IOSR Journal Of Pharmacy *www.iosrphr.org*
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 6, Issue 6 Version. 2 (June 2016), PP. 46-65

The pharmacological activities of *Cuminum cyminum* - A review

Prof Dr Ali Esmail Al-Snafi
Department of Pharmacology, College of Medicine, Thi qar University, Nasiriyah, P O Box 42, Iraq .

Abstract: Phytochemical analysis showed that *Cuminum cyminum* contained: alkaloid , coumarin, anthraquinone, flavonoid, glycoside, protein, resin, saponin, tannin and steroid. The previous pharmacological studies revealed that *Cuminum cyminum* exerted antimicrobial, insecticidal, anti-inflammatory, analgesic, antioxidant, anticancer, antidiabetic, antiplatelet aggregation, hypotensive, bronchodilatory, immunological, contraceptive, anti-amyloidogenic, anti-osteoporotic, aldose reductase , alpha-glucosidase and tyrosinase inhibitory effects, protective and central nervous effects. This review highlights the chemical constituents and pharmacological effects of *Cuminum cyminum.*

Keywords: *constituents, pharmacology, Cuminum cyminum.*

I. INTRODUCTION

The World Health Organization (WHO) estimates that 4 billion people, 80 percent of the world population, presently use herbal medicine for some aspect of primary health care[(1)]. Plant showed wide range of pharmacological activities including antimicrobial, antioxidant, anticancer, hypolipidemic, cardiovascular, central nervous, respiratory, immunological, anti-inflammatory, analgesic antipyretic and many other pharmacological effects[(2-70).]

Phytochemical analysis showed that *Cuminum cyminum* contained: alkaloid , coumarin, anthraquinone, flavonoid, glycoside, protein, resin, saponin, tannin and steroid. The previous pharmacological studies revealed that *Cuminum cyminum* exerted antimicrobial, insecticidal, anti-inflammatory, analgesic, antioxidant, anticancer, antidiabetic, antiplatelet aggregation, hypotensive, bronchodilatory, immunological, contraceptive, anti-amyloidogenic, anti-osteoporotic, aldose reductase , alpha-glucosidase and tyrosinase inhibitory effects, protective and central nervous effects. This review highlights the chemical constituents and pharmacological effects of *Cuminum cyminum.*

II. PLANT PROFILE

Synonyms:

Cuminia cyminum J. F. Gmel., *Cuminum aegyptiacum* Mérat ex DC., *Cuminum hispanicum* Mérat ex DC., *Cuminum odorum* Salisb., *Cuminum sativum* J. Sm., *Cyminon longeinvolucellatum* St.-Lag[(71)].

Taxonomic classification:

Kingdom: Plantae; **Subkingdom**: Viridiplantae; **Infrakingdom**: Streptophyta; **Superdivision**: Embryophyta; **Division**: Tracheophyta; **Subdivision**: Spermatophytina; **Class:** Magnoliopsida; **Superorder**: Asteranae; **Order**: Apiales; **Family**: Apiaceae; **Genus**: Cuminum; **Species**: *Cuminum cyminum*[(72)].

Nomenclature and Common names:

The word cumin was derived from the Latin cuminum, which itself was derived from Greek (kyminon)[(73)]. The common names of the plant were**: Arabic**: Kamoun, Kamun; **Chinese**: Ou shi luo, Ma qin (Ma ch'in), Xian hao, Xiang han qin, Zi ran.**; English**: Cumin, Roman caraway; **French**: Cumin, Cumin de Malte, Cumin blanc, Cumin du Maroc, Faux anis; **German**: Kreuzkümmel, Römischer Kümmel, Weißer Kreuzkümmel; **Greek**: Kimino, Kiminon; **India**: Jiiraa (Jeera), Zeera (zira, ziira), afed ziiraa (Safed zira), Safed jiiraa (Safaid jeera); **Italian**: Cumino; **Japanese**: Hime unikyoo, Kumin; **Portuguese**: Cominho; **Russian:** Kmin, Kmin rimskii, Kmin tminovyi (Kmin tminovyj); **Spanish**: Comino; **Swedish**: Spiskummin[(74)].

III. DISTRIBUTION

Cumin was native to Egypt and has been cultivated in the Middle East, India, China and Mediterranean countries for millennia. The plant possibly originated from the Mediterranean area, perhaps Egypt and Syria. Nowadays it cultivated extensively in Turkey, India, China, Iraq, Libya, and Palestine. In the past, the largest cumin exporter to the United States was Iran. However, currently Turkey, India and China have provided alternatives. Now, the major production of cumin was came from India (states of Rajasthan and Gujarat)[(75-77)].

Description

The plant is a delicate, glabrous annual 10 to 50 cm high. The stem is bifurcated at the base and glabrous. The leaves are glabrous and finely pinnatifid with oblong-linear tips, of which the lower are mostly doubly trifoliate.

The flowers are in umbels radiating in groups of 3 to 5. The petals are white or red, oblong and deeply bordered with a long indented tip. The involucral bracts are long and simple. The style is short and turned outward at the end. The ovary is inferior and 3-Iocular. The fruit is a schizocarp, about 6 mm long and 1.5 mm wide and crowned with awl-shaped calyx tips. The mericarp is almost round in transverse section, with 5 thread-like, bristly main ribs and bristly secondary ribs[78].

Traditional uses:

In traditional medicine, cumin was used to treat hoarseness, jaundice, dyspepsia and diarrhoea. Its seeds were used for stomachic, diuretic, carminative, stimulant, astringent and abortifacient properties[79-80]. The oil of cumin was used in perfumery and as a seasoning in curry powders, soups, stews, sausages, cheeses, pickles, meats and chutneys[81]**.** In America, Africa and India the drug is used as an abortive and as an emmenagogue. In Indonesia, it was used in cases of bloody diarrhea and headache (paste is applied to the forehead). It was also taken orally for rheumatic ailments. In India, cumin was used as an abortifacient, for kidney and bladder stones, chronic diarrhea, leprosy and eye disease[78]. In Unani system of medicine, the fruits of *Cuminum cyminum* were used as an astringent, carminative, emmenagogue, for the treatment of corneal opacities, ulcers, boils, styes and to relieve cough and inflammation[75].

Parts used:

The medicinal parts were the Cumin oil extracted from the ripe fruit and the ripe, dried fruit[78].

Physicochemical characteristics:

Moisture content: 8%, PH: 7.3, total ash: 7.5, acid insoluble ash: 18%, alcohol soluble extractive: 6.58% , water soluble extractive: 138% and ether soluble extractive: 11.44 ± 0.20 and 12.36 ± 0.23% in the wet and dry fruits[73]. Crude protein 18.40 ± 0.16 and 19.88 ± 0.20%, crude fibers 21.82 ± 0.13 and 23.57 ± 0.13%, total carbohydrate 55.58 and 60.05% in the wet and dry fruits respectively[82]. Physical properties of the essential oil of cumin seeds: extraction percentage: 2.3-5.7 %, color: colorless or pale yellow, refractive index (20 ºC): 1.47-1.50, density (20 ºC): 0.90-0.94, alcohol solubility (80% v/v): 1:1.3-1:2, aldehyde percentage (on the basis of cuminaldehyde): 35-63%, acidity (on the basis of cuminic acid): 0.36-1.8, alcohol percentage (on the basis of cuminol): 3.5, carbonyl index: 9.32 and steric index: 19.24[83].

Chemical constituents:

Phytochemical analysis showed that *Cuminum cyminum* contained: alkaloid , anthraquinone, coumarin, flavonoid, glycoside, protein, resin, saponin, tannin and steroid[73].

Nutrient contents of cumin (in 2 g of seeds) were included: calories 7.50, calories from fat 4.00, calories from saturated fat 0.28, protein (g) 0.36, carbohydrates (g) 0.88, dietary fibre (g) 0.22, total fat (g) 0.44, saturated fat (g) 0.04, monounsaturated fat (g) 0.28, polyunsaturated fat (g) 0.06, water (g) 0.16, Ash (g) 0.16, vitamin A (IU) 25.40, vitamin A (RE) 2.54, α-carotenoid (RE) 2.54, beta carotene (µg) 15.24, thiamin – B1(mg) 0.02, niacin – B3(mg) 0.10, niacin equiv 0.10, vitamin C 0.16, vitamin E alpha equiv 0.02, vitamin E (IU) 0.04, vitamin E (mg) 0.02, folate(µg) 0.20, vitamin K (µg) 0.11, calcium(mg) 18.62, copper(mg) 0.02, iron(mg) 1.32, magnesium (mg) 7.32, manganese (mg) 0.06, phosphorus (mg) 9.98, potassium (mg) 35.76, selenium(µg) 0.10, sodium (mg) 3.36, zinc (mg) 0.10, palmitic acid (g) 0.02, oleic (g) 0.28, linoleic acid (g) 0.06 and omega 6 fatty acids (g) 0.06[79].

Organic acids (aspartic, citric, malic, tartaric, propionic, ascorbic, oxalic, maleic and fumaric acids) were isolated from seeds of *Cuminum cyminum*[84].

Cumin fruits contained 2.5 to 4.5% volatile oil and 10% fixed oil[75]. It appeared that the constituents of *Cuminum cyminum* essential oil were differ according to the area from which the *Cuminum cyminum* samples were taken. The major compounds in the Turkish cumin (*Cuminum cyminum*) seed oil were cuminaldehyde (19.25-27.02%), p-mentha-1,3-dien-7-al (4.29-12.26%), p-mentha-1,4-dien-7-al (24.48-44.91%), γ-terpinene (7.06-14.10%), p-cymene (4.61-12.01%) and β-pinene (2.98-8.90%)[85].

Cuminaldehyde, γ-terpinene, o-cymene, limonene and β-pinene were determined to be the major constituents of Syrian *Cuminum cyminum* [86].

The major compounds in cumin essential oil of Egyptian cultivars were cumin aldehyde (35.25%), tetradecene (12.25%), γ-terpenene (12%), β-ocimene (9.72%), p-mentha-2-en-ol (9%), α-terpinyl acetate (5.32%), α-terpinolene (3%), lmonine (0.5%), myrcene (0.2%), β-pinene (0.9%) and α-pinene (0.19%)[82].

Tunisian variety of *Cuminum cyminum* contained cuminlaldehyde (39.48%), gamma-terpinene (15.21%), O-cymene (11.82%), beta-pinene (11.13%), 2-caren-10-al (7.93%), trans-carveol (4.49%) and myrtenal (3.5%) as major components[87].

Analysis of the fruit oil of *Cuminum cyminum* from Delhi showed that the major constituents were transdihydrocarvone (31.11%), γ-terpinene (23.22%), p-cymene (15.8%), α- phellandrene (12.01%) and p-menth-2-en-7-ol (3.48%) and cuminlaldehyde constituted only 0.58%[88].

Analysis of cumin oil samples from four different German regions showed that the major compounds in all samples were monoterpenes beta -pinene, p-cymene, gamma –terpinene, the terpenoid aldehydes, cuminic aldehyde and the isomeric menthadien carboxaldehydes[89].

However, Li and Jiang found that Chinese cumen seed oil contained cuminal (36.31%), cuminic alcohol (16.92%), γ-terpinene (11.14%), safranal (10.87%), p-cymene (9.85%) and β-pinene (7.75%) as major components[90].

Thymol (40.65%), γ-terpinene (24.51%), b-pinene (5.38%), a-pinene (3.47%), camphene (2.31%), terpinene- 4 – ol (2.00%), cuminaldehyde (1.79%), a-thujene (1.45%), a-terpinolene (1.17%), myrcene (1.07%), limonene (1.04%), α-phyllanderene (0.94%), acetoxylinalool (0.57%) and sabinene (0.37%) represented the major components isolated from cumin essential oils from Kurdistan mountain of Iran[91].

Romeilah *et al.*, isolated 20 compounds from the *Cuminum cyminum* (seeds) oil including: α-pinene 2.14, sabinene 1.01, β-pinene 4.89, β-myrcene 1.45, α-terpinene 0.84, p-cymene 1.77, limonene 0.24, γ-terpinene 1.07, α-terpinolene 0.08, Camphor 0.12, Terpinen-4-ol 0.04, α-terpineol 2.47, geraniol 0.07, geranyl acetate 4.11, β-caryophyllene 3.44, α-phellandrene 1.09, cuminaldehyde 60.01, thymol 2.04, β-farnesene 3.01 and caryophyllene oxide 6.12[92].

However, Gachkar *et al.*, isolated 32 compounds from *Cuminum cyminum* oil including: isobutyl isobutyrate 0.8, *a*-thujene 0.3, *a*-pinene 29.1, sabinene 0.6 , myrcene 0.2 , *d*-3-carene 0.2, *p*-cymene 0.3, limonene 21.5, 1,8-cineole 17.9, (*E*)-ocimene 0.1, *g* -terpinene 0.6, terpinolene 0.3, linalool 10.4, *a*-campholenal 0.03, *trans*-pinocarveole 0.07 , *d*-terpineole 0.09, terpinene-4-ol 0.5, *a*-terpineole 3.17, *trans*-carveole 0.4, *cis*-carveole 0.07, geraniol 1.1, linalyl acetate 4.8, methyl geranate 0.2, *a*-terpinyl acetate 1.3, neryl acetate 0.09, methyl eugenol 1.6, *b*-caryophyllene 0.2, *a*-humulene 0.2, spathulenol 0.07, caryophylleneb epoxide 0.1, humulene epoxide II 0.08 and acetocyclohexane dione-2 0.4[93].

