Pharmacognosy Reviews, 2023; 17(33):135-143.
www.phcogrev.com

Review Article

Phytochemistry, Pharmacological Properties and Medicinal Uses of *Apium leptophyllum*: A Review

Tariq Ahmad Sheikh, Shahid Yousuf Ganie, Mohd Salim Reshi*

Department of Zoology, Toxicology and Pharmacology Laboratory, School of Biosciences and Biotechnology, Baba Ghulam Shah Badshah University, Rajouri, Jammu and Kashmir, INDIA.

ABSTRACT

Apium leptophyllum seeds are used as an important drug in Ayurveda from ancient times. The main constituents of the seed are fats, fibre, carbohydrates and essential oils, about 50% of which consists of Thymol. Chromatographic analysis of the seed showed various essential compounds viz. Pentacosanol, β-Sitosterol, 1-nonadecanol, 8-hydroxy cuminic acid, Corosolic acid and Stigmasterol. The seeds have shown strong antioxidant properties along with various other pharmacological properties like anti-microbial, anti-fungal, anti-diabetic, anti-inflammatory, anti-diarrheal, anti-asthmatic and anti-cancer properties. This review aims to provide a comprehensive overview of scientific research literature on the chemical composition and pharmacological activities of Apium leptophyllum. We are the first to report vast and updated review of this plant, as much of the work has not been done on this plant. So this review may be helpful for the researchers to explore the pharmacological properties of this plant which may lead to new discoveries in drug development.

Keywords: Pharmacology, Phytochemistry, Antioxidant.

Correspondence:

Dr. Mohd Salim Reshi,

Assistant Professor, Department of Zoology, Toxicology and Pharmacology Laboratory, School of Biosciences and Biotechnology, Baba Ghulam Shah Badshah University, Rajouri, Jammu and Kashmir, INDIA.

E-mail: reshisalim@gmail.com

Received: 20-07-2022;
Revised: 27-08-2022;
Accepted: 08-09-2022.

INTRODUCTION

There is a rising demand for plant-based medicines, pharmaceuticals, food supplements, health products, cosmetics etc which are derived from plants. From times immemorial, various societies have resorted to nature, mainly to plants as medicine and health sources. Today, a large number of people particularly in under developed and developing countries uses these traditional plants for primary needs of medicinal assistance.[1] As an estimate of the World Health Organization (WHO), about 80% of the world population still uses these herbs and other traditional medicines for their medicinal use. Polysaccharides from medicinal herbs have received a lot of significance in recent decades because of their notable bioactivities, such as anti-proliferative, antioxidant, anticoagulant, radioprotection effect, antiviral activity, hypolipidemic, antidiabetic and immunomodulatory activities, which make them worthy for medicinal uses.[2] Traditional medicines and medicinal herbs are widely used as curative agents in most underdeveloped countries for maintaining of sound health.[3] The antibacterial, antioxidant and antipyretic actions of phytochemicals present in these plants could explain their medicinal properties.[4] So these plants should be investigated to have good comphrension of their qualities, protection, and efficacy.[5] The word "herbal drug" refers to the plant parts (seeds, leaves, flowers, roots, barks, stems, and so on) that are used to make medications. Furthermore, the World Health Organization (WHO) defines medicinal plants as herbal remedies made by subjecting plant materials to extraction, fractionation, purification and concentration and which can be made for utilization or as a base for herbal products. Because information on the usage of plant species has been passed down through oral tradition from one generation to the next, knowledge of therapeutic plants has begun to dwindle. As a result of a shift in socio-economic changes and attitude, knowledge of therapeutic plants has become obsolete.[6] The Ayurveda system in India has detailed a vast number of plant or plant product-based remedies. The exploration of their morphological, pharmacognostical or pharmacological uses can help us understand their active principles and mode of action, which can help in exploring different medicinal plants.

