Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
www.phytojournal.com
JPP 2021; 10(2): 1255-1263
Received: 01-01-2021
Accepted: 03-02-2021

Nisha Mehra
Department of Chemistry, G. B. Pant University of Agriculture and Technology Pantnagar, Uttarakhand, India

Garima Tamta
Department of Chemistry, G. B. Pant University of Agriculture and Technology Pantnagar, Uttarakhand, India

Viveka Nand
Department of Chemistry, G. B. Pant University of Agriculture and Technology Pantnagar, Uttarakhand, India

Corresponding Author:
Nisha Mehra
Department of Chemistry, G. B. Pant University of Agriculture and Technology Pantnagar, Uttarakhand, India

A review on nutritional value, phytochemical and pharmacological attributes of *Foeniculum vulgare* Mill

Nisha Mehra, Garima Tamta and Viveka Nand

DOI: https://doi.org/10.22271/phyto.2021.v10.i2q.13983

Abstract
Foeniculum vulgare is a cuisine spice of the Apiaceae genus, which is extensively cultivated in the world's tropical and temperate areas. Fennel seeds are developed mostly from dry and semi-dry regions in India. Recent studies have revealed pharmacological properties including antimicrobials, antidiabetic, antioxidants, anticancer and other activities. Fennel contains flavonoids, glycosides and other phytoconstituents present in it which used in medicinal ailments purpose. Phenolic compounds present in fennel can promote to the human health. Trans-anethole, estragole, fenchone and bioactive compounds kaempferol, quercetin, rosmarinic acid have been isolated from this plant and several associate with prospective human body mechanisms. The objective of this review to focusing on the nutritional value, botanical studies, phytochemicals and some major pharmacological actions of fennel to reveal the medicinal potential and future investigation aspects.

Keywords: *Foeniculum vulgare*, nutritional value, phytochemical, anti-inflammatory, anti-carcinogenic, antispasmodic, analgesic

Introduction
From prehistoric times, medicinal plants also termed as therapeutic herbs have been recognized and used in traditional medicinal practises. Medicinal plants are those natural products which are used since primitive time for the prevention of specific human diseases. Due to numerous favourable implementations, medicinal herbs and spices remain strongly in demand, in the functional food and biopharmaceutical industries. In view of market preferences, Medicinal plants industries are highly preferred [1]. For a long time, aromatic herbs and spices have been used in Mediterranean cuisine not only to enhance or change food taste, but also to avoid its degradation [2]. Spices have been historically used as an important additives in food processing which directly providing the foodstuffs with flavour, fragrance and taste. Many therapeutic characteristics and actions are being attributed to spices [3]. Due to food-borne illness, severe health problems are generated in the world, in well-developed countries too. Because of the resistant microorganisms have developed against pathogens, certain biologically active substances isolated from herbs and spice is used to prevent the growth of pathogenic micro bodies [4]. Pharmacological properties of plant-centred therapeutic agents also termed as phytochemicals [5]. *Foeniculum vulgare* Mill., referred as Fennel a small, erect and aroma herb of the Apiaceae genus. Studies have recorded a variety of chemical components and different therapeutic impacts of this herb [6]. Fennel seeds tend to be used for their antimicrobial anti-inflammatory, antispasmodic functions [7].
Fennel plant and seeds are shown in fig. 1.

Geographical description
Plant profile
Synonyms: *F. officinale*; fenkel; *Anethum foeniculum*; capillaceum; sweet fennel; common fennel [8].

Common names: French: fenouli**; Spanish:** hinojo**; Italian:** finnochio**; Russian:** fynkhel; **Hindi**: saunf**; German**: fenchel**; Arabic**: shamar [8].

Table 1: Taxonomic classification [9]

Kingdom	Plantae
Subkingdom	Virideplantae
Superdivision	Embryophyta
Division	Tracheophyta
Subdivision	Spermatophytina
Class	Magnoliopsida
Order	Apiaels
Family	Apiaceae
Genus	Foeniculum Mill.
Species	*Foeniculum vulgare* Mill.

Fig 1.1: Fennel plant and seeds

Fennel was endemic to Mediterranean and European countries but is now broadly distributed in the world's tropical and temperate areas and therefore it is extensively grown. Fennel is a famous and very economical medicinal plant in China [10]. Fennel grows wild through naturalization and cultivation in the eastern, western and northern hemispheres, especially in Asia, Europe and North America [11]. Fennel grows throughout India, basically in the region of Gujarat, West Bengal, Haryana, Uttar Pradesh and Rajasthan.

Table 1.2: World production of Fennel

Country	Production (tonnes)
India	58,400
China	48,002
Bulgaria	36,500
Iran	32,771
Mexico	29,251
Syria	27,668
World	970,404

Table 1.3: India production of Fennel

State	Production	% Share production
Gujrat	96.77	74.81
Rajasthan	30.72	23.75
West Bengal	1.03	0.80
Uttar Pradesh	0.67	0.52
Haryana	0.17	0.13

Botanical description

Fennel plants with bulbous leaves and yellow flowers are green and white. It is double achene oval shaped, ribbed, which is bluish initially then brownish grey [12]. The crunchy bulb and the fennel plant seeds both have a mild, liquorice-like taste. But seed flowers are more active because of their essential oils. It is a strongly aromatic and spicy herb used in cooking, and is one of the key ingredients of absinthe, along with the similar-tasting anise. Fennel requires cool and dry climatic conditions for its better growth and yield. Dry and cool climatic condition will result in good yield and quality of seeds.

