate conditions, soil characteristics, and used protocols (Table 1) [27, 34].

Anethole is the most important chemical constituent of anise and is the most used in food, and medicine, as well as in the industry of pharmaceuticals, perfumery, flavouring, and pesticides [7, 30, 31, 38]. Generally, anise is constituted of protein that occupies 18% of the mass, lipids mainly fatty acids (palmitic and oleic acids) take 8–11% of the mass, volatile oil constitutes 1.5–6.0% mass of Anise and is principally composed from *trans*-anethole, and approximately 4% of carbohydrates [39]. The most important proteins and carbohydrates are Lignin-Carbohydrate-Protein Complexes (LC1, LC2, and LC3), isolated from hot water extract of *P. anisum* seeds by a combination of gel filtration, anion-exchange, and hydrophobic interaction column chromatographies [40]. Further, Ghilissi et al. [41] have currently revealed that Galactose at 33.47%, β-D-Glucose at 26.71%, and α-D-Mannose at 18.21% were the major monosaccharides components presenting in polysaccharide preparation from *Pimpinella anisum* seeds, while β-D-Galactose, D-Fructose, α-D-Glucose, α-L-Galactose, and arabinose were the minor constituents. In essential oil, eugenol *trans*-anethole, anisaldehyde, methylchavicol, estragole, scopoletin, coumarins, umbelliferone, terpene hydrocarbons, estrols, polyenes, and polyacetylenes were the major compounds of *Pimpinella anisum* seed extracts [42]. In fruits, the extracts showed also a higher quantity of *trans*-anethole (93.9%) and minimum fractions of estragole (2.4%), methyleugenol, α-himachalene, α-cuparene, β-bisabolene, *p*-anisaldehyde, and *cis*-anethole (0.06%) [7].

From the analysis of 11 samples of fruit essential oils from 11 European countries, Orav et al. [11] revealed that

trans-anethole (76.9–93.7%) was the major component, followed by γ-himachalene with 0.4–8.2%, *trans*-pseudoisoeugenyl 2-methylbutyrate with 0.4–6.4%, *p*-anisaldehyde with 5.4%, and methylchavicol with only 0.5–2.3%, while the minor components were nonanal with 0–1.4%, isogeijerene, 0–0.9%, *cis*-anethole (0–2.0%), pregeijerene (0–0.5%, and bourbonene (0–0.9%). These chemicals were variable from country to another and the highest content of *trans*-anethole with a fraction superior to 90% was found in the samples of Greece, Scotland, Hungary, Italy, Lithuania, and Germany. In Middle East, the analysis (GC–MS) of essential oil extracted from seeds showed 51 components, with the dominance of *trans*-Anethole or Anisole (71.52%), followed by benzocycloheptene (6.59%), and Isoeugenyl acetate (4.63%) in samples from Iraq [36], and 4-allylanisole (85.28%), Limonene (5.53%), Fenchone (4.12%), Anethole (3.54%), Acide linoléique (trace), and Camphene (trace) in samples from Yemen. In North Africa, 4-allylanisole (76.70%), Limonene (9.75%), Anethole (7.40%), Fenchone (6.16%), linoleic Acide (trace), and Camphene (trace) were the principal chemicals in Moroccan samples, while in Algerian samples, *trans*-anethole (92.4%) followed by estragol (1.9%), *o*-isoeugenol (1.9%), and γ-himachalene (1.1%) were the major chemical constituents [16].

In terms of variation of chemical constituents according to used methods, via Supercritical fluid extraction using CO₂ and GCMS, Rodrigues et al. [43] obtained anethole (90%), γ-himachalene (4%), *p*-anisaldehyde (up to 1%), methylchavicol (up to 1.5%), *cis*-pseudoisoeugenyl 2-methylbutyrate (3%), and *trans*-pseudoisoeugenyl 2-methylbutyrate (1.3%) as major chemical constituents of *P. anisum*. by Silver Ion HPLC, Denev et al. [44] revealed the composition of fatty acids in of *P. anisum* seed oils, counting the positionally isomeric 18:1 fatty acids, followed by oleic acid (*cis* 9–18:1), petroselinic acid (*cis* 6–18:1), and *cis*-vaccenic acid (*cis* 11–18:1). By Soxhlet, hydrodistillation using Clevenger apparatus (HDC), Ultrasonic-assisted (UAE), subcritical water extraction (SWE), ethanol (ScCO₂-Et), supercritical carbon dioxide extraction (ScCO₂) using three solvents (methanol (ScCO₂-Met), and hexane (ScCO₂-H) and supercritical 1,1,1,2-tetrafluoroethane (ScR134a) methods, Nasir et al. [45] revealed Anethole as the main component with different values, 94.5% by SWE, 94.5% by Soxhlet respectively. The highest TPC value was 508.5 mg GAE/100 g kb in ScR134a extract, while the lowest value was 27.77 mg GAE/100 g kb in HDC extracts, the highest antioxidant capacity was IC₅₀ = 1.58 mg/mL in ScCO₂-H and the lowest was IC₅₀ = 0.07 mg/mL in Soxhlet extracts. Also, as we mentioned above, three lignin-carbohydrate-protein complexes were purified from hot water seed extracts of *Pimpinella anisum* by a combination of anion-exchange, gel filtration, and hydrophobic interaction column chromatographies [40, 46].

Table 1 Variation and diversity of chemical components in *P. anisum* in Europe, Africa, and Asia

Continent	Region	Sample origin	Dominant climate	<i>trans</i> -Anethole	<i>p</i> -Anisaldehyde	<i>trans</i> -Pseudoisoeugenyl 2-methylbutyrate	Himachalene	Methyl chavicol	<i>cis</i> -anethole	4-allylanisole	
Europe	Mediterranean	France	Mediterranean	76.9	5.4	5.7	3.1	1.5			
		Spain	Mediterranean	87.9	2.2	2.3	2.3	1.4			
	Eastern Europe	Italy	Mediterranean	92.2	tr	1.5	2.2	1.3			
		Greece	Mediterranean	90.2	2.8	0.9	2.6	1.3			
	Baltic	Hungary	Continental climate and the oceanic climate	91.3	0.2	1	3.9	0.5			
		Russia	Humid continental and subarctic	87.7	1.8	1.7	2.5	1.5			
	Western Europe	Czech	Temperate climate	88.4	3.1	2.9	0.7	0.9			
		Lithuania	Humid continental climate	93	0.7	0.7	1.5	2			
		Estonia	Temperate and mild	78.1	0.1	6.4	8.2	0.6			
		Scotland	Temperate maritime climate	93.6	0.7	0.4	1.4	1.9			
Africa	Northwest Africa	Germany	Temperate and rainy	93.7	1	1.3	0.4	2.3			
		Algeria	Mediterranean and Saharan	92.4					0.5		
	Northeast Africa	Tunisia	Mediterranean and Saharan	94.3	0.17		0.12				
Asia	Middle east	Morocco	Mediterranean and semi-arid	7.4					7.4	76.7	
		Egypt	Mediterranean and Saharan	90.41	0.1		0.11				
	Central Asia	Iraq	Continental and subtropical semi-arid type	71.52	0.19						
Europe	Limonene	Iran	Extremely continental	92.9	0.1				0.1		
		Pakistan	Extremely continental	82.1			0.44		0.14		
	Fenchone	linalool	Estragol	γ -Himachalene	Zingiberene	Anisylacetone	<i>o</i> -Isoeugenol	Butanoic acid, 2-methyl- 4-methoxy-2-(3- methyloxiranyl) phenyl ester	Oil yield (mL kg ⁻¹)	References	
										10.0 ^a	[11]
										25.4	
										20.4	
										48.3	
										26.1	
										23.1	
									23.3		
									23		
									53.6		
									13.1 ^a		
									25.3		