Fir-leafed celery and Marsh parsley are common names for *Apium leptophyllum*, which belongs to the Apiaceae (Umbelliferae) family. It's called "Ajmoda" in Hindi. The plant is found in North America, but it is present all over the world, from warm tropical to temperate latitudes, and it is known as noxious weed in many places. It's a herb with tap-rooted branching and thread-like green leaves that grows to just over half a metre.

CLASSIFICATION

Kingdom	:	Plantae
Division	:	Magnoliophyta
Class	:	Magnoliopsida
Subclass	:	Rosidae

DOI: 10.5530/097627870185

Publishing Partner : EManuscript Tech. [www.emanuscript.in]

Order	:	Apiales
Family	:	Apiaceae
Genus	:	*Apium*
Species	:	*leptophyllum*
Synonym	:	*Cyclospermum leptophyllum*
Other Names	:	Hindi: Ajmoda, Ajmod
English	:	Oregano
Urdu	:	Ajmod
Kashmiri	:	Fakhazur, Banjuan
Parts used for medicine uses	:	Leaves, Seeds, Root,
Group	:	Dicot

Ajamoda (*Apium leptophyllum*) was discovered in Pakistan, South America, Sri Lanka, Queensland, India and the tropics.[7] The Umbelliferous fruit '*Apium leptophyllum*' is an essential drug in the Siddha, Ayur-veda, and Unani systems of medicine. Fruits of *Apium leptophyllum* are used in the drug formulations. Ajmoda is an annual plant that can reach a height of 2 feet. It thrives on soils that are acidic, neutral, or basic (alkaline). Cooked leaves are consumed, while the plant's seeds are utilized as a condiment. The plant's seeds are tiny and yellowish brown and have a pleasant scent and a slightly bitter-pungent flavour.

Apium leptophyllum is a member of the Apiaceae family.[8] *Apium leptophyllum* leaves are used in Ethiopia to treat "Mitch," a disorder characterized by sweet inflammation and loss of appetite and are used in traditional system of medicine to cure flatulence, dyspepsia and diarrhoea.[9,10] The extracts of fruit also showed high antioxidant activity and chemopreventive ability.[11-12] Flavonoids isolated during phytochemical examination of the fruits are,[13] Coumarins,[14] D-mannitol, 2, 3 dihydro-2-methyl-6-hydroxybenzofuran-5carboxylic acid[15] and 8-hydroxy cuminic acid.[16] The plant *Apium leptophyllum* and its seeds are shown in Figure 1.

Figure 1: *Apium leptophyllum.*

Morphological Features of *Apium leptophyllum* (pers.) F. Muell ex Benth

Color - Light brown to yellow

Shape- Oval and spherical to spherical and mericarps are not curved

Size - 2mm length and about 2mm in width

Surface- Glabrous to naked eye and ridges straight

Microscopic Characters

Microscopy is required for the observation of adulterants and defilement in herbal production, as well as for determining the validity and quality of herbal remedies. During microscopic study of crude pharmaceuticals, the shape, size, and relative position of distinct cells and tissues, as well as the chemical nature of cell walls and the form and nature of cell contents, are all taken into account.

Saraswathya and other coworkers in 2013 demonstrated the microscopic characters of *Apium leptophyllum*. They have reported that the epidermal cells are straight walled; they are generally 80 microns long, 50 microns broad and papillae present. The vascular system's patchy extensions with pitted sclerenchymatous cells are present in the mesocarp, but there is no full mesocarpic sclerenchymatous layer. Parquetry arrangement is not found in endocarp. A vascular bundle of spiral, tracheids, and reticulate vessels and sclerenchyma cells with oblong pits supports the ridges; thin xylem fibres are also present. The seed is endospermous, a single layer called testa is on the posterior side, but it is present with some more tissue layers on the commissural side, embryo is embedded in the endosperm; cell walls of the endosperm uniformly thick, cells packed with aluerone grains.[17] These studies will be helpful in the identification of *Apium leptophyllum* for researchers who want to work on this plant.