Table 2: Nutritional values of *Foeniculum vulgare* Mill. Reported in details

S. No.	Nutritional composition in fennel	Amount	References
1	Moisture content	8.04% 6.24±0.24%	[13] [10]
2	Ash content	12.87% 12.97±0.51%	[13] [10]
3	Crude fat	9.76±0.34% 10.71%	[10] [13]
4	Crude fibre	18.01% 18.21±0.73%	[13] [10]
5	Protein content	9.38±0.39%	[10]
6	Nitrogen free extract	43.44±1.82%	[10]
7	Carbohydrate	40.19%	[13]
8	Fatty acids	ω-3 fatty acids, ω-6 fatty acids and linoleic acid	[14]
9	Vitamin B_3	6.4 mg/kg	[15]
10	Vitamin C	8.7–340 mg/kg	[15]
11	Folates	270 mg/kg	[15]
12	K	849.45 mg/100g 4,241-5,851 mg/kg 852.45±33.25 mg/100 g	[13] [15] [10]
13	Ca	20,500–23,000µg/g 580.6±24.39mg/100 g 56-363 mg/kg 583.6 mg/100g	[16] [10] [15] [13]
14	Mg	1,310–3,460 µg/g 209.35mg/100g 82-389 mg/kg	[16] [13] [15]
15	Mn	209.35 mg/100g 211.35±7.40 mg/100 g 31–51 µg/g	[13] [10] [16]
16	Fe	1,140–1,900 µg/g 9.72±0.38 mg/100 g 6.33mg/100g	[16] [10] [13]

17	Na	77 to 512 mg/kg 16.21±0.65mg/100 g	[15] [10]
18	Zn	37–45 µg/g 2.89 mg/100g	[16] [13]
19	P	470 mg/100g	[13]

Phytochemical activities

Phytochemical are the compounds that produced by plants and these have biological activity. Fennel seed methanolic extract screened for existence of various phytochemicals are phenols, alkaloids, terpenoids, flavonoids, glycosides, tannins and saponins [17]. Total phenolic content were evaluated as Gallic acid equivalent (GAE) in water and ethanol extracts of *F. vulgare* seeds [18]. Trans-anethole, fenchone, estragole (methyl chavicol), and α-phellandrene (shown in fig. 2) are the main components have been identified in *F. vulgare* essential oil.

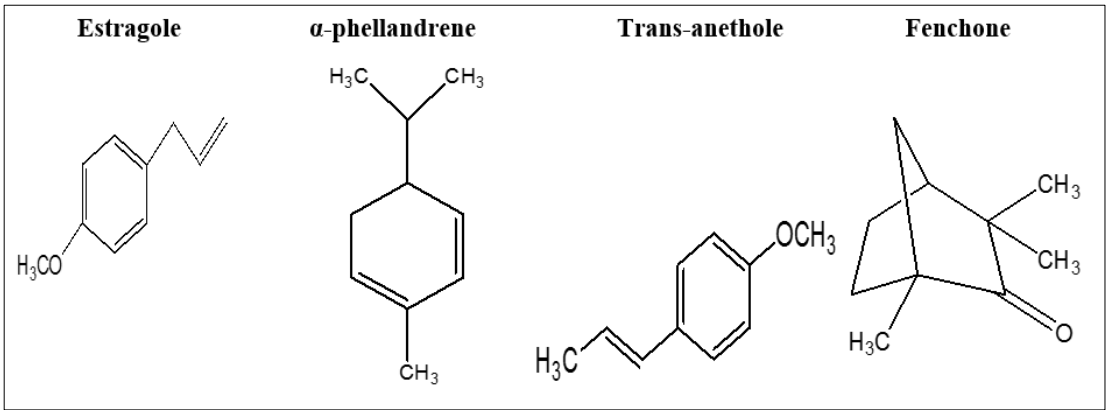

Fig 2: Structure of bioactive components isolated from *Foeniculum vulgare* [12]

The relative concentration of these compounds differs greatly depends on the fennel morphological state and origin [19]. Phenolic constituent included in *F. vulgare* is observed to be related to the mitigation of oxidative stress caused disorder such as cardiovascular diseases, inflammation and cancer. Phenols and phenolic glycosides are other categories of the phytochemicals included in *F. vulgare*. Such phenolic compounds have achieved significant attention from food scientists, dieticians and users for their role in public health [20]. Mostly naturally existing plant-based phytoconstituents are ascorbates, polyphenolics, carotenoids, terpenoids and tocopherols have been evaluated and used as appropriate chemotherapeutic drugs to cure numerous oxidative stress disorders that result in free radicals being accumulated. Results demonstrated that Fennel seed extracts contained significant amount of total phenol content (627.21–967.50 GAE, mg/100 g) and total flavonoid content (374.88–681.96 CE, mg/100 g) [4]. 3,8-Binaringenin and 3,4-dihydroxy-phenethylalchohol-6-o-caffeoyl-β-D-glucopyranoside are two phenolic constituents have been obtained from the wild herb fennel illustrated in fig. 3 [21].

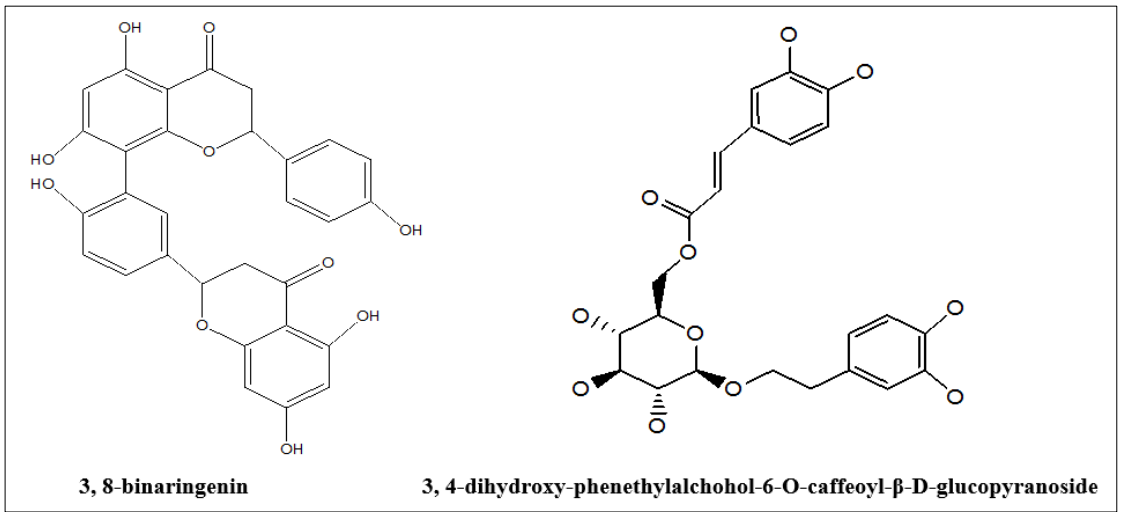

Fig 3: Structure of phenolic compounds isolated from *Foeniculum vulgare* [19]

The dendrogram study was administered to evaluate the genetic variability based on essential oil components of fennel genotypes. Results of this analysis informed significant variation (0.99-8.65%) in essential oil content. Trans-anethole (18.43–69.69%) was found to be key component, while estragole (methyl chavicol) 0.27–29.55% was second most vital component of fennel. Most of trans-anethole was recorded in the PI649464 genotype oil, whereas the highest concentration of estragole was shown in PI414189 genotype. NSL6409 genotype was found finer in case of phenolic quantities as compared with other genotypes [22].