49 components were identified in the essential oil constituents of the *Cuminum cyminum* fruit grown in Delhi, which represented 99.78% of total detected constituents. The essential oil was characterized by the presence of monoterpene (79.61%), sesquiterpene (2.66%), aromatic (16.55%) and aliphatic compounds (0.66%). Among thirty four monoterpenes detected, there were fourteen hydrocarbons (41.28%), twelve alcohols (5.76%), six keto compounds (31.92%), one aldehyde (0.54%) and two esters (0.11%). The predominant monoterpene hydrocarbon was γ-terpinene (23.22%) followed by α-phellandrene (12.01%), α-pinene (1.78%) and α-terpinene (1.24%). Among twelve monoterpenic alcohols, p-menth-2-en-7-ol (3.48%) was the major alcoholic constituent and trans-dihydrocarvone (31.11%) was the prominent monoterpenic ketone in the essential oil. The sesquiterpenes identified in the oil were teresantalol (2.62%) and karvaknol (0.04%). The aromatic compounds detected were p-cymene (15.87%), 8a-methyl octahydro-2(1H)- naphthalenone, 2-isopropyl-5-methyl phenol, p-cymen-7-ol, o-cymen-5-ol, p-cymen-3-ol, 6-allyl-4,5-dimethoxy-1,3-benzodioxole and 2,a,8,8-tetramethyl decahydrocyclopropanal [d] naphthalene. The aliphatic compounds included 1-(1, 2, 3-trimethyl-2- cyclopenten-1-yl) ethanone, 3-isopropyl phenol, 2-methyl-4-isopropyliden-cyclopentan-1-al, 1-methyl-4-iso propyl-3-cyclohexen-1-ol, 2-isopropenyl-5-methyl-hex-4-enal, 4-isopropyl cyclohex-1,3-dien-1-yl) methanol, 4-isopropyl-1-cyclohexen-1-carbaldehyde, hexadecylene oxide and (3,4-dimethyl-2-oxo-cyclopenten-1-yl) acetic acid[88].

Analysis of the methanolic extract of the fruits of *Cuminum cyminum* led to the isolation of five terpenic and steroidal constituents, they were characterized as 1,4,5,8-tetrahydroxynaphthyl geranilan-10′-al 1′-oate, lanost-5,20 (22)-dien-3α-olyl *n*docosanoate, labdan-6α,16,20-triol-16-(10′,11′- dihydroxy anthraquinone-2′-oate), stigmast-5-en- 3β-O-D-arabinopyranosyl-2′-benzoate and lanost-5,24-dien-3β-ol 3β-O-D- arabinopyronosyl-2′-*n*octadec- 9″, 12″-dienoate[94].

The characteristic odour of cumin was attributed to the presence of sminaldehyde, 1, 3-p-menthadien-7al, 1-4-p-menthadien-7-al. 14 free amino acids were also isolated from the seeds. While, flavonoid glycosides isolated from the plant were included apigenin-7-glucoside, luteolin-7-glucoside, luteolin-7-glcuronosyl glucoside, luteolin and apigenin[95].

Total polypheols in cumin were 4.98± 0.31. (mg GAE/g DW)[96]. Phenols (salicylic acid, gallic acid, cinnamic acid, hydroquinone, resorcinol, P-hydroxybenzoic acid, rutin, coumarine, quercetin) were isolated from seeds of *Cuminum cyminum*[84].

However, *Cuminum cyminum* roots, stems and leaves, and flowers were investigated for their total phenolics, flavonoids, and tannins contents. In all *Cuminum cyminum* organs, total phenolics content ranged from 11.8 to 19.2 mg of gallic acid equivalents per gram of dry weight (mg of GAE/g of DW). Among the polyphenols studied, 13 were identified in roots, 17 in stem and leaves, and 15 in flowers. The major phenolic compound in the roots was quercetin (26%), whereas in the stems and leaves, p-coumaric, rosmarinic, trans-2-dihydrocinnamic acids and resorcinol were predominant. In the flowers, vanillic acid was the main compound (51%)[97].

A total of 19 phenolic compounds were successfully identified during the ripening of cumin seeds. Rosmarinic acid was the major phenolic acid for the unripe seeds, while, half ripe and full ripe seeds were dominated by p-coumaric acid[98].

IV. PHARMACOLOGICAL EFFECTS

Antimicrobial effect:

Ethanol extracts of seed of *Cyminum cuminum* were tested for antimicrobial activity *in vitro* by the microdilution method. Ethanol extract of seed exhibited antimicrobial activity against biofilm *Escherichia coli*[99].

All essential oils, and cuminic aldehyde, were tested, using agar diffusion and serial dilution methods, against different Gram-positive and Gram-negative bacteria isolated from different sources of food (pork fillet, minced meat and sausages) and clinical isolates, as well as three different *Candida albicans* isolates. All cumin oils and cuminic aldehyde exhibited a considerable inhibitory effect against all the tested organisms, except *Pseudomonas* spp[89].

The volatile oil of *Cuminum cyminum* was active against *Staphylococcus epidermidis, S. aureus, S. haemolyticus, Propionibacterium acnes, Corynebacterium diphtheriae, Erysipelothrix rhusiopathiae, Bacillus cereus, Clostridium tetani, C. difficile, Escherichia coli, Salmonella typhi, Klebsiella pneumoniae, Vibrio cholerae, Aeromonas hpydrophila, Mycobacterium tuberculosis* and *Neisseria gonorrhoeae*, *Asperigillus niger, Saccharomyces cerevisae* and *Colletrotrichum gloeosporioides*. The antimicrobial activity induced by methanolic, hydroalcoholic and aqueous extracts was less that that produced by volatile oils[88].

The essential oil of Bulgarian *Cuminum cyminum* was active against *Aspergillus niger, Bacillus subtilis, Staphylococcus epidermidis, Saccharomyces cerevisiae* and *Candida albicans*[100].

The inhibitory effect of steam distilled essential oil of cumin fruits was tested against 3 Gram-negative bacteria (*Pseudomonas fluorescens, Escherichia coli*, and *Serratia marcescens*), 4 Gram-positive bacteria (*Staphylococcus aureus*, *Micrococcus* spp., *Sarcina* spp., and *Bacillus subtilis*), an acid fast bacterium (*Mycobacterium phlei*), and one yeast (*Saccharomyces cerevisiae*). The results showed that cumin oils possessed strong antimicrobial activity[101].

The essential oils from seeds of *Cuminum cyminum*, exerted antifungal activity against *Aspergillus flavus*[102].

The cumin essential oil showed activity against *E. coli, Pseudomonas aeruginosa* and *Salmonella sp.* and their inhibitory zones were 18, 10 and 23 mm, respectively[103].

The antimicrobial activity of the essential oil of cumin (*Cuminum cyminum*) seeds was studied against different strains of microorganisms. Antimicrobial testing showed high activity of the essential *Cuminum cyminum* oil against *Candida albicans, Aspergillus niger*, the Gram positive bacteria *Bacillus subtilis* and *Staphylococcus epidermidis* as well as the yeast (*Saccharomyces cerevisiae*) [104].

Cuminum cyminum essential oil exhibited strong antimicrobial activity against *E. coli, S. aureus* and *L. monocytogenes*. Complete death time on exposure to *Cuminum cyminum* oil was 20, 180 and 90 min for *E. coli, S. aureus* and *L. monocytogenes*, respectively[105].

Cuminum cyminum essential oils possessed antifungal activity against *Botrytis cinerea, Rhizopus stolonifer* and *Aspergillus niger*. The incorporation of 750 µl/1 from *Cuminum cyminum* oils to PDA medium was completely inhibited the growth of *B. cinerea, R. stolonifer* and *A. niger*[106].

The fungicidal activities of p-isopropyl benzaldehyde and p-isopropyl benzoic acid extracted from *Cuminum cyminum* were studied against *Alternaria solani, Verticillium dahliae, Rhizoctonia cerealis, Alternaria alternata, Gaeumannomyces graminis, Sclerotinia sclerotiorum, Phytophthora capsici, Thanatephorus cucumeris, Blumeria graminis* [*Erysiphe graminis*] and *Botrytis cinerea*. The bioassay results showed that both compounds had fungicidal activities *in vivo* and *in vitro*. P-isopropyl benzaldehyde and p-isopropyl benzoic acid had better inhibitory effects against *Sclerotinia sclerotiorum*, and their EC_{50} were 2.1 and 7.3 mg/l respectively. In a concentration of 1000 mg/l, the protective effects of p-isopropyl benzaldehyde and p-isopropyl benzoic acid treatments were higher than 50% against *Blumeria graminis*. At the same concentration, the control effect of p-isopropyl benzoic acid treatment was 57.52% against *Sclerotinia sclerotiorum*, which was comparable to sumilex treatment[107].

The effectiveness of the essentials oils from cumin (*Cuminum cyminum*) was studied on the growth of some bacteria commonly used in the food industry, *Lactobacillus curvatus, Lactobacillus sakei, Staphylococcus carnosus* and *Staphylococcus xylosus* or related to food spoilage *Enterobacter gergoviae, Enterobacter amnigenus*. The agar disc diffusion method was used to determine the antibacterial activities of the oils. *Cuminum cyminum* essential oils showed an inhibitory effect against all the tested bacteria[108].

The antifungal activities of the essential oils obtained from *Hyssopus officinalis, Cuminum cyminum, Thymus vulgaris* and cones of *Cupressus arizonica* were evaluated against *Aspergillus flavus*. Different concentrations of the essential oils on conidial germination and germ tube elongation were determined *in vitro*. Essential oils were applied in 5 levels (0, 0.125, 0.25, 0.375 and 0.5%). The results showed that the essential oil of *Cuminum cyminum* was more effective in comparison with others[109].

The storage life of the strawberry fruits was increased by the use of Cumin (*Cuminum cyminum*) essential oils significantly, because they inhibited the fungi (*Botrytis cinerea*)[110].

Cuminum cyminum oil exhibited higher antibacterial and antifungal activities with a high effectiveness against *Vibrio spp*. strains with a diameter of inhibition zones ranging from 11 to 23 mm, and MIC and MBC values ranging from (0.078-0.31 mg/ml) to (0.31-1.25 mg/ml) respectively[87].

A great inhibition of *Cuminum cyminum* essential oil was recorded on *Pseudomonas syringae* pv. Syringae[111].

The ranges of minimum inhibitory concentration of *Cuminum cyminum* oils against several food-borne pathogens (*Staphylococcus aureus*, *Bacillus cereus*, *Escherichia coli* O157:H7, *Salmonella enteritidis* and *Listeria monocytogenes*) were 0.37-3.0 mg/ml. Moreover, the combination of *B. persicum* and *Cuminum cyminum* essential oils confirmed synergistic and additive activities against the pathogens[112].

The antifungal activity of the volatile parts (at doses from 5 to 20 microl) of the essential oil of fruits of *Cuminum cyminum* was tested on dermatophytes and phytopathogens, fungi, yeasts and some new *Aspergilli*. Antifungal testing showed that *Cuminum cyminum* was active on all fungi but in particular on the dermatophytes, where *Trichophyton rubrum* was the most inhibited fungus at the lowest dose of 5 µl. Phytopathogens were less sensitive to the treatment [113].

The chemical composition of essential oils from cumin (*Cuminum cyminum*), laurel (*Laurus nobilis*), oregano (*Oreganum onites*), rosemary (*Rosmarinus officinalis*), anise (*Pimpinella anisum*) and clove (*Syzygium aromaticum*) was determined and their antibacterial activities were tested aginst *Salmonella typhimurium* CCM 5445, *Staphylococcus aureus* (MRSA) RSKK 95047, *Staphylococcus aureus* ATCC 6538P, *Escherichia coli* ATCC 29998 and *Escherichia coli* O157:H7 RSKK 232 by two different methods (disc diffusion and agar dilution). The results showed that oregano essential oil showed the highest inhibition (0.0625-0.125 mg/ml) effect followed by cumin (0.0625-2.0 mg/ml) and clove (0.25-1.0 mg/ml)[114].

Antibacterial activity of seed extracts of cumin (*Cuminum cyminum*) was investigated against 10 Gram positive and Gram negative bacteria. Disc diffusion method was used to test the antibacterial activity. Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were determined by using standard procedures. The highest inhibition zone of 16.67±0.47 mm was found at 250 mg/ml against *Escherichia coli.* On the other hand, the inhibition zones 15.00±0.82 mm for ethanol, 15.33±0.47 for methanol, and 15.67±0.82 for acetone were recorded against *Bacillus subtilis, Sarcina lutea* and *Klebsiella pneumonia*, respectively. MIC value (20 to 50 mg/ml) and MBC value (40 to 60 mg/ml) were recorded against the studied bacteria[115].

Antibacterial activity of *Cuminum cyminum* essential oil was observed against Gram-positive and Gram-negative bacterial species. The activity was particularly high against the genera *Clavibacter*, *Curtobacterium*, *Rhodococcus*, *Erwinia*, *Xanthomonas*, *Ralstonia*, and *Agrobacterium*, which were responsible for plant or cultivated mushroom diseases worldwide. In general, a lower activity was observed against bacteria belonging to the genus *Pseudomonas*[116].

Antimicrobial activities and biofilm-formation preventive properties of *Cuminum cyminum* essential oils and chlorhexidine were assessed against *Streptococcus mutans* and *Streptococcus pyogenes*. The minimal bactericidal concentrations (MBC) of the oils and chlorhexidine and microbial decimal reduction time (D value) were determined. *Cuminum cyminum* induced mild antibacterial and *in vivo* biofilm preventive effects (less than chlorhexidine). *In vivo* experiments conducted on male and female volunteers who brushed with essential oil blended toothpastes indicated that lower concentrations of the oils were significantly higher ($p<0.001$) and effective during the course of the study as compared to chlorhexidine[117].