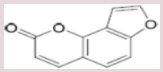
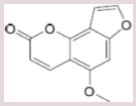
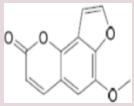
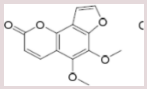
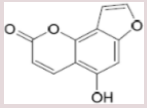
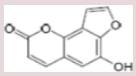
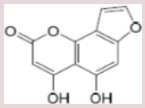
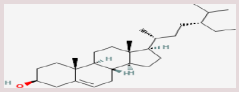
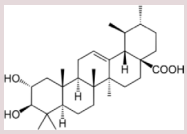
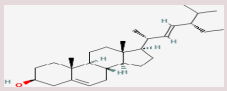
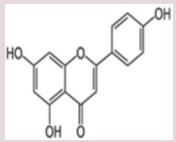
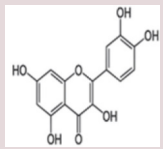
Chemical Composition and Isolated Compounds

Chemical composition of *Apium leptophyllum* is given in Table 1 and isolated compounds from *Apium leptophyllum* and their structures are given in Table 2. The major chemical components of the seeds of *Apium leptophyllum* are fibre, fat and carbohydrates. The major minerals in the seeds are phosphorus, calcium, and iron while carotene, thiamine, riboflavin and niacin are main vitamins. Salehi and other researchers in 2019 reported that Phytochemical constituents of the *Apium* plants as per USDA Nutrient Database contain Glucides (fructose, sucrose), Lipids (fatty acids), Stearic acids, Palmitic acids, Oleic acids, carbohydrates, Linoleic acids, alkaloids, glycosides, flavonoids, saponins and steroids, tannins and Linoleic acids. Carbohydrates, alkaloids, glycosides, flavonoids, saponins and steroids, tannins and the majority of macro and microelements were found in large

Table 1: Isolated compounds from *Apium leptophyllum*.

Isolated compounds (Phytoconstituents)	Parts investigated	Methods used	References
Thymol	Seed	Hydro-distillation	[24]
Thymoquinol dimethyl ether), γ-terpinene, isothymolmethyl ether, p-cymene and thymol methyl ether	Leaves	Hydro-distillation	[21]
p-cymene and γ-terpinene, thymohydroquinone dimethyl ether monomethoxy cymene isomers, cuminaldehyde	Seed	GC MS	[22]
Pentacosanol, β- sitosterol, nonadecanol, 8-hydroxy cuminic acid, Corosolic acid and 7α-hydroxstigmasterol	Seed	Gel chromatography	[23]
Apigenin and Quercetin	Seed	FTIR, NMIR	[24]
Germacrene D, Germacrene B, n-Hexanal, n-Heptanal, α-Thujene	Seed	GC MS	[23]
Glucides (fructose, sucrose), fatty acids, flavonoids, saponins, steroids, tannins, phenols, furocoumarins, 3-butilphtalide.	Leaves, seed, root	Chromatography	[18]
Thujene, α-Pinene Sabinene, β-Pinene, β-Myrcene, α-Terpinene, p-Cymene, β-Phellandrene, cis-β-Ocimene, trans-β-Ocimene, γ-Terpinene, Terpinen-4-ol, Isothymol methyl ether, Thymol methyl ether, Cuminaldehyde, Carvacrol methyl ether,	Seeds	GC MS	[10]

Table 2: Isolated compounds from *Apium leptophyllum* and their structures.

Isolated compound	Structure	References
Angelicin		[18]
Isobergapten		
Sphondin		
Pimpinellin		
Isobergaptol		
Sphondinol		
5,6 dihyydroxy Anglocenin		
Pentacosonal		[23]
1-nonadecanol		
β- Sitosterol		
Corosolic acid		
7-hydroxy-Stigmasterol		
Apigenin		[24]
Quercetin		