Table 1 (continued)

Continent	Limonene	Fenchone	linalool	Estragol	γ -Himachalene	Zingiberene	Anisylacetone	<i>o</i> -Isoeugenol	Butanoic acid, 2-methyl-4-methoxy-2-(3-methoxyiranyloxy) phenyl ester	Eugenol acetate	Oil yield (mL kg ⁻¹)	References
Africa			0.3	1.9	1.1	0.3	0.3	1.9	0.3			[16]
			0.13	0.2	2.32	0.3		0.14				[18]
	9.75	6.16										[35]
Asia			0.04	3.74	1.08	0.25		0.22				[18]
			0.44			1.02				0.91		[36]
						0.4						[37]
					7	0.77						[25]

6 Nutritional and Industrial Uses

Various ethnobotanical studies have shown that *Pimpinella anisum* plants, seeds, roots, and/or leaves are used in cuisine for food, while their derivatives containing essential oils and extracts serve as aroma for different receipts and drinks [17, 47, 48]. In North Africa from Morocco to Egypt, *P. anisum* is mainly used as a fragrance and spice in cooking of Cakes and dishes (46.1%) [17]. It is often used as a “licorice” flavor substitute or added to licorice candy, while the flavoured components are used alcohols, liqueurs, dairy products, gelatins, puddings, meats, and candies. Generally, seeds are used as a breath freshener, and it is sold as a spice.

Nath et al. and Sharaf and Goma [49, 50] were among the author that studied the nutritional uses of *P. anisum*. Sharaf and Goma [50] demonstrated that extract and *Pimpinella anisum* oil mixed with food have positive oestrogenic effects in immature rabbits and ovariectomized rats. Further, Nath et al. [49] demonstrated a significant nutritional potential of the residue resulting after the distillation of steams for essential oil in Kumauni bullocks of about 200 kg liveweight. Equally, the use of anise seed (*Pimpinella anisum* L.) powder supplemented to the drinking water (0, 500, 750, and 1000 mg/L) for 1-day-old Hubbard Classic chicks for 56 days, significantly improved blood RBC, WBC, Hgb, HCT, TP, albumin, globulin, GLU, P, and Ca levels of broilers, and the highest levels of anise seed powder, i.e., 1000 and 750 mg/L, had a stimulating effect on the physiological traits of the birds [51].

During last decades, Cabaroglu and Yilmaztekin [52] have proven one of *P. anisum*'s productive uses in industry. In order to make the traditional Turkish alcoholic beverages known as “Raki,” aniseed *P. anisum* is used. The beverages are made from raw materials such as raisins, grapes, and molasses by double or triple distilling either (1) suma, a distillate of raw materials that have undergone fermentation, or (2) suma combined with agricultural ethanol and aniseed flavoring [53]. The beverage is aromatized by adding 6–10% (w/v) of aniseed [52]. Turkey produces several different varieties of raki (the most preferred spirit among other distilled spirits) [54], and are consumed by the people in Turkey and exported to other countries, and the most preferred spirit among other distilled spirits in Turkey. Sales of these alcoholic drinks have more than doubled since 2000, with 614 million liters to 1.127 billion liters in 2012.

Currently, Das et al. [1] have demonstrated a new way to substitute artificial preservatives to control the contaminations that causing significant loss in nutritive value of stored food commodities, with derivatives of *P. anisum* plants. The authors encapsulated essential oil of *P. anisum*

in chitosan nanobiopolymer (CS-PAEO-Nm) to improve its sensorial suitability and bioefficacy for application in food system. Obtained results showed a higher inhibitory effect against fungal infestation and aflatoxin B1 contamination, which make the essential oil of *P. anisum* a green food preservative against deterioration of nutritional qualities. Similarly, the co-encapsulate binary synergistic formulation of *P. anisum* and *C. sativum* essential oils (0.75:0.25) into chitosan nanoemulsion (Nm-PC) showed effective inhibition against fungal proliferation, aflatoxin B1 secretion (AFB1), and peroxidation of lipids in stored rice [1]. The encapsulated essential oils caused irreversible destruction of plasma membrane in cells of toxigenic *Aspergillus flavus* and significant diminution of methylglyoxal [1]. Poly-lactic acid films comprising diverse percentage of anise essential oil (0, 0.5, 1 and 1.5% v/v) showed significant antibacterial inhibitory *L. monocytogenes* and *V. parahaemolyticus* in a concentration-dependent manner, which suggests the significant potency of anise essential oil to be used as an antibacterial agent in active food packaging [55].

7 Agronomic Uses

7.1 Uses Against Pathogens

7.1.1 Insecticidal Potential

Extracts of seeds and leaves of *Pimpinella anisum* have widely tested against pathogen insects from the seventies. These tests were realized in fields and laboratory on different phytopathogen insects that impact most important crops. Obtained results were variable depending on used quantities, type of extracts, and pathogens (Table 2).

First study of toxicology of anise bioactive compounds was realized by Marcus and Lichtenstein [56] who tested the impacts of nine anise compounds counting anethole, estragole, anisyl alcohol, anisic acid, *p*-creosol, *p*-cresol, eugenol, anisaldehyde, acetaldehyde, and hydroquinone combined with insecticides counting parathion, paraoxon, carbofuran, carbaryl, DDT, or pyrethrum against houseflies. In results, anethole at 0.5% of diet of the insect combined with insecticide was effective.

