SCIENCE OF SPICES & CULINARY HERBS

LATEST LABORATORY, PRE-CLINICAL, AND CLINICAL STUDIES

Editors:
Atta-ur-Rahman
M. Iqbal Choudhary
Sammer Yousuf

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(Volume 6)

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PREFACE

Spices and culinary herbs have been among the richest sources of medicines, fragrances, and recreational substances since antiquity. The modern concept of "food and medicine homology" is largely based on the use of spices as food and medicine. We have recently coined the term "phytodietoceuticals" for all those plant parts that are not only rich in nutrition but also prevent and treat diseases. Extensive research studies on spices and culinary herbs have proven their utility as anti-oxidants and anti-infectious, anti-inflammatory and neuroprotective agents. Volume 6 of the *e*book series titled "*Science of Spices & Culinary Herbs"* is an excellent compilation of ethnobotanical, phytochemical, pharmacological and clinical work being conducted on the most commonly consumed spices and herbs globally. The book series is an attempt to demystify the existing information about these fascinating natural products by presenting comprehensive reviews of scientific studies and their results. This makes *e*book series a must to have in general libraries, pharmaceutical R&D institutions, and nature-based healthcare facilities.

The review by Ceyda Sibel Kilic provides an excellent account of the ethnomedicinal uses and phytochemistry, as well as pharmacological, dietary, and cosmetic applications of aniseed or anise (*Pimpinella anisum* L.). *Sinapis alba* L., commonly called white or yellow mustard, is the focus of the article contributed by Hattab *et al.* The authors have explained the taxonomy, phytochemical methods, essential oil extraction, and chemical and biological properties of aniseeds. Maithanil *et al.* updated the literature review on world-famous herb cinnamon bark powder (*Cinnamomum verum* J. Presl), covering recent work on tremendous health benefits and mechanisms of action, largely due to the presence of its main constituent, cinnamaldehyde. Recent studies on the globally famous spice tamarind (*Tamarindus indica* L.) were reviewed by Ahmad *et al*. The authors have explained the phytochemicals of the pulp of tamarind and their pharmacological and clinical properties. Curcumin, a key constituent of *Curcuma longa*, has been the subject of extensive research in recent years due to its numerous medicinal properties. Badavath *et al.* reviewed the work conducted on the synthetic analogs of curcumin for improved anticancer and anti-oxidant properties. *Glycyrrhiza glabra* L. is the source of licorice derived from its dried roots and rhizomes and used as a natural sweetener. Aksoyalp *et al.* commented on the novel aspect of licorice pharmacology. They reviewed recent studies on the interplay between the use of licorice constituents and human gut microbiota and resulting therapeutic effects on neurodegenerative diseases.

We gratefully acknowledge the scholarly contributions of all authors and the production team of Bentham Science Publishers for a job very well done. Among them, Mrs. Fariya Zulfiqar (Manager Publications) and Mr. Mahmood Alam (Editorial Director) of Bentham Science Publishers deserve special recognition. We sincerely hope that the contributions of the authors and the production team will help readers better understand and appreciate the therapeutic effects and disease-preventive potential of colorful, tasty, and aromatic spices and herbs.

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CHAPTER 1

Pimpinella anisum L. (Anise, Aniseed)

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Abstract: *Pimpinella anisum* L. is an aromatic species of the Apiaceae (Parsley) family, commonly known as anise or aniseed. Fruits of the plant, which are also known as seeds, have widespread usage throughout the world for culinary and medicinal purposes, in cosmetics industry, and also is used in the flavoring of some alcoholic beverages, candies *etc*. Usage of the plant for medicinal purposes dates back to ancient Egypt and the plant is currently being used mainly for its digestive properties and hormonal activities such as increasing milk production in breast feeding mothers. The plant is sometimes confused with star anise, another species called *Illicium verum* Hook. f. from Schisandraceae family due to the fact that they both have *trans*-anethole within the composition of their volatile oils, though anise is an annual herbaceous plant and star anise is an evergreen tree. In this chapter composition, traditional usages, biological activities and some issues related to the utilization of this world-renowned plant are focused on.

Keywords: *Pimpinella anisum*, anise, aniseed, Apiaceae, Parsley family, volatile oil, anethole.