quantities in *Apium* plants, while terpenoids were found in limited amounts or even absent. Volatile oils, sesquiterpene, alcohols and fatty acids were also found in aqueous and ethanolic extract of *Apium leptophyllum*.[18] Ganesh and other coworkers discovered phenols, flavonoids, coumarins, terpeniods and alkaloids.[19] The dominant part, phenolic ether, apiole, was recognize by the Brazilian source, while no other sources mentioned even traces of this compound, some reported thymohydroquinone dimethyl ether as the dominant component while the major ones were γ-terpinene, thymol methyl ether and p-cymene and in addition either carvacrol methyl ether) or isothymol methyl ether.[10-20] It has been reported that the leaves of *Apium leptophyllum* yielded colorless essential oil on hydrodistillation. The oil contains γ-terpinene, isothymol methyl ether, thymoquinol dimethyl ether), p-cymene and thymol methyl ether, sesquiterpenes (germacrene D), Bicyclic monoterpene hydrocarbons (β-pinene, sabeinene, α-thujene and α-pinene), Acyclic monoterpene hydrocarbons (trans-β-ocimene, β-myrcene and cis-β-ocimene), Monocyclic oxygenated monoterpenes (carvacrol methyl ether, cuminaldehyde and terpinen-4-ol) and Monocyclic monoterpene hydrocarbons (β-phellandrene and α-terpinene).[21] Helal and other researchers in 2015 revealed GC-MS analysis of ripe fruit, unripe fruit, root and green aerial part of *Apium leptophyllum* and showed presence of various compounds via n-Heptanal, α-Thujene, n-Hexanal, α –Pinene, Sabinene, Myrcene, Car-3-ene,

α –Terpinene, β-Pinene, p-Cymene, trans-Ocimene, cis-Sabinene hydrate, γ –Terpinene, Terpinolene, p-Cymenene, Linalool, Terpinen-4-ol, n-Decanal, Isothymol methyl ether, Thymol methyl ether, Carvacrol methyl ether, Cuminaldehyde, Car-2-en-10-al, γ -Terpinen-7-al, Carvacrol, α-Copaene, B-Bourbonene, Thymohydroquinone dimethyl ether, 3-Methoxy cuminaldehyde, α-Humulene, Germacrene D, α-Zingiberene, Methoxy cuminaldehyde isomer, Caryophyllene oxide, Humulene epoxide II, Cumin alcohol isovalerate, 2-Pentadecanone, Palmetic acid.[22] Asamenew and other researchers in 2008 have isolated 20 compounds from *Apium leptophyllum* seeds through GC MS analysis viz α-Thujene, β-Pinene, β-Myrcene, α-Pinene Sabinene α-Terpinene, p-Cymene, cis-β-Ocimene, β-Phellandrene trans-β-Ocimene, Isothymol methyl ether, Thymol methyl ether, Cuminaldehyde, γ-Terpinene, Terpinen-4-ol, Carvacrol methyl ether, Thymoquinol dimethyl ether α-Humulene, Germacrene D, Germacrene B.[10] It has been reported by Helal and other coworkers in 2017 that silica gel chromatographic analysis of seeds of *Apium leptophyllum* showed presence of six compounds that are Pentacosanol, β- sitosterol, 1-nonadecanol, 8-hydroxy cuminic acid, Corosolic acid and 7α-hydroxstigmasterol.[23] Sahoo and other researchers in 2015 have has isolated two compounds from the flavonoidal fraction of *Apium leptophyllum* and purified as Apigenin and Quercetin. The structural elucidation of each compound was carried out by MS, FTIR and NMR spectroscopy and the structure of these compounds were analyzed.[24] Phytochemical compounds and their pharmacological properties are shown in Table 3.