Further, essential oil nanoemulsions of *P. anisum* were tested against the red flour beetle, (*Tribolium castaneum* Herbst) considered as one of the most an economically important Coleoptera pest of stored crops [57]. The nanoemulsion of essential oil containing 81.2% of (*E*)-anethole exhibited poisonousness on *T. castaneum* ($LC_{50}=9.3\%$ v/v), with important effect on its progeny and scanning electron microscopy (SEM) revealed Morphological and histological

damages against insects. Tunç et al. [58] also tested the insecticidal activity of essential oil vapours from anise *Pimpinella anisum*, eucalyptus *Eucalyptus camaldulensis*, cumin *Cuminum cyminum*, rosemary *Rosmarinus officinalis*, and oregano *Origanum syriacum* var. *bevanii* against another two stored-product pathogen insects, the Mediterranean flour moth (*Ephesia kuehniella*) and the confused flour beetle (*Tribolium confusum*). Further, 100% mortality of the eggs was obtained in essential oils from anise and cumin, compared to 77% and 89% in Oregano against *T. confusum* and *E. kuehniella*, respectively and 45% and 65% in eucalyptus and rosemary respectively. At a concentration of 98.5 µL anise essential oil/l air, the LT_{99} values were 60.9 for *E. kuehniella* and 253.0 h for *T. confusum*, respectively. In another study, essential oils of *Pimpinella anisum* and other 39 plant species were tested against larvae of *Lycoriella ingenua* that cause serious crop loss, using a fumigation bioassay. In results, among all tested essential oils, anise and garlic were the most effective with insecticidal activity against the larvae. The constituents counting allyl isothiocyanate followed by *trans*-anethole, diallyl disulfide, and *p*-nivaldehyde were the most toxic agents against larvae of *L. ingenua* [59]. Against three mosquito species *Aedes aegypti*, *Anopheles stephensi*, *Culex quinquefasciatus*, essential oils of *Pimpinella anisum* and *Juniperus macropoda* showed effective insecticidal activity against larvae and eggs. icidal and ovicidal [60]. Against another mosquito *Culex pipiens*, the essential oil of *Pimpinella anisum* showed the highest insecticidal activity as compared to *Eucalyptus camaldulensis*, *Mentha piperita*, *Ocimum basilicum*, and *Laurus nobilis* [61]. We investigated the acaricidal activity of *p*-anisaldehyde produced from anise seed oil and commercially available components of anise seed oil against *Dermatophagoides farina* and *D. pteronyssinus*, two species of home dust mites. The findings indicated that *p*-anisaldehyde and benzyl benzoate were the two substances that were most poisonous to these dermatophagoides, and as a result, *p*-anisaldehyde may be beneficial as a lead drug for the selective control of house dust mites [62].

In current studies, the insecticidal activity of *Pimpinella anisum* essential oils were test with positive results against different stages (eggs, larvae and adults) of a wide range of pathogens counting aphids (i.e. *Brevicoryne brassicae*, *Myzus persicae*) on kale plants [63], moskitos (i.e. *Culex quinquefasciatus*) [64], insect vectors (i.e., the common housefly *Musca domestica* and the lymphatic filariasis and Zika virus vector *Culex quinquefasciatus*) [65], non-target organism such as *Daphnia magna* [64], and beneficial organisms such as the earthworm *Eisenia fetida* and the aphid predator *Harmonia axyridis* (Benelli et al. 2018). For examples, essential oils of *P. anisum* were effective on larvae of *Spodoptera littoralis* ($LC_{50}=57.3\ \mu\text{g/Larvae}$) and *Culex quinquefasciatus* ($LC_{50}=25.4\ \mu\text{l/L}$), while they were

Table 2 The inhibition capacity of *P. anisum* against phytopathogens

Type of pathogens	Crop	Treatment substances	Treated parts	Treated species	Used concentration	Effectiveness	References
Insects	Various stored crops	Essential oil nanoemulsions	Individuals	Houseflies	0.50%	LC ₅₀ =9.3% v/v	[56]
		Essential oil nanoemulsions	Individuals	Red flour beetle, (<i>Tribolium castaneum</i> Herbst)	14%, v/v of the total coarse emulsion), ethanol (3%, v/v), and Tween 80 (3%, v/v), representing 20% (v/v) of the total emulsion		[57]
	Grain crops	Fumigant of essential oil vapours	Eggs	The Mediterranean flour moth (<i>Ephesia kuehniella</i>) and the confused flour beetle (<i>Tribolium confusum</i>)	98.5 µL anise essential oil/L air	LT ₉₉ values were 60.9 for <i>E. kuehniella</i> and 253.0 h for <i>T. confusum</i>	
Acarians	Green bean plants	Essential oil nanoemulsions	Adult Individuals	House dust mites, <i>Dermatophagoides pteronyssinus</i> and <i>D. farina</i>	Concentrations of anise oil (10, 20, 30, or 40 µL/L)	LD50 values, to <i>D. farinae</i> was <i>p</i> -anisaldehyde (1.11 µg/cm ²), 3-carene (42.10 µg/cm ²), and estragol (43.23 µg/cm ²). Against <i>D. pteronyssinus</i> , <i>p</i> -anisaldehyde (0.98 µg/cm ²), 3-carene (39.84 µg/cm ²), and estragol (40.11 µg/cm ²)	[62]
			Adults	The two-spotted spider mite, <i>Tetranychus urticae</i>		40 µL/L killed 96.0% of the red spiders after 72 h	[66]
Viruses	<i>Chenopodium amaranticolor</i>	Essential oils		Tobacco mosaic virus (TMV), potato virus X (PVX), and tobacco ring spot virus (TRSV)	Agar diffusion method at 0.01%, 0.1%, and 100% (v/v)	Concentration of 3000 ppm totally inhibited the formation of lesions	[69]
Bacteria	Sugar Beet	Essential oil and Extracts		<i>Pectobacterium betavascularum</i>	Agar diffusion method at 0.01%, 0.1%, and 100% (v/v)	Diameter of the inhibition zone (mm) in pure concentration 12.87±0.83 and 5.08±0.49 in 10-1 concentration	[67]

definitely non-toxic effects on predators of aphids counting *Harmonia axyridis* and *Eisenia fetida* [65]. These findings represent a milestone to product and commercialize eco-friendly or green formulations or bio pesticide to be used in crop protection.

7.1.2 Acaricid Potential

As the insects, Acarians cause also huge losses in crops as well as diseases to human health unpleasant odours, allergies and stains. The most problematic issue is the development of resistance to the available chemicals. However, essential oils of *Pimpinella anisum* showed significant effects against some of these pathogens, including resistant ones (Table 2).

Lee [62] have compared the effectiveness of two types of home dust mites, *Dermatophagoides pteronyssinus* and *D. farina*, on the commercially available components of anise seed oil and *p*-anisaldehyde derived from anise seed oil. According to the findings, *p*-anisaldehyde was more successful in killing these dermatophagoides than chemical and commercial chemicals (i.e. benzyl benzoate) [62]. Currently, El-Sayed et al. [66] investigated how the two-spotted spider mite (*Tetranychus urticae*), one of the most dangerous pests in agriculture and a major source of significant losses of various crops (including green bean plants), would react to the essential oil from *P. anisum* seeds. In the experiment, spiders were applied to green bean seedlings for a week before the plants were treated with various quantities of *P. anisum* essential oil for 24, 48, and 72 h. The findings demonstrated that anise oils have considerable, dose- and time-dependent acaricidal effects against *T. urticae*. Anise oil inhibited acetylcholinesterase at all concentrations, and when the plants were treated with 30 or 40 L/L of anise oil, the spiders' protease activity decreased. The protease activity of *T. urticae* mites was unaffected by the concentrations of 10 and 20 L/L.