The effect of different concentrations of *Cuminum cyminum* essential oil (0, 15, 30 and 45 µl/100 ml) and nisin (0, 0.5 and 1.5 µg/ml) combination at different temperatures (10, 25 and 35°C) was studied on growth of *Salmonella typhimurium* and *Staphylococcus aureus* in the brain-heart infusion (BHI) broth model. The concentrations of 0 µl/100 ml for essential oil and 0 µg/ml for nisin imply the negative control. The growth of *S. typhimurium* was significantly decreased by the concentration of essential oil ≥ 30 µl/100 ml in combination with nisin ≥ 0.5 µg/ml at temperature = 10°C ($p<0.05$). Also, in combination of the essential oil ≥ 15 µl/100 ml and nisin ≥ 0.5 µg/ml at temperature ≤ 25°C, the growth of S. aureus was significantly reduced ($p<0.05$). The results indicated that the combination of essential oil and nisin inhibited the growth of *S. typhimurium* and *S. aureus* bacteria and there was the possibility of using them as substitutes for chemical food preservatives[118].

The antimicrobial activity of cumin oil against many pathogenic bacteria, showed that *E. coli*, *S. aureus*, and *S. faecalis* were sensitive to various oil dilutions[119].

The antmicrobial activity of *Cuminum cyminum* essential oil was evaluated against: *Micrococcus luteus* LA 2971, *Bacillus megaterium* NRS, *Bacillus brevis* FMC 3, *Enterococcus faecalis* ATCC 15753, *Pseudomonas pyocyaneus* DC 127, *Mycobacterium smegmatis* CCM 2067, *Escherichia coli* DM, *Aeromonas hydrophila* ATCC 7966, *Yersinia enterocolitica* AU 19, *Staphylococcus aureus* Cowan 1, *Streptococcus faecalis* DC 74 bacteria, and *Saccharomyces cerevisiae* WET 136, *Kluvyeromyces fragilis* DC 98 fungi). *Cuminum cyminum* essential oil (2 µl) exerted antibacterial effect against all the tested microorganisms with MIC ranged from 10-60mm. While the inhibition zone was higher in the bacteria *E. faecalis*, it was lowest in *E. coli* and *P.*

pyocyaneus. Among the fungi, the inhibition zone against *K. fragilis* was higher than *S. cerevisiae*. In combined application of *Cuminum cyminum* essential oil (2 µl) and gentamicin antibiotics discs, a synergistic effect in *P. pyocyaneus* and *A. hydrophila*, an antagonistic effect in other bacteria were noted [(120)].

The antimicrobial effects of garlic, bay, black pepper, origanum, orange, thyme, tea tree, mint, clove, and cumin essential oils were studied against *Listeria monocytogenes* AUFE 39237, *Escherichia coli* ATCC 25922, *Salmonella enteritidis* ATCC 13076, *Proteus mirabilis* AUFE 43566, *Bacillus cereus* AUFE 81154, *Saccharomyces uvarum* UUFE 16732, *Kloeckera apiculata* UUFE 10628, *Candida albicans* ATCC 10231, *Candida oleophila* UUPP 94365, and *Metschnikowia fructicola* UUPP 23067. Thyme, origanum, clove, and orange essential oils were the most inhibitory against bacteria and yeasts. Cumin, tea tree, and mint oils inhibited the yeasts actively[(121)].

The activity of cumin seed essential oil and alcoholic extract against *Klebsiella pneumoniae* ATCC 13883 and clinical *K. pneumoniae* isolates was studied by evaluating the effect of subminimum inhibitory concentrations (sub-MICs) on cell morphology, capsule expression and urease activity. Growth of *K. pneumoniae* strains exposed to sub-MICs of *Cuminum cyminum* extracts resulted in cell elongation and repression of capsule expression. Urease activity was decreased[(122)].

The effects of the essential oils (EOs) of *Cuminum cyminum* on growth and aflatoxins production by *A. parasiticus* was evaluated. Minimal inhibitory concentrations (MICs) and minimal fungicidal concentrations (MFCs) of the EOs were determined. Determination of aflatoxin (AFB1, AFB2, AFG1, and AFG2) production was performed by immunoaffinity column extraction using reverse phase-high performance liquid chromatography. *Cuminum cyminum* oil exhibited strong activity (MIC_{90}: 1.6; MFC: 3.5 mg/ml) against *A. parasiticus*. Aflatoxin production was inhibited at 0.25 mg/ml of *Cuminum cyminum* [(123)].

Chloroformic and isoamyl alcohol extracts of *Cuminum cyminum* were investigated for their *in vitro* antibacterial activity against six human bacterial pathogens. The antibacterial activity was evaluated and based on the zone of inhibition using agar disc diffusion method. The tested bacterial strains were included *Streptococcus pyogenes, Staphylococcus epidermidis, Klebsiella pneumonia, Staphylococcus aurues, Serratia marcesnces,* and *Pseudomonas aeruginosa*. Chloroform and isoamyl alcohol extracts of *Cuminum cyminum* had significant effect against *P. aeruginosa, S. marcesnces* and *S. pyogenes*[(124)].

The potential of *Cuminum cyminum* (cumin) seed essential oil (EO) (as a plant based shelf life enhancer) was studied against fungal and aflatoxin contamination and lipid peroxidation. The EO showed efficacy as a preservative in food systems (stored wheat and chickpeas). The minimum inhibitory concentration and minimum aflatoxin inhibitory concentration of EO were 0.6 and 0.5 µl/ml respectively. The EO showed toxicity against a broad spectrum of food borne fungi. The antifungal action of EO on ergosterol content in the plasma membrane of *A. flavus* was determined. As a fumigant in food systems, the EO provided sufficient protection of food samples against fungal association without affecting seed germination. In view of the antifungal and antiaflatoxigenic nature, free radical scavenging potential and efficacy in food system, cumin seed EO may be able to provide protection of food commodities against quantitative and qualitative losses, thereby enhancing their shelf life[(125)].

The *in vitro* antifungal activities of essential oil from *Cuminum cyminum* were studied against *C. albicans* ATCC 14053, *C. dubliniensis* ATCC CD60, *C. glabrata* ATCC 90030, *C. krusei* ATCC 6258 and *C. parapsilosis* ATCC 22019. *Cuminum cyminum* oil had a broad-spectrum antifungal activity against different pathogenic Candida species. Inhibition zone values were ranged from 7 to 50mm against the tested organisms. The best minimal inhibitory concentration (MIC) of *Cuminum cyminum* oil was recorded against *C. albicans* and *C. dubliniensis* (289 mg/l)[(126)].

The antifungal activity of cumin oil was evaluated on mycelia growth of 90 fungal isolates (eighty-seven species and 3 species varieties belonging to 32 genera). The agar-well diffusion method was used to evaluate fungal growth inhibition at a concentration of 100%. Cumin oil was highly effective against all the isolates of tested fungi. It was completely inhibited mycelial growth of all fungi when added to solid medium[(127)].

The effect of *Cuminum cyminum* essential oil was studied in the growth and FUM1 gene expression of fumonisin-producing *Fusarium verticillioides* strains isolated from maize. FUM1 transcript levels were quantified using a reverse transcription-polymerase chain reaction (RT-PCR) protocol. Minimum inhibitory concentration (MIC) values of *Cuminum cyminum* oil against *F. verticillioides* strains varied from 0.195 to 0.781 µl/ml (mean MIC value: 0.461 µl/ml) indicating 54.5% of the fungal strains were inhibited at 0.390 µl/ml. PCR analysis of FUM1 gene expression revealed that DNA fragment of 183 bp was amplified in all the isolates of *F. verticillioides* before treatment with *Cuminum cyminum* essential oil. Based on RT-PCR analyses, reduction in the expression of fumonisin biosynthetic genes was significant only for FUM1 gene ($p<0.05$), while no effect was observed on ITS gene[(128)].

The essential oils of *Cuminum cyminum* showed antiviral activities against herpes simplex virus 1 (HSV-1) using cytopathicity (CPE) assay. At concentration of 1000 µg the antiviral activity reached 91.60 ± 1.93[(129)].

V. INSECTICIDAL EFFECTS

The electrophysiological, behavioural (repellency, irritancy) and toxic effects of the of *Cuminum cyminum* essential oils was studied against *Anopheles gambiae* strain (Kisumu). Aldehydes elicited the strongest responses and monoterpenes the weakest responses in electroantennogram (EAG) trials. However, EAG responses did not correlate consistently with results of behavioral assays. In behavioral and toxicity studies, several of the single compounds exhibited repellency, irritancy or toxicity in *An. gambiae*; however, the activity of essential oils did not always correlate with activity expected from the major components. The biological activity of essential oils appeared complex, suggesting interactions between individual compounds and the insect. Data also indicated that the three effects appeared independent, suggesting that repellency mechanism(s) may differ from mechanisms of irritancy and toxicity[130].

Fumigant activity of essential oil vapours distilled from cumin was recorded against the eggs of two stored-product insects, the confused flour beetle, *Tribolium confusum*, and the Mediterranean flour moth, *Ephestia kuehniella*. The exposure to vapours of essential oils resulted in 100% mortality of the eggs at a concentration of 98.5 µl cumin essential oil/l air[131-132].

Antidiabetic effect:

The orally administered seed powder (2 g/kg) lowered the blood glucose levels in hyperglycaemic rabbits[133]. The Antidiabetic effects of cumin seed, was examined in streptozotocin induced diabetic rats. An eight week dietary regimen containing cumin powder (1.25%) was found to be remarkably beneficial, as indicated by reduction in hyperglycaemia and glucosuria. This was also accompanied by improvement in body weights of diabetic animals. Dietary cumin also countered other metabolic alterations as revealed by lowered blood urea level and reduced excretions of urea and creatinine by diabetic animals[134].

Cuminaldehyde and cuminol were identified as potent insulinotrophic components. Cuminaldehyde and cuminol (25 µg/ml) showed 3.34- and 3.85-fold increased insulin secretion, respectively. The insulinotrophic action of both components was glucose-dependent and due to the closure of the ATP-sensitive K (K^+ -ATP) channel and the increase in intracellular Ca^{2+} concentration. An inhibitor of insulin secretion with potent β-cell protective action was also isolated from the same petroleum ether fraction. The authors concluded that *Cuminum cyminum* was able to lower blood glucose without causing hypoglycaemia or β-cell burn out[135].

The effect of methanolic extract of seeds of *Cuminum cyminum* (CC) on diabetes, oxidative stress and formation of advanced glycated end products (AGE) were investigated compared with glibenclamide. *In vitro* studies indicated that CC inhibited free radicals and AGE formation. Treatment of streptozotocin-diabetic rats with CC and glibenclamide for 28 days induced a reduction in blood glucose, glycosylated hemoglobin, creatinine, blood urea nitrogen and improved serum insulin and glycogen (liver and skeletal muscle) content when compared to diabetic control rats. Significant reductions in renal oxidative stress and AGE were observed with CC when compared to diabetic control and glibenclamide. CC and glibenclamide also improved antioxidant status in kidney and pancreas of diabetic rats. Diabetic rats showed increase in rat tail tendon collagen, glycated collagen, collagen linked fluorescence and reduction in pepsin digestion[136].

The role of *Cuminum cyminum* supplementation on the plasma and tissue lipids was studied in alloxan diabetic rats. Oral administration of 0.25 g/kg body weight of *Cuminum cyminum* for 6 weeks to diabetic rats resulted in significant reduction in blood glucose and an increase in total haemoglobin and glycosylated haemoglobin. It also prevented a decrease in body weight. *Cuminum cyminum* treatment also resulted in a significant reduction in plasma and tissue cholesterol, phospholipids, free fatty acids and triglycerides. Histological observations demonstrated significant fatty changes and inflammatory cell infiltrates in diabetic rat pancreas, but supplementation with *Cuminum cyminum* to diabetic rats significantly reduced the fatty changes and inflammatory cell infiltrates. Moreover, *Cuminum cyminum* supplementation was found to be more effective than glibenclamide in the treatment of diabetes mellitus[137].

VI. ANTICANCER EFFECT

At a concentration of 0.1 microl/ml, oil of *Cuminum cyminum* destructed Hela cells by 79%[119]. Cancer chemopreventive potentials of different doses of a cumin seed-mixed diet were evaluated against benzo(α)pyrene [B(α)P]-induced forestomach tumorigenesis and 3-methylcholanthrene (MCA)-induced uterine cervix tumorigenesis. Results showed a significant inhibition of stomach tumor burden by cumin. Tumor burden was 7.33 ± 2.10 in the B(α)P-treated control group, whereas it reduced to 3.10 ± 0.57 ($p<0.001$) by a 2.5% dose and 3.11 ± 0.60 ($p<0.001$) by a 5% dose of cumin seeds. Cervical carcinoma incidence, compared with the MCA-treated control group (66.67%), reduced to 27.27% ($p<0.05$) by a diet of 5% cumin seeds and to 12.50% ($p<0.05$) by a diet of 7.5% cumin seeds. The effect of 2.5 and 5% cumin seed-mixed diets was also examined on carcinogen/xenobiotic metabolizing phase I and phase II enzymes, antioxidant enzymes, glutathione content, lactate dehydrogenase (LDH), and lipid peroxidation in the liver of Swiss albino mice. Levels of cytochrome P-450 (cyt P-450) and cytochrome b5 (cyt b5) were significantly augmented ($p<0.05$) by

the 2.5% dose of cumin seed diet. The levels of cyt P-450 reductase and cyt b5 reductase were increased (from $p<0.05$ to $p<0.01$) by both doses of cumin. Among the phase II enzymes, glutathione S-transferase specific activity increased ($p<0.005$) by the 5% dose, whereas that of DT-diaphorase increased significantly ($p<0.05$) by both doses used (2.5 and 5%). In the antioxidant system, significant elevation of the specific activities of superoxide dismutase ($p<0.01$) and catalase ($p<0.05$) was observed with the 5% dose of cumin. The activities of glutathione peroxidase and glutathione reductase remained unaltered by both doses of cumin. The level of reduced glutathione measured as nonprotein sulfhydryl content was elevated (from $p<0.05$ to $p<0.01$) by both doses of cumin. Lipid peroxidation measured as formation of MDA production showed significant inhibition ($p<0.05$ to $p<0.01$) by both doses of cumin. LDH activity remained unaltered by both doses of cumin. The results were strongly suggested the cancer chemopreventive potentials of cumin seed and could be attributed to its ability to modulate carcinogen metabolism[138].