INTRODUCTION

Pimpinella anisum L. is an annual plant of the Apiaceae family, formerly known as Umbelliferae. The plant is known to be cultivated since ancient Egypt (for at least ~4000 years) for its beneficial usages. While texts of ancient Egyptians stated the usage of the plant for digestive problems, as diuretic and against toothache, Greeks and Romans also mentioned the cultivation and uses of the plant for different purposes; furthermore, it has been used in China as a traditional remedy since the 5th century [1, 2]. It is reported to be used in embalming of Scythian kings [3]. The plant is reported to be used in Serbia during medieval times as carminative, digestive, against splenomegaly, stomachache, female genitalia disorders, bruising, to increase spermatogenesis, lactation [4]. The plant

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is still being used traditionally in many countries as an anticonvulsant and for the treatment of gastrointestinal, inflammatory, dermatological diseases, against nightmares, melancholy, seizures, epilepsy [5 - 7]. Not only the seeds, but volatile oil of the fruits/seeds are also being used for their medicinal activities [8].

In addition to the plant's utilization for medicinal and culinary purposes, volatile oil obtained from the seeds is used in the cosmetic industry in the making of toothpastes, lotions, soaps, skin care products; used in the production of different alcoholic beverages in different countries (e.g. rakı in Türkiye, ouzo in Greece, Anisette or Pastis in France, anesone in Spain, Sambuca in Italy and arak mainly in Armenia and Syria) [1, 9]. A Cuban refreshment called Pru was also prepared with the species once, however basic Pru recipes do not include the plant currently [10]. Furthermore, volatile oil is also used in the aromatization of candies and tobacco [1, 7, 11]. The plant is considered to be a functional food and nutraceutical preparations are also being prepared with the volatile oil of the plant [12, 13]. With all these different usages, it is no surprise that anise seed is listed in various pharmacopoeia such as British, German and European Pharmacopoeia [14, 15], and is also approved by Herbal Medicinal Products Committee (HMPC) of European Medicines Agency (EMA) as a traditional herbal medicinal product [16].

The plant can be up to 30-50 cm in height, peak height is reported to be 50-60 cm; leaves are heterophyllous, petiolate basal leaves are simple, 2-5 cm long, reniform/ovate shaped with dentate margins; lower cauline leaves are pinnate having ovate/obovate segments and upper cauline leaves are 2-3 pinnate with linear-lanceolate lobes and sheathing petioles. The plant has white flowers, umbels 7-15 rayed, has 1 bract or none, and bracteoles also none or few, very narrow if present. Approximately 10 white flowers are present per umbellule and has greenish-grey to brown colored schizocarp fruits of 2-5 mm with a conical stylopodium. The flowering period of the plant is June and fruits are harvested in August [17 - 19]. The general appearances of the plant and the fruits are given in Fig. (**1**).

The plant is known by different names in various countries, some examples are listed in Table **1**.

(a)

(b)

(c)

Fig. (1). (**a**) *Pimpinella anisum* field; (**b**) General appearance of *P. anisum* (Photos by A.M. Gençler Özkan); (**c**) *P. anisum* fruits (Photo by C.S. Kılıç).

Table 1. Vernacular names of *P. anisum* in different countries.

Vernacular Name	Country	Refs.
Habathlawa, Nafaa	Algeria	[20, 21]
Andres huaylla, anisa, anis	Bolivia	[22, 23]
Erva-doce,	Brazil	[24, 25]
Anis	Ecuador	[26]
Anise	England	[27]
Anise vert	France	[27]
Anisa, Badian, Kuppi, Muhuri, Saunf, Sop	India	[27]
Anison, Badian rami, Vaveshing	Iran	[28 - 30]
Yansun, Razyane	Iraq	[31, 32]
Annesella, Matafaluga, Anice, Anici, Anesc	Italy	[27, 33, 34]

(Table 1) cont.....

