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REVIEW ARTICLE

The medicinal Umbelliferae plant Fennel (*Foeniculum vulgare* Mill.): Cultivation, traditional uses, phytopharmacological properties, and application in animal husbandry

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Abstract *Foeniculum vulgare* Mill., commonly called fennel is one of the most popular perennial herbaceous plants used as herbal medicine and spices worldwide. It belongs to the family Umbelliferae or Apiaceae and is characterized by a distinct floral arrangement with an umbrella-like shape. In addition to other well-known Umbelliferae plants, such as carrot, celery, and angelica, fennel has been utilized ethnobotanically to cure various ailments, including gastrointestinal issues, hormonal disorders, reproductive, and respiratory diseases. This review aims to update the information on conventional usage, cultivation, phytopharmacological properties, and other applications of *F. vulgare* Mill. in animal husbandry. Ethnobotanical studies have shown its medicinal uses worldwide; some tribes have reported its medicinal uses and how they use different parts of the plant. Alkaloids, essential oils, phenols, fatty acids, and amino acids are examples of natural phytochemicals that have been characterized and biologically tested for their medicinal potential. Fennel has been used to treat ten categories of diseases over the last two decades. Pharmacological studies revealed that the Umbelliferae plant has antiviral, antimicrobial, antioxidant, anti-inflammatory, anti-anxiety, gastro-protective, estrogenic-like, cardiovascular, lipid, anti-mutagenic, anti-diabetic, anti-cancer activity, hepatoprotective, and memory-protective properties. Fennel extract is used as a potential phytogenic agent to enhance the productivity and quality of animal husbandry. Finally, the present study may provide up-to-date information on the medicinal application of *F.*

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vulgare from ethnobotanical and phytopharmacological perspectives and could be further explored to provide a broader benefit to humankind.

1. Introduction

Medicinal plants contribute significantly to human civilization through their biological functions that protect people from sickness. One example among common plant families that have been previously reported to be used in human health is Apiaceae or Umbelliferae. It comprises a vast group of plants, including vegetables, spices, and herbal plants (Ferrie and Caswell, 2016). Their utilization is also diverse, not only for particular medicinal purposes but also as flavors, liqueurs, and confectionery. Although members of this plant family are found worldwide, almost all Umbelliferae plants are originally from Mediterranean countries (Shelef and HERBS, 2003). An important member of the Umbelliferae family is *Foeniculum vulgare* Mill. Like other members of the Umbelliferae family, *F. vulgare* is thought to be endemic to the Mediterranean area (Rather et al., 2016) and has spread worldwide, including Asia, Africa, America, Europe, and Oceania (Khammassi et al., 2018; Weiping and Baokang, 2011). Therefore, vernacular names have been documented in many countries. Some of them are *sweet fennel* (English), *fenouille* (French), *adas* (Indonesian), *hui xiang* (Chinese), *phak chi* (Thai), *venkel* (Dutch), *bisbas* (Arabic), *bitterfenchel* (Germany), *bari saunf* (Indian), and *sohoehyang* (Korean).

Indonesia is an archipelago with 17,000 islands and more than 1,000 tribes. It is a tropical country with diverse ecosystems. In addition, it is home to almost 30,000 medicinal plants, including *F. vulgare*. Fennel possesses phytopharmacological components that are useful in healing various diseases. These phytopharmacological components have been reported to be partly found in roots, stems, leaves, seeds, flowers, and fruits. However, different modes of preparations for a specific medicinal healing process have been documented in the ethnobotanical literature. This mode of preparation is usually transferred from one generation to another through oral traditions or daily practice/rituals. In addition, this mode of preparation is sometimes region-specific (Guarrera and Savo, 2013). Several studies have shown that *F. vulgare* can effectively prevent and control many bacterial, fungal, viral, mycobacterial, and protozoan infections (Badgujar et al., 2014; Dua et al., 2013; Kaur and Arora, 2008). Moreover, it also has antitumor and chemopreventive, antioxidant, cytoprotective, hepatoprotective, hypoglycemic, and estrogenic-like effects (Chang et al., 2016; Badgujar et al., 2014; El-Soud et al., 2011; Gulfraz et al., 2008).

Fennel is also characterized by its main essential oil component, detected using gas chromatography-mass spectrometry (GC–MS). These include *trans*-anethole, estragole, and 28 other chemical components (Diao et al., 2014). In addition, fennel can be consumed directly in raw forms, such as snacks or salads, cooked and baked in a variety of cuisines. Additionally, fennel may also be used to season cheese, seafood, bread or toast, alcohol beverages, desserts, and vegetables (Khammassi et al., 2018). In Italy, fennel pollen is also a common ingredient, although it is very expensive (Kimberly and Jazmine, 2013; Malhotra, 2012).

Metabolite identification and the pharmacological use of fennel constituents still attract many researchers worldwide. Some literature reviews gathered information on fennel's therapeutic and phytochemical content (Kooti et al., 2015; Rather et al., 2016). However, these previous review articles need more information regarding the ethnobotanical use of fennel within society. Traditional people have also used fennel for other purposes, including controlling animal health (Mwale et al., 2006). None of the earlier review articles include the application of fennel in the veterinary domain. Therefore, it is worth noting that a study on ethnobotany is also essential in understanding and exploring fennel's human and veterinary pharmacology potential.

On the other hand, reviews describing fennel cultivation are still limited. High demand for industrial purposes poses a need for more fennel material. Traditionally, this herbal or aromatic plant is propagated through its seeds. However, this propagation system also possesses limitations. Low seed viability and genetic inconsistency of the plant quality are considered significant problems (Mor et al., 2009). Plant tissue culture rises as a good alternative for fennel propagation. It offers rapid and efficient propagation of fennel (Dwivedi et al., 2020). Taken together, providing comprehensive information covering data from botanical characteristics to the broad range of fennel applications and functions is necessarily needed. This present review attempts to update and complete the information on the botanical, cultivation, traditional use, phytochemicals, phytopharmacological properties, and other functions of F. vulgare Mill. on animal husbandry.

2. Botanical aspect and cultivation of *Foeniculum vulgare* Mill.

Foeniculum is classified botanically into two sub-species: *piperitum* and *vulgare*. According to the literature, *F. vulgare* is categorized into two types of varieties: sweet fennel or var. *dulce* and bitter fennel or var. *vulgare* (Coşge et al., 2008; Khammassi et al., 2018). However, it has been reported that fennel consists of three varieties, and they include var. *Piperium* (cria) Cout. (bitter fennel), var. *dulce* DC Batt. Et Trab (sweet fennel) and var. *azoricum* Thell. (Florence fennel, finocchio, or Italian fennel) (Seidemann, 2005). Each variety has its own specific use. Bitter fennel is known for its fruits and essential oils. The leaves of Florence fennel are usually used for food preparation and eaten as vegetables. Similar to the Florence fennel, sweet fennel is frequently cultivated for its fruits, expanded leaf base, and fruit-derived essential oils.

Fennel is a tropical herb that has been used and cultivated for centuries. The plant is characterized by many branches, soft leaves, and hairy-like foliage. It may reach a height of 2 m, and the foliage consists of 3–4 pinnate leaves. In addition, it has a slippery green stem and small yellow flowers. The fruit is elongated, and the seeds are greenish-yellow. They reproduce using their seeds or vegetative multiplication using their root fragments (Badgujar et al., 2014). Several studies have described this species as a perennial herb; however, some researchers have classified fennel as an annual or a biennial plant. Fennel seems to have a typical annual plant characteristic. When the plant enters its flowering and then fructification time, it gradually senesces and dies. Interestingly, a new bud will grow on the basal end of the stem after cutting, making it possible to cultivate fennel annually or polyannually. However, a previous study showed that the yield might differ between the old plant and the new fennel that grew after cutting (Carrubba et al., 2003).