Cumin seeds also augmented the levels of carcinogen/xenobiotic metabolizing phase I enzymes, cytochrome P-450 (cyt P-450) and cytochrome b5 (cyt b5), the levels of cyt P-450 reductase and cyt b5 reductase, and the phase II enzymes, such as glutathione-*S*-transferase and DT-diaphorase. These results, in addition to antioxidant effects, strongly suggest the cancer chemopreventive potential of cumin seed, which attributed to its ability to modulate carcinogen metabolism. Cumin seeds also decreased significantly the incidence of both B[*a*]P-induced neoplasia and 3'MeDAB induced hepatomas in Wistar rats[79, 139].

VII. ANTIOXIDANT EFFECTS

The antioxidant capacity of cumin by ABTS and DPPH assays was3.26 ± 0.29 and2.16 ± 0.06 (mmol TE/g DW) respectively[140].

The antioxidant activity of cumin was studied. The oil showed higher antioxidant activity compared with that of BHT and BHA. The cumin essential oil exhibited a dose-dependent scavenging of DPPH radicals and 5.4 microg of the oil was sufficient to scavenge 50% of DPPH radicals/ml[119].

Antioxidant activity of essential oils was evaluated by DPPH radical scavenging assay, radical inhibition of *Cuminum cyminum* essential oils was 83.59% , the scavenging activities of the essential oil was increased with the increased of the essential oil concentrations[129].

It appeared that the full ripe seeds were richer on polyphenols and condensed tannin than unripe ones, and consequently exhibited higher antioxidant activities. However, the unripe seeds had a higher total flavonoid content compared to those of half ripe and full ripe ones. The comparison of two extraction methods, the soxhlet extracts contained the greatest amount of polyphenols and flavonoids, while maceration samples exhibited higher antiradical and bleaching power assay. Total phenolic contents and IC_{50} values in cumin seed during their maturation allowed to conclude that antioxidant activity does not depend only on the high content of total phenolics but also on the phenolic composition[98].

The antioxidant activities of β-pinene, p-cymene, γ-terpinene, cuminaldehyde and cumin oils (cumin oleoresin/COR, cumin essential oil/CEO, distillation residue/DR and distillate condensed from cold trap/CT) were investigated in the present study. IC_{50} values and kinetics rates were used to evaluate the efficiency of tested samples in scavenging the alkyl peroxyl radical generated in the β-carotene-linoleic acid system and the 2,2-diphenyl-1-picrylhydrazyl radical (DPPH). In kinetic approach, antioxidant activities of tested samples were expressed as the rate of β-carotene bleaching (R(β-carotene)) and DPPH scavenging (R(DPPH)), respectively. The order of antioxidant activities of cumin oils was DR=COR>CEO>CT. γ-Terpinene exhibited lower R (β-carotene) value and the lowest IC_{50}(β-carotene) value, which indicated the stronger response in alkyl peroxyl radical scavenging. The R2(DPPH) values for γ-terpinene, followed by DR and COR, showed high response in scavenging DPPH, with IC50 values of 22.73, 6.72, 8.53mg/ml, respectively. γ–terpinene appeared the most efficient antioxidant compounds in cumin oils[141].

Thiobarbituric acid reactive substances (TBARS) assay was used to evaluate the lipid peroxidation of *Cuminum cyminum* extract. The extract also produced significant lipid peroxidation inhibition in comparison with known antioxidant ascorbic acid in both rat liver and brain[142].

The antioxidant activities of *Cuminum cyminum* essential oils and acetone extracts obtained from the three organs were assessed using four tests [1,1-diphenyl-2-picrylhydrazyl (DPPH), β-carotene/linoleic acid, reducing power, and chelating power assays]. The acetone extract of flowers was strongly effective as a DPPH radical scavenger, lipid peroxidation inhibitor, and reducing agent, with IC_{50} values of 4, 32, and 8 μg/ml, respectively. Moreover, the acetone extract of stems and leaves showed the highest chelating power. However, the essential oils exhibited moderate activities in the different tests[97].

Two complementary assays were used to assess the antioxidant activity of cumin and caraway methanolic and acetonic seed extracts: the DPPH free radical scavenging assay and the β-carotene bleaching assay. Both cumin and caraway seed extracts were able to neutralize free radicals over a period of 60 min in the DPPH assay, with most of the neutralization occurring quickly within the first 30s. The steady state was reached within 10min, and it appeared that the acetonic extracts of both seeds had less antioxidant activity than the methalonic extracts. The

methanolic and acetonic extracts of cumin showed slightly higher neutralization ability than the respective extracts from caraway within three minutes of assay initiation (57.0 and 52.4% for cumin and 44.7 and 39.5% for caraway[143].

The effect of *Cuminum cyminum* was investigated on alcohol and thermally oxidized oil induced hyperlipidaemia. The results showed increased activity of aspartate transaminase (AST), alkaline phosphatase (ALP) and gamma glutamyl transferase (GGT) and increased levels of cholesterol, triglycerides and phospholipids in the plasma of rats given alcohol, thermally oxidized oil and alcohol+ thermally oxidized oil when compared with the normal control group. The levels of tissue (liver and kidney) cholesterol and triglycerides were increased significantly in rats groups given alcohol, thermally oxidized oil and alcohol+ thermally oxidized oil when compared with the normal control rats. The levels were decreased when cumin was given along with alcohol and thermally oxidized oil. The level of phospholipids decreased significantly in the liver and kidney of groups given alcohol, thermally oxidized oil and alcohol+ thermally oridized oil when compared with the normal control rats. The level increased when cumin was administered along with alcohol and thermally oxidized oil. The activity of phospholipase A and C increased significantly in the liver of groups given alcohol, thermally oxidized oil and alcohol+ thermally oxidized oil when compared with the normal control rats, whereas the activity was decreased with the cumin treatment. The results indicate that cumin can decrease the lipid levels in alcohol and thermally oxidized oil induced hepatotoxicity[144].

VIII. ANTIINFLAMMATORY AND ANALGESIC EFFECTS

Acetic-acid induced writhing, hot plate, Carrageenan-induced paw oedema and Cotton-pellet granuloma methods were used for evaluation of analgesic and anti-inflammatory effects of *Cuminum cyminum* extracts (200 and 500 mg/kg for aqueous and ethanolic extract). Both the aqueous and ethanolic extracts showed highly significant analgesic activity in Acetic-acid induced writhing, while the ethanolic extracts were effective in hot plate method. Both the aqueous and ethanolic extracts showed significant anti-inflammatory activity in Carrageenan-induced paw oedema and Cotton-pellet granuloma models when compared to the control group[145].

The anti-inflammatory effects of cumin essential oil (CuEO), in lipopolysaccharide- (LPS-) stimulated RAW 264.7 cells and the underlying mechanisms were investigated. Mitochondrial-respiration-dependent 3-(4,5-dimethylthiazol-2-yl)- 2,5-diphenyl tetrazolium (MTT) reduction assay demonstrated that CuEO did not exhibit any cytotoxic effect at the employed concentrations (0.0005–0.01%). Real-time PCR tests showed that CuEO significantly inhibited the mRNA expressions of inducible nitric oxide synthase (iNOS), cyclooxygenase (COX-2), interleukin- (IL-) 1, and IL-6. Moreover, western blotting analysis revealed that CuEO blocked LPS-induced transcriptional activation of nuclear factor-kappa B (NF-κB) and inhibited the phosphorylation of extracellular signal regulated kinase (ERK) and c-Jun N-terminal kinase (JNK). The results revealed that CuEO exerted anti-inflammatory effects in LPS-stimulated RAW264.7 cells via inhibition of NF-κB and mitogen-activated protein kinases ERK and JNK signaling[146].

The potential anti-nociceptive and anti-inflammatory activities of the fruit essential oil of *Cuminum cyminum* has been evaluated in chemical (formalin test) and thermal (tail-flick test) models of nociception and formalin model of acute inflammation in rats and mice. The essential oil at the doses ranging between 0.0125 and 0.20 ml/kg exhibited a significant and dose-dependent analgesic effect in both model of chronic and inflammatory pain. However, the essential oil was devoid of anti-inflammatory activity. Moreover, the essential oil had no analgesic effect in tail flick test as a model of acute pain[147].

The antiinflammatory activity of cumin volatile oil was investigated in carrageenan-induced rat paw oedema. The volatile oil showed dose–dependent inhibition of rat paw oedema, at dose of 0.1ml/kg, ip, when compared to control group. The activity was comparable with that of the standard drug, diclofenac sodium[75].

The methanolic extract of *Cuminum cyminum* inhibited lipoxygenase (LOX) activity. Activity-guided screening of the *Cuminum cyminum* crude extracts helped the identification and isolation of cuminaldehyde as a 15-LOX inhibitor. The enzyme kinetics analysis suggested cuminaldehyde to be a competitive inhibitor and the IC_{50} value derived from LB plots is 1.370 μM[148].

IX. CENTRAL NERVOUS EFFECT

The effect of the fruit essential oil of *Cuminum cyminum* on the epileptiform activity induced by pentylenetetrazol (PTZ) was evaluated using intracellular technique. The results demonstrated that extracellular application of the essential oil of *Cuminum cyminum* (1% and 3%) dramatically decreased the frequency of spontaneous activity induced by PTZ in a time and concentration dependent manner. In addition it showed protection against pentylenetetrazol-induced epileptic activity by increasing the duration, decreasing the amplitude of after hyperpolarization potential (AHP) following the action potential, the peak of action potential, and inhibition of the firing rate[149].

The memory-enhancing and antistress activities of *Cuminum cyminum* were studied in rats. Antistress activity was evaluated by inducing stress via forced swimming and the urinary vanillylmandelic acid (VMA) and ascorbic acid were estimated as biomarkers. Memory-enhancing activity was studied by conditioned avoidance response using Cook's pole climbing apparatus in normal and scopolamine-induced amnestic rats. Daily administration of cumin at doses of 100, 200, and 300 mg/kg bw, 1h prior to induction of stress, it inhibited the stress-induced urinary biochemical changes in a dose-dependent manner without altering the levels in normal control groups. The cognition, as determined by the acquisition, retention, and recovery in rats, was observed to be dose-dependent. The extract also produced significant lipid peroxidation inhibition in comparison with known antioxidant ascorbic acid in both rat liver and brain[142].

The effects of fruit essential oil (FEO) of *Cuminum cyminum* on acquisition and expression of morphine tolerance and dependence were investigated in mice. Animals were rendered dependent on morphine using the established method in which morphine (50, 50, 75 mg/kg; sc) was injected three times daily for 3 days. FEO (0.001, 0.01, 0.1, 0.5, 1 and 2%; 5 ml/kg, ip) or Tween-80 (5 ml/kg, ip) were given 60 min prior to each morphine injection (for acquisition) or the last injection of morphine on test day (for expression). Morphine tolerance was measured by tail-flick before and after administration of a single dose of morphine (50 mg/kg, sc) in test day (4^{th} day). Morphine dependence was also evaluated by counting the number of jumps after injection of naloxone (5 mg/kg, ip) on the test day. The results showed that Cumin FEO, only at the dose of 2%, significantly attenuated the development of morphine tolerance ($p<0.01$) and dependence ($p<0.05$). It was significantly effective on expression of morphine tolerance (1 and 2%) and dependence (0.5, 1 and 2%) in a dose-dependent manner. Accordingly, the essential oil of *Cuminum cyminum* ameliorated the morphine tolerance and dependence in mice[150].

The effects of *Cuminum cyminum* fruit essential oil (FEO) on the acquisition and expression of morphine-induced conditioned place preference (CPP) was studied in mice. CPP was induced by subcutaneous injection of morphine (5mg/kg) in 3 days conditioning schedule. Intraperitoneal administration of Cumin FEO (0.001%, 0.01%, 0.1%, 0.5%, 1% and 2%; 5 ml/kg) or Tween-80 (0.5%, 5 ml/kg) did not show any conditioning effects. Administration of Cumin FEO (0.001-2%, 5 ml/kg; ip), 60 min before test on day 5 (expression) decreased the conditioning scores at the doses of 1% and 2% while ip injection of Cumin FEO (0.001-2%, 5 ml/kg), 60 min before morphine injection (5mg/kg, sc) during 3 days of conditioning session (acquisition) significantly resulted in decrement of rewarding properties of morphine at the doses of 0.1%, 0.5%, 1% and 2% in dose-dependent manner[151].