Vernacular Name	Country	Refs.
Anise seed	Japan	[27]
Jintan manis	Malaysia	[35]
Gros lani, Gro anis	Mauritius	[36, 37]
Anise verde	Mexica	[38]
Habbat hlawa, Anis vert, Maadnos	Morocco	[39 - 42]
Yansoon	Saudi Arabia	[27]
Anis, anason	Serbia	[4]
Anason	Türkiye	[27, 43]
Anise, star anise	USA	[27]

DISTRIBUTION AND STATUS OF THE SPECIES

According to the World Flora Online, the genus *Pimpinella* L. consists of 197 taxa, however some of them are unchecked names awaiting taxonomic scrutiny [44]. The genus is distributed through Europe, Asia and Africa [45]. The plant is reported to be native to Southwest Asia, Middle East and the Mediterranean region, and is being cultivated in many countries, such as Brazil, Bulgaria, China, Egypt, Greece, France, India, Iran, Italy, Mexico, Spain, Syria, Russia, Tunisia, Türkiye and United States due to its aromatic fruits, which are also called seeds, commercially [7, 27, 46 - 48]. However, it is now considered to as no longer exist in the wild and is only being cultivated [49].

TRADITIONAL/ETHNOMEDICINAL USES

Since the plant has been known for thousands of years by mankind, it has been used in the treatment of certain diseases for centuries. In addition, different parts of the plants, like leaves and especially the aromatic seeds are edible and used for culinary purposes [50, 51]. Some examples for ethnobotanical/traditional uses of the species are given in Table **2**:

Table 2. Ethnobotanical/traditional usages of *P. anisum*.

Plant Part	Preparation Method	Usage/Activity	Country	Refs.
Fruits	Infusion	Carminative, digestive, sedative	Italy	[33]
Fruits	NA	Renal diseases	Morocco	[39]
Aerial parts	Infusion	Diarrhoea, digestive disorders, bronchitis	Bolivia	[22]
Fruits	Decoction (along with chamomile, 3 white rose petals)	Digestive	Italy	[52]

(Table 2) cont.....

Plant Part	Preparation Method	Usage/Activity	Country	Refs.
Fruits	Decoction	Sedative, soporific (for babies)	Türkiye	[53]
Seeds	Powdered, decoction	Against cough, flu, stomachache	Türkiye	[54]
Fruits	Decoction	Sedative, against insomnia		
Seeds	Decoction	Stomachache	Italy	[55]
Seeds	Infusion, decoction	Against flatulence, asthma, female fertility, abdominal pain	Iraq	[56]
Leaves, seeds	Tea	Stomachache, flatulence, soothing, against flu, fever, toothache	Brazil	[24]
Fruits	Decoction, infusion	Colic, both renal and GIS originated, anxiety, upper respiratory tract disorders	Egypt	[57]
Seeds	-	Digestive and for disorders of the respiratory tract	Mexico	[38]
Seeds	Infusion	Stomachache, inflammatory	Bolivia	[23]
Seeds	Decoction with *Mentha piperita* L.	Stomachache	Mauritius	[36]
Fruits	Infusion	Flatulence, anthelmintic, colic, stomachache, as antacid, antidiarrheal	Iran	[28]
Fruits	Internally	Carminative, culinary usage	Iran	[30]
Seeds	Decoction	Flatulence	Mauritius	[37]
Seeds	NA	Flatulence, indigestion	Iraq	[31]
Seeds	Infusion, maceration	Digestion problems, intestinal gas, asthma, bronchitis, cough, painful menstruation period	Morocco	[40]
Fruits	Infusion	Stomachache, colic, as anthelmintic, antacid, antidiarrheal	Iran	[29]
Seeds, leaves	Decoction, powder	For menopause, diarrhea of children, increases breast milk, as stomachic, appetizing, against worms, ascaris	Iraq	[32]
Fruits	Decoction	Eliminates gastric colic	Iran	[58]
Fruits	Infusion	Against stress and insomnia	Algeria	[59]
Seeds	Decoction, infusion	Used for digestive, gynecological, respiratory, urological, neurological purposes	Saudi Arabia	[60]
Seeds	Infusion, handful of seeds themselves	Diabetes treatment	Morocco	[61]
Aerial parts	NA	For the kidneys, strengthens breast (in respect to respiration)	Poland	[62]
Whole plant	Decoction	Against dyspepsia, hepatoprotective, hypolipidemic, antifungal and antibacterial	Tunisia	[63]

(Table 2) cont.....