Fennel is commonly cultivated in tropical and temperate regions. To some extent, this herbaceous plant is grown in semi-arid or arid environments (Agarwal et al., 2018). The herb is cultivated using seeds, and normally, germination takes approximately 7–14 days. Heidari et al. (2014) showed that temperature had a significant effect on germination. In addition, other factors, including genotype, physiology, and environmental stress, influence the seed germination of this medicinal plant.

With regard to cultivation, the nutritional requirement of fennel is dependent on the soil condition of the region. In addition, there is an increased demand for pesticide-free and chemical-fertilizer-free fennel (Malhotra and Vashishtha, 2008). Moreover, some studies have reported that environmental and agricultural practices may have an impact on fennel productivity or yield and quality (Díaz-Maroto et al., 2006; Ozcan et al., 2006). Different phytochemical and antioxidant properties of essential oils produced from some organic variety of fennel in Egypt have also been identified (Shahat et al., 2011).

Recent developments in agricultural systems have tended towards organic farming models. The negative impact of pesticides and chemical fertilizers on the environmental damage and human or animal health is the main reason for the development of green agriculture. However, high crop productivity and quality still need to be considered (Pretty and Bharucha, 2014). Agricultural systems, including intercropping, which takes advantage of two plant species with different characteristics, might be used to organically reduce weeds and pests (Poggio, 2005). Insect management using intercropping systems that consist of both medicinal and aromatic plants, has also been reported previously. *F. vulgare* Mill. has been used as an intercrop to reduce aphid populations in mustard (*Brassica juncea* L.) (Singh and Kothari, 1997). In addition, intercropping of fennel and dill (*Anethum graveolens* L.) increased grain and biomass yields. However, a higher proportion of fennel in this system should be considered (Carrubba et al., 2008). Another research discovered that the intercropping of fennel with colored cotton (*Gossypium hirsutum*) resulted in a significant reduction in fennel aphids (*Hydaphis foeniculi* (Pass.)) (Fernandes et al., 2013).

An increase in fennel demand in the market has improved its cultivation, and the plant has become critically important. Agricultural systems, including methods to improve soil fertility in marginal areas, need to be continuously developed. The selection of genetically good quality fennel also determines biomass yield and essential content. The application of phosphorous (P) fertilizer is widely used by farmers to improve soil nutrients, as P is an essential macronutrient for plant development. However, this may be costly and would have a negative impact on the environment. The use of phosphate-solubilizing microorganisms as organic fertilizers is an alternative method to improve P availability. Mishra et al. (2016) showed that phosphate-solubilizing bacteria not only increase seed yield but also enhance essential oil content. Crop propagation based on cross-pollination or allogamy could increase heterozygosity among populations and decrease the quality and performance of the plants. Therefore, many attempts have been made to solve the problem of fennel propagation while maintaining its quality. Micropropagation or *in vitro* plant culture has been applied to preserve, improve, and produce secondary metabolites of fennel. *In vitro* propagation using shoots, calluses, somatic embryogenesis, and inflorescences and the optimization of culture medium using a combination of plant growth regulators (PGRs) have been applied to accelerate plant regeneration (Table 1).

Table 1 Micropropagation of *F. vulgare* using different growth media and plant growth regulators.

No	Explant	Medium supplemented with PGRs	Other additives	Type of Culture	References
1	Buds	MS with 0.01 mg/l IAA + 1 mg/l BA	3 % Glucose	Bud culture	Garcia-Rodriguez et al. (1978)
2	Buds	MS with 0.1 mg/l NAA + 0.1 mg/l BA	3 % Glucose	Bud culture	Paupardin et al. (1980)
3	Buds	0.5 MS with 0.1 mg/l NAA + 0.1 mg/l BA	2 % Glucose, 1 mg/l thiamine, 0.5 Ca pantothenate, 0.1 biotin, 100 mg/l *meso*-inosit, 0.1 mg/l riboflavine, 1 mg/l nicotinic acid, 0.01 folic acid	Bud culture	Badoc (1982)
4	Apical buds	BM with 0.1 IAA + 0.1 mg/l BA	2 % Sucrose, MS vitamins, 0.1 biotin, 0.1 folic acid	Bud culture	Du Manoir et al. (1985)
5	Hypocotyls	MS liquid with 1 mg/l 2,4-D		Cell suspension	Umetsu et al. (1995)
6	Hypocotyls	MS with 2.6 µM NAA + 2.3 µM KIN	3 % Sucrose	Callus and shoot regeneration	Anzidei et al. (2000); Bennici et al. (2004)
7	Callus generated from hypocotyls	MS with 3.3 µM GA3	3 % Sucrose	Somatic embryo	Anzidei et al. (2000)
8	Petioles	LS with 10^{6} M 2,4-D + 10^{-6} M KIN	0.35–0.65 M Glucose	Cell suspension and protoplast culture	Miura and Tabata (1986)
9	Immature inflorescenses	MS with 4.25 µM BA + 4 µM NOA	3 % Sucrose,	Embryogenic callus	Fiore et al. (2012)
10	Stem or petiole pieces	MS with 1 mg/l 2,4-D + 0.3 mg/l KIN	Thiamine-HCl, myo-inositol, 3 % glucose	Callus and cell suspensions	Hunault (1984)
11	Embryo	B5 with 100 mg/l Cefotaxime + 1 mg/l BAP	30 g/l sucrose, vitamins	Shoot proliferation	Shahi et al. (2017)
12	Stem	MS with 0.88 µM 2,4-D	3 % Sucrose	Callus induction	Anzidei et al. (1996)
13	Cotyledonary node	MS with 1 mg/l BAP	29.92 µM of $ZnSO_4$	Shoot multiplication	Dwivedi et al. (2020)

Note: 2,4-D, 2,4-Dichlorophenoxyacetic acid; BM, Basal medium; BA, Benzyladenine; MS, Murashige and Skoog; IAA, Indole-3-acetic acid; BAP, 6-Benzylaminopurine; KIN, Kinetin; LS, Linsmaier-Skoog; NOA, β-Naphthoxyacetic acid.

3. Traditional and medicinal use of *Foeniculum vulgare*

Indonesia is an Asian country with a tropical climate, megabiodiversity, ethnicity, rituals, local languages, and diverse local medicine. The country is very rich in natural resources that have not been explored and are well-documented (Jadid et al., 2020). One example is the Tengger tribe, which applies local wisdom in their daily lives, including knowledge about how to deal with diseases and interact with natural resources. Local knowledge of medicinal plants can be obtained through ethnobotany, and in this case, the ethnobotany of fennel is discussed. Fennel possesses ethnobotanical usage, phytochemical content, pharmacological, and biological properties. We collected ethnobotanical data for two previous decades. The data showed that *F. vulgare* has been used in a broad range of traditional medicinal treatments. We clustered the diseases that have been treated using different organs of *F. vulgare* into 10 categories. These categories included dermatological problems; respiratory (ear, nose, mouth/dental, and throat) issues; internal medical diseases; urogenital and gynecological problems; eye diseases; gastrointestinal disorders; musculoskeletal and disorders of the connective tissue; parasitic and contagious diseases; nervous system disorders; and others (Table 2). Diseases vary, ranging from minor illnesses (such as coughs, colds, and sores) to various very complicated diseases (for example, kidney disease and cancer).