7.1.3 Antibacterial Potential

The anti-bacterial capacity of *P. anisum* is not widely investigated. Currently, Rastgou et al. [67] have investigated the effect of twenty-nine plant extracts, including *Pimpinella anisum*, and 27 essential oils against *Pectobacterium betavasculorum* isolate C3, the Causative Agent of Bacterial Soft Rot and Vascular Wilt of Sugar Beet [68]. The author extracted and the antibacterial activities of these plants against *P. betavasculorum*, using the agar diffusion method at 0.01%, 0.1%, and 100% (v/v). This was the first report of essential oils and extracts having antibacterial action against *Pectobacterium betavasculorum* (Table 2).

Pure *Pimpinella anisum* L. oil had the strongest antibacterial properties among three different concentrations of essential oils and extracts, followed by *Thymus vulgaris* L. oil and

Rosa multiflora Thunb. extract. The impact of advantageous essential oils and extracts on the in vivo germination and growth of sugar beet seedlings of the Ic1 cultivar was also studied. The Ic1 cultivar's seed germination was impaired at every concentration of essential oil used. Only the plant extracts of *Pimpinella anisum* L., *Brassica oleracea* L., *Salvia rosmarinus* Spenn., *Eucalyptus globulus* Labill., *Rosa multiflora* Thunb., *Lactuca serriola* L., *Syzygium aromaticum* (L.) Merr. and L.M. Perry, and essential oils of *Mentha pipe* and *Ocimum basilicum* L. are permitted.

7.1.4 Antiviral Potential

In agronomy, only Rastgou et al. [69] have tested the inhibition capacity of *P. anisum* against phytopathogen viruses (Table 2). The authors applied different concentrations of *P. anisum* and *Foeniculum vulgare* essential oils against three viruses counting tobacco mosaic virus (TMV), potato virus X (PVX), and tobacco ring spot virus (TRSV) and obtained results showed that at a concentration of 3000 ppm both essential oils totally inhibited the formation of local lesions on the hypersensitive host *Chenopodium amaranticolor*.

7.2 Improvement of Productivity

7.2.1 Improvement of Broiler Performance

Sharaf and Goma and Nath et al. [49, 50] were among the author that studied the nutritional uses of *P. anisum*. Sharaf and Goma [50] demonstrated that extract and *Pimpinella anisum* oil mixed with food have positive oestrogenic effects in immature rabbits and ovariectomized rats. Further, [49] demonstrated a significant nutritional potential of the residue resulting after the distillation of steams for essential oil in Kumauni bullocks of about 200 kg liveweight. Equally, the use of anise seed (*Pimpinella anisum* L.) powder supplemented to the drinking water (0, 500, 750, and 1000 mg/L) for 1-day-old Hubbard Classic chicks for 56 days, significantly improved blood RBC, WBC, Hgb, HCT, TP, albumin, globulin, GLU, P, and Ca levels of broilers, and the highest levels of anise seed powder, i.e., 1000 and 750 mg/L, had a stimulating effect on the physiological traits of the birds [51]. In another study, Ciftci et al. [70] added 400 mg/kg of anise oil to the diet of day-old broilers which improved feed conversion ratio by approximately 6% compared to antibiotic group. So anise oil can be considered as a natural growth promoter for poultry [70].

7.2.2 Improvement of Milk Production

The effects of adding aniseed and fenugreek seeds to the diet on the effectiveness of the does and kits were investigated. Findings showed that kits in the anisum-fenugreek group

consumed the same amount of milk every day as control rabbits. Additionally, there was no discernible difference in the two groups' body weights after 17 days. The differences in litter size, litter weight, kit weight, and 1–35-day weight gain between the anisum-fenugreek group and the control groups at 35 days of nursing were not statistically significant. In conclusion, additional research is required to determine the ideal dosage and taste of these spices in the feed for breastfeeding rabbits [71].

8 Traditional Medicine Uses

For thousands of years ago, *Pimpinella anisum* have been used for in traditional medicine, with significant roles in maintaining human health and improving their life quality [72–74]. In modern era, many populations, such as in Iranian, North African, and Turkish, are yet using similar old treatments based on *Pimpinella anisum* and its derivatives. However, these uses vary between countries, used parts of plant, and targeted diseases [3, 5].

In Iran, seed extracts of *Pimpinella anisum* are habitually as aromatic, carminative, and disinfectant for hands, while against illnesses, they are used as analgesic in migraine and in diuretic [75]. Further, Aniseed plant has dry and warm nature and is used to increase menstruation, sweat, and urine secretion, as well as to make good complexion. It is also used in polishing of teeth and mentioned for nightmare, melancholy, and in epilepsy and seizure treatment [6, 76]. In central areas of Morocco, *Pimpinella anisum* plant and extracts are used for therapeutic treatments for neurologic, digestive, gynecologic, and respiration disorders [17, 35, 77, 78]. In Southern areas (i.e. Tan-Tan), *Pimpinella anisum* is used in phytotherapy mainly in urinary tract infections principally against pyelonephritis and cystitis [79]. In Algeria, plant parts counting seeds, leaves are habitually used against respiratory disorders, chronic uremic in Algerian inflammatory-malnutrition, and currently against COVID19 infection [80–82]. In Turkey, seeds of *Pimpinella anisum* are mixed in herbal tea and used for weight loss [83], while in Egypt, it is used for treatment Kidney Stones [84, 85]. In Italy, seeds of *Pimpinella anisum* are used as flavoring in bread, sweet and meat dishes for carminative, digestive treatments [86–88].

9 Pharmacological Properties

9.1 Antiviral Activity

The anti-viral activity is widely tested in various extracts of *Pimpinella anisum* on different viruses. The first test was realized in Iraq when Alwan et al. [89] studied the antiviral activity of aqueous and ethanolic extract of 17 plant

species including *Pimpinella anisum* against rinderpest virus (RPV). However, during antiviral in vivo and in vitro tests, the inhibitory effects were variable depending on the viruses and used *Pimpinella anisum* materials.