Pharmacological activities

This review article aims to understand the different pharmacological activities of *Foeniculum vulgare.*

Antimicrobial activity

F. vulgare shows anti-microbial activity to a wide variety of microorganisms. *In vitro* assay for antibacterial activity of *F. vulgare* essential oil for *B. megaterium* and *E. coli* and 27 Pathogenic bacteria and two mycopathogenic species responsible for the growth of mushroom diseases [23]. The essential oil of Fennel demonstrates antibacterial efficacy against all isolates of *A. baumanni*. Susceptibilities of isolates were determined using a broth microdilution method. MIC and MBC of isolates to fennel essential oil were analyzed. The susceptibilities of isolates to different antibiotics were evaluated using the agar disc diffusion method. Fennel essential oil demonstrates an antibacterial activity against all isolates of *A. baumanni.* However more appropriate studies must be carried out to verify the possibility of using it to fight against bacterial infections in human [24]. The methanol extract of dried fennel seeds was determined antibacterial potential by calculating minimum inhibitory concentration, growth inhibition zone and cell damage against pathogenic bacteria: *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa and Bacillus pumilus* [25]. The fennel essential oil exhibited antibacterial potential *against Bacillus subtilis, Staphylococcus albus, Shigella dysenteriae, Salmonella typhimurium* and *Escherichia coli.* Among these bacteria *S. dysenteriae* was most susceptible to fennel essential oil and representing the lower MIC and MBC values of 0.125 and 0.25 mg/ml respectively [26]. Antibacterial activity of *F. vulgare* seeds evaluated against *Escherichia coli, Staphylococcus aureus, Listeria monocytogenes, Bacillus pumilus* and *Enteropathogenic E. coli* (EPEC). Fennel's extract exhibits maximum antibacterial activity against *Staphylococcus aureus* showing 20.00 mm of inhibition zone [27].

Antifungal activity

F. vulgare oil exercised varying potential of anti-fungal effects on *Alternaria alternata's* experimental mycelial growth. The fennel oil concentrations of 40 ppm represent inhibitory impact on mycelial growth of *A. Alterneria* on the other hand 10 ppm was unworkable [28]. *F.vulgare* plant essential oil derived a natural therapeutic impact against dermatophyte. Antifungal potential of fennel essential oil determined from variety of features, such as minimum fungicidal concentration, MIC, growth of mycelia, biomass and germination of spores. *Trichophyton rubrum* ATCC40051, *Trichophyton tonsurans* 10-0400 e.t.c. had effective antifungal activities [29].

Antioxidant activity

Lipid oxidation adversely affects on food degredation and quality of life. The antioxidant activity of water and ethanolic extract of *F. vulgare* seeds are determined. Strong antioxidant activity was seen in water and ethanol extract of *F. vulgare* seed. In the linoleic acid system, 100 µg of water and ethanol extracts exhibited 99.1% and 77.5% inhibition of peroxidation respectively, and greater than equivalent dose of α-tocopherol (36.1%) [18]. *F. Vulgare* essential oil and extracts displayed strong DPPH scavenging activity, showing IC_{50} 32.32 and 23.61-26.75 µg/ml and peroxidation inhibition 45.05 and 48.80-70.3 % respectively. 80% of the ethanol extracts have highest antioxidant activity. Result demonstrated that significant ($p<0.05$) variation in antioxidant activity of fennel essential oil and extracts [4]. IC_{50} represented the equivalent DPPH scavenging effect in methanol and aqueous seed extract of *F. vulgare* less than ascorbic acid at 30µg/ml. At 240µg/ml concentration, the methanol extract of fennel demonstrated the maximum OH- scavenging potential of 71.61%. Extract reduction power (FRAP activity) was 7-48 µm Fe (II)/g [30].

Antioxidant activity in olive oil at concentration of BHT (75 ppm), BHA (75 ppm) and Â 1:1 BHA to BHT ratio in which FSE antioxidant activity was greater than BHT (75 ppm), BHA (75 ppm) and BHT to BHA in 1:1 at 150 ppm. Finest antioxidant activity was exhibit at 150 ppm concentration [31]. Fennel essential oil have important antioxidants (IC_{50} values range in the DPPH is 11.83-36.90 mg/ml, in ABTS•+ is 7.65-20.13 mg /ml and EC_{50} values range in the reducing power assay is 3.65-15.24 mg/ml) and phytotoxic activity [32].

Anti-inflammatory activity

Anti-inflammatory drugs affect the central nervous system to block pain signalling to brain reduces inflammation. Oral administration (200 mg/kg) of *F. vulgare* fruit methanol extract demonstrated the inhibitory effect against acute and subacute inflammatory diseases. It also significantly increased plasma superoxide dismutase (SOD) and catalase activity as well as high density lipoprotein-cholesterol levels. The malondialdehyde MDA (as an indicator of lipid peroxidation) level considerably decreased in methanol extract of *F.vulgare* relative to control group ($P<0.05$). Results demonstrated that *F. vulgare* fruit methanol extract is used in relieving inflammation. [33]. *F. vulgare* essential oil possess an anti-inflammatory property as similar to etodolac in 0.050 and 0.200 ml/kg doses in the carrageenan-induced rat paw edema model [34]. Anti-inflammatory function of *F. vulgare* has a high potential for 5-lipoxygenase inhibitions [35].