Plant Part	Preparation Method	Usage/Activity	Country	Refs.
Seeds	NA	As digestive, for respiratory, cardiovascular and genitourinary disorders	Morocco	[64]
Branch, leaf, seeds	-	As soothing, against gas and pain	Brazil	[25]
Seeds	Decoction	Against kidney stones	Morocco	[41]
Seeds	Decoction	Against sciatica	Morocco	[65]
Seeds	Infusion	As carminative, antiulcer	Morocco	[66]
Fruits, seeds	Decoction	Burns belly fats, aids weight loss	Türkiye	[67]
Seeds	NA	Carminative, digestive	Italy	[34]
NA	NA	Against intestinal gas, as vermifuge, antispasmodic	Algeria	[20]
Seeds	Powder added to water	Used against colon cancer	Morocco	[68]
Seeds	NA	Against flatulence	Türkiye	[69]
Fruits	Infusion	Soothing and calming	Morocco	[21]
NA	Tea	For rheumatism	Brazil	[70]
Seeds	Fresh or dried	Digestive	Italy	[71]
Fruits	Infusion	Abdominal pain	Ghana	[72]
	Decoction	Diabetes, depression		
Seeds	Decoction, powder/infusion	Gastrointestinal problems	Morocco	[42]
Fruits	Decoction, maceration	Gastrointestinal problems, endocrine disorders, aids weight loss	Saudi Arabia	[73]
Seeds	NA	Gastrointestinal problems, to relieve pain of the joints, head and throat, febrifuge	Ecuador	[26]
Seeds	Decoction	Against hypertension	Morocco	[74]
Leaves, seeds	Crushed, decoction	Inappetence, stomach disorders	Türkiye	[75]
Aerial parts, seeds	Decoction/infusion	Against intestinal gases	Algeria	[76]
Seeds	NA	Against genitourinary diseases	Morocco	[77]
Seeds	Infusion	Digestive, for urogenital disorders	Algeria	[78]
Seeds	Powder	Against hypercholesterelomia	Morocco	[79]
Seeds	Maceration, powder; added in bread; powder added to olive oil	Anticancer	Morocco	[80]
Seeds	Decoction	As aphrodisiac, against asthma, diabetes, menstrual pain	Morocco	[81]

(Table 2) cont.....

Plant Part	Preparation Method	Usage/Activity	Country	Refs.
Seeds	Decoction	Against inflammation	Morocco	[82]
Seeds	Tea	Against abdominal pain (for children) and colic in infants	Cyprus	[83]
Seeds	Infusion	Anti-inflammatory	Morocco	[84]
Fruits	Decoction	In mouth care as gargle	Morocco	[85]

NA: Not Available.

COMPOSITION

When we search the literature, we can see that several studies have been performed on the chemical composition of the plant. However, most of them are related to the volatile oil of fruits/seeds of the plant. In general, all of these studies state that *trans*-anethole, a phenylpropene derivative is the major compound of the volatile oil [43, 46, 86 - 105]. However, some studies suggest that other compounds are also found in high quantities, for example 4-allylanisole is the major component [106] and estragole was also found to be in high quantities, though much lower [107]; and these differentiations were attributed to geographical differences or harvesting time.

In addition, new compounds are increasingly being isolated from the volatile oil, and their structures are being elucidated. Besides anethole, anise oil is also found to include phenylpropanoids such as umbelliprenine [108, 109].

Phytochemical composition of anise other than the volatile components is given in Table **3**.

Table 3. Phytochemical composition of *P. anisum* (major components are listed).

Plant Part	Phytochemical and/or Mineral Composition	Refs.
Fruits	Fatty acids (linoleic, petroselinic, palmitic, palmitoleic oleic and stearic acids), phenolic acids (caffeic, ferulic, sinapinic, chlorogenic, neochlorogenic, caffeoylquinic, cryptochlorogenic, *p*-coumaric, gallic acids), flavonoids (apigenin, apigenin 2'-O-pentosyl-6-C-hexoside, apigenin-6-*C*-glucoside, apigenin-7-*C*-glucoside catechin, luteolin, luteolin-6-*C*-glucoside luteolin-7-*O*-glucoside, luteolin-8-*C*-glucoside, rutin, quercetin-3-glucuronide)	[110 - 123]
Fruits	Minerals (Fe, Mn, Zn, Cu, Ni, Pb, Al, P, Ca, Mg)	[124]
Fruits	Sterols (β-sitosterol, campesterol, spinasterol, Δ7-stigmasterol, spinasterol), terpenes (α-amyrin)	[113, 116, 125]
Seeds	Monosaccharides (galactose, glucose, mannose)	[126, 127]
Seeds	Iridoid (oleuropein)	[120]
Seeds	Phenlypropene (estragole)	[128]

(Table 3) cont.....