Fennel's leaves, stem bark, roots, fruits, seeds, apical shoots, and whole aerial sections of the plant, have all been employed. Additionally, some modes of administration include decoction, oral infusion, inhalation, raw-eaten, and chewing, and plants could be administered as a paste, powdered, and squeezed form. Among these modes of administration decoction is the most utilized mode, and this the reports of previous studies. The decoction is mainly used because it is a simple, cheap, and "easy to handle" method.

F. vulgare is also used to treat approximately 68 specified diseases. Among these, we noted that most of the diseases treated by *F. vulgare* were internal medical diseases (15 diseases), followed by gastrointestinal disorders (11 diseases), respiratory-nose, ear, mouth/dental, throat issues (10 diseases), urogenital, obstetric and gynecological (9 diseases), musculoskeletal system and connective tissue disorders (5 diseases), dermatological diseases (3 diseases), and infectious or contagious and parasitic diseases (2 diseases). The nervous system diseases include only one type of disease: epilepsy. Moreover, diseases that are not covered by previous clusters belong to "others". The latter include motion sickness, insomnia, refreshment agents, hypnotics, aperitifs, mosquitocides, sedatives for children, fat deduction, anxiety, and poisoning (Fig. 1). These records strongly support several previous studies demonstrating that many medicinal plants have been used to treat and cure internal medicinal diseases and gastrointestinal issues (Jadid et al., 2020; Wali et al., 2022).

4. Phytochemical composition of fennel

Fennel is a plant rich in potassium, sodium, phosphorus, and calcium. Badgujar et al., (2014) reported, according to USDA data, that fennel is rich in vitamins and promotes health, and its nutrition is relatively essential to humans. Proximate analysis of *F. vulgare,* according to previous studies, showed that the organs of fennel have different nutritional values, and their leaves contain the highest moisture content. Carbohydrate (approximately 42.3 %) represents the most dominant macronutrients in all the organ parts of the plant; however, the protein constituent was reported to be less abundant, and it contains only 9.5 % in their stems and flowers (Badgujar et al., 2014; Rather et al., 2016).

Different phytochemical works have been carried out in order to isolate lipids, phenols, hydrocarbon-based compounds, volatile substances, and several other groups of specialized metabolites from each organ part of the fennel (Gross et al., 2009). These chemical components strongly support various pharmacological effects, such as antioxidants, anti-inflammatory properties, anti-microbial, and anti-viral effects. To extract the phytochemical constituents of the plant, several chemical solvents were utilized, including water, methanol, ethanol, acetone, hexane, and dichloromethane (Suppl 1).

Some scientific reports have discovered that the major phytochemical substances of fennel are volatile compounds and essential oils (Parejo et al., 2004). We grouped the metabolites derived from this plant into several classes (Suppl 1); they include terpenoid-derived molecules such as monoterpenes, diterpenes, and sesquiterpenes, and some major substances such as anethole (Díaz-Maroto et al., 2005) and estragole (Afifi et al., 2021) belong to some phenylpropanoid-derived substances found in this plant. It is worth noting that different stages of plant development might affect the quantity of these compounds. Mature organs have lower phytochemical concentrations than immature organs (Telci et al., 2009). The presence of phenolic and phenolic glycoside constituents also makes *F. vulgare* to be a phyto-antioxidant bio-resource. It contains 3-O-caffeoylquinic acid and quercetin glucoside. Some other substances have also been found in this plant but in small quantities (Suppl. 1).

5. Pharmacological properties

F. vulgare has been utilized globally for centuries by ancient societies (Table 2) to treat and cure medical ailments owing to the broad range of phytochemical compounds they contain (Zeller and Rychlik, 2006). Some pharmaceutical importance, such as anti-microbial, anti-viral, anti-oxidant, anti-inflammatory, anti-anxiety, gastro-protective, estrogenic, cardiovascular, lipid, antidiabetic, antimutagenic and chemopreventive, anti-cancer, hepato-protective, and memory-protective properties, in the plant have been recorded. Besides its medicinal uses, *F. vulgare* is also used in several other sectors such as animal husbandry.

5.1. Antifungal, antibaterial, and antiviral activities

F. vulgare is used to treat various ailments caused by bacterial, fungal, viral, and mycobacterial infections (Roby et al., 2013; Singh et al., 2006). Several studies have reported that fennel exhibits antimicrobial and antiviral properties through bioactive compounds such as fenchone, oleic acid, estragole, *trans*-anethole, scopoletin, and coumarin, which have antimicrobial activities (Kooti et al., 2015; Mota et al., 2015). A combination of herbal medicine consisting of *F. vulgare* and *Nigella sativa* displayed potent antifungal properties against *Candida albicans* (Naeini et al., 2017). According to Pecarski (2017), fennel

Table 2 Ethnobotanical uses of *F. vulgare* in medical treatments in some regions worldwide.

No	Disease Categories	Specified disease name	Plant part used	Mode of preparation	Localities	References
1	Dermatological diseases	Urticaria/hives	Leaves	Decoction, Pounded	Probolinggo, East Java, Indonesia	Jadid et al. (2020)
		Hair problems	Fresh fruits and shoots	Decoction, external usage	Middle Navarra	Cavero et al. (2011)
			Seeds	Decoction, oral/topical infusion	Tiaret region, Northwest of Algeria	Djahafi et al. (2021)
		Eczema	Fruits and first leaves	Infusion	Turkey	Alan et al (2021); Fakir et al. (2009)
2	Respiratory-nose, ear, oral/dental, throat problems	Cough	Leaves	Decoction	Probolinggo, East Java, Indonesia	Jadid et al. (2020)
			Whole plant	Oral infusion	Guerrero, Mexico	Juárez-Vázquez et al. (2013)
			Whole plant	Decoction	Southern Spain	Benítez et al. (2010)
			Whole plant	–	Western cape of South Africa	Aston Philander (2011)
			Roots, seeds	Decoction	Basilicata, Italy	Guarrera et al. (2005)
			Fruits and floral tops	Decoction, internal usage/inhalation	Campania, Southern Italy	Savo et al. (2011)
			Fruits	Infusion	Turkey	Fakir et al. (2009)
			Fruits	Pills, powders, oiling agent, stewing granules, and ointment	India	Li et al. (2022)
			Fruits, leaves, roots, and root barks	Tablets and granules	China	Li et al. (2022)
			Leaves	Fresh leaves are directly chewed to relieve cough	Shishi Koh Valley, Chitral, Pakistan	Wali et al. (2021)
			Seeds	Decoction, seeds are boiled and mixed with 2–3 spoons of sugar. The mixture is used at night for the treatment of cough	Shishi Koh Valley, Chitral, Pakistan	Wali et al. (2021)
			Seeds	Decoction	Bahawalpur, Pakistan	Afzal et al. (2021)
			Seeds	Infusion	Calabria, Southern Italy	Mattalia et al. (2020)
			Seeds, leaves, and leaflets	Decoction, intenal usage	Western Aegean Region, Turkey	Güler et al. (2020)
		Bronchitis	Fruits	Infusion	Turkey	Fakir et al. (2009)
			Seeds	The seeds are fried in butter and by addition of a little bit flour and water; a soup is made which is used against bronchitis	Shishi Koh Valley, Chitral, Pakistan	Wali et al. (2021)
		Toothache	Leaves	A few leaves are chewed	South Africa	Van Wyk (2008)
			Leaves	Fresh leaves are directly chewed to relieve toothache	Shishi Koh Valley, Chitral, Pakistan	Wali et al. (2021); Shah et al. (2016)
			Fruits	Fruits are smoked and used to relieve toothache	Cava de' Tirreni area, Southern Italy	Mautone et al. (2019)
		Mouth ulcers	Tender or delicate green leaves	Chowed down and clamped on an ulcer	Basilicata, Italy	Guarrera et al. (2005)
		Gum disorders	Fruits and seeds	Used as a mouthwash	Central Serbia	Jarić et al. (2007)
			Leaves and seeds	Decoction, oral administration, used as a mouthwash	Casablanca, Morocco	Kachmar et al. (2021); Zougagh et al. (2019)
			Seeds	Employed as mouthwash	Calabria, Southern Italy	Mattalia et al. (2020)