Anticarcinogenic activity

Cancer is a gene disorder disease in which abnormal cell division and damage body tissue. *F. vulgare* has estrogenic, lactagogue, diuretic, immune booster property that makes anticarcinogenic study necessary. In well known genetic model mutant mice and Drosphila, the possible antimutagenic and cancer chemopreventive effects of hot water crude extract of *F.vulgare* seed were analyzed. Before and after treatment with 5 or 0.5mg/kg body weight or in combination with fennel crude extract as (24h) acute and subacute (5 consecutive days) doses, Mitomycin C (MMC) was administered to mice as a positive control alone, respectively. Fennel extract alleviated the toxic effects of MMC [36]. *F. vulgare* methanol extract may have significant potential for anticancer against breast cancer cell line (Hepg-2) and liver cancer cell line (MCF-7). The mean±standard deviation of 50% inhibitory concentrations were 50±0.03 µg/ml for the MCF7 breast cancer cell line and 48±022 µg/ml for the Hepg-2 liver cancer cell line [37]. The cytotoxicity of fennel plant extract was determined using sulphodiamine-B assay (SRB assay). SRB assay results represent that *F.vulgare* extracts were inhibited the anticarcinogenic activity with IC50 value for MCF-7 (human breast cancer cell line) is 24.5±0.08 while for HePG-2 (human hepatocellular carcinoma cell line) is 28.7±0.04 and for HCT 116 (colon carcinoma cell line) is 59.8±0.09µg/ml [38].

Antidiabetic activity

Diabetes mellitus is a chronic disease due to inaccurate insulin action associated with an abnormal high blood glucose concentration. The optimal extraction conditions with optimum value of angiotensin converting enzyme (ACE) inhibition activity was found for 8 hrs (50.8%) in methanol extract at 37˚C. Via optimization method, inhibition levels of α-amylase and α-glucosidase in methanol extract were observed up to 8 hrs with 82.43% and 82.26% data value. It is possible to infer that phenolic constituents extracted from *F. vulgare* have potent activity in antidiabetic but gentle activity in antihypertensive [39]. Approximate *F. vulgare* extract on lipid profile, lipid peroxidation and amino transferase enzyme activity in adult male rats induced by streptozocin. Execution of *F. vulgare* extract to diabetic rats reduced total cholesterol, blood glucose, triglycerides, HDL, LDL, MDA, ALT, AST and increased HDL proportion [40]. Three specific n-butanol, ethyl acetate and benzene extract of *F. vulgare* seeds screened with α-amylase and α-glucosidase inhibition assay for their antidiabetic activity *in vitro*. The results demonstrated that in comparison with the standard acarbose values, these three extracts contained high α-glucosidase inhibitory effect than α-amylase [41].

A remarkable bring down was noted in blood glucose level after 2 hours of fennel administration in diabetic patients which signified a good short term anti-diabetic activity. Before fennel administration, the mean values exhibited as 313.5±108.69 and 279.33±96.24 for patients having 100 mg per kg body weight and having 50 mg per kg body weight. After 2 hours, the blood glucose levels showed mean values of 262±88.69 for individuals having 100mg per kg body weight and 246.5±91.93 for individuals having 50mg per kg of body weight. And the mean values for control group showed as 272.16±89.84 before and 330.5±91.87 after 2 hours [42].

Bronchodilatory effect

The relaxant effect of *F. vulgare* on isolated tracheal guinea pig chains has demonstrated in the previous research. The present research assessed the inhibitory effect of this plant on the contracted tracheal chains of guinea pigs to analysis the mechanism responsible for this effect. The relaxant effects of aqueous, ethanol extracts and essential oil of *F. vulgare* have been compared with negative control (saline for aqueous extract and essential oil and ethanol for ethanol extract) and positive control (diltiazem) using isolated tracheal chains of guinea pig precontracted by 10 µm methacholine (group 1) and 60 mm KCl (group 2, n=7 for each group). In Group 1, experiments diltiazem, ethanol extract, and essential oil of *F. vulgare* showed a significant relaxant effect on methacholine induced contraction of tracheal chains as compare to negative controls ($p<0.05$ to $p<0.001$). Furthermore, the effect of ethanol extract was significantly higher than diltiazem ($p<0.001$). Only diltiazem showed a significant relaxant effect on KCl induced contraction of tracheal chains ($p<0.001$) in group 2 experiments. The relaxant effects of ethanol extracts and essential oil obtained in group 2 experiment were significantly lesser than group 1 experiment ($p<0.05$ to $p<0.001$). These results verify the bronchodilatory effects of *F. vulgare* ethanol extracts and its essential oil [43].

Gastrointestinal effect

The study were undertaken to evaluate the anti-ulcerogenic effects of *F. vulgare* aqueous extracts (FVE) on ethanol-induced gastric lesions in rats. 75, 150 and 300 mg/kg doses of FVE were administered by gavage and famotidine was used at 20 mg/kg dose. All the rats were given 1 ml of ethanol (80%) after 60 min by gavage. All the groups were sacrificed after one hour of ethanol administered and the gastric ulcer index was measured. It was reported that FVE pretreatment significantly reduced ethanol-induced gastric damage. This FVE impact was higher and statistically important in the 300 mg/kg group as compared with control (4.18±2.81 vs 13.15± 4.08, $P<0.001$). Pretreatment with FVE significantly decreased the MDA levels, while enhanced the levels of GSH, nitrite, nitrate, ascorbic acid, retinol, and β-carotene [44]. Recent research was conducted to assess the efficacy of heated fennel therapy in accelerating the recovery of gastrointestinal function. This surgeon-blinded, prospective randomised controlled trial included 381 patients with hepatobiliary, pancreatic, and gastric tumours were divided into 2 groups. Patients in the experimental groups received heated fennel therapy and those in the control groups received heated rice husk therapy. In the heated fennel therapy group, the time to first flatus and first defecation and the fasting time were significantly less than those in control groups ($P<0.05$ each); and in the experimental groups abdominal distension was also relieved ($P<0.001$). Heated fennel therapy had no significant beneficial effects on inflammatory markers but enhanced serum albumin (ALB) levels of patients at postop day 9 ($P<0.001$) [45].