Plant Part	Phytochemical and/or Mineral Composition	Refs.
Aerial parts	Pectin	[126]
Whole plant	Isoflavone (daidzein), monocarboxylic acid (cinnamic acid), phenolic acid (ellagic acid) flavonoids (rutin, quercetin, naringenin)	[129 - 130]
Seeds	Coumarins (scopoletin, umbelliprenin)	[131]
Seeds	Oxadiazole compounds	[132]

BIOLOGICAL ACTIVITIES

The plant has a long history of traditional utilization in countries where it grows naturally and also where it is being cultivated. These utilizations are confirmed with some scientific studies and some of them are focused on in this section.

Anticancer Activity

Cancer is an important health problem having high ratio of mortality. Although we have come a long way in the treatment of different types of cancers, it still is a major cause of mortality and researchers are seeking for treatment alternatives with less or no side effects. Since natural sources are mainly explored in this respect, it is no surprise that anise seed was also tested for its anticancer activity. In a study by Kadan *et al.* [133], ethanol extract from the seeds was tested for its antiproliferative and apoptotic efficacy against PC-3 (human prostate cancer) cell line and L6 (rat skeletal muscle) cell line used as normal cell line, and it was understood that the seeds had significant anticancer activity against PC-3 cells while it did not harm L6 cells.

Ethanolic extract and volatile oil of the seeds were tested for their cytotoxic activities in gastric cell line (AGS) and it was shown that AGS cell growth was inhibited, and furthermore angiogenesis in HUVEC cells was also inhibited; thus it had the potential to be used in gastric cancer as a plant based cure alternative [134]. However, different cancer cell lines do not always yield the same response. For example, while anise had moderate chemopreventive effect against E2 (17β-estrogen)-induced mammary tumorigenesis in August-Copenhagen-Irish (ACI) rat model in a study by Aqil *et al.* [135] in which seeds were powdered, lyophilized then added to the animal feed, it had significant cytotoxic activity against KB (human epithelial carcinoma cells) cell line. In this study, powdered seeds were first extracted with ethyl acetate, and then diluted with DMEM to yield solutions of five different concentrations [136].

Trans-anethole found within the composition of the volatile oil is considered to have anticancer activity. In a study by Garzoli *et al.* [137], this compound was reported to have cytotoxic and antiproliferative activities against He-La cell line with an IC_{50} of 0.25 mg/mL.

Anticariogenic and Dental Activities

Due to antibacterial activities of anise extracts and volatile oil, anticariogenic activity was also examined with the help of some caries causing bacteria. For example, *Streptococcus mutans, Lactobacillus rhamnosus* and *Actinomyces millefolium* were found to be sensitive to the growth inhibitory activity of the hydroalcoholic extract of the seeds [138]. In another study, dental plaque samples obtained from 3-5 years old children were used in a study in which anticariogenic activity of hydroalcoholic anise extract was examined. As a result, it was demonstrated that plant extract had antimicrobial activity against bacteria that lead to dental caries (*S. mutans, S. sanguinis* and *S. salivarius*) [139]. Methanol extract of the seeds was also found to have antimicrobial activity against *S. sanguinis* [140]. In addition to these bacteria, volatile oil of the seeds was also found to be effective against other periodontal pathogens such as *Enterococcus faecalis*, *Aggregatibacter actinomy-cetemcomitans, Lactobacillus casei* and *Actinomyces naeslundii* leading to different dental disorders [141].