(*continued on next page*)

Table 2 (*continued*)

No	Disease Categories	Specified disease name	Plant part used	Mode of preparation	Localities	References
		Cold	Roots, seeds	Decoction	Basilicata, Italy	Guarrera et al. (2005)
			Fruits and floral tops	Decoction, internal usage/inhalation	Campania, Southern Italy	Savo et al. (2011)
			Seeds	Decoction	Bahawalpur, Pakistan	Afzal et al. (2021)
		Gingival wound	Fruits	Paste	Uttarakhand, India	Bhat et al. (2012)
			Entire plant organs	Decoction	Andalusia, Spain	Benítez et al. (2010)
		Asthma	Roots	Decoction, oral infusion	Northeastern Marocco	Kachmar et al. (2021)
			Seeds	Decoction, oral administration	Northern Morocco	Redouan et al. (2020)
		Tracheitis	Fruits, leaves, roots, and root barks	Tablets and granules	China	Li et al. (2022)
		Unspecified respiratory disorders	Leaves, stems, and flowers	Powder, extract, paste, ash	Bahawalpur, Pakistan	Afzal et al. (2021)
3	Internal medical diseases	Hypertension	Leaves	Directly chewed	North-Eastern Majorcan area	Calvo et al. (2011)
		Fever	Leaves	Oral infusion	South Africa	Lewu and Afolayan (2009)
			Fruits, roots, and seeds	Decoction	China	Li et al. (2022)
		Cancer	Leaves and flower	Oral infusion	Loja, Ecuador	Tene et al. (2007)
		Abdominal pains	Whole plant	Decoction, internal usage	Campania, Southern Italy	Savo et al. (2011)
			Leaves and seeds	Infusion	Northern Badia, Jordan	Aburjai et al. (2007)
			Leaves	Paste	Manisa, Turkey	Bulut and Tuzlaci (2013)
			Whole plant	Oral infusion	Guerrero, Mexico	Juárez-Vázquez et al. (2013)
			Fruits	Fresh or boiled/infusion/decoction, internal usage	Middle Navarra	Cavero et al. (2011)
			Seeds	Decoction	Liguria, Italy	Cornara et al. (2009)
			Seeds, leaves, and stems	Infusion, directly consumed	North Iran	Ghorbani (2005)
			Aerial parts, fruits, seeds	Infusion	Komen and Izola, Slovenia	Vitasović-Kosić et al. (2021)
			Seeds	Decoction	Liguria, Italy	Cornara et al. (2009)
			Fruits, leaves, roots, and root barks	Powders, pills, tablets, and granules	China	Li et al. (2022)
			Seeds	Decoction, seeds are boiled and mixed with 2–3 spoons of sugar. The mixture is used at night for the treatment of abdominal pain	Shishi Koh Valley, Chitral, Pakistan	Wali et al. (2021); Shah et al. (2016)
			Whole plant	Macerated, oral administration	Fangoga area, Sennar State, Sudan	Ahmed et al. (2020)
			Seeds	Infusion	Calabria, Southern Italy	Mattalia et al. (2020)
			Seeds and roots	Decoction, oral administration	Northern Morocco	Redouan et al. (2020); Haouari et al. (2018)
			Bulbs	Raw or infusion	Bordj Bou Arreridj, Northeast Algeria	Miara et al. (2019)

Table 2 (*continued*)

No	Disease Categories	Specified disease name	Plant part used	Mode of preparation	Localities	References
		Colic	Leaves and fruits	Infusion	Brazil	de Albuquerque et al. (2007)
			Fruits	Pills, powders, oiling agent, stewing granules, and ointment	India	Li et al. (2022)
			Seeds	Infusion	Marche region, Central Italy	Lucchetti et al. (2019)
		Nausea and vomiting	Fruits	Simple powder	North-Eastern Majorcan area	Carrió and Vallès (2012)
			Fruits, leaves, roots, and root barks	Tablets and granules	China	Li et al. (2022)
		Tachycardia	Fruits	Infusion	Turkey	Fakir et al. (2009)
		Anaemia	Seeds	Decoction, oral/topical infusion	Tiaret region, North west of Algeria	Djahafi et al. (2021)
			Seeds	Infusion	Marche region, Central Italy	Lucchetti et al. (2019)
		Obesity	Seeds	Decoction, oral/topical infusion	Tiaret region, North west of Algeria	Djahafi et al. (2021)
			Seeds	Infusion to lose weight	Calabria, Southern Italy	Mattalia et al. (2020)
		Dizziness	Fruits, roots, and seeds	Decoction	China	Li et al. (2022)
		Hiccup	Fruits, leaves, roots, and root barks	Tablets and granules	China	Li et al. (2022)
		Anorexia	Fruits, leaves, roots, and root barks	Powders, pills, tablets and granules	China	Li et al. (2022)
			Fruits	Pills, powders, oiling agent, stewing granules, and ointment	India	Li et al. (2022)
		Diabetes	Seeds	Decoction	Morocco	Bouyahya et al. (2021)
			Aerial parts	Infusion	Croatia	Končić and Bljajić (2019)
		Headache	Seeds	Infusion	Calabria, Southern Italy	Mattalia et al. (2020)
			Fresh leaves	Decoction made with *Matricaria chamomilla* heads	Cava de' Tirreni area, Southern Italy	Mautone et al. (2019)
		Dysphagia	Seeds	Decoction, oral administration	Northern Morocco	Redouan et al. (2020)
4	Urogenital, obstetry and gynecological	Leucorrhoea	Seeds	Powdered with other recipes (*Papaver somniferum* and *Coriander sativum*)	Rajasthan, India	Jain et al. (2007)
			Fruits, leaves, roots, and root barks	Tablets and granules	China	Li et al. (2022)
		Unspecified kidney diseases	Aerial parts	Infusion	Alto, Bolivia	Macía et al. (2005)
			Seeds	Decoction	Gujranwala, Pakistan	Mahmood et al. (2013)
		Diuretic	Tender parts	Raw or boiled	Rome, Italy	Guarrera and Savo (2013)
			Whole plant	–	South Africa	Aston Philander (2011)
			Seeds	Decoction	South-Europe	Jarić et al. (2011)
			Seeds, roots, and fresh leaves	Decoction	Northern Portugal, Miami, Florida, USA	Neves et al. (2009); Halberstein (2012)
			Leaves	Oral infusion	South Africa	Lewu and Afolayan (2009)
			Roots	Infusion	Marche region, Central Italy	Lucchetti et al. (2019)

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Table 2 (*continued*)