In medicine, many tests were conducted by researchers to evaluate the effects of essential oils and other extracts on viruses that infect human health. Sokmen et al. and Sökmen [90, 91] tested the effects of crude extracts from 24 callus and 11 cell suspension counting *P. anisum* against herpes simplex viruses, HSV-I and HSV-II, but the results were negative. In huge Sudanese screening, 152 water and methanol extracts of 71 plants frequently used in traditional medicine were tested against C virus (HCV) protease (PR), and in results, 34 extracts counting those of *P. anisum* showed significant inhibitory activity superior to 60% at 100 µg/mL [92]. Further, three lignin–carbohydrate–protein complexes were isolated from *Pimpinella anisum* by the mixture of gel filtration, anion-exchange, and hydrophobic interaction column chromatographies, and tested against human cytomegalovirus (HCMV), herpes simplex virus types 1 and 2 (HSV-1 and -2) and measles virus [40]. All LCs were found to inhibit the adsorption of viruses to the host cell surface and disable them via induction of iNOS mRNA of cytokines including IL-1β and IL-10. Currently, seed extracts of *P. anisum* showed significant effects against the acute respiratory syndrome coronavirus 2 (SARS-CoV-2) considered a serious health hazard internationally [93]. Preparation of green synthesis combining zinc oxide nanoparticles, seed extracts of *P. anisum* and *Nigella sativa* loaded nanostructured oil carriers (NLC) (composed from black seed and olive essential oils) were extensively characterized (high docking energy scores (ranging from –7.9 to –9.9 kcal/mol) and tested against SARS-CoV-2 main protease (3CLpro or Mpro). Obtained results showed no conformational change in the protein during simulations.

9.2 Antibacterial Effect

The anti-bacterial activity of *P. anisum* was tested against different strains counting pathogen and non-pathogen agent [94, 95]. The scientists used the plant and its derivatives to demonstrate the inhibition effects against this king and microorganism [95]. Equally, *P. anisum* was combined with other plants, industrial substances and materials to increase their effectiveness against resistant pathogens [94].

Using the disc diffusion method, the aqueous 50% (v/v) acetone, methanol, and petroleum ether extracts of *P. anisum* fruits were found to have antibacterial effects against four pathogenic bacteria, including *Streptococcus pyogenes*, *Staphylococcus aureus*, *Klebsiella pneumonia*, and *Escherchia coli* [96]. The obtained results demonstrated that acetone and petroleum extracts were unable to suppress the growth of the same harmful test bacteria, while

both methanol and aqueous extracts shown fair inhibition effects against all tested bacteria. The aqueous extract demonstrated noticeably more efficacy than the methanolic extract.

In another study, Gülçin et al. [42] used the disc diffusion method to examine the antibacterial properties of ethanolic and aqueous extracts of *P. anisum* against 10 bacterial species, including *Candida albicans*. As a result, water extract was found to have an inhibitory impact against *Candida albicans* but not against Gram-negative bacteria like *Escherichia coli* and *Pseudomonas aeruginosa* [42]. The ethanolic extract, in contrast hand, exhibited a strong inhibitory effect against all of the examined microorganisms but was ineffective against *Candida albicans*. Alcoholic extracts from *P. anisum* seeds have demonstrated positive antibacterial activity against *Mycobacterium smegmatis* and *Micrococcus luteus* [97]. Based on the disc diffusion method, the antibacterial potential of four plants' aqueous decoctions against 176 microbial isolates from 12 genera, including anise, coriander, black pepper, and bay leaf, was discovered [98]. As a result, although an aniseed decoction only displayed 18.1% antibacterial activity against the studied microorganisms, black pepper had greater inhibitory effects with 75% antibacterial activity. *Micrococcus roseus* was the target of *P. anisum*'s strongest antibacterial effects. Dental plaque samples from kids aged 3 to 5 years old were gathered after detecting the bacterial colonies of *Streptococcus mutans*, *S. sanguinis*, and *S. salivarius* in an in vitro investigation. Then, using macrodilution and microdilution techniques, the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of ethanolic and methanolic extracts of *P. anisum* and *Oregano vulgare* were determined [99]. As a consequence, there was a statistically significant difference between the mean MIC and MBC of *P. anisum* and *O. vulgare* extracts alone and in combination against *S. sanguinis*, *S. mutans*, and *S. salivarius*. These extracts together revealed the lowest MIC and MBC levels.

In terms of combination with other substances, Al-Bayati [100] have studied the synergic antibacterial effects between essential oil and methanol extract of both *Thymus vulgaris* and *P. anisum* against nine pathogenic bacteria. The combination of methanol extract and essential oil of these species exhibited significant inhibitory activity against most tested pathogens, with superior inhibition levels against three bacteria *Bacillus cereus*, *Staphylococcus aureus*, and *Proteus vulgaris*. Moreover, this combination showed an improved effect against most tested bacteria, particularly *Pseudomonas aeruginosa* [100]. Zayed et al. [94] used the disk diffusion method to assess the in-vitro antibacterial properties of metal nanoparticles biosynthesized using optimized *P. anisum* extract against *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans*. Comparing biosynthesized AgNPs

to AuNPs and *P. anisum* extract, they demonstrated greater antibacterial activity.

9.3 Antifungal Effects

The essential oils of *P. anisum* were also tested against fungi, with a positive result [69]. In a promoting study, Kosalec et al. have evaluated the antifungal effects of essential oil and fluid extract of *P. anisum* fruits on four dermatophytes species and on seven yeast species using broth dilution method and the diffusion technique with cylinders. The obtained results showed that the fluid extract of *P. anisum* showed antimycotic inhibition against *Candida albicans*, *C. tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. pseudotropicalis*, and the biggest inhibition zone was detected for *C. albicans*. Similarly, the fluid extract of *P. anisum* exhibited inhibitory activities against all dermatophyte species, *Trichophyton mentagrophytes*, *T. rubrum*, *Microsporum gypseum*, and *M. canis*, and the superior inhibitory zone was measured for *T. mentagrophytes*. Similarly, the essential oil of *P. anisum* showed robust antifungal effects against dermatophytes and yeasts, and the superior inhibition zone was recorded against *C. parapsilosis* with 30 mm, followed successively by *C. albicans*, *C. glabrata*, and then *Geotrichum* spp. Generally, essential oil of anise demonstrated robust antifungal effects rather than extracts against both yeasts and dermatophytes [101]. Inhibitory activity of anise essential oil also was mentioned by Özcan and Chalchat [7] against *Aspergillus niger*, *Aspergillus parasiticus*, and *Aternaria alternata*, and the most effected fungus was *A. parasiticus*. The results of other studies utilizing methanolic extracts of anise against four dermatophyte species and a saprophyte fungus revealed that the extract only suppressed the growth of *Trichophyton mentagrophyte*, *Candida albicans*, and *Microsporum canis*. On the other hand, saprophyte *A. niger* was not inhibited by aniseed's methanolic extracts in any way [102].

Özcan and Chalchat [94] used the disk diffusion method to assess the in-vitro antibacterial properties of metal nanoparticles biosynthesized using optimized *P. anisum* extract against *Aspergillus flavus*. Comparing biosynthesized AgNPs to AuNPs and *P. anisum* extract, they demonstrated greater antifungal activity.