Estrogenic property

Foeniculum vulgare seed is used for polycystic ovarian syndrome (PCOS) treatment with phytoestrogen compound present in it. The renoprotective action of *F. vulgare* aqueous extract (AEF) in female rats with PCOS is examined. Forty female rats were divided into five groups. The first group worked as control, was injected with an equal volume (0.2 ml) of normal saline, and provided regular diet. Non-polycystic ovary syndrome (PCOS) rats in the second groups were treated with intragastric administration of *F. vulgare's* aqueous extract (150 mg/kg b.w.). The intraperitoneal injection of estradiolvalerate (4 mg in 0.2 ml of sesame oil) was injected in the third groups. The fourth groups were treated with the same route using EV and AEF (150 mg/kg b.w.). EV and AEF (100 mg/kg b.w.) were administered to the fifth group. After 4 weeks of analysis, all the rats were sacrificed, their kidney's tissues were processed for light microscopy, and some biochemical parameters of serum were calculated. The mean values of blood urea nitrogen in PCOS rats treated with low dose of AEF and EV and non-treated, were significantly ($p<0.05$) increased as compared to non-PCOS and PCOS rats treated with higher dose of AEF. Moreover histopathological improvements in kidney samples were comparable in PCOS rats with respect to the treated groups with AEF [46].

Hepatoprotective activity

Liver is a vital organ which detoxifies various metabolites and secret out xenobiotics from the body. Hepatoprotection is a chemical substance capable of preventing liver damage. Hepatoprotective property of *F. vulgare* essential oil was examined in rats using a carbon tetrachloride-induced liver fibrosis model. The hepatotoxicity generated by chronic carbon tetrachloride administration was found to be inhibited by the *F. vulgare* essential oil with confirmation of reduced levels of serum aspartate aminotransferase, alanine aminotransferase, bilirubin and alkaline phosphatase. Histopathological results also conclude that *F. Vulgare*

essential oil prohibits the development of chronic liver damage [47]. The study was undertaken to find out the chlorpyrifos (CPF) hepatotoxicity and to evaluate the hepatoprotective action of *F. vulgare* essential oil (FEO) in male rats. Two doses of oil (0.3 and 0.5 ml/kg b.wt.), with or without CPF (1/10 LD50), were given orally for 28 days. Administration of CPF caused rise in hepatic cytochrome P450, lipid peroxidation (LPO) and change in various serum biomarkers (e.g. alanine aminotransferase (ALT), γ-glutamyl transferase (GGT), acid phosphatase (AcP), cholinesterase (ChE), albumin and total protein). Compared to the control values, body weight reduced, while relative liver weight is increased. Even CPF-group demonstrated degenerative alteration, mononuclear cell infiltration and focal necrotic cells in the liver [48].

Effect of hepatoprotective on two cultivars of *F. vulgare* methanolic extract is examined. A total of 100, 200 mg/kg BW fennel seed extracts and 100, 200 mg/kg of silymarin (standard) were administered on dissimilar groups of rats for CCl_4 administration histopathology testing. It has been found that the hepatotoxicity produced by CCl_4 administration significantly inhibits $p \leq 0.05$ (dose dependent), using both 100 and 200 mg/kg BW of FV methanol extract could inhibit CCl_4 induced acute hepatotoxicity by decreasing the levels of serum aspartate amino transferase (AST), alkaline phosphatase (ALP), alanine amino transferase (ALT) and bilirubin. It could be assumed that silymarin at the two doses is appropriate treatment of liver intoxicated with CCl_4, followed by F1 and F2 [49].

Hypolipidemic activity

F. Vulgare demonstrated hypolipidemic activity and therefore can be used for prevention of cardiovascular diseases. It is strongly suggested that fennel should be used in diets for patients with hyperlipidemia or those with a family history of hyperlipidemia. Hyperlipidemia (mainly increased level of triglycerides (TG), total cholesterol (TC), and low-density lipoprotein (LDL) cholesterol with a decrease in high-density lipoprotein (HDL)-cholesterol) is the predictor of coronary artery disease (CAD). Hyperlipidemia is a significant risk factor in development and progression of atherosclerotic impasse [50]. Following 24-hour therapy, triglycerides, total plasma cholesterol, apolipoprotein B and LDL-cholesterol reduced by 50%, 35%, 60% and 50% respectively, and enhanced in apolipoprotein A-I and HDL-cholesterol by 52% and 56% respectively. It effectively decreases the deposition of triglycerides in the form of fatty liver and facilitates the blood motion in coronary arteries by blocking deposition of lipid in the light of coronary arteries by reducing serum and liver lipids [51].

Antispasmodic activity

Primary dysmenorrhoea is painful menstrual cramps without any evident diagnosis to account for them and it appears in up to 50% of menstruating women and causes significant disturbance in quality of life and absenteeism. [52]. The usual treatment of primary dysmenorrhoea is therapeutic treatment, such as mefenamic acid [non-steroidal anti-inflammatory drugs (NSAIDs)] and oral contraceptive pills, both of them functioned by reducing myometrial activity. Fennel may be helpful in treatment of primary dysmenorrhoea as it contains antispasmodic and anethole agents. The purpose of this research was to examine the consequences of oral fennel drop on the treatment of primary dysmenorrhoea. Sixty college students suffering from primary dysmenorrhoea were randomly divided into two groups and carried out for two cycles. Using SPSS version 16, statistical analysis was performed. $P<0.05$ was considered to be statistically significant. Parametric and non-parametric tests were used. Comparison of pain intensity in the two groups demonstrated that there was no significant difference in pain relief between the two groups. Comparison of bleeding severity in the study group before and after the treatment was demonstrated from first day to the fifth day (PV on the first day, second day, third day, fourth day, and fifth day 0.948, 0.330, 0.508, 0.583, 0.890, respectively). It appears that fennel would be effective in reducing the severity of dysmenorrhoea [53].