No	Disease Categories	Specified disease name	Plant part used	Mode of preparation	Localities	References
		Amenorrhoea and oligomenorrhoea	Aerial parts	Freshly consumed with carrot	Rome, Italy	Guarrera and Savo (2013)
			Fruits	Simple powder	Northeastern Majorcan area	Carrió and Vallès (2012)
			Seeds	–	Haryana, India	Kumar et al. (2012)
			Fruits, leaves, roots, and root barks	Tablets and granules	China	Li et al. (2022)
			Roots	Decoction, oral administration	Italy	Motti et al. (2019)
		Milk stimulant in pregnant women (Galactagogue)	Leaves	Oral infusion	South Africa	Lewu and Afolayan (2009)
			Fruits	As condiment or chewed	Rome, Italy	Guarrera and Savo (2013)
			Fruits	Simple powder	Northeastern Majorcan area	Carrió and Vallès (2012)
			Aerial parts	Infusion	Alto, Bolivia	Macía et al. (2005)
			Fruits	Infusion	Turkey	Fakir et al. (2009)
			Seeds, roots, leaves, and aerial parts	Raw or decoction, oral administration	Italy	Motti et al. (2019); Motti and Motti (2017)
			Seeds	Infusion	Marche region, Central Italy	Lucchetti et al. (2019)
		Problem of repeated abortions	Seeds	Powdered with other recipes (*Trapa natans)*	Rajasthan, India	Jain et al. (2007)
		Kidney stones	Leaves and seeds	Decoction, infusion, or made into herbal tea	North-Eastern Morocco	Bencheikh et al. (2021)
		Dysmenorrhoea	Fruits, roots, and seeds	Decoction, powders, and pills	China	Li et al. (2022)
			Seeds	Decoction, administered orally	Italy	Motti et al. (2019); Fortini et al. (2016)
		Urinary calculi	Fruits, leaves, roots, and root barks	Tablets and granules	China	Li et al. (2022)
5	Eye diseases	Eye Irritation	Aerial parts	Heated and put in the eyes, external usage	Balikesir, Turkey	Polat and Satıl (2012)
			Seeds, roots, and leaves	–	Northern Portugal	Neves et al. (2009)
			Seeds	Infusion, directly consumed	Gujranwala, Pakistan	Mahmood et al. (2013)
			Leaves and/or fruits	Eye drops	South Africa	Van Wyk (2008)
		Conjunctivitis	Leaves and flowers	Aqueous infusion, drink	Loja, Ecuador	Tene et al. (2007)
6	Gastrointestinal disorders	Diarrhea	Seeds, roots, and fresh leaves	–	Northern Portugal	Neves et al. (2009)
			Seeds	Paste and mixed with *Hemidesmus indicus*	Bhandara, Maharashtra, India	Gupta et al. (2010)
			Bulbs	Raw or infusion	Bordj Bou Arreridj, Northeast Algeria	Miara et al. (2019)
		Constipation	Seed of fennel	Decoction	South Europe	Jarić et al. (2011)
				Combined with sugar	Jammu and Kashmir, India	Kumar et al. (2009)
				Infusion or directly consumed	Gujranwala, Pakistan	Mahmood et al. (2013)
				Decoction, oral/topical infusion	Tiaret region, North west of Algeria	Djahafi et al. (2021)

Table 2 (*continued*)

No	Disease Categories	Specified disease name	Plant part used	Mode of preparation	Localities	References
		Stomatitis	Leaves and flowers	Honey-sweetened drink	Loja, Ecuador	Tene et al. (2007)
		Gastric distension		Aqueous infusion, decoction	Liguria, Central Italy	Guarrera et al. (2005)
			Fruits, roots, and seeds	Decoction, powders, and pills	China	Li et al. (2022)
		Gastralgia	Leaves	Decoction	Southern Spain	Benítez et al. (2010)
		Dyspepsia	Fruits	Infusion	Turkey	Fakir et al. (2009)
			Fruits	Pills, powders, oiling agent, stewing granules, and ointment	India	Li et al. (2022)
			Fruits, leaves, roots, and root barks	Tablets and granules	China	Li et al. (2022)
			Seeds	Decoction, orally administered	Northern part of Morocco	Redouan et al. (2020); Haouari et al. (2018)
		Irritable bowel syndrome	Leaves and seeds	Infusion	Northern Badia, Jordan	Alzweiri et al. (2011)
		Liver pain	Seeds	–	Pernambuco, Northeast Brazil	de Albuquerque et al. (2007)
		Other digestive system problems	Fruits	Decoction	Basilicata, Italy	Guarrera et al. (2005)
			Seeds	Decoction, oral administration	Balikesir, Turkey	Polat and Satıl (2012)
			Whole plant	–	Western region of South Africa	Aston Philander (2011)
			Fruits	Powder for digestive ailments	Middle, Western, and Southern part of Bosnia	Šarić-Kundalić et al. (2010)
			Seeds	Decoction	South Europe	Jarić et al. (2011)
			Seeds, roots, and fresh leaves	–	Northern region of Portugal.	Neves et al. (2009)
			Seeds	Decoction	South region of Spain	Benítez et al. (2010)
			Fruits and floral tops	Decoction, internal usage	Campania, Southern Italy	Savo et al. (2011)
			Shoots, leaves, and stems	Fresh or boiled/infusion/decoction, internal usage	Middle Navarra	Cavero et al. (2011)
			Seeds	Infusion	Marche region, Central Italy	Lucchetti et al. (2019)
		Flatulence	Leaves and fruits	Infusion	Brazil	de Albuquerque et al. (2007)
			Leaves and seeds	Infusion	Northern part of Jordan	Mitra and Mukherjee (2010)
			Fresh fruits	Decoction	North Bengal, India	Alzweiri et al. (2011)
			Tender parts	Raw or boiled	Rome, Italy	Guarrera and Savo (2013)
			Whole plant	–	Western area of South Africa	Aston Philander (2011)
			Seeds	Decoction	Southern region of Europe	Jarić et al. (2011)
			Seeds, leaves, and stems	Infusion or directly consumed	North Iran	Ghorbani (2005)
			Shoots, leaves, and stems	Fresh or boiled/infusion/decoction, internal usage	Middle Navarra	Cavero et al. (2011)
			Leaves and/or fruits	–	South Africa	Van Wyk (2008)
			Seeds	Decoction, oral/topical infusion	Tiaret region, Northwestern of Algeria	Djahafi et al. (2021)
			Aerial parts, fruits, seeds	Infusion	Komen and Izola, Slovenia	Vitasović-Kosić et al. (2021)
			Aerial parts (flowers,	Infusion	Liguria, Italy	Cornara et al. (2009)

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Table 2 (*continued*)