9.4 Muscle Relaxant Effect

Boskabady and Ramazani-Assari [103] initiated the investigations about the relaxant effects of *P. anisum*. These authors have studied the relaxant roles of *P. anisum* on isolated tracheal chains of guinea pig and the possible involved mechanism. They used ethanol and aqueous extracts, and essential oil of *P. anisum* on precontracted isolated tracheal chains (10 mM methacholine) under two different conditions; group 1 of non-incubated tissues (1 mM propranolol)

and group 2 of 1 mM chlorpheniramine incubated tissues. The results revealed that all treatments including ethanol and aqueous extracts, essential oil, and theophylline displayed significant relaxant effects compared to those of under control. Further, the relaxant effects of essential oil were significantly lower than those of theophylline, while the relaxant effects were similar between aqueous and ethanol extracts, and theophylline. Equally, the relaxant effects were similar between examined groups. As possible mechanism, the results of Boskabady and Ramazani-Assari [103] showed that the inhibitory effects on muscarinic receptors is the potential cause of the relaxant effect of this plant. The effects of three hydroalcoholic extracts from the aerial portions of *P. anisum*, comprising ethanol/water; 40/60, 60/40, and 80/20, on the rat anococcygeus smooth muscle were examined in a different study by Tirapelli et al. [104]. As a consequence, all three hydroalcoholic extracts reduced the contraction caused by acetylcholine. This study also noted that, in contrast to the other two hydroalcoholic extracts, only the 60% ethanol extract produced concentration-dependent relaxation of acetylcholine-precontracted tissues. The authors hypothesized that the NO-cGMP pathway's activation is mostly responsible for the relaxing effect.

9.5 Anticonvulsant Effect

The anticonvulsant effects of an essential oil from the fruits of *Pimpinella anisum* against seizures induced by pentylenetetrazole (PTZ) or maximal electroshock were investigated in male mice (MES). This study shows that *P. anisum* decreases the threshold for inducing clonic seizures by intravenous PTZ infusion and can stop tonic convulsions by intraperitoneal PTZ injection. In addition, *P. anisum* contains anticonvulsant qualities that protect against tonic seizures caused by MES [105]. The effects of an anise methyl alcohol extract on a mouse model of picrotoxin-induced epilepsy were also the subject of his research by Heidari and Ayeli [106]. The results showed that mice pretreated with various dosages of anise extract experienced a delayed onset of seizures, with 200 mg/kg being the most effective amount ($P < 0.05$). In addition, when compared to phenobarbital (40 mg/kg), this dose ($P < 0.01$) significantly prolonged the time to death in mice [106]. The results of the other study, which examined the effects of the leaves and stems of some Arab medicinal plants, including *Pimpinella anisum*, on picrotoxin-induced seizures in mice, revealed that *Rosmarinus officinalis*, *Pimpinella anisum*, *Matricaria chamomilla*, and *Artemisia vulgaris* extracts delayed the onset of the seizures and decreased mortality [107]. Janahmadi et al. [108] conducted research on the cellular mechanisms underlying the antiseizure effects of anise fruits in 2008. In this study, it was evaluated if anise fruit essential oil affected snail neurons' bioelectrical activity under control conditions

or following the induction of epileptic activity by pentylenetetrazol (PTZ). The findings suggest that augmentation of Ca^{2+} , K^+ channel activity or suppression of voltage and/or Ca^{2+} dependent K^+ channel activity underpinning post-hyperpolarization potential are likely candidate cellular processes underlying the hyperexcitability caused by anise oil [108].

9.6 Effect on Gastrointestinal System

9.6.1 Effect on Gastric Ulcer

Indomethacin and other toxic substances were used to induce acute stomach ulceration in rats in order to examine the effectiveness of anise's aqueous suspension against these lesions. The findings demonstrated that anise considerably reduced the damage to the stomach mucosa brought on by necrotizing agents and indomethacin. Histological evidence further supported the antiulcer efficacy [109].

9.6.2 Palliation of Nausea

In a case study, 25 patients in a hospice and palliative care program with nausea symptoms received an aromatherapy treatment that included *P. anisum*, *Foeniculum vulgare*, var. dulce, *Anthemis nobilis*, and *Mentha piperita*. Most patients who received aromatherapy treatments reported feeling better. However, all study participants were also receiving a range of additional therapies for their problems [110].

9.6.3 Effect on Constipation

In a randomized clinical trial with 20 patients who met the criteria for chronic constipation according to the American Association of Gastroenterology, the laxative efficacy of a phytotherapeutic compound containing *P. anisum* L., *Foeniculum vulgare* Miller, *Sambucus nigra* L., and *Cassia augustifolia* was examined. Colonic transit time (CTT), which was assessed radiologically, served as the main endpoint. The quantity of evacuations each day, how well the bowels appeared to be working, side effects, and quality of life were considered secondary objectives. When compared to a placebo, the study's findings showed that phytotherapeutic substance had considerable laxative effects. A reduction in colonic transit time and an increase in daily evacuations served to highlight this effect. This substance can be a safe alternative for the treatment of constipation even though there were no appreciable differences in quality of life across the research periods [111].

9.7 Effect on Morphine Dependence

We investigated the effects of *Pimpinella anisum* essential oil on the expression and development of conditioned place preference (CPP), a morphine-induced behavior in mice. The results demonstrated that subcutaneous injections of morphine (2–5 mg/kg) produced place preference in a dose-dependent manner and that injections of *P. anisum* essential oil may cause conditioned place aversion in mice, i.e., the essential oil has some unpleasant effects as investigated by a place conditioning paradigm. Additionally, the oil possesses GABAergic effects [112].

9.8 Anti-Inflammatory and Analgesic Effect

The extracts of *Tribulus terrestris* and *Pimpinella anisum* shown considerable analgesic effect against benzoquinone-induced writhing and in thermal testing, according to a screening of several Iraqi medicinal plants for analgesic action [113]. *P. anisum* essential oil demonstrated a significant analgesic effect in a study by Tas that was comparable to morphine and aspirin [114]. Additionally, mice were used to test the analgesic and anti-inflammatory effects of fixed oil of anise. The results demonstrated that the fixed oil of anise has an anti-inflammatory impact equivalent to indomethacin's strength, as well as analgesic effects comparable to morphine and aspirin at the 30-min mark [115].

9.9 Effect on Menopausal Hot Flashes

Anise extract's impact on menopausal hot flashes in 72 postmenopausal women was investigated in a double-blind clinical experiment. In this study, postmenopausal women who took three capsules of anise extract daily for 4 weeks saw a significant decrease in the frequency and intensity of their hot flashes [116].