The inhibitory effects of the *Cuminum cyminum* essential oil on the fibrillation of α-SN, which was a critical process in the pathophysiology of several neurodegenerative diseases, especially Parkinson's disease, was investigated. Analysis of different fractions from the total extract, identified cuminaldehyde as the active compound involved in the antifibrillation activity. In comparison with baicalein, a well-known inhibitor of α-SN fibrillation, cuminaldehyde showed the same activity in some aspects and a different activity on other parameters influencing α-SN fibrillation. The presence of spermidine, an α-SN fibrillation inducer, dominantly enforced the inhibitory effects of cuminaldehyde even more intensively than baicalein. Furthermore, the results from experiments using preformed fibrils and monobromobimane-labeled monomeric protein also suggested that cuminaldehyde prevents α-SN fibrillation even in the presence of seeds, having no disaggregating impact on the preformed fibrils. Structural studies showed that cuminaldehyde stalls protein assembly into β-structural fibrils, which might be achieved by the interaction with amine groups through its aldehyde group as a Schiff base reaction. This assumption was supported by FITC labeling efficiency assay. In addition, cytotoxicity assays on PC12 cells showed that cuminaldehyde is a nontoxic compound, treatment with cuminaldehyde throughout α-SN fibrillation showed no toxic effects on the cells[152].

X. EFFECT ON PLATELET FUNCTION

Extract of cumin inhibited arachidonate-induced platelet aggregation. It also inhibited thromboxane B2 production from exogenous (^{14}C) arachidonic acid (AA) in washed platelets, in addition, a simultaneous increase in the formation of lipoxygenase-derived products was also observed[153].

XI. HYPOTESIVE EFFECT

The anti-hypertensive potential of standardized aqueous extract of *Cuminum cyminum* seeds and its role in arterial endothelial nitric oxide synthase expression, inflammation, and oxidative stress were evaluated in renal hypertensive rats. Renal hypertension was induced by the two-kidney one-clip (2K/1C) method in rats. Systolic blood pressure (SBP), plasma nitrate/nitrite, carotid–eNOS, renal–TNF-α, IL-6, Bax, Bcl-2, thioredoxin 1 (TRX1), and thioredoxin reductase 1 (TRXR1) mRNA expressions were studied to demonstrate the anti-hypertensive action of *Cuminum cyminum*. *Cuminum cyminum* seed was administered orally (200 mg/kg bw) for a period of 9 weeks, it improved plasma nitric oxide and decreased the systolic blood pressure in hypertensive rats. It also up-regulated the gene expression of eNOS, Bcl-2, TRX1, and TRXR1; and down-

regulated Bax, TNF-α, and IL-6. The data revealed that *Cuminum cyminum* seeds augment endothelial functions and ameliorate inflammatory and oxidative stress in hypertensive rats[154].

XII. HYPOLIPIDEMIC AND WEIGHT REDUCTION EFFECTS

The hypocholesterolemic effect of methanolic extract of *Cuminum cyminum* (MCC) was evaluated in ovariectomized (OVX) rats. MCC 1000 mg/kg and estradiol benzoate equivalent to 0.15 mg/kg of estradiol were administered to OVX rats per orally for 10 weeks. The results indicated that estradiol as well as MCC protected OVX rats against increased cholesterol levels due to ovariectomy, MCC was better than estradiol[155].

The effect of cumin powder on body composition and lipid profile was studied in overweight and obese women in a randomized clinical trial. 88 overweight/obese women were randomly assigned into two groups. The experimental group was given 3 g/day cumin powder with yogurt at two meals for 3 months. The same amount of yogurt without cumin powder was prescribed for the control group. All patients received nutrition counseling for weight loss in a similar manner. Anthropometric and biochemical parameters were determined before and after the intervention. Cumin powder reduced serum levels of fasting cholesterol, triglyceride, and LDL and increased HDL. Weight, BMI, waist circumference, and fat mass were also significantly reduced. However, it exerted no effect on FBS and fat-free mass[156].

The effects of cumin extract supplementation on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, triglycerides, High density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), apolipoprotein A1 (Apo A1), and apolipoprotein B (Apo B) were studied in the patients with hypercholesterolemia. The results demonstrated that there was a significant decrease in the level of oxLDL after receiving cumin. Paraoxonase and arylesterase activities increased in serum after taking cumin extract. Paraoxanase 1 (PON1) played a protective role against the oxidative modification of plasma lipoproteins and hydrolyzes lipid peroxides in human atherosclerotic lesions [157].

The effects of *Cuminum cyminum* intake on weight loss and metabolic profiles among overweight subjects was studied by a randomized double-blind placebo-controlled clinical trial which conducted among 78 overweight subjects (male, n = 18; female, n = 60) aged 18-60 years old. Participants were randomly assigned into three groups to receive: (1) *Cuminum cyminum* capsule (n = 26); (2) orlistat 120 capsule (n = 26) and (3) placebo (n = 26) three times a day for 8 weeks. Anthropometric measures and fasting blood samples were taken at baseline and after 8 weeks of intervention. Consumption of the *Cuminum cyminum* and orlistat120 resulted in a similar significant decrease in weight (-1.1 ± 1.2 and -0.9 ± 1.5 compared with placebo 0.2 ± 1.5 kg, respectively, p = 0.002) and BMI (-0.4 ± 0.5 and -0.4 ± 0.6 compared with placebo 0.1 ± 0.6 kg/m(2), respectively, p = 0.003). In addition, *Cuminum cyminum* L., compared with orlistat and placebo, led to a significant reduction in serum insulin levels (-1.4 ± 4.5 vs. 1.3 ± 3.3 and 0.3 ± 2.2 μIU/ml, respectively, p = 0.02), HOMA-B (-5.4 ± 18.9 vs. 5.8 ± 13.3 and 1.0 ± 11.0, respectively, p = 0.02) and a significant rise in QUICKI (0.01 ± 0.01 vs. -0.005 ± 0.01 and -0.004 ± 0.01, respectively, p = 0.02)[158].

XIII. GASTROINTESTINAL EFFECT

The stomach of pentobarbitone-anesthetized rats was perfused at 0.15 ml/min with aqueous extracts of cumin or acetylcholine (1 microgram/ml or 10 micrograms/ml solutions, in 40 min blocks, twice in each experiment bracketed by saline perfusions. The acid content in the samples was estimated by titration with 0.1N NaOH with phenolphthalein as indicator. Cumin increased stomach acid secretion from 0.08 to 0.02. ($p < 0.05$)[159].

The antiulcer activity of the aqueous extracts of leaves of dried fruits of *cumin* against the diclofenac sodium induced stomach ulceration has been studied in rats in comparison with omeprazole. Cumin extract accelerated the healing process to different extents. Healing activity of the aqueous extracts of combination of *piper betel* and *cumin* was found to be beter than healing activity of aqueous extracts of cumin and piper betel alone. Aqueous extract also enhance gastric mucin protection and regeneration[160].

The effect of aqueous extract of *Cuminum cyminum* seeds (ACCS) was studied against diarrhoea on albino rats. The animals were divided into five groups and the control group was given 2% acacia suspension, the standard group with loperamide (3 mg/kg) or atropine sulphate (5mg/kg) and three test groups administered orally with 100, 250 and 500 mg/kg of ACCS. The antidiarrhoeal effect was investigated by castor oil induce diarrhoea model, prostaglandin E2 (PGE2) induced enteropooling model and intestinal transit by charcoal meal test. The ACCS showed significant ($p< 0.001$) inhibition in frequency of diarrhoea, defecation time delaying, secretion of intestinal fluid as well as intestinal propulsion as compared to control. The graded doses of the tested extract showed dose dependent protection against diarrhea[161].

Protective effects:

The effect of *Cuminum cyminum* (Cumin) on kidney exposed to profenofos was evaluated in female swiss albino mice. The results showed that cumin was effective in normalizing the uric acid and creatinine level[162].

Depression in growth, hepatotoxicity and nephrotoxicity were observed in rats that had been given paracetamol at 500 mg/kg orally for 4 weeks. These findings were accompanied by leucopenia, macrocytic normochromic anemia and alterations of serum aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase activities and concentrations of cholesterol, urea and other serum constituents. Serum bilirubin did not change. In rats given the mixture of paracetamol 500 mg/ kg plus 6% *Cuminum cyminum* fruit for 4 weeks, the recovery of paracetamol hepatotoxicity was evidenced by increase in body weight, absence of hepatocellular fatty vacuolation and significant improvement of serbiochemical and hematological parameters[163].

The effects of cumin on sperm quality and testicular tissue was evaluated following experimentally induced copper poisoning (copper sulphate 100 mg/kg) in mice. *Cuminum cyminum* was used at dose of 1 mg/kg. The results showed that sperm concentration, motility and viability in copper group were significantly decreased at weeks 4 and 6, and severe degenerative changes were observed in testicular tissues in comparison with the control group. In cumin treated group, significant improvement in the sperm count, motility and viability, and normal architecture in most seminiferous tubules with organized epithelium was observed compared to the copper group[164].

Bronchodilatory effects:

The relaxant effects of the macerated and aqueous extracts of *Cuminum cyminum* (0.25, 0.5, 0.75 and 1.0 g%) was investigated on the tracheal chains of guinea pig in comparison with saline and theophylline (0.25, 0.5, 0.75, and 1.0 mM) In Group 1 experiments (contracted by KCl) only the last two concentrations of theophylline and the highest concentration of macerated extract showed significant relaxant effect compared to that of saline ($p<0.001$ and $p<0.05$ for theophylline and macerated extract respectively). The effects of the last two concentrations of theophylline in this group were significantly greater than those of the macerated and aqueous extracts ($p<0.001$). However, in Group 2 experiments (contracted by methacholine) both the extracts and theophylline showed concentration-dependent relaxant effect compared to that of saline ($p<0.05$ to $p<0.001$). The effects of the two last concentrations of both extracts were significantly lower than those of theophylline in Group 2 experiments ($p<0.05$ to $p<0.001$). In Group 3 (non-incubated, contracted by methacholine) the extracts of *Cuminum cyminum* did not show any relaxant effect of tracheal chains. The relaxant effects of macerated and aqueous extracts in Groups 1 and 3 were significantly lower than those of Group 2 ($p<0.05$ to $p<0.001$)[165].

Immunological effect:

The health modulating effects and immunomodulatory properties of *Cuminum cyminum* were evaluated using flowcytometry and ELISA in normal and immune-suppressed animals. *Cuminum cyminum* stimulated the T cells and Th1 cytokines expression in normal animals. Swiss albino mice subjected to Cyclosporine-A induced immune-suppression were dosed orally with *Cuminum cyminum* (25, 50, 100 and 200 mg/kg) on consecutive days. The results showed that administration significantly increased T cells (CD4 and CD8) count and Th1 predominant immune response in a dose dependent manner, suggesting immunomodulatory activity through modulation of T lymphocytes expression. In restraint stress induced immune-suppressed animals, *Cuminum cyminum* countered the depleted T lymphocytes, decreased the elevated corticosterone levels and size of adrenal glands and increased the weight of thymus and spleen[166].

Contraceptive effect:

The contraceptive efficacy of *Cuminum cyminum* isolated fractions (CcFr) was investigated in male albino rats. Oral dose of CcFr 50 mg/rat/day for 60 days revealed no significant changes in body weight, while marked abnormalities in spermatogenesis were observed with decreased counts ($P \leq 0.001$) in round spermatids, preleptotene spermatocytes and secondary spermatocytes. Cross sectional surface area of Sertoli cells as well as number of mature Leydig cell were decreased significantly ($p \leq 0.001$). Testicular as well as accessory sex organ biochemical parameters were significantly changed ($p \leq 0.001$). Sperm motility, density and morphology were resulted in 100% negative fertility. Testosterone levels were declined significantly. The authors concluded that *Cuminum cyminum* inhibited spermatogenesis in rats and can be acting as herbal male contraceptive[167].

Anti-amyloidogenic effect:

The active anti-amyloidogenic compounds of the cumin oil was studied. After fractionation, the highest inhibitory effect was observed in the toluene-ethyl acetate part of the oil. Gas chromatography-mass spectrometry (GC-MS) analysis of this fraction indicated that eight compounds were predominantly present in the fraction. Two compounds including terpinolene and limonene (having very similar chemical structures) inhibited fibrillation. PC12 cells (derived from a transplantable rat pheochromocytoma) were affected by HEWL fibrils, whereas the inhibited forms of fibrils in the presence of terpinolene led to higher levels of viability, as appeared by 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT), lactate dehydrogenase (LDH) and flow cytometry assays. Molecular local docking analysis suggested a site of interaction for

terpinolene in the flexible cleft of the protein. This interaction site was close to tryptophan -62 and -63 and two other hydrophobic residues in the hot spot regions of the protein[168].

Anti-osteoporotic effect:

The anti-osteoporotic activity of *Cuminum cyminum* was evaluated in rats. Adult Sprague-Dawley rats were bilaterally ovariectomized (OVX) and randomly assigned to 3 groups. Additional animals were sham operated. OVX and sham control groups were orally administered with vehicle while the other two OVX groups were administered 0.15 mg/kg estradiol and 1 g/kg of methanolic extract of *Cuminum cyminum* fruits (MCC) in two divided doses for 10 weeks. At the end of the study blood, bones and uteri of the animals were collected. Serum was evaluated for calcium, phosphorus, alkaline phosphatase and tartarate resistant acid phosphatase. Bone density, ash density, mineral content and mechanical strength of bones were evaluated. Scanning electron microscopic (SEM) analysis of bones (tibia) was performed. MCC (1 g/kg, po) significantly reduced urinary calcium excretion and significantly increased calcium content and mechanical strength of bones in comparison to OVX control. It showed greater bone and ash densities and improved microarchitecture of bones in SEM analysis. Unlike estradiol it did not affect body weight gain and weight of atrophic uterus in OVX animals. MCC prevented ovariectomy-induced bone loss in rats with no anabolic effect on atrophic uterusl[169].