Antinociceptive activity

The purpose was to examine antinociceptive activity of some components of *Foeniculum vulgare* Mill., commonly referred as fennel. Trans-anethole, α-pinene, α-copaene, limonene and fenchone were examined for analgesic activity in mice using tail-flick tests which is commonly employed as pain model. The medications were injected intravenously in the doses of 0.05, 0.1 and 0.2 ml/kg. In the tail-flick test, fenchone and α-pinene caused substantial reduction in the nociceptive threshold. Other compounds examined did not show analgesic activity [54].

Antihirsutism activity

Foeniculum vulgare is a herb used as an estrogenic agent. The study were undertaken to investigate the therapeutic effects of idiopathic hirsutism to topical fennel extract. In a double blind trial, 38 patients were treated with creams containing 1%, 2% fennel extract and placebo. Effectiveness of treatment with the cream containing 2% fennel is higher than the 1% fennel and these two were more powerful than placebo. Patients that receiving creams containing 1%, 2% and 0% (placebo) show mean values of hair diameter reduction were 7.8%, 18.3% and -0.5% respectively. [55]. A randomised, double-blind, placebo-controlled clinical study was conducted in Sari, Iran from 2009 to 2011. 44 women with mild to moderate idiopathic hirsutism were randomly categorised into case and control groups, each group included 22 cases. The case group received fennel gel 3% and control group received placebo. The effect of fennel gel 3% was described as reduction in thickness of facial hair in micrometer by microscope as compared to placebo. Measurements were conducted at zero and 24 weeks after treatment. Before intervention, the hair thickness between two groups was identical. The hair thickness reduced from 97.9±31.5 to 75.6±26.7 micron in patients accepting fennel gel after 24 weeks ($P<0.001$). The study reflected that Fennel gel 3% is effective in reducing hair thickness in females with mild to moderate idiopathic hirsutism [56].

Antithrombotic activity

In vivo, *F. vulgare* essential oil and anethole administered orally in mice through a sbacute treatment (30 mg/kg per day for 5 days) to demonstrate antithrombotic potential preventing the paralysis induced by collagen-epinephrine intravenous injection (70% and 83% protection, respectively). At the antithrombotic dosage they were free from prohemorrhagic side effects, in contrast with acetylsalicylic acid used as the reference drug. In addition, *F. vulgare* essential oil and anethole (100 mg/kg oral administration) conferred protection towards ethanol induced gastric lesions in the rats. These findings demonstrated that *F. vulgare* essential oil and its key component anethole exhibits a safe antithrombotic activity

due to their large range of anti-platelet activity, clot destabilizing effect and vasorelaxant effect [57].

Antidepressant activity

To examine the effect of methanolic extract of *F. vulgare* fruits on depression using force swim test in rats, potentiation of nor epinephrine toxicity in mice and haloperidol induce catalepsy in mice. The extract of *F. vulgare* (250 and 500 mg/kg) was given orally to the rats used in FST and 500mg/kg was administered in HIC and same dose administered in NE toxicity in mice. 250 mg/kg and 500 mg/kg dose of extract significantly (p<0.001) reduced the stability time in rats but the dose of 500 mg/kg demonstrated more powerful impact than imipramine (30 mg/kg). So this dose was used for HIC and NE toxicity in mice. But it has been noted in NE toxicity model that MEFV is not an appropriate adrenergic component. It was noted that a significant (P<0.001) reduction in period of catalepsy in the MEFV treated group and Fluoxetine group as compared to the haloperidol treated group. Mice were sacrificed on seventh day and TBARS, glutathione, and nitrite activities were determined in HIC. Monoamine oxidase inhibiting effect and antioxidant effect of *F. vulgare* can contribute suitably to antidepressant-like activity. [58]

Conclusion

Foeniculum vulgare is a plant that has a broad range of chemical components and has several pharmacological actions. The bioactive fennel molecules can be used in the production of pharma drugs. The production of novel drugs from *Foeniculum vulgare* is highly promised to cure human diseases because of its efficacy and safety measures. As this plant has highly medicinal property therefore, it is highly recommended plant for researchers to developed therapeutic drugs for treatment of many diseases. Phytochemical studies of this plant acknowledge the various volatile components flavanoid, glycosides, and phenols having therapeutic effect. Fennels are enriched with nutrients and used in food processing. Further studies should be focussed on the development of pharmaceutical drugs from bioactive chemical constituents in *Foeniculum vulgare* seeds extract and oil which involve in pharmacological actions.