Table 3: Phytochemicals and their pharmacological properties found in *Apium leptophyllum*

Phytochemicals	Pharmacological properties	References
Thymol methyl ether	Antioxidant, Antibacterial, Anti-inflammatory	[45]
γ-terpinene	Antioxidant, Acaricidal, Antimicrobial	[46] [47] [48]
p-cymene	Anticancer	[49] [50]
Carvacrol methyl ether	Antioxidant, Antimicrobial	[51] [52]
β-pinene	Antimicrobial, Antibacterial, Antifungal	[53] [53]
α-thujene	Anti-inflammatory Antifungal	[54] [55]
α-pinene	Antimicrobial Oxidative stress	[53] [56]
Cuminaldehyde	Antibacterial	[57]
β-phellandrene	Antibacterial	[58]
Germacrene D	Antibacterial Anti-toxic	[59] [60]
Pentacosanol	Anti-cancer	[61]
β- sitosterol	Hypocholesterolemic, Anti-inflammatory	[62] [64]
8-hydroxy cuminic acid	Anticancer activity	[23]
Corosolic acid	Antiangiogenic	[64]

Antioxidant Properties

Oxidative stress and an increase in free radical levels are two of the most important core markers linked to a variety of progressive pathological illnesses, including neurological disorders, cancer, ageing, and endocrine disease.[25] Many chronic health disorders are caused by free radicals and antioxidants can help us by preventing free radical formation. New sources of antioxidants of natural origin that are both economically viable and safe are being researched. Medicinal plants as natural antioxidants have gained in popularity as a therapeutic choice. Natural antioxidants found in medicinal plants include flavonoids, Vitamin C, tocopherol, and other phenolic substances.[26] Secondary metabolites protect living organisms against harm caused by unrestricted formation of reactive oxygen species (ROS), DNA strand breaking, protein damage, and concurrent lipid peroxidation.[27] Because of the presence of various important active chemicals such as phenol, tannins, flavonoid, coumarins, and terpenoids, medicinal plants are currently found to have free radical scavenging action.[28] Among the different naturally occurring traditional medicinal plants, *Apium leptophyllum* has been reported for its strong antioxidant activities of *in-vivo* and *in-vitro* studies. When compared to conventional ascorbic acid, *Apium leptophyllum* seed extracts showed considerable antioxidant activity by reducing hydroxyl, DPPH, nitric oxide and superoxide radicals, which could be owing to the high phenolic and flavonoidal content.[29] Due to its high free radical scavenging activity the essential oil of *Apium leptophyllum* is used for the curative agent of "Mitch", the inflammatory disease which causes the formation of free radicals. Scavenging of such radicals by the oil is helpful to control the general symptoms of "Mitch" such as inflammation.[10] DPPH radical scavenging activity is being performed to screen the antioxidant potential of plant extracts. The scavenging effect percentage of DPPH on various extracts of *Apium leptophyllum* with different concentrations was studied by Sahoo and other researchers in 2013. They have found the IC_{50} values of methanolic, aqueous, ethanolic extract and Ascorbic acid at 97.9, 123.52, 217.32, 20.98 μg/ml respectively. Thus, they have revealed in their study that the methanol extracts showed higher DPPH radical scavenging activity as compared to other extracts.[11] The radical scavenging activity of the essential oils of *Apium leptophyllum* on DPPH was also determined spectrophotometerically by Asamenew and other researchers in 2008. They found that adding the volatile oil to the mix decreased DPPH in a concentration dependent manner.[10] The constituents terpinene and terpinene-4-ol, which have been stated in the literature to have strong

Table 4: Antioxidant activities of *Apium leptophyllum*.