Aldose reductase and alpha-glucosidase inhibitory effects:

The inhibitory activity of *Cuminum cyminum* seed oil component was evaluated against lens aldose reductase and alpha-glucosidase isolated from Sprague-Dawley male rats and compared with quercitrin as an aldose reductase inhibitor and acarbose as an alpha-glucosidase inhibitor. The biologically active constituent of *Cuminum cyminum* seed oil was characterized as cuminaldehyde by various spectral analyses. The IC_{50} value of cuminaldehyde is 0.00085 mg/ml against aldose reductase and 0.5 mg/ml against alpha-glucosidase. Cuminaldehyde was about 1.8 and 1.6 times less inhibitory than quercitin and acarbose, respectively[170].

Tyrosinase inhibitory effect:

Cuminaldehyde was identified as a potent mushroom tyrosinase monophenol monooxygenase inhibitor. It inhibited the oxidation of L-3,4-dihydroxyphenylalanine (L-DOPA) by mushroom tyrosinase with an ID_{50} of 7.7 g/ml (0.05 mM). Its oxidized analogue, cumic acid (*p*-isopropylbenzoic acid), also inhibited this oxidation with an ID_{50} of 43 g/ml (0.26 mM). These two inhibitors affected mushroom tyrosinase activity in different ways[171].

Effect on erythrocyte hemolysis:

The effect of methanolic and acetonic seed extracts of Cumin (*Cuminum cyminum*) was studied on on human erythrocyte hemolysis in comparison with caraway. Both seed extracts were able to protect erythrocytes from hemolysis. Methanolic cumin extract showed higher percentage of protection than caraway[143].

Side effect and toxicity:

Health risks or side effects following the proper administration of designated dierapeutic dosages are not recorded[78]. The LD_{50} of essential oils in mice was 0.59 ml/kg[77]. *Cuminum cyminum* fruits were fed to male Wistar rats at 2% or 10% of standard diet for 6 weeks. A mixture (5% *Cuminum cyminum* fruits + 5% *T. vulgaris* leaves) was also fed to rats for a similar period. Diets containing 2% *Cuminum cyminum* fruits, was not toxic to rats. Impairment of growth and enterohepatonephropathy were observed in the rats fed a diet containing 10% *Cuminum cyminum* fruits. These changes were also recorded in the rats fed the mixture of the 2 plants and were accompanied by leukopenia, anemia and increases in serum AST activity and urea and by decreased total protein and albumin levels[172].

Acute and subchronic toxicity of cumin essential oil were studied in a 30 day oral toxicity study in rats. A 17.38% decrease in WBCs count, and 25.77%, 14.24%, and 108.81% increase in hemoglobin concentration, hematocrit, and platelet count respectively, were noted. LDL/HDL ratio was reduced to half[119].

Dose:

Daily dosage: The average single dose is 300 to 600 mg of drug (equivalent to 5 - 10 fruits). However, cumin was used both internally and externally in ground form and as a pressed oil[78].

XIV. CONCLUSION

This review discuss the chemical constituent, pharmacological and therapeutic effects of *Cuminum cyminum* as promising herbal drug because of its safety and effectiveness.

REFERENCES

[1]. Davidson-Hunt I. Ecological ethnobotany: stumbling toward new practices and paradigms. MASAJ 2000; 16: 1–13.

[2]. Al-Snafi AE. Chemical constituents and pharmacological importance of *Agropyron repens* – A review. Research Journal of Pharmacology and Toxicology 2015; 1 (2): 37-41.

[3]. Al–Snafi AE. Pharmacology and medicinal properties of *Caesalpinia crista* - An overview. International Journal of Pharmacy 2015; 5(2): 71-83.

[4]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Calendula officinalis* - A review. Indian Journal of Pharmaceutical Science & Research 2015; 5(3): 172-185.
[5]. Al-Snafi AE. The constituents and pharmacological properties of *Calotropis procera* - An Overview. International Journal of Pharmacy Review & Research 2015; 5(3): 259-275.
[6]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with hypolipidemic, hemostatic, fibrinolytic and anticoagulant effects (part 1). Asian Journal of Pharmaceutical Science & Technology 2015; 5(4): 271-284.
[7]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their effect on reproductive systems (part 1). Ind J of Pharm Sci & Res 2015; 5(4): 240-248.
[8]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their gastro-intestinal effects (part 1). Ind J of Pharm Sci & Res 2015; 5(4): 220-232.
[9]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their antiparasitic, antiprotozoal, molluscicidal and insecticidal activity (part 1). J of Pharmaceutical Biology 2015; 5(3): 203-217.
[10]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with antidiabetic effects (part 1). J of Pharmaceutical Biology 2015; 5(3): 218-229.
[11]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with antifungal activity (part 1). Int J of Pharm Rev & Res 2015; 5(3):321-327.
[12]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their dermatological effects (part 1). Int J of Pharm Rev & Res 2015; 5(4):328-337.
[13]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with anticancer activity (part 1). Int J of Pharmacy 2015; 5(3): 104-124.
[14]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with anti-inflammatory, antipyretic and analgesic activity (part 1). Int J of Pharmacy 2015; 5(3): 125-147.
[15]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their immunological effects (part 1). Asian Journal of Pharmaceutical Research 2015; 5(3): 208-216.
[16]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their antibacterial activity (part 1). International Journal of Pharmacology and Toxicology 2015; 6(3): 137-158.
[17]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with antioxidant activity (part 1). International Journal of Pharmacology and Toxicology 2015; 6(3): 159-182.
[18]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their respiratory effects (part 1). International Journal of Pharmacological Screening Methods 2015; 5(2):64-71.
[19]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their antiviral activity (part 1). International Journal of Pharmacological Screening Methods 2015; 5(2): 72-79.
[20]. Al-Snafi AE. Galactagogue action of the crude phenolic extracts of grape seeds (*Vitis vinifera*). International Journal of Biological & Pharmaceutical Research 2015; 6(8): 577-580.
[21]. Al-Snafi AE. Mammary gland stimulating effects of the crude phenolic extracts of green tea (*Camellia sinensis*). International Journal of Biological & Pharmaceutical Research 2015; 6(7): 573-576.
[22]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants with cardiovascular effects (part 1). Int J of Pharmacology & Toxicology 2015; 5(3): 163-176.
[23]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of medicinal plants with central nervous effects (part 1). Int J of Pharmacology & Toxicology 2015; 5(3): 177-192.
[24]. Al-Snafi AE. The pharmacological Importance of *Antirrhinum majus* - A review. Asian J of Pharm Sci & Tech 2015; 5(4): 313-320.
[25]. Al-Snafi AE. Chemical constituents and pharmacological effects of *Astragalus hamosus* and *Astragalus tribuloides* grown in Iraq. Asian J of Pharm Sci & Tech 2015; 5(4): 321-328.
[26]. Al-Snafi AE. The Pharmacological Importance of *Ballota nigra* –A review. Ind J of Pharm Sci & Res 2015; 5(4): 249-256.
[27]. Al-Snafi AE. Chemical constituents and pharmacological importance of *Bidens tripartitus* - A review. Ind J of Pharm Sci & Res 2015; 5(4): 257-263.
[28]. Al-Snafi AE. The pharmacological importance of *Brassica nigra* and *Brassica rapa* grown in Iraq. J of Pharm Biology 2015; 5(4): 240-253.
[29]. Al-Snafi AE. The chemical constituents and pharmacological importance of *Celosia* cristata – A review. J of Pharm Biology 2015; 5(4): 254-261.
[30]. Al-Snafi AE. The pharmacological importance of *Centaurea cyanus*- A review. Int J of Pharm Rev & Res 2015; 5(4): 379-384.
[31]. Al-Snafi AE. The chemical constituents and pharmacological importance of *Chrozophora tinctoria*. Int J of Pharm Rev & Res 2015; 5(4): 391-396.
[32]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of plants affected smooth muscles functions (part 1). Int J of Pharmacy 2015; 5(2): 90-97.

[33]. Al-Snafi AE. Medicinal plants with anti-urolithiatic effects (part1). Int J of Pharmacy 2015; 5(2): 98-103.
[34]. Al-Snafi AE, Allahwerdi, IY. and Jawad IA. Using of topical 5% urtica dioica ointment in treatment of psoriasis. European Journal of Biomedical and Pharmaceutical Sciences 2015; 2(4):103-111.
[35]. Al-Snafi AE. The pharmacological importance of Capsicum species (*Capsicum annuum* and *Capsicum frutescens*) grown in Iraq. Journal of Pharmaceutical Biology 2015; 5(3): 124-142.
[36]. Al-Snafi AE. Therapeutic properties of medicinal plants: a review of their detoxification capacity and protective effects (part 1). Asian Journal of Pharmaceutical Science & Technology 2015; 5(4): 257-270.
[37]. Al-Snafi AE. Cardiovascular effects of *Carthamus tinctorius*: A mini-review. Asian Journal of Pharmaceutical Research 2015; 5(3): 199-209.
[38]. Al-Snafi AE, Wajdy JM and Tayseer Ali Talab. Galactagogue action of *Nigella sativa* seeds. IOSR Journal of Pharmacy 2014; 4(6): 58-61.
[39]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Adiantum capillus-veneris* - A review. Asian Journal of Pharmaceutical Science and Technology 2015; 5(2): 106-111.
[40]. Al-Snafi AE. The pharmacological and therapeutic importance of *Agrimonia eupatoria*- A review. Asian Journal of Pharmaceutical Science and Technology 2015; 5(2): 112-117.
[41]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Ammannia baccifera* - A review. International Journal of Pharmacy 2015; 5(1): 28-32.
[42]. Al-Snafi AE. The chemical constituents and pharmacological importance of *Carthamus tinctorius* - An overview. Journal of Pharmaceutical Biology 2015; 5(3): 143-166.
[43]. Al-Snafi AE. Clinically tested medicinal plant: A review (Part 1). SMU Medical Journal 2016; 3(1): 99-128.
[44]. Al-Snafi AE. The pharmacological importance of *Artemisia campestris*- A review. Asian Journal of Pharmaceutical Research 2015;5(2): 88-92.
[45]. Al-Snafi AE. Chemical constituents and pharmacological effects of *Asclepias curassavica* – A review. Asian Journal of Pharmaceutical Research 2015; 5(2): 83-87.
[46]. Al-Snafi AE. The pharmacological importance of *Asparagus officinalis* - A review. Journal of Pharmaceutical Biology 2015; 5(2): 93-98.
[47]. Al-Snafi AE. The medical importance of *Betula alba* - An overview. Journal of Pharmaceutical Biology 2015; 5(2): 99-103.
[48]. Al-Snafi AE. Bioactive components *and* pharmacological effects of *Canna indica*- An overview. International Journal of Pharmacology and toxicology 2015; 5(2):71-75.
[49]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Capsella bursa-pastoris* - A review. International Journal of Pharmacology and toxicology 2015; 5(2):76-81.
[50]. Al-Snafi AE. The pharmacological importance of *Ailanthus altissima*- A review. International Journal of Pharmacy Review and Research 2015; 5(2):121-129
[51]. Al-Snafi AE. *Alhagi maurorum* as a potential medicinal herb: An Overview. International Journal of Pharmacy Review and Research 2015; 5(2):130-136.
[52]. Al-Snafi AE. The pharmacological importance of *Aloe vera*- A review. International Journal of Phytopharmacy Research 2015; 6(1) : 28-33.
[53]. Al-Snafi AE. The constituents and biological effects of *Arundo donax* - A review. International Journal of Phytopharmacy Research 2015; 6(1): 34-40.
[54]. Al-Snafi AE. The nutritional and therapeutic importance of *Avena sativa* - An Overview. International Journal of Phytotherapy 2015; 5(1): 48-56.
[55]. Al-Snafi AE. The Pharmacological importance of *Bellis perennis* - A review. International Journal of Phytotherapy 2015; 5(2): 63-69.
[56]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Capparis spinosa* - An overview. Indian Journal of Pharmaceutical Science and Research 2015; 5(2): 93-100.
[57]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Carum carvi* - A review. Indian Journal of Pharmaceutical Science and Research 2015; 5(2): 72-82.
[58]. Al-Snafi AE. The pharmacological importance of *Casuarina equisetifolia* - An Overview. International Journal of Pharmacological Screening Methods 2015; 5(1): 4-9.
[59]. Al-Snafi AE. The chemical constituents and pharmacological effects of *Chenopodium album* - An overview. International J of Pharmacological Screening Methods 2015; 5(1): 10-17.
[60]. Al-Snafi AE. Chemical constituents and pharmacological effects of *Clerodendrum inerme*- A review. SMU Medical Journal 2016; 3(1): 129-153.
[61]. Ali Esmail Al-snafi. Chemical constituents and pharmacological effects of *Citrullus colocynthis* - A review. IOSR Journal Of Pharmacy 2016; 6(3): 57-67.
[62]. Ali Esmail Al-Snafi. Medical importance of *Cichorium intybus* – A review IOSR Journal Of Pharmacy 2016; 6(3): 41-56.