References

1. Goswami N, Chatterjee S. Assessment of free radical scavenging potential and oxidative DNA damage preventive activity of *Trachyspermum ammi* L. (carom) and *Foeniculum vulgare* Mill. (fennel) seed extracts. Biomed Res Int 2014.
2. Mata AT, Proença C, Ferreira AR, Serralheiro MLM, Nogueira JMF, Araújo MEM. Antioxidant and antiacetylcholinesterase activities of five plants used as Portuguese food spices. Food Chem 2007;103(3):778-786.
3. Gupta M. Pharmacological properties and traditional therapeutic uses of important Indian spices: A review. Int J Food Prop 2010;13(5):1092-1116.
4. Anwar F, Ali M, Hussain AI, Shahid M. Antioxidant and antimicrobial activities of essential oil and extracts of fennel (*Foeniculum vulgare* Mill.) seeds from Pakistan. Flavour Fragr J 2009;24(4):170-176.
5. Mahomodally MF. Traditional medicine in Africa: An appraisal of ten potent African medicinal plants. Evid Based Complement Alternat Med 2013;13:1-14.
6. Khan and Musharaf. *Foeniculum vulgare* Mill. A Medicinal Herb. Med Plant Res 2014;4(6):46-54.
7. Grover S, Malik CP, Hora A, Kushwaha HB. Botany, cultivation, chemical constituents and genetic diversity in fennel (*Foeniculum vulgare* Mill): a review. Int J Life Sci 2013;2(2):128-139.
8. Charles DJ. Antioxidant properties of spices, herbs and other sources. Springer Science & Business Media 2012.
9. ITIS, *Foeniculum vulgare* https://www.itis.gov/servlet/SingleRpt/SingleRpt? search_topic =TSN&search_value=29509#null
10. Bukhari H, Shehzad A, Saeed K, Sadiq BM, Tanveer S, Iftikhar T. Compositional profiling of fennel seed. Pak J Food Sci 2014;24(3):132-36.
11. Krishnamurthy HK. Medicinal plants: Madhurikā, saunf or fennel (*Foeniculum vulgare*, Gaertn). J New Approaches Med Health 2011;19(1):1-4.
12. Rizvi MA, Saeed A, Zubairy HN. Medicinal Plants. Karachi, Pakistan: Hamdard Institute of Adv Studies Res 2007.
13. Saber JI, Eshra DH. Using Fennel and Its Oil as A Preservative and Functional Food to Produce Food and Drink Products to be used to Alleviate Cough Symptoms. Alexandria Sci Exchange J 2019;40:406-414.
14. Barros L, Carvalho AM, Ferreira IC. The nutritional composition of fennel (*Foeniculum vulgare*): Shoots, leaves, stems and inflorescences. LWT-Food Sci and Tech 2010;43(5):814-818.
15. Koudela M, Petříková K. Nutritional compositions and yield of sweet fennel cultivars-*Foeniculum vulgare* Mill. ssp. vulgare var. azoricum (Mill.) Thell. Hort Sci 2008;35(1):1-6.
16. Endalamaw FD, Chandravanshi BS. Levels of major and trace elements in fennel (*Foeniculum vulgare* Mill.) fruits cultivated in Ethiopia. Springer Plus 2015;4(1):5.
17. Khandelwal KR. Preliminary phytochemicals screening, Practical Pharmacognosy Techniques and Experiments 2001;8:149-156.
18. Oktay M, Gülçin İ, Küfrevioğlu Öİ. Determination of *in vitro* antioxidant activity of fennel (*Foeniculum vulgare*) seed extracts. LWT-Food Sci Technol 2003;36(2):263-271.
19. Díaz-Maroto MC, Pérez-Coello MS, Esteban J, Sanz J. Comparison of the volatile composition of wild fennel samples (*Foeniculum vulgare* Mill.) from Central Spain. J Agric Food Chem 2006;54(18):6814-6818.
20. De Marino S, Gala F, Borbone N, Zollo F, Vitalini S, Visioli F *et al*. Phenolic glycosides from *Foeniculum vulgare* fruit and evaluation of antioxidative activity. Phytochemistry 2007;68(13):1805-1812.
21. Ghanem MT, Radwan HM, Mahdy ESM, Elkholy YM, Hassanein HD, Shahat AA. Phenolic compounds from *Foeniculum vulgare* (Subsp. Piperitum) (Apiaceae) herb and evaluation of hepatoprotective antioxidant activity. Phcog Res 2012;4(2):104.
22. Yaldiz G, Camlica M. Variation in the fruit phytochemical and mineral composition, and phenolic content and antioxidant activity of the fruit extracts of different fennel (*Foeniculum vulgare* L.) genotypes. Ind Crops Prod 2019;142:111852.
23. Lo Cantore P, Iacobellis NS, De Marco A, Capasso F, Senatore F. Antibacterial activity of *Coriandrum sativum* L. and *Foeniculum vulgare* Miller var. vulgare (Miller) essential oils. J Agric Food Chem 2004;52(26):7862-6.