Parts used	Type of extract	Method used	IC_{50} VALUE	Responsible phytochemicals	References
Seed	Methanolic Ethanolic Aqueous	DPPH	97.9 µg/ml 123.52 µg/ml 217.32 µg/ml	Phenolics and Flavonoids	[11]
Seed (OIL)	Aqueous Ethanolic	DPPH	4.3 µg/ ml	α-terpinene, γ-terpinene and terpinen-4	[10]
Seed oil	Aqueous Ethanolic	DPPH	180 µg/ml 98 µg/ml	Phenol, tannins, flavonoid, coumarins, terpeniods	[19]
Seed	Methanolic Ethanolic Aqueous	Hydroxy Radical Scavenging	89.02 µg/ml 111.02µ g/ml 195.22 µg/ml	Phenolics and Flavonoids	[11]
Seed	Aqueous Ethanolic	Hydroxy Radical Scavenging	250 µg/ml 218 µg/ml	Phenol, tannins, flavonoid, coumarins, terpeniods	[19]
Seed	Methanolic Ethanolic Aqueous	NO	135.37µg/ml 179.82 µg/ml 282.81 µg/ml	Phenolics and Flavonoids	[11]
SEED	Aqueous Ethanolic	NO	180 µg/ml 110 µg/ml	Phenol, tannins, flavonoid, coumarins, terpeniods	[19]
SEED	Methanolic Ethanolic Aqueous	SO	127.73 µg/ml 144.01µg/ml 207.67µg/ml	Phenolics and Flavonoids	[11]
SEED	Aqueous Ethanolic	Reducing power assay	170 µg 100 µg	Phenol, tannins, flavonoid, coumarins, terpeniods	[19]

radical scavenging activity.[30,31] Shukla and other researchers in 2001 also reported concentration dependent free radical scavenging activity of aqueous and ethanolic extracts of *Apium leptophyllum* by DPPH assay. Through oxidation of essential thiol (-SH) groups Hydrogen peroxide a oxidizing agent that inactivates a few enzymes directly.[32] Various researchers have evaluated the H_2O_2 scavenging activity of *Apium leptophyllum* to check the antioxidant property of *Apium leptophyllum*. They reported a concentration dependent inhibition of H_2O_2 radical scavenging.[11,19] Methanolic extract have been found to have better hydroxyl radical scavenging ability.[11] Nitric oxide inhibition is another powerful assay to check the antioxidant activity of plant extracts. The works on the principle that sodium nitroprusside in aqueous solution at physiological pH, generates nitric oxide which interacts with oxygen to produce nitrite ions that can be estimated using Griess reagent. Various studies have been conducted to evaluate the nitric oxide scavenging activity of *Apium leptophyllum* and found inhibition of nitric oxide radicals in a dose dependent manner.[11,19] Sahoo and other researchers in 2013 have also reported superoxide radical scavenging of *Apium leptophyllum* in a concentration dependent manner. They found that the methanolic extract is more effective than other extracts of *Apium leptophyllum*.[11] Reducing power assay method works on the principle that substances having reduction potential, react with potassium ferricyanide (Fe^{3+}) to form potassium ferrocyanide (Fe^{2+}), which then reacts with ferric chloride to form ferric–ferrous complex that has an absorption maximum at 700 nm. Presence of the polyphenolic compounds in the plant extracts is responsible for the reducing power capacity.[33] The reducing power of seed extracts of *Apium leptophyllum* was determined by various researchers to evaluate its antioxidant property; they have reported concentration dependent effect of *Apium leptophyllum*.[34,19] The antioxidant activities of *Apium leptophyllum* are shown in Table 4.

Pharmacological Properties of *Apium leptophyllum*

The fruit has long been used as an anti-nephritic and anti-rheumatic as well as for the treatment of anorexia, tumors, vomiting and Mitch.[24] The presence of coumarins, phenolics, alkaloids, and a major source of flavonoids has been proven in previous research to have antibacterial, antioxidant, chemo preventive, and anti-mutagenic activity in the Volatile oil of the fruit and leaves.[10,11,24] Moreover, some Indian traditional practitioners have found the fruits to be beneficial in the treatment of bronchitis, cough, and asthma. In asthmatic patients, fruits have thermogenic and antispasmodic properties.[35] *Apium leptophyllum* is used to cure stomachaches and diarrhoea because of its powerful antibacterial, antifungal and anti-inflammatory qualities.[36]

Anti-microbial Properties

Abd and co-workers in 1992 have reported that the oil of *Apium leptophyllum* had shown strong activity against both Gram-negative bacteria and Gram-positive. *Apium leptophyllum* was found significantly active against *E. coli*, *S. dysenteriae*, *P. aeruginosa* and *V. cholerae* strains tested. *S, aureus* and

Table 5: Antimicrobial activities of the leaf essential oil of *Apium leptophyllum*.