[63]. Ali Esmail Al-Snafi. Pharmacological importance of *Clitoria ternatea* – A review IOSR Journal Of Pharmacy 2016; 6(3): 68-83.
[64]. Ali Esmail Al-Snafi. The medical Importance of *Cicer arietinum* - A review IOSR Journal Of Pharmacy 2016; 6(3): 29-40.
[65]. Ali Esmail Al-Snafi. Medical importance of *Antemis nobilis* (*Chamaemelum nobilis*)- A review. Asian Journal of Pharmaceutical Science & Technology 2016; 6(2): 89-95.
[66]. Ali Esmail Al-Snafi. *Adonis aestivalis*: pharmacological and toxicological activities- A revew. Asian Journal of Pharmaceutical Science & Technology 2016; 6(2): 96-102.
[67]. Al-Snafi AE. Study of drugs prescribing pattern of specialists and general practitioners in Tikrit city. Med J Tikrit Univ 1997; 3: 12-17 .
[68]. Al- Snafi AE. Antimicrobial drugs. Al Diaa Publication house, Iraq 2013.
[69]. Al- Snafi AE. Pharmacology and therapeutics. Al Diaa Publication house, Iraq 2013.
[70]. Al-Snafi, AE. The best lysosomal stabilizing and hypolipoproteinemic mono/ polyunsaturated fatty acids combination . Med. J Tikrit Univer 2002, 8:148-153 .
[71]. The plant list. A working list of all plant species. *Cuminum cyminum*, http://www. theplantlist.org/tpl/record/kew-2747364
[72]. ITIS (Integrated Taxonomic Information System) report, *Cuminum cyminum* L., http://www.itis.gov/servlet/SingleRpt/SingleRpt? search_topic=TSN&search _value=501839
[73]. Rai N, Yadav S, Verma AK, Tiwari L and Sharma RK. A monographic profile on quality specifications for a herbal drug and spice of commerce- *Cuminum cyminum* L. International Journal of Advanced Herbal Science and Technology 2012; 1(1): 1-12.
[74]. USDA, ARS, National Genetic Resources Program. Germplasm Resources Information Network-(GRIN). National Germplasm Resources Laboratory, Beltsville, Maryland. URL: http://www.ars-grin.gov.4/cgi-bin/npgs/html/taxon. pl?12617 (05 Nov 2015)
[75]. Shivakumar SI, Shahapurkar AA, Kalmath KV and Shivakumar B. Antiinflammatory activity of fruits of *Cuminum cyminum* Linn. Der Pharmacia Lettre 2010; 2(1): 22–24.
[76]. Zohary D and Hopf M. Domestication of plants in the old world, third edition. Oxford University Press 2000: 206.
[77]. Parashar M, Jakhar ML and Malik CP. A review on biotechnology, genetic diversity in cumin (*Cuminum cyminum*). Life Science 2014; 4(4): L17-L34.
[78]. PDR for Herbal Medicines. Medical Economics Company, Inc. at Montvale, 2000: 237-238.
[79]. Parthasarathy VA, Chempakam B and Zachariah TJ. Chemistry of spices. CAB International 2008: 211-226.
[80]. Prajapati ND, Purohit SS, Sharma AK and Kumar T. A Hand Book of Medicinal Plant: a Complete Source Book. Agrobios (India) 2003: 928.
[81]. Farrell KT. In: Spices, Condiments and seasonings. The AVI Publishing Co., Inc., Westport, Connecticut 1985: 98–100.
[82]. Moawad SA, El-Ghorab AH, Hassan M, Nour-Eldin H and El-Gharabli MM. Chemical and microbiological characterization of Egyptian cultivars for some spices and herbs commonly exported abroad. Food and Nutrition Sciences 2015; 6: 643-659.
[83]. Gohari AR and Saeidnia S. A review on phytochemistry of *Cuminum cyminum* seeds and its standards from field to market. Pharmacognosy Journal 2011;3(25): 1-5.
[84]. Hashum F and Al-Hashemi Y. Chromatographic separation and identification of some volatile oils, organic acids and phenols from the seeds of *Cuminum cyminum* growing in Iraq. IJRRAS 2014; 19 (1): 80-90.
[85]. Baser KHC, Kürkcüoglu M and Özek T. Composition of the Turkish cumin seed oil. Journal of Essential Oil Research 1992; 4(2): 133-138.
[86]. Rihawy MS, Bakraji EH and Odeh A. PIXE and GC-MS investigation for the determination of the chemical composition of Syrian *Cuminum cyminum* L. Appl Radiat Isot 2014; 86:118-125.
[87]. Hajlaoui H, Mighri H, Noumi E, Snoussi M, Trabelsi N, Ksouri R and Bakhrouf A. Chemical composition and biological activities of Tunisian *Cuminum cyminum* L. essential oil: a high effectiveness against *Vibrio* spp. strains. Food and Chemical Toxicology 2010; 48(8/9): 2186-2192.
[88]. Chaudhary N, Husain SS and Ali M. Chemical composition and antimicrobial activity of cumin oil (*Cuminum cyminum*, Apiaceae). Journal of Pharmacy and Pharmaceutical Sciences 2014; 3(7): 1428-1441.
[89]. Wanner J, Bail S, Jirovetz L, Buchbauer G, Schmidt E, Gochev V, Girova T, Atanasova T and Stoyanova A. Chemical composition and antimicrobial activity of cumin oil (*Cuminum cyminum*, Apiaceae). Natural Product Communications 2010; 5(9): 1355-1358 .

[90]. Li R and Jiang Z. Chemical composition of the essential oil of *Cuminum cyminum* L. from China. Flavour and Fragrance Journal 2004; 19(4): 311-313.
[91]. Moghadam ARL. Essential oil of the seeds of *Cuminum cyminum* L.(Apiaceae). Bull Env Pharmacol Life Sci 2015; 4(3):161-163.
[92]. Romeilah RM, Fayed SA and Mahmoud GI. Chemical compositions, antiviral and antioxidant activities of seven essential oils. Journal of Applied Sciences Research 2010; 6(1): 50-62.
[93]. -Gachkar L, Davood Y, Mohammad BR, Masood T, Shakiba AA. and Iraj R. Chemical and biological characteristics of *Cuminum cyminum* and *Rosmarinus officinalis* essential oils. Food Chemistry 2007; 102(3): 898-904.
[94]. Chaudhary N, Husain SS and Ali M. New phenolic, triterpenic and steroidal constituents from the fruits of *Cuminum cyminum* L. Journal of Pharmacognosy and Phytochemistry 2014; 3 (1): 149-154.
[95]. Leug AY and Foster S.. Encyclopedia of common natural ingredients used in food, drugs and cosmetic. Wiley- Interscience Publication, Johan Wiley & Sons Inc 1980: 409.
[96]. Vallverdú-Queralt A, Regueiro J, Martínez-Huélamo M, Rinaldi Alvarenga JF, Leal LN and Lamuela-Raventos RM. A comprehensive study on the phenolic profile of widely used culinary herbs and spices: rosemary, thyme, oregano, cinnamon, cumin and bay. Food Chem 2014; 154:299-307.
[97]. Bettaieb I, Bourgou S, Wannes WA, Hamrouni I, Limam F and Marzouk B. Essential oils, phenolics, and antioxidant activities of different parts of cumin (*Cuminum cyminum* L.). J Agric Food Chem 2010; 58(19): 10410-10418.
[98]. Rebey IB, Kefi S, Bourgou S, Ouerghemmi I, Ksouri R, Tounsi MS and Marzouk B. Ripening stage and extraction method effects on physical properties, polyphenol composition and antioxidant activities of cumin (*Cuminum cyminum* L.) seeds. Plant Foods Hum Nutr 2014; 69(4): 358-364.
[99]. Bameri Z, Amini-Boroujeni N, Saeidi S and Bazi S. Antimicrobial activity of *Cyminum cuminum* against biofilm E. coli. International Research Journal of Applied and Basic Sciences 2013; 5 (10): 1232-1234.
[100]. Jirovetz L, Buchbauer G, Stoyanova AS, Georgiev EV, Stanka T and Damianova ST. Composition, quality control and antimicrobial activity of the essential oil of cumin (*Cuminum cyminum* L.) seeds from Bulgaria that had been stored for up to 36 years. Int J Food Sc Techn 2005; 40: 305-310.
[101]. Farag RS, Daw ZY, Hewedi FM and El-Baroty GSA. Antimicrobial activity of some Egyptian spice essential oils. Journal of Food Protection 1989; 52(9): 665-667.
[102]. -Dwivedi SK and Dubey NK. Potential use of the essential oil of *Trachyspermum ammi* against seed-borne fungi of guar (*Cyamopsis tetragonoloba* L. Taub). Mycopathologia 1993; 121(2): 101-104.
[103]. Stefanini MB, Figueiredo RO, Ming LC and Junior AF. Antimicrobial activity of the essential oils of some spice herbs. Acta Horticulturae 2003; 597:215-216.
[104]. Leopold J, Buchbauer G, Stoyanova AS, Georgiev EV and Damianova ST. Composition, quality control and antimicrobial activity of the essential oil of cumin (*Cuminum cyminum* L.) seeds from Bulgaria that had been stored for up to 36 years. International Journal of Food Science & Technology 2005; 40(3): 305-310.
[105]. Fakoor MH and Rasooli I. Pathogen control by antioxidative characteristics of *Cuminum cyminum* and *Rosmarinus officinalis* essential oils. Acta Horticulturae 2008; 786: 125-136.
[106]. Hadian J, Ghasemnezhad M, Ranjbar H, Frazane M and Ghorbanpour M. Antifungal potency of some essential oils in control of postharvest decay of strawberry caused by *Botrytis cinerea*, *Rhizopus stolonifer* and *Aspergillus niger*. Journal of Essential Oil-Bearing Plants 2008; 11(5):553-562.
[107]. Hu L, Chen C, Yi X, Feng J and Zhang X. Inhibition of p-isopropyl benzaldehyde and p-isopropyl benzoic acid extracted from *Cuminum cyminum* against plant pathogens. Acta Botanica Boreali-Occidentalia Sinica 2008; 28(11): 2349-2354.
[108]. Manuel V, Ruiz-Navajas Y, Fernandez-Lopez J and Perez-Alvarez JA. Antibacterial activity of different essential oils obtained from spices widely used in Mediterranean diet. International Journal of Food Science & Technology 2008; 43(3): 526-531.
[109]. Karbin S, Rad AB, Arouiee H and Jafarn S. Antifungal activities of the essential oils on post-harvest disease agent *Aspergillus flavus*. Advances in Environmental Biology 2009; 3(3): 219-225.
[110]. Marjanlo AA, Mostofi Y, Shoeibi S and Fattahi, M. Effect of cumin essential oil on postharvest decay and some quality factors of strawberry. Journal of Medicinal Plants 2009; 8(31): 25-43.
[111]. Mahmoudi H, Rahnama K and Arabkhani MA. Antibacterial effect essential oil and extracts of medicinal plant on the causal agents of bacterial canker and leaf spot on the stone fruit tree. Journal of Medicinal Plants 2010; 9(36): 34-42.
[112]. Oroojalian F, Kasra KR, Azizi M and Bassami MR. Synergistic antibacterial activity of the essential oils from three medicinal plants against some important food-borne pathogens by microdilution method. Iranian Journal of Medicinal and Aromatic Plants 2010; 26(2): 133-146.