No	Disease Categories	Specified disease name	Plant part used	Mode of preparation	Localities	References
			leaves, shoots), and seeds			
			Seeds	Decoction, oral administration	Northern part of Morocco	Redouan et al. (2020)
			Fresh leaves	Infusion	Cava de' Tirreni area, Southern Italy	Mautone et al. (2019)
			Bulbs	Raw or infusion	Bordj Bou Arreridj, Northeast Algeria	Miara et al. (2019)
		Hernia	Fruits, leaves, roots, and root barks	Powders, pills, tablets, and granules	China	Li et al. (2022)
7	Muskuloskeletal system and connective tissue disorders	Arthritis	Leaves	Oral infusion	South Africa country	Lewu and Afolayan (2009)
			Whole plant	Macerated, oral administration	Fangoga area, Sennar State, Sudan	Ahmed et al. (2020)
		Rheumatism	Roots	Decoction, oral infusion	Northeastern part of Marocco	Kachmar et al. (2021)
		Neck pain	Fruits, roots, and seeds	Decoction	China	Li et al. (2022)
		Backache	Fruits, leaves, roots, and root barks	Tablets and granules	China	Li et al. (2022)
		Low back pain	Seeds	Fried in butter	Shishi Koh Valley, Chitral, Pakistan	Wali et al. (2021); Shah et al. (2016)
8	Infectious and parasitic disease	Dysentery	Fruits	Pills, powders, oiling agent, stewing granules, and ointment	India	Li et al. (2022)
		Rabies	Fruits, leaves, roots, and root barks	Tablets and granules	China	Li et al. (2022)
9	Nervous system disease	Epilepsy	Fruits, roots, and seeds	Decoction	China	Li et al. (2022)
10	Others	Motion sickness	Leaves	Squeezed	Probolinggo, East Java, Indonesia	Jadid et al. (2020)
		Insomnia	Leaves	Infusion	Brazil	Oliveira et al. (2012)
		Refreshing	Roots/whole plant	Decoction/crushed, internal usage	Campania, Southern Italy	Savo et al. (2011)
		Hypnotic	Seeds, leaves, and stems	Infusion or directly consumed	North Iran	Ghorbani (2005)
		Appetizer	Delicate part of the plant	Eaten fresh/raw	Rome, Italy	Guarrera and Savo (2013)
		Mosquitocidal	Roots	Drinking as tea	Somali Region, Ethiopia	Mesfin et al. (2012)
		Sedative for children	Apical shoots	–	Liguria, Italy	Cornara et al. (2009)
			Apical shoots	–	Southern part of Punjab, Pakistan	Jabbar et al. (2006)
		Fat reduction	Green fruits	Chewed	South Africa country	Lewu and Afolayan (2009)
		Anxiety	Seeds	Decoction, oral/topical infusion	Tiaret region, Northwestern of Algeria	Djahafi et al. (2021)
		Poisoning	Fruits	Powders and pills	China	Li et al. (2022)

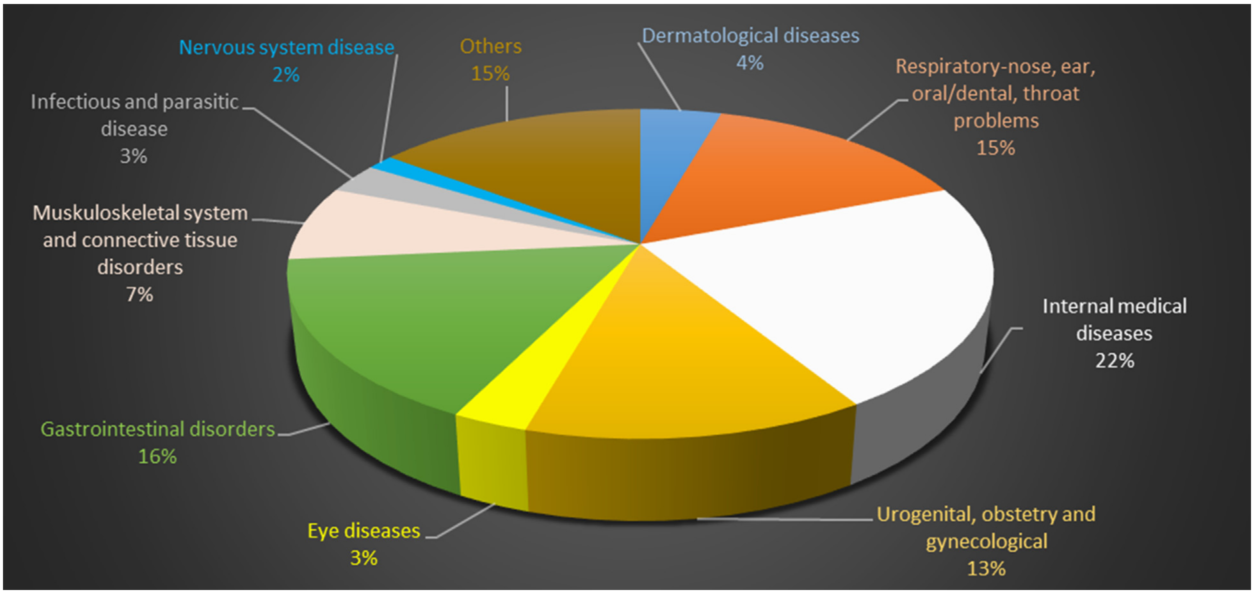

Fig. 1 Percentage of specified diseases treated using *Foeniculum vulgare* Mill.

showed antibacterial activity against *Candida albicans* and *Staphylococcus aureus* through the formation of imbibition and diameter zones, probably owing to the content of Geranyl diphosphate (GPP) derived monoterpenes (i.e: p-cymene, limonene, and α-pinene) in fennel fruit extract. Another study investigated the anti-bacterial activity of fennel extract on a nosocomial pathogen such as *Acinetobacter baumannii*. Their finding results revealed that fennel extract has an antibacterial effect on all the strains of the bacteria and can be used to control double bacterial antibiotic resistance (Jazani et al., 2009). A recent study showed that the combination of the essential oil of *F. vulgare* and silver nanoparticles (AgNPs) increased the bacteriostatic activity of several bacteria, including *Escherichia coli, Pseudomonas aeruginosa, Enterobacter cloaceae, Staphylococcus aureus, and S. epidermidis* (Qaralleh et al., 2022). Additionally, AgNPs was also strongly recommended for increasing the accumulation of specialized metabolite in the plant through *in vitro* culture (Rahmawati et al., 2022). Recently, Yoshino et al. (2022) stated that a fennel *n*-hexane extract has bactericidal action. They reported that a combination of fennel extract and petroselenic acid could be used for periodontitis treatment caused by *Porphyromonas gingivalis*.

In addition to its antimicrobial activities, fennel also exhibited anti-viral properties (Orhan et al., 2012). Its essential oils showed potent antiviral activities against HSV-1 herpes simplex virus and RNA-based influenza virus. Furthermore, another study also revealed the anti-viral effect of *F. vulgare* against hepatitis viruses (Ibrahim and Moussa, 2021). This antiviral activity is linked to the essential oils found in *F. vulgare*, and this has been corroborated by an *in silico* study, which showed the interaction of essential oils with some viral proteins, including Severe Acute Respiratory Syndrome (SARS) associated corona virus proteins (spike glycoprotein) (Saab et al., 2022). The antiviral compound in *F. vulgare* that function against covid-19, include anethole and limonene (Kulkarni et al., 2020).

5.2. Antioxidant activity

Antioxidants play a vital role in reducing radical damages, which may be detrimental to biological systems and may subsequently disturb human health. Many research have been undertaken to evaluate the antioxidant activities of fennel (Jadid et al., 2016), and fennel from different locations may exhibit distinct antioxidant activities (Faudale et al., 2008). For instance, a DPPH assay using the methanolic extract of fennel seed derived from several regions in Tunisia resulted in IC_{50} 977.33 to 23.66 μg/mL. The essential oil extracted from marocain fennel using GC MS was predominantly monoterpene hydrocarbons (El Ouariachi et al., 2014).