24. Hosseini Jazani N, Zartoshti M, Babazadeh H, Ali Daiee N, Zarrin S, Hosseini S. Antibacterial effects of Iranian fennel essential oil on isolates of Acinetobacter baumannii. Pak J Bio Sci 2009;12(9):738-41.
25. Dua A, Garg G, Mahajan R. Polyphenols, flavonoids and antimicrobial properties of methanolic extract of fennel (*Foeniculum vulgare* Miller). Eur J Exp Biol 2013;3(4):203-208.
26. Diao WR, Hu QP, Zhang H, Xu JG. Chemical composition, antibacterial activity and mechanism of action of essential oil from seeds of fennel (*Foeniculum vulgare* Mill.). Food Control 2014;35(1):109-116.
27. Bano S, Ahmad N, Sharma AK. Phytochemical investigation and evaluation of anti-microbial and anti-oxidant activity of *Foeniculum vulgare* (fennel). Int J Pharma Sci Res 2016;7(7):310-314.
28. Özcan MM, Chalchat JC, Arslan D, Ateş A, Ünver A. Comparative essential oil composition and antifungal effect of bitter fennel (*Foeniculum vulgare* ssp. piperitum) fruit oils obtained during different vegetation. J Med Food 2006;9(4):552-561.
29. Zeng H, Chen X, Liang J. *In vitro* antifungal activity and mechanism of essential oil from fennel (*Foeniculum vulgare* L.) on dermatophyte species. J Med Microbiol 2015;64(1):93-103.
30. Chatterjee S, Goswami N, Bhatnagar P. Estimation of Phenolic Components and *in vitro* Antioxidant Activity of Fennel (*Foeniculum vulgare*) and Ajwain (*Trachyspermum ammi*) seeds. Adv Biores 2012;3(2):109-18.
31. Chang S, Bassiri A, Jalali H. Evaluation of antioxidant activity of fennel (*Foeniculum vulgare*) seed extract on oxidative stability of olive oil. J Chem Health Risks 2013, 3(2).
32. Sabzi Nojadeh M, Pouresmaeil M, Younessi-Hamzekhanlu M, Venditti A. Phytochemical profile of fennel essential oils and possible applications for natural antioxidant and controlling *Convolvulus arvensis* L. Nat Prod Res 2020, 1-5.
33. Choi EM, Hwang JK. Anti-inflammatory, analgesic and antioxidant activities of the fruit of *Foeniculum vulgare*. Fitoterapia 2004;75(6):557-565.
34. Özbek H. The anti-inflammatory activity of the *Foeniculum vulgare* L. essential oil and investigation of its median lethal dose in rats and mice. Int J Pharmacol 2005;1(4):329-331.
35. Albano SM, Miguel MG. Biological activities of extracts of plants grown in Portugal. Ind Crops Prod 2011;33(2):338-343.
36. Ebeed NM, Abdou HS, Booles HF, Salah SH, Ahmed ES, Fahmy KH. Antimutagenic and chemoprevention potentialities of sweet fennel (*Foeniculum vulgare* Mill.) hot water crude extract. J Am Sci 2010;6:831-842.
37. Mohamad RH, El-Bastawesy AM, Abdel-Monem MG, Noor AM, Al-Mehdar HAR, Sharawy SM *et al*. Antioxidant and anticarcinogenic effects of methanolic extract and volatile oil of fennel seeds (*Foeniculum vulgare*). J Med Food 2011;14(9):986-1001.
38. Zaahkouk SA, Aboul-Ela EI, Ramadan MA, Bakry S, Mhany AB. Anti-carcinogenic activity of Methanolic Extract of Fennel Seeds (*Foeniculum vulgare*) against breast, colon, and liver cancer cells. Int J 2015;3(5):1525-1537.
39. Abu-Zaiton A, Alu'datt M, Wafa M. Evaluating the effect of *Foeniculum vulgare* extract on enzymes related with blood pressure and diabetes (*in vitro* study). Int J Chem Engg Biol Sci 2015;2(2):77-80.
40. Parsaeyan N. The effect of *Foeniculum vulgare* (fennel) extract on lipid profile, lipid peroxidation and liver enzymes of diabetic rat. Iran J Diabetes Obesity 2016;8(1):24-29.
41. Godavari A, Amutha K, Moorthi NM. *In-vitro* hypoglycemic effect of *Foeniculum vulgare* Mill. Seeds on the carbohydrate hydrolysing enzymes, alpha-amylase and alpha-glucosidase. Int J Pharm Sci Res 2018;9:4441-4445.
42. Zulifqar S. Influence of *Foeniculum vulgare* Mill in the Management of Hyperglycemia. Int J Innovative Sci Res Tech 2019;4(5):1117-22.
43. Boskabady MH, Khatami A, Nazari A. Possible mechanism (s) for relaxant effects of *Foeniculum vulgare* on guinea pig tracheal chains. Die Pharmazie-An Int J Pharm Sci 2004;59(7):561-564.
44. Birdane FM, Cemek M, Birdane YO, Gülçin İ, Büyükokuroğlu ME. Beneficial effects of *Foeniculum vulgare* on ethanol-induced acute gastric mucosal injury in rats. World J Gastroenterol: WJG 2007;13(4):607.
45. Chen B, He Y, Xiao Y, Guo D, Liu P, He Y *et al*. Heated fennel therapy promotes the recovery of gastrointestinal function in patients after complex abdominal surgery: A single-center prospective randomized controlled trial in China. Surgery 2020.
46. Sadrefozalayi S, Farokhi F. Effect of the aqueous extract of *Foeniculum vulgare* (fennel) on the kidney in experimental PCOS female rats. Avicenna J Phytomed 2014;4(2):110.
47. Özbek H, Ugras S, Bayram I, Uygan I, Erdogan E, Öztürk A *et al*. Hepatoprotective effect of *Foeniculum vulgare* essential oil: A carbon-tetrachloride induced liver fibrosis model in rats. Scand J Lab Anim Sci 2004;31(1):9-17.
48. Mansour SA, Heikal TM, Refaie AA, Mossa AH. Antihepatotoxic activity of fennel (*Foeniculum vulgare* Mill.) essential oil against chlorpyrifos-induced liver injury in rats. Glob J Environ Sci Technol 2011, 1(10).
49. El Baz FK, Salama ZA, Abdel Baky HH, Gaafar AA. Hepatoprotective effect of sweet Fennel (*Foenculum vulgare* L.) methanol extract against carbon tetrachloride induced liver injury in rats. Int J Pharm Sci Rev Res 2014;25(2):194-201.
50. Helal EG, Eid FA, El-Wahsh AM, Ahmed D. Effect of fennel (*Foeniculum vulgare*) on hyperlipidemic rats. Egypt J Hosp Med 2011;43(1):212-225.
51. Oulmouden F, Ghalim N, El Morhit M, Benomar H, Daoudi EM, Amrani S. Hypolipidemic and anti-atherogenic effect of methanol extract of fennel (*Foeniculum vulgare*) in hypercholesterolemic mice. Int J Sci Knowl 2014;3(1):42-52.
52. Dawood MY. Primary dysmenorrhea: advances in pathogenesis and management. Obstet Gynecol 2006;108(2):428-441.
53. Bokaie M, Farajkhoda T, Enjezab B, Khoshbin A, Mojgan KZ. Oral fennel (*Foeniculum vulgare*) drop effect on primary dysmenorrhea: effectiveness of herbal drug. Iran J Nurs Midwifery Res 2013;18(2):128.
54. Him A, Ozbek H, Turel I, Oner AC. Antinociceptive activity of alpha-pinene and fenchone. Pharmacologyonline 2008;3:363-369.
55. Javidnia K, Dastgheib L, Samani SM, Nasiri A. Antihirsutism activity of fennel (fruits of *Foeniculum*

vulgare) extract-a double-blind placebo controlled study. Phytomedicine 2003;10(6-7):455-458.
56. Akha O, Rabiei K, Kashi Z, Bahar A, Zaeif-Khorasani E, Kosaryan M *et al.* The effect of fennel (*Foeniculum vulgare*) gel 3% in decreasing hair thickness in idiopathic mild to moderate hirsutism, A randomized placebo controlled clinical trial. Caspian J Intern Med 2014;5(1):26.
57. Tognolini M, Ballabeni V, Bertoni S, Bruni R, Impicciatore M, Barocelli E. Protective effect of *Foeniculum vulgare* essential oil and anethole in an experimental model of thrombosis. Pharmacol Res 2007;56(3):254-260.
58. Singh JN, Sunil K, Rana AC. Antidepressant activity of methanolic extract of *Foeniculum vulgare* (fennel) fruits in experimental animal models. J Appl Pharm Sci 2013;3(9):65-70.