Antidepressant / Anxiolytic Activities

Depression and anxiety due to stress are among important mental disorders that are seen in every society with a high prevalence. Since the disorder is triggered by stress and is quite common due to various factors such as daily tasks, diseases, disasters, latest COVID-19 pandemic *etc*., antidepressants are among the most used medications to relieve these two disorders throughout the world. However, having many side effects on their own, scientists are searching for safer alternatives. In this respect, plants/plant-based remedies are sought for and *P. anisum* is also tested for this biological activity. Aqueous and 70% ethanolic extracts of the fruits were tested for their antidepressant activities in a study by Shahamat *et al.* [142] and it was found that anise plant had significant antidepressant activity that was comparable to the synthetic agent fluoxetine. The anxiolytic activity was also examined in a previous study and intraperitoneal injection of the hydro-alcoholic seed extract was found to have anxiolytic activity in male Wistar rats as shown in elevated plus maze model by increased number of entries to the open arm and decreased time spent in close arms [143]. In another study by Es-safi *et al.* [120], hydro-ethanolic extract prepared after defattening of the seeds with hexane extraction was found to have potent antidepressant and anxiolytic activities possibly due to monoaminergic involvement.

Antidiabetic Activity

Diabetes is a chronic disease leading to secondary complications, and in the search of finding natural antidiabetic sources, anise plant is also being examined among the plants tested for their antidiabetic activities. As a result of various

studies, methanolic extracts of the seeds were shown to have inhibitory effects on α-amylase and α-glucosidase enzymes, pointing out to the antidiabetic potential of the plant [111]. Similarly, in another study, aerial parts of the plant were ground and then aqueous infusions were prepared and tested for their α-amylase inhibitory activities, and it was concluded that the plant might be useful against diabetes [116]. Volatile oil was also tested and yielded hypoglycemic activity, which might be beneficial for diabetic patients [88].

Anti-inflammatory Activity

Anise plant is examined for anti-inflammatory activity, as well. In a study by Taş *et al.* [144], it was shown that the fixed oil of the seeds had anti-inflammatory activity that is comparable to indomethacin's. In another study that was carried out to confirm the traditional usage of anise in respiratory diseases, volatile oil of the seeds was found to have significant anti-inflammatory activity against HBEpC (primary airway bronchial epithelial cells) and HTEpC (primary airway tracheal epithelial cells) cells and mucus hypersecretion with neutralization of pro-inflammatory cytokines [145]. Another study examined the anti-inflammatory activity of lyophilized seed extract and it was observed that the extract prevented ovalbumin induced asthmatic complications, probably by inhibiting eosinophil trafficking and blockade of Th2 cytokines responses. As a result, anise reduces inflammation of the airways and could be an alternative for the treatment of allergic asthma [146].

Anti-lipase Activity

Obesity has become an important health issue throughout the world. Anti-obesity agents without serious side effects are being sought for by researchers in order to reduce obesity related complications and/or mortality rates.

In a study by Ado *et al.* [35] in which 98 plant materials were tested for their activities on porcine pancreatic lipase activities, methanolic extract of the anise seeds was reported to stimulate porcine pancreatic lipase by 186.5%, and thus resulted in anti-obesity activity.

Antimicrobial Activity

Volatile oils are known to have antimicrobial activities, and anise oil is no exception. Thus, anise oil has been used in different applications for its antimicrobial activities. Studies related to these activities are given summarized as follows:

Antibacterial Activity

Alcoholic extract of the fruits was tested for its antibacterial activity on some Gram (-) and (+) bacteria, and it was found to be effective against *Bacillus cereus, Bacillus subtilis, Cirobacter koseri, Enterobacter aerogenes, Escherichia coli*, *Helicobacter pylori, Klebsiella pneumonia, Micrococcus luteus, Proteus mirabilis, Pseudomonas aeruginosa*, *Salmonella typhimurium, Staphylococcus* aureus, *Staphylococcus epidermidis* and *Streptococcus pneumoniae*, *Streptococcus pyogenes* [19, 38, 103, 147 - 152].

The volatile oil of the seeds was tested for its antibacterial activity by different researchers, as well. For example, different researchers showed that, the oil had antibacterial activity against *B. subtilis*, *Clostridium butyricum, C. perfringens, E. coli*, *P. aeruginosa*, *S. aureus*, *S. pyogenes, S. pneumoniae* [101, 105, 153 - 159]. In another study by AlBalawi *et al.* [128], methanol extract of the seeds was found to inhibit multidrug resistant bacteria growth and thus has the potential to constitute a potential anti-virulence option.