DPPH assay is a potent tool for screening the potential antioxidant activity of plant-based compounds (Jadid et al., 2017). A good DPPH inhibition was demonstrated by fennel derived from Pakistan, with an IC_{50} value of 23.61–26.75 μg/mL (Anwar et al., 2009), and cirsiliol is the predominant phenolic compound found in the plant (Khammassi et al., 2022). The anti-oxidant properties of fennel seed extracts from Egypt and China have been documented to be robust yet possess distinct IC_{50} value (Ahmed et al., 2019). It has also been discovered that the anti-oxidant properties of wild and cultivated fennel vary. Conforti et al. (2006) demonstrated that the DPPH test revealed that the ethanolic extract of wild *F. vulgare* (IC_{50}: 31 μg/mL) was greater than that of cultivated fennel (83 μg/mL). Besides the methanolic and ethanolic extracts of fennel seed, some reports showed similar results from other solvent extracts and fennel organs. For example, peroxidation assay showed that the acetone extract of fennel has a high percentage of free radical inhibition (Ruberto et al., 2000), whereas *n*-butanol extract from fennel fruit demonstrated modest antioxidant activities (De Marino et al., 2007). The overall results of antioxidant assay showed that fennel extract has the potential to be developed as a pharmaceutical agent with strong antioxidant activities.

5.3. Anti-inflammatory activity

Inflammation can be defined as the physiological and defensive responses of the body against pathogenic microbes or viruses. Several research have been undertaken to assess the impact of utilizing *F. vulgare* extract as an anti-inflammatory agent. Choi and Hwang (2004) revealed that the methanol extract of fennel fruit (200 mg/kg) demonstrated remarkable inflammatory inhibition, with an increase in several anti-oxidant enzymes, including catalase (CAT) and superoxide dismutase (SOD). In addition, the use of *F. vulgare* with other medicinal plants (*Nigella sativa*, *Brassica nigra*, *Trigonella foenum-graceum* demonstrated good anti-inflammatory activities owing to their phenols and flavonoid constituents (Gias et al., 2020). These constituents have been reported to have analgesic and anti-inflammatory effects; they show strong anti-inflammation by inhibiting prostaglandin synthesis (Elizabeth et al., 2014). Inhibition of inflammation was also reported by Yang et al. (2015) that imperatorin, which is extracted from fennel, inhibits pro-inflammatory cytokines. In addition, Kooti et al., (2015) reported that the possible anti-inflammatory mechanism may be through the preventive effects of methanol extract on acute and subacute diseases and type 4 allergic reactions through the inhibition of cyclooxygenase-2 (COX-2) and 5-lipoxygenase; this report was corroborated by the report of Crescenzi et al. (2022), which showed that the quercetin glucoside in fennel is capable of inhibiting COX-2 (IC_{50} value 9.34), and COX-2 inhibition subsequently reduces prostaglandins, which are involved in inflammatory responses (Crescenzi et al., 2022).

5.4. Anti-anxiety and anti-depressant effects

Anxiety is a distressing sensation of worry and paranoia. Anxiety disorders are diagnosed when anxiousness becomes extreme. Fennel has traditionally been used as natural remedy to alleviate anxiety and psychiatric issues (Amaghnouje et al., 2020). Anxiolytic effect of an ethanolic extract of fennel fruit injected to experimental mice was observed to be comparable to 1 mg/kg diazepam (anti-anxiety medication as control) (Kishore et al., 2012). Another study showed that 250 and 500 mg/kg of methanolic fennel extract given orally to experimental mouse exhibited anti-depressant effect (Jamwal et al., 2013). Furthermore, a herbal medicine that contained 21–27 mg of fennel-derived anethole was reported to significantly improve depressed postmenopausal women (Ghazanfarpour et al., 2018). Similarly, Alvarado-García et al. (2022) showed that essential oil (mainly *trans*-anethole) derived from fennel seeds exhibited more effective anxiolytic activity than antidepressants. In contrast, the aerial part of the fennel extract demonstrated moderate anxiolytic activity.

5.5. Gastrointestinal protection

A previous ethnobotanical study showed that fennel fruit cures gastrointestinal disorders such as indigestion, flatulence, and diarrhea (Table 2) (Mitra and Mukherjee, 2010). Peptic ulcer, another gastrointestinal disorder, is considered a chronic disease and it occurs in the proximal duodenum and stomach: extract of *F. vulgare* has been proven to act as antiulcerogenic agent, and a pre-treatment using fennel extract showed strong inhibition of mucosal lesion induced by ethanol in the rat. The highest percentage of mucosal lesion inhibition was demonstrated by 300 mg/kg of fennel extract pre-treatment (Birdane et al., 2007). Another report showed that the extracts of polyherbs such as betel, clove, fennel, and black catechu have significant gastro-protective activity (Reddy et al., 2013). This was proven by an anti-ulcer protection test in mice ulcer induced by aspirin and ethanol. The result revealed that liquid extract of fennel (250 and 500 mg/kg) has gastro-protective activity, and ulcer and gastric lesions were successfully prevented by 65 and 75 %, respectively, compared to omeprazole drugs (98 %). Das et al. (2022) did a recent investigation which demonstrated that seed-derived fennel extract exhibited a protective function on transepithelial electrical resistance on T84 colonic cells. They reported that fennel extract reduces the activation of Signal Transducer and Activator of Transcription (STAT), which strongly correlate with inflammatory responses. Interestingly, mice administered with fennel extract showed an increase in ulcer indications (Das et al., 2022).

5.6. Estrogenic-related activities

A reduced protein total content was detected in the testes and seminal vesicles of rats treated with acetone extract of fennel seeds. Interestingly, female rats demonstrated vaginal cornification and oestrus cycle after the treatment (Rahimi and Ardekani, 2013). Another study reported that *F. vulgare* was involved in the enhancement of milk secretion (galactogenic activity), facilitating birth and menstruation cycle induction (Albert-Puleo, 1980; Rather et al., 2016). Furthermore, some phyto-constitutents of fennel extract (dianethole, photoane, and diosgenin) were reported to be involved in prolactin secretion, which facilitate ovarian folliculogenesis effect in female mice (Khazaei et al., 2011).

5.7. Cardiovascular and lipid activity

Patients with the cardiovascular disorders often receive antithrombotic therapy. *In vivo* study of essential oil derived from fennel extract, especially anethole, was shown to possess antithrombotic activity. Fennel essential oil (30 mg/kg/day) given orally to mice treated with Acetylsalicylic acid (ASA) for five days, demonstrated significant antithrombotic activity by exhibiting 70 % paralysis inhibition, and *in vitro* tests showed similar results. The essential oil from fennel and anethole, which can also be found in fennel, significantly inhibited platelet aggregation (Tognolini et al., 2007). In addition, studies on the anti-cholesterol and atherogenesis inhibition effects of methanol extract of fennel showed a significant reduction in plasma lipid levels. The anti-atherogenic effect can prevent atherogenic dyslipidemia (AD) and enhance blood circulation in the coronary arteries. Thus, the presence of hypolipidemic and anti-atherogenic activity in fennel extract can be used to control cardiovascular disorders (Oulmouden et al., 2014).