[113]. Romagnol, C, Andreotti E, Maietti S, Rai M and Mares D. Antifungal activity of essential oil from fruits of Indian *Cuminum cyminum*. Pharmaceutical Biology 2010; 48(7): 834-838.
[114]. Basmacıoglu MH , Özdemir P and Hames EE . Chemical compositions and antibacterial activity of the essential oils from some plant species. Ege Üniversitesi Ziraat Fakültesi Dergisi 2011; 48(1): 11-18.
[115]. Sheikh MI, Islam S, Rahman A, Rahman M, Rahim A and Alam F. Control of some human pathogenic bacteria by seed extracts of cumin (*Cuminum cyminum* L). Agriculturae Conspectus Scientifi cus 2010; 75 (1):39-44.
[116]. Iacobellis NS, Lo Cantore P, Capasso F and Senatore F. Antibacterial activity of *Cuminum cyminum* L. and *Carum carvi* L. essential oils. J Agric Food Chem 2005; 53(1): 57-61.
[117]. Shayegh S, Rasooli I, Taghizadeh M and Astaneh SD. Phytotherapeutic inhibition of supragingival dental plaque. Nat Prod Res 2008; 22(5):428-439.
[118]. Tavakoli HR, Mashak Z, Moradi B and Sodagari HR. Antimicrobial activities of the combined use of *Cuminum cyminum* L. essential oil, nisin and storage temperature against *Salmonella typhimurium* and *Staphylococcus aureus in vitro*. Jundishapur J Microbiol 2015; 8(4): e24838.
[119]. Allahghadri T, Rasooli I, Owlia P, Nadooshan MJ, Ghazanfari T, Taghizadeh M and Astaneh SD. Antimicrobial property, antioxidant capacity, and cytotoxicity of essential oil from cumin produced in Iran. J Food Sci 2010; 75(2): H54-61.
[120]. Toroglu S. *In-vitro* antimicrobial activity and synergistic/antagonistic effect of interactions between antibiotics and some spice essential oils. Journal of Environmental Biology January 2011; 32 (1): 23-29.
[121]. Irkin R and Korukluoglu M. Growth inhibition of pathogenic bacteria and some yeasts by selected essential oils and survival of *L. monocytogenes* and *C. albicans* in apple-carrot juice. Foodborne Pathog Dis 2009; 6(3):387-394.
[122]. Derakhshan S, Sattari M and Bigdeli M. Effect of subinhibitory concentrations of cumin (*Cuminum cyminum* L) seed essential oil and alcoholic extract on the morphology, capsule expression and urease activity of *Klebsiella pneumoniae*. Int J Antimicrob Agents 2008; 32(5):432-436.
[123]. Khosravi AR, Shokri H and Minooeianhaghighi M. Inhibition of aflatoxin production and growth of *Aspergillus parasiticus* by *Cuminum cyminum*, *Ziziphora clinopodioides*, and *Nigella sativa* essential oils. Foodborne Pathog Dis 2011; 8(12): 1275-1280.
[124]. Awan UA, Andleeb S, Kiyani A, Zafar A, Shafique I, Riaz N, Azhar MT and Uddin H. Antibacterial screening of traditional herbal plants and standard antibiotics against some human bacterial pathogens. Pak J Pharm Sci 2013; 26(6): 1109-1116.
[125]. Kedia A, Prakash B, Mishra PK and Dubey NK. Antifungal and antiaflatoxigenic properties of *Cuminum cyminum* (L.) seed essential oil and its efficacy as a preservative in stored commodities. Int J Food Microbiol 2014; 168-169: 1-7.
[126]. Naeini A, Naderi NJ and Shokri H. Analysis and *in vitro* anti-Candida antifungal activity of *Cuminum cyminum* and *Salvadora persica* herbs extracts against pathogenic Candida strains. J Mycol Med 2014; 24(1): 13-18.
[127]. El-Said AHM and El-Hady G. Antifungal activities of *Cuminum cyminum* and *Pimpinella anisum* essential oils. Int J Curr Microbiol App Sci 2014; 3(3): 937-944.
[128]. Khosravi AR, Shokri H and Mokhtari AR. Efficacy of *Cuminum cyminum* essential oil on FUM1 gene expression of fumonisin-producing *Fusarium verticillioides* strains. Avicenna J Phytomed 2015; 5(1): 34-42.
[129]. Romeilah RM, Fayed SA and Mahmoud GI. Chemical compositions, antiviral and antioxidant activities of seven essential oils. Journal of Applied Sciences Research 2010; 6(1): 50-62.
[130]. Deletre E, Chandre F, Williams L, Duménil C, Menut C and Martin T. Electro-physiological and behavioral characterization of bioactive compounds of the *Thymus vulgaris, Cymbopogon winterianus, Cuminum cyminum* and *Cinnamomum zeylanicum* essential oils against *Anopheles gambiae* and prospects for their use as bednet treatments. Parasit Vectors 2015; 8: 316.
[131]. Clark L. Dermal contact repellants for starlings: foot exposure to natural plant products. Journal of Wilderness Management 1998; 61(4): 1352–1358.
[132]. Tunc I, Berger BM, Erler F and Dagli F. Ovicidal activity of essential oils from five plants against two stored product insects. Journal of Stored Product Research 2000; 36: 161–168.
[133]. Jain SC, Purohit M and Jain R. Pharmacological evaluation of *Cuminum cyminum.* Fitoterapia 1992; 63(4): 291–294.
[134]. Willatgamuva SA, Platel K, Sarawathi G and Srinivasan K. Antidiabetic influence of dietary cumin seeds (*Cuminum cyminum*) in streptozotocin induced diabetic rats. Nutr Res 1998; 18:131–42.
[135]. Patil SB, Takalikar SS, Joglekar MM, Haldavnekar VS and Arvindekar AU. Insulinotropic and β-cell protective action of cuminaldehyde, cuminol and an inhibitor isolated from *Cuminum cyminum* in streptozotocin-induced diabetic rats. Br J Nutr 2013; 110(8):1434-1443.

[136]. Jagtap AG and Patil PB. Antihyperglycemic activity and inhibition of advanced glycation end product formation by *Cuminum cyminum* in streptozotocin induced diabetic rats. Food Chem Toxicol 2010; 48(8-9): 2030-2036.
[137]. Dhandapani S, Subramanian VR, Rajagopal S and Namasivayam N. Hypolipidemic effect of *Cuminum cyminum* L. on alloxan-induced diabetic rats. Pharmacol Res 2002; 46(3): 251-255.
[138]. Gagandeep, Dhanalakshmi S, Méndiz E, Rao AR and Kale RK. Chemopreventive effects of *Cuminum cyminum* in chemically induced forestomach and uterine cervix tumors in murine model systems. Nutr Cancer 2003; 47(2):171-180.
[139]. Aruna, K and Sivaramakrishnan VM. Anticarcinogenic effects of some Indian plant products. Food and Chemical Toxicology 1992; 30(11): 953–956.
[140]. Vallverdú-Queralt A, Regueiro J, Martínez-Huélamo M, Rinaldi Alvarenga JF, Leal LN and Lamuela-Raventos RM. A comprehensive study on the phenolic profile of widely used culinary herbs and spices: rosemary, thyme, oregano, cinnamon, cumin and bay. Food Chem 2014; 154: 299-307.
[141]. Chen Q, Gan Z, Zhao J, Wang Y, Zhang S, Li J and Ni Y. *In vitro* comparison of antioxidant capacity of cumin (*Cuminum cyminum* L) oils and their main components. Food Science and Technology 2013; 55(2): 632-637.
[142]. Koppula S and Choi DK. *Cuminum cyminum* extract attenuates scopolamine-induced memory loss and stress-induced urinary biochemical changes in rats: a noninvasive biochemical approach. Pharm Biol 2011; 49(7): 702-708.
[143]. Atrooz OM. The Effects of *Cuminum cyminum* L and *Carum carvi* L seed extracts on human erythrocyte hemolysis. International Journal of Biology 2013; 592: 57-63.
[144]. Aruna K, Rukkumani R, Suresh Varma P and Venugopal MP. Therapeutic role of *Cuminum cyminum* on ethanol and thermally oxidized sunflower oil induced toxicity. Phytotherapy Research 2005; 19(5): 416–421.
[145]. Bhat SP, Rizvi W and Kumar A. Effect of *Cuminum cyminum* L seed extracts on pain and inflammation. Journal of Natural Remedies 2014; 14(2): 186-192.
[146]. Wei J, Zhang X, Bi Y,Miao R, Zhang Z and Su H. Anti-inflammatory effects of cumin essential oil by blocking JNK, ERK, and NF- κB signaling pathways in LPS-stimulated RAW 264.7 cells. Evidence-Based Complementary and Alternative Medicine 2105, http://dx.doi.org/10.1155/2015/474509
[147]. Sayyah M, Peirovi A and Kamalinejad M. Anti-nociceptive effect of the fruit essential oil of *Cuminum cyminum* L in rat. Iranian Biomedical Journal 2002; 6 (4): 141-145.
[148]. Tomy MJ, Dileep KV, Prasanth S, Preethidan DS, Sabu A, Sadasivan C and Haridas M. Cuminaldehyde as a lipoxygenase inhibitor: *in vitro* and in silico validation. Appl Biochem Biotechnol 2014; 174(1): 388-397.
[149]. Janahmadi M, Niazi F, Danyali S and Kamalinejad M. Effects of the fruit essential oil of *Cuminum cyminum* Linn (Apiaceae) on pentylenetetrazol-induced epileptiform activity in F1 neurones of Helix aspersa. J Ethnopharmacol 2006; 104(1-2): 278-282.
[150]. -Haghparast A, Shams J, Khatibi A, Alizadeh AM and Kamalinejad M. Effects of the fruit essential oil of *Cuminum cyminum* Linn (Apiaceae) on acquisition and expression of morphine tolerance and dependence in mice. Neurosci Lett 2008; 440(2): 134-139.
[151]. Khatibi A, Haghparast A, Shams J, Dianati E, Komaki A and Kamalinejad M. Effects of the fruit essential oil of *Cuminum cyminum* L on the acquisition and expression of morphine-induced conditioned place preference in mice. Neurosci Lett 2008; 448(1):94-98.
[152]. Morshedi D, Aliakbari F, Tayaranian-Marvian A, Fassihi A, Pan-Montojo F and Pérez - Sánchez H. Cuminaldehyde as the major component of *Cuminum cyminum*, a natural aldehyde with inhibitory effect on alpha-synuclein fibrillation and cytotoxicity. J Food Sci 2015; 80(10): H2336-2345.
[153]. Srivastava KC. Extracts from two frequently consumed spices-cumin (*Cuminum cyminum*) and turmeric (*Curcuma longa*)- inhibit platelet aggregation and alter eicosanoid biosynthesis in human blood platelets. Prostaglandins Leukot Essent Fatty Acids 1989; 37(1):57-64.
[154]. Kalaivani P, Saranya RB, Ramakrishnan G, Ranju V, Sathiya S, Gayathri V, Thiyagarajan LK, Venkhatesh JR, Babu CS and Thanikachalam S. *Cuminum cyminum*, a dietary spice, attenuates hypertension via endothelial nitric oxide synthase and NO pathway in renovascular hypertensive rats. Clin Exp Hypertens 2013; 35(7): 534-542.
[155]. Shirke SS and Jagtap AJ. Effects of methanolic extract of *Cuminum cyminum* on total serum cholesterol in ovariectomized rats. Indian J Pharmacol 2009; 41(2): 91-93.
[156]. Zare R, Heshmati F, Fallahzadeh H and Nadjarzadeh A. Effect of cumin powder on body composition and lipid profile in overweight and obese women. Complement Ther Clin Pract 2014; 20(4): 297-301.

[157]. Samani KG and Farrokhi E. Effects of cumin extract on oxLDL, paraoxanase 1 activity, FBS, total cholesterol, triglycerides, HDL-C, LDL-C, Apo A1, and Apo B in in the patients with hypercholesterolemia. Int J Health Sci (Qassim) 2014; 8(1):39-43.
[158]. Taghizadeh M, Memarzadeh MR, Asemi Z and Esmaillzadeh A. Effect of the *Cuminum cyminum* L intake on weight loss, metabolic profiles and biomarkers of oxidative stress in overweight subjects: A randomized double-blind placebo-controlled clinical trial. Ann Nutr Metab 2015; 66(2-3):117-124.
[159]. Vasudevan K, Vembar S, Veeraraghavan K and Haranath PS. Influence of intragastric perfusion of aqueous spice extracts on acid secretion in anesthetized albino rats. Indian J Gastroenterol 2000; 19(2): 53-56.
[160]. Pratyusha AC, Manmohan B, Raju S, Bhanuprasad T, Sruthi VV and Kishore RN. Comparative study of anti ulcer activity of aqueous extracts of leaves of *Piper betel* Linn and dried fruits of *Cuminum cyminum* Linn and their combination in rats. International Journal of Advanced Research 2013; 1(4): 192-195.
[161]. Sahoo HB, Sahoo SK, Sarangi SP, Sagar R and Kori ML. Anti-diarrhoeal investigation from aqueous extract of *Cuminum cyminum* Linn seed in albino rats. Pharmacognosy Res 2014; 6(3):204-209.
[162]. Kumar A, Singh JK, Ali M, Kumar R, Kumar A, Nath A, Roy AK, Roy SP and Singh JK. Evaluation of *Cuminum cyminum* and *Coriandrum sativum* on profenofos
[163]. induced nephrotoxicity in Swiss albino mice. Elixir Appl Botany 2011; 39 : 4771-4773.
[164]. Elhabib EM. Homeida MMA and Adam SEI. Effect of combined paracetamol and *Cuminum cyminum* or *Nigella sativa* used in Wistar Rats. Journal of Pharmacology and Toxicology 2007; 2: 653-659.
[165]. Sakhaee E, Emadi L, Azari O, Kheirandish R, Esmaili Nejad MR and Shafiei BH. Effects of *Cuminum cyminum* L essential oil on some epididymal sperm parameters and histopathology of testes following experimentally induced copper poisoning in mice. Andrologia. 2015, doi: 10.1111/and.12476.
[166]. Boskabady MH, Kiani S and Azizi H. Relaxant effect of *Cuminum cyminum* on guinea pig tracheal chains and its possible mechanism(s). Indian Journal of Pharmacology 2005; 37(2): 111-115.
[167]. Chauhan PS, Satti NK, Suri KA, Amina M and Bani S. Stimulatory effects of *Cuminum cyminum* and flavonoid glycoside on cyclosporine-A and restraint stress induced immune-suppression in Swiss albino mice. Chem Biol Interact 2010; 185(1): 66-72.
[168]. Saxena P, Gupta R and Gupta RS. Contraceptive studies of isolated fractions of *Cuminum cyminum* in male albino rats. Nat Prod Res 2015; 29(24): 2328-2331.
[169]. Morshedi D, Kesejini TS, Aliakbari F, Karami-Osboo R, Shakibaei M, Marvian AT, Khalifeh M and Soroosh M. Identification and characterization of a compound from *Cuminum cyminum* essential oil with antifibrilation and cytotoxic effect. Res Pharm Sci 2014; 9(6): 431-443.
[170]. Shirke SS, jadhav SR and Jagtap AG. Methanolic extract of *Cuminum cyminum* inhibits ovariectomy-induced bone loss in rats. Exp Biol Med 2008; 233(11): 1403-1410.
[171]. Lee HS. Cuminaldehyde: aldose reductase and alpha-glucosidase inhibitor derived from *Cuminum cyminum* L seeds. J Agric Food Chem 2005; 53(7): 2446-2450.
[172]. Kubo I and Kinst-Hori I. Tyrosinase inhibitors from cumin. Journal of Agricultural and Food Chemistry 1998; 46(12): 5338–5341.
[173]. Haroun EM, Mahmoud OM and Adam SE. Effect of feeding *Cuminum cyminum* fruits, *Thymus vulgaris* leaves or their mixture to rats. Vet Hum Toxicol 2002; 44(2):67-69.