9.10 Effect on Dysmenorrhea

In a research by Karami et al. [117], 180 female students (aged 17–28) with primary dysmenorrhea had their response to a herbal capsule containing dried extracts of celery, saffron, and anise compared to a capsule containing mefenamic acid. Both the herbal and the mefenamic acid groups significantly reduced their levels of pain when compared to the placebo group, according to the data. Additionally, the outcomes showed that herbal capsules were more successful in relieving pain than mefenamic acid and could be a good substitute for primary dysmenorrhea [117].

9.11 Antioxidant Activity

In a study by [42] antioxidant activities of natural and synthetic antioxidants, including butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), and -tocopherol, were compared. The antioxidant properties of water and ethanolic extracts of aniseeds were evaluated using various antioxidant tests. In comparison to BHA, BHT, and -tocopherol, both aniseed extracts demonstrated strong antioxidant activity, reducing power, DPPH radical and superoxide anion scavenging, hydrogen peroxide scavenging, and metal chelating activities. Water extract also demonstrated a higher antioxidant capacity than ethanolic extract [42]. Additionally, research on the in vivo and in vitro antioxidant capability of aniseeds revealed that the aniseed's ethanolic extract has concentration-dependent scavenging activity against nitric oxide, superoxide, and 1,1-diphenyl, 2-picrylhydrazyl (DPPH) radicals as well as reducing power [118]. Anise seed oleoresins and essential oil were investigated for their antioxidant properties. Through the suppression of linoleic acid peroxidation, 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging, Fe^{3+} reducing power, and different lipid peroxidation assays, the antioxidant properties were evaluated. The results demonstrated that anise oil and its methanol oleoresin had the strongest antioxidant activity, surpassing both BHA and BHT. Other oleoresins had somewhat lower antioxidant activity [119]. The 2, 2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging test was used to examine the antioxidant capacity of some Umbelliferae fruits from Iran, including *P. anisum*. It revealed that all the extracts had antioxidant capacity, with *P. anisum* extract having the strongest activity ($\text{IC}_{50} = 614.109.80$) and the highest activity and flavonoid content.

The strength of the antioxidants and the flavonoid content of the fractions were shown to be positively correlated [120]. In a different study, the antioxidant activity of anise seeds, dill seeds, and water and alcohol extracts of chamomile flowers was examined. In both linoleic acid and liposome model systems, the extracts demonstrated noticeable antioxidant activity, while the water extracts displayed greater antioxidant activity than the comparable alcohol extracts. Additionally, aniseeds' antioxidant activity was lower than that of chamomile flowers and dill seeds [121]. Thirteen herbal teas, including anise tea, had their antioxidant capacities tested in vitro. The results suggest that compared to other herbal teas, anise tea had poor antioxidant activity in the Trolox equivalent Antioxidant Capacity (TEAC) assay and a modest impact on the hypochlorite and peroxy nitrite quenching assays [122]. At different phases of ripening, Rebey et al. [18] looked at the bioactive components and antioxidant activity of four populations of *P. anisum*, including accessions from

Egypt, Tunisia, Serbia, and Turkey. As a result, all aniseed accessions had their peak antioxidant activity, DPPH scavenging activity, chelating capacity, and reducing power at full maturity. These results suggest that it may be crucial for certain industries to determine the best times and provenances for antioxidant buildup in order to assess the quality of aniseeds. In-vitro antioxidant activity of metal nanoparticles biosynthesized based on optimized *P. anisum* extract was investigated by Zayed et al. [94]. The authors evaluated the free radical scavenging abilities of silver and gold nanoparticles against 1,1-diphenyl-2-picryl-hydrazyl in order to accomplish this goal (DPPH). Comparing biosynthesized AgNPs to AuNPs and *P. anisum* extract, they demonstrated better antioxidant activity. According to our findings, *P. anisum* seed extract can be widely exploited in the environmentally friendly manufacture of prospective antioxidant and antibacterial AgNPs for secure biomedical applications.

9.12 Effects on Diabetic Patients

Aniseeds and coriander seeds were evaluated in type 2 diabetes patients for their antidiabetic, hypolipidemic, and antioxidant properties [118, 123]. Two groups of type 2 diabetic patients received the seed powders (5 g/day) for 60 days. The results showed an 11% increase in fasting blood sugar in controls, a 36% decrease in type 2 diabetics receiving anise treatment, and a 13% decrease in those receiving coriander treatment. Additionally, a significant reduction in blood cholesterol and triglycerides was seen in patients who received either aniseed or coriander seed treatment. Both treated groups showed a reduction in protein oxidation in serum and lipid peroxidation in erythrocytes and plasma when compared to baseline levels. Both groups demonstrated an increase in serum levels of carotene and vitamin A, which may have led to a marked reduction in the amount of lipid peroxidation in RBC and plasma. Both the coriander and anise groups also demonstrated an increase in vitamin C. In a diabetic patient, both seeds have antidiabetic, hypolipidemic, and antioxidant properties [118, 123]. To test *P. anisum*'s ability to heal wounds, Hashemnia et al. [124] produced full-thickness excisional wounds on the backs of male Sprague–Dawley rats with diabetes. The rats were divided into four treatment groups at random: a control group, *P. anisum* 10% for 14 days, doxycycline (3%), and 1 mL basal cream. Five animals from each group were put to death at days 7, 14, and 21 after the injury, and the wounds were examined grossly, histopathologically, and for oxidant/antioxidant levels. In addition, the skin sample's dry matter

and hydroxyproline contents were examined. As result, *P. anisum*-treated animals showed a considerable reduction in wound size compared to other groups. Additionally, *P. anisum* therapy improved early fibroblast counts, lowered lymphocyte counts, and increased late-stage fibrocyte counts in the process of wound healing. When compared to the control, other variables like re-epithelialization, tissue alignment, more mature collagen fibers, and big capillary-sized blood vessels showed substantial modifications. Malondialdehyde, glutathione peroxidase, and total antioxidant capacity alterations brought on by diabetic wounds were all considerably reversed by *P. anisum*. At various stages of wound healing, it also markedly enhanced the dry matter and hydroxyproline contents.

9.13 Effect on Glucose Absorption

Aniseed oil's impact on the absorption of glucose from the jejunum and water from the colon and renal tubules was examined by Kreydiyyeh et al. [132], along with the oil's mode of action [125–127]. The findings showed that aniseed oil significantly increased the rate of glucose absorption in the rat jejunum. The sodium gradient that drives mucosal glucose transport was increased as a result of the oil's stimulation of the $\text{Na}^+ - \text{K}^+$ ATPase activity. However, adding anise oil at a concentration of 0.05% had no appreciable effect on the colon's ability to absorb water, indicating that the colon's ATPase is immune to the oil's action. Aniseed oil was also added to drinking water to reduce the amount of urine the rats generated and to increase the activity of the renal $\text{Na}^+ - \text{K}^+$ ATPase even at extremely low doses [125].