5.8. Anti-diabetic and anti-obesity activity

Fennel essential oil protect patient from hyperglycemia and pathological defects in diabetic mice through antioxidant effects and restoration of redox homeostasis. *In vivo* studies on hyperglycemia-induced rats showed that essential oil from fennel has significant anti-hyperglycemia activity. The corrected hyperglycemia status may correlate with an increase in glutathione peroxidase activity as antioxidant (El-Soud et al., 2011), and a recent study by Zolkepli et al. (2022) corroborated this finding. The encapsulated essential oil from fennel by nanoemulsion exhibited a considerable reduction in the blood glucose content (Zolkepli et al., 2022). The aqueous extract of fennel given to certain diabetic rats, influenced the reduction of blood glucose. The extract also exhibited a strong inhibitory concentration of 50 % radicals (at 43 ± 1.19 μg/ml) (El-Ouady et al., 2020). Furthermore, the combination of *F. vulgare* and black cumin (2.5 g each) on female patient food significantly affects the body mass index (BMI) and cholesterol level of the female patients (AbdElwahab et al., 2021).

5.9. Anti-mutagenic and anti-cancer activities

The potential antimutagenic and cancer chemopreventive effects of fennel have been elucidated in several studies. For example, the crude and fractioned extracts of fennel seed have been demonstrated to possess significant cytotoxic activity against breast cancer cell lines (Megeressa et al., 2020). In addition, *in silico* analysis of α-pinene and D-limonene through molecular docking showed strong binding energy (each represents −6 and −5.9 kcal/mol) to the breast cancer cell target (Kaur et al., 2022); however, it is important to note that the effect is apparently dependent on the cancer cell lines, because the crude extract of fennel did not show significant inhibition (Megeressa et al., 2020). Furthermore, potential anti-hepatocellular carcinoma was exhibited by the ethanol extract of fennel seed, which showed an inhibitory effect on hepatocellular carcinoma by binding with oncoprotein survivin (Ke et al., 2021).

The apoptotic activity of crude methanol and ethanol extract of *F. vulgare* leaves was examined in a cervical cancer cell line (HeLa). Apoptosis induction was indicated by fragmented DNA in the HeLa cell lines treated with methanol plant extract. Fragmented DNA was occured at different concentrations of plant samples (Devika and Mohandass, 2014).

5.10. Hepato-protective activity

Fennel plants have a protective effect on the liver. The active compound of fennel was tested to evaluate its impact on hepatoprotective activity through hyperglycemia-induced liver injury in rats. Some markers, which include serum aminotransferase such as ALT and AST were tested. Although these markers are supposed to increase following a liver injury, a study by Samadi-Noshahr et al. (2021) reported a lower ALT and AST levels. The 400 mg/kg of fennel extract was able to reduce lipid peroxidation. The hepatotoxicity induced by carbon tetrachloride (CCL_4) in rats was inhibited by combining fennel oils with *Anethum graveolens* (Rabeh et al., 2014). It has been reported that treatments using combined *A. graveolens* and *F. vulgare* extracts increases enzymatic antioxidants (SOD). Moreover, a decrease in MDA level was detected, indicating that the extract successfully inhibited the formation of oxidative radicals following the induction of CCL_4 (Rabeh et al., 2014). Furthermore, fennel essential oil has been proven to have a positive effect on the histopathological liver tissues of sodium valproat-induced hepatotoxicity in rats (Al-Amoudi, 2017). Wang et al. (2012) studied the effects of fennel on cytokines in mice with liver fibrosis; the findings revealed that lipid breakdown and inflammation were reduced in the fennel-treated rats.

5.11. Memory-protective activity

Fennel plants can be used to improve memory and intelligence (Kooti et al., 2015). Together with *Origanum vulgare*, *F vulgare* displayed an effective antioxidant activity related to learning and memory enhancement. A recent study by Ghaderi et al., (2020) demonstrated that animal in vivo experiments suggested potential property of water extract of *O. vulgare* to enhance memory in male rats. Joshi and Parle, (2006) investigated the effects of fennel extract as a neutropic factor and anti-acetylcholinesterase in amnesic mice. The results demonstrated that the activity of acetylcholinesterase was inhibited. Fennel, therefore, may be useful the treat cognitive disorders such as schizophrenia and Alzheimer's disease.

6. Application of *F. vulgare* in animal husbandry

Numerous scientists have been interested in using natural remedies derived from plant as phytobiotics due its importance in improving animal health and performance. Essential oils contained in plants, such as sunflowers, alfalfa, and *Moringa oleifera*, have been proven to play important roles in increasing animal immunity, nutrient digestibility, reproductive function, and animal productivity (Alharthi et al., 2021; Khan et al., 2021; Ullah et al., 2022). Furthermore, Khan et al. (2022) recently reported the use of *F. vulgare* as an alternative to phytobiotics in animal husbandry.

The supplementation of broiler feedstock with fennel seeds enhanced feed consumption (Saleh et al., 2018), probably owing to the good palatability, odor, and antimicrobial effects of fennel seed, which might have also increased the digestion capacity of the broilers and led to their weight gain (Zahira et al., 2017). However, this effect may be different in other poultry species (Safaei-Cherehh et al., 2018), and it seems that the booster effect on feed consumption depended on the proportion of the bioactive constituents in the plant and its ratio within the animal meals. Similarly, fennel in the feed of Holstein calves increased their consumption rate (Kargar et al, 2021); for example, 0.4 and 0.8 % (dry matter basis) of fennel seed was observed to increase the body weight of Holstein calves (Saeedi et al., 2017), and 1.5 % of fennel powder increased the weight of experimental lambs than control lambs (Hajalizadeh et al., 2019). Furthermore, some essential oils from fennel (estragole, anethole, and fenchone) are thought to be responsible for changes in consumption behavior (Hajalizadeh et al., 2019).

The effects of fennel supplementation (50 mg/kg) on egg production have been reported; they include enhanced oviduct size, increased albumin production, and increased shell membrane strength in laying hens (Kazemi-Fard et al., 2013; Reza et al., 2018). Bollengier-Lee et al. (1998) showed that fennel extract increases egg yolk formation, and fennel seed plays a significant role in increasing ovary, egg duct, and oviduct of Japanese quail (Yazarlou et al., 2012). Similarly, the effect of fennel extract on human and animals fed fennel include increased potential to scavenge free radicals by enhancing the production of SOD, CAT, and glutathione peroxidase (Khan et al., 2022). Furthermore, animals fed diet containing fennel has been reported to show increased total protein, albumin, red blood cell, high-density lipoproteins (HDL), and haemaglobin (Mohammed and Abbas, 2009 (Safaei-Cherehh et al., 2018)).

7. Conclusion

Fennel (*F. vulgare* Mill.) has been recognized by the society as a traditional medicinal plant and serves as a potent phytopharmacological bioresources. Effective and efficient plant cultivation through *in vitro* culture is necessary to meet the high demand of the plant, and its sustainability in nature should be considered while maintaining its genetic stability. This study gathered information on plant *in vitro* culture techniques that have been performed and could be developed and used as a biosystem to boost the phytochemical content of plants *in vitro*. This study also offers details on the traditional uses of the plant to treat ailments worldwide. The traditional uses were classified into 10 categories, and they are closely linked to the phytochemical constituents of the plant, which has been biologically tested. The bioactive compounds and activities include antimicrobial and antiviral, anti-inflammatory, anti-oxidant, gastro-protective, anti-anxiety, estrogenic-like activity, cardiovascular protection and lipid, anti-diabetic, anti-mutagenic, anti-cancer, hepatoprotective, and memory-protective activities. This study also demonstrated the phytogenic properties of the fennel to enhance the productivity and quality of animals in animal husbandry. However, further investigation and biological studies on the potential uses of fennel is still important, especially in terms of developing novel fennel bioactive-based drugs and other applications to provide beneficial impacts on humankind.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.arabjc.2023.104541.

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