In addition to the volatile oil and the extracts, anethole isolated from the oil is also active against some bacteria, such as *Vibrio cholera*, the causative agent of cholera [160]. 5% suspension of the seeds was found to be effective against another *Vibrio* sp. (*V. parahaemolyticus*) resulting in mild food-borne gastroenteritis [161]. Other researchers have also found that anethole was effective against *Bacillus cereus, E. coli, K. pneumonia, P. mirabilis, S. aureus* [162].

Moreover, different formulations were also prepared with anise and tested against various bacteria. For example, silver nanoparticles containing aqueous seed extract solution were found to be effective against *Staphylococcus pyogenes, Acinetobacter baumannii, K. pneumoniae, Salmonella typhi, P. aeruginosa* and were reported to be an eco-friendly alternative with excellent antimicrobial activity [163]. Zayed *et al.* [164] synthesized metal nanoparticles with optimized anise seed extract prepared by different solvents (hexane, methylene chloride, 70% aqueous methanol, water) and methanol extract and silver nanoparticles prepared by this extract were found to have the highest antibacterial activity against *E. coli, S. aureus*. Similarly, copper oxide particles containing anise volatile oil had antibacterial activity against *E. coli, P. aeruginosa* and are considered to be beneficial in future therapeutic applications [165]. In another study [166] an emulgel was prepared with the volatile oil and it was found that the emulgel had significant activity against *E. coli*.

Antifungal Activity

Fluid extract and volatile oil prepared from the seeds were reported to have potent antifungal activity against yeasts isolated from clinical specimens of blood, wounds, and urine, i.e. *Candida albicans, C. parapsilosis, C. tropicalis, C. pseudotropicalis,* and *C. krusei* [167]. Volatile oil was also tested for its antifungal effects and *Candida albicans* and *Saccharomyces cerevisiae* yeasts were found to be sensitive to the volatile oil and the compounds found within the composition [101]. Methanolic extract of the seeds was also found to have high fungicide activity against *C. albicans, Microsporum canis* and *Trichophyton mentagrophyes* [168]. However, in a previous study, volatile oil was shown to have mild activity against *C. albicans* [169]. The volatile oil again was tested for its antifungal activity against some fungal isolates and was found to be active against the mycelial growth of *Chaetomium oblatum, Drechslera erythrospila, D. euphorbiae, Fusarium sulphureum, Gibberella tricincta, Scopulariopsis brevicaulis,* and *Setosphaeria rostrata,* when the volatile oil was added to the solid medium [170]. A homogenous peptide isolated from the seeds was also tested for its antimicrobial activity and found to be effective against *C. albicans*, as well [171]. The volatile oil of the seeds was tested for their activity against fungi isolated from chronic einiatrophic oral candidiasis cases (*C. albicans, C. parapsilossis, C. glabrata, C. krusei*) and concluded to be a promising agent in the prevention and/or treatment of fungal infections of the oral tissue [97]. In another study, volatile oil of the seeds was examined for its antifungal activity against some *Penicillium* species (*P. brevicompactum, P. citrinum, P. crustosum, P. expansum, P. funiculosum, P. glabrum, P. chrysogenum, P. oxalicum, P. polonicum*) and found to have antifungal activity at varying extents [172]. In the aforementioned study by Zayed *et al.* [164] related to antibacterial activity, silver nanoparticles synthesized with methanol extract from the seeds were found to have high antifungal activity against *Aspergillus flavus* and *C. albicans* and could be a safe alternative for biomedical applications. *Aspergillus fumigatus* and *A. niger* were also found to be sensitive to the methanol extract of the seeds, whereas aqueous extract has lower activity [173].

Methanolic extract of the seeds was tested for its activity against some fungi that cause infection on finger and/or toenails (*onychomycosis*) and found to be active against *Tricophyton rubrum, T. mentagrophytes, Microsporum canis, M. gypseum, C. albicans*) due to the phenolic compounds that is possesses [174].

In addition to these aforementioned antimicrobial activities, seeds of the plant are also known to have antiamoebic activity, and methanolic extract of the seeds was demonstrated to be effective against *Entamoeba histolytica* [175].