9.14 Immunomodulatory Effects

The ability of aniseed (*Pimpinella anisum*) and ginger (*Zingiber officinale*) extract mixture to enhance growth and immunomodulatory in broiler chicks with dose dependent has been studied by Raziq et al. [128]. The dose dependence trials (2 + 4 g, 2.5 + 5 g, and 3 + 6 g for both plants in drinking water) were conducted by the authors. Two hundred forty (240) day-old broiler chicks were separated into two subgroups for each of the four groups, which were randomly assigned the letters A, B, C, and D. Ten checks per duplicate for various treatments were performed for each of the three replications of each subgroup. One of the subgroups received the recommended doses of the vaccines against infectious bronchitis, new castle disease, and infectious bursal disease. Group B, C, and D were treated with an extract mixture of aniseed and ginger at the rates of (2 + 4 g), (2.5 + 5 g), and (3 + 6 g/L of drinking water, respectively.

Group A was kept as a control. In terms of mean feed intake and water intake, there were substantial differences between body weight and feed conversion ratio (FCR). Comparing group D and the vaccination groups to other groups, the mean antibody titer against ND, IB, and IBD was considerably higher in group D. Conclusion: Adding an extract mixture of aniseed and ginger to the water that poultry birds consume is better for promoting body weight gain, achieving the best FCR, and enhancing immunological response. Similar to that, it is rather safe, has no adverse effects, is environmentally friendly, and can be found nearby.

10 Guidelines for Future Research

10.1 Extraction Methods

Variation in extraction approaches is habitually dependent on the particle size of the plant tissues, solvent used, the solvent-to-sample ratio, temperature, length of the extraction period, and pH of the solvent. The fundamental principle is to grind the herb dry or wet material finer, which rises the surface space for extraction thus increasing the amount of extraction.

In *Pimpinella anisum*, various extraction methods were used, such as the sprouts of glycine max, water, and ethanol extraction. these traditional extraction methods involve several drawbacks such as low selectivity for biomolecules, high extraction time, and low extraction efficiency. Therefore, more advanced methods are needed to increase the efficiency, reduce time, solvents, and cost of extractions. In this point, we suggest new methods such as supercritical fluid (SFE) and pressurized liquid extractions (PLE) techniques known for their high selectivity toward targeted biomolecules, short extraction times, and use the of non-toxic solvents [129]. In fact, effective identification of bioactive molecules from plant material is basically reliant on the nature of solvent used in the extraction method [129]. Generally, good solvent for extractions must be ease of evaporation at inferior temperatures, promote of fast physiologic absorption of the extract, low toxicity, preserve nature, action mod, and ability of extracted molecules [130]. As the end product in extraction will contain traces of residual solvent, the solvent should be non-toxic and should not interfere with the bioassay [131]. In our case, we suggest to use optimization simulators that enable to select more suitable solvent, or a mixture of solvent with optimised fractions. At this point, we suggest mixture designs techniques as a good tool to explore needed solvents, quantities, time of extraction for extraction of higher quantity of molecules in *Pimpinella anisum* [132]. Equally, these approaches permit to combine between solvents which allows to extract large spectra of molecules based on solubility ability of solvents [133].

10.2 Tests Against More Devastating Agents

A huge number of agents impact human life, productivity of crops and animals. The most devastating agents to human life are pathogenic bacteria are *Serratia marcescens*, *Pseudomonas aeruginosa*, *Vibrio cholerae*, *Francisella tularensis*, *Lactobacillus plantarum*, *Salmonella typhimurium*, *Mycobacterium marinum* [134], fungi are fungus *Cryptococcus*, *Ajellomyces dermatitidis*, *Ajellomyces capsulatus*, *Paracoccidioides lutzii*, *Lacazia loboi*, *Coccidioides immitis*, *Coccidioides posadasii* [135, 136], and viruses are influenza viruses, and HIV. These pathogens and their vectors (i.e. insects) infect humans and cause neurologic, immunity, and other metabolic disorders. In crops insects, fungi, viruses are causing every year losses of cereals, rice, potato, and other important crops that ensure the food security of humans. Further, the majority of cited agents have developed resistance to the available chemical treatments. Therefore, the selections of biological materials to treat them will be of great importance. In this case, we suggest applying in vitro, in vivo, and in the field the extracts, essential oils, purified molecules of *Pimpinella anisum* against these pathogens, then select promoting results to produce plant-based treatments for vulnerable agents.

10.3 Climate Change and Adaptation

Counting aromatic and medicinal plants *Pimpinella anisum* are an essential part of human health care because they represent the primary source of medicine for about 95% of inhabitants, largely in underdeveloped nations, and they are increasingly used by many people living in wealthy countries, as many authors have noted [39, 76]. Millions of people also make a living as traditional healers, herb collectors, or sellers. As the value of the global export trade for herbal compounds was recently projected to be over US\$32.6 billion per year, the gathering and trade of medicinal plants serve as a significant source of income for both rural and urban people [137]. However, the life of many plants as well as their chemical makeup are threatened by climate change, which disrupts temperature regimes and precipitation profiles. According to a recent study, over 600 plant species, including APMs, have vanished from the planet in the last 250 years [138].

In *Pimpinella anisum*, all cited studies didn't include any aspect of climate change. Determining the effects of climate change on the plant morphology, metabolism, and genetic is suggested to clarify, how this plant react physiologically, morphologically to this change. Equally, it will allow to identify the impact of climate change on synthesis of biomolecules. At the end, if the climate change impact the

wild populations of the species, scientists and responsible will know how to ensure the conservation of it.

11 Conclusion

Due to *Pimpinella anisum* L.'s beneficial characteristics, including its hypolipidemic, antidiabetic, anticancer, antioxidant activities, and antimicrobial properties, both the seeds and essential oils of anise are promising for use as raw ingredients and superfood supplements in the food, agronomy, and pharmaceutical industries. The main constituents of anise seed oil include anethol, eugenol, pseudisoeugenol, estragole, methyl chavicol, anisaldehyde, and coumarins. Other important constituents include umbelliferon, scopoletin, terpene hydrocarbons, estrols, and polyacetylenes. The antimicrobial, antifungal, antiviral, hepatoprotective, anti-inflammatory, anticonvulsant, antispasmodic, estrogenic, expectorant, and insecticidal effects are among the pharmacological and agronomic effects, as are clinical effects like nausea, constipation, bronchodilation, menopause, diabetes, obesity, and sedative action. However, further clinical and experimental investigations using novel extraction techniques, solvents, and agents are required to fully understand the myriad compounds in ginseng and how they affect crop protection and public health. On the other hand, it is advised to investigate how plants adapt to abiotic and biotic stresses in order to understand the current status of the species and assure its conservation.

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Declarations

Conflict of Interest The authors declare no conflict of interest.

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