Parts used	Method used and type of extract	Activity Against	References
Leaf (oil)	Oil distillation by GCMS, DMSO Extract	*Staphylococcus aureus* *S. aureus* *Bacillus pumilus*	[10] [18]
Leaf	DMSO extract	*Escherichia coli* *E. coli* *Pseudomonas aeruginosa* *Shigella dysenteriae*	[10] [18]
Seed	Ethanolic extract	*Helicobacter pylori* *Salmonella typhi* *Aspergillus flavus*	[18]

Table 6: Anti-fungal activities of the leaf essential oil of *Apium leptophyllum*.

Parts used	Method used and type of extraction	Activity Against	References
Leaf (oil)	Oil distillation by GCMS, DMSO Extract	*Aspergillus niger*	[10]
Leaf (oil)	DMSO	*Candida albicans* *Penicillium funiculosum* *P. notatum*	[10]
Seed	Ethanolic	*Aspergillus fumigatus and A. flavus*	[18]
Seed	Ethanolic	*C. albicans, C. kreussei, and C. parapsilosis*	[40]

Shigella spp. demonstrated moderate action against the oil.[37,10] The oil's anti-bacterial activity, especially against *S. aureus* is responsible for a variety of human clinical disorders marked by inflammation, tissue necrosis and abscess development.[38] The bacterial infection induced by *S. aureus* is most likely to blame for "Mitch" inflammation; therefore the use of fresh leaves of *Apium leptophylum* is used in the Ethiopian medicinal system for the curative agent of "Mitch".[10] Salehi and other researchers in 2019 determined the antimicrobial activity of the essential oil of *Apium leptophyllum* against *Helicobacter pylori*. Moderate antimicrobial activity was found against *Salmonella typhi* that are resistant to various antibiotics. They also demonstrated that the ethanolic fraction of *Apium leptophyllum* were significant effective against *A. flavus*. Due to presence of, selinene, free hydroxyls, limonene and other constituents that can combine with the carbohydrates and proteins in the bacterial cell wall, as well as the lipophilic character of these compounds, led to enzyme inhibition or accumulation in membranes, resulting in energy depletion, which is linked to their antibacterial properties.

Table 7: Phytochemicals present in *Apium leptophyllum* and the type of cancer against which they are used.

Phytochemicals	Type of cancer cells against which they are used	References
β- sitosterol	HepG2, MCF	[23]
1-nonadecanol	PC3, HepG2, MCF	
8-hydroxy cuminic acid	HepG2, MCF, HCT	
Apeginin	A549, MCF, HCT	[65] [66]
Quercetin	HCT, MCF	[67]
Corosolic acid	MCF, APC	[68], [69]

The antimicrobial properties of *Apium leptophyllum* are shown in Table 5.

Anti-fungal Properties

Asamenew and other co-workers in 2008 have reported the antifungal activity of the oil of *Apium leptophyllum* and found that maximum fungal inhibitory potential against *A. niger* was 83.3 percent, somewhat greater than that observed against *P. notatum* (77.3 percent).[10] According to several studies, *Apium leptophyllum* harvested in Egypt had strong antifungal activity against *Candida albicans* and moderate activity against Cocciand rods, Gram-negative bacteria and Gram-positive bacteria and.[39,37] According to Salehi and other coworkers, the presence of Dillapiol and Myristicin in essential oils may have a synergistic impact, which could explain the greater antifungal activity against *Asperigillus fumigatus* and *Aspergillus flavus*. The methanolic extract of *Apium leptophyllum* also showed the strongest antifungal activity against *Candida parapsilosis, Candida kreussei* and *Candida albicans*.[40] The anti- fungal properties of *Apium leptophyllum* are shown in Table 6.

Anti-inflammatory and Anti-diabetic Properties

Various researchers have demonstrated anti- inflammatory activity of *Apium leptophyllum*. The *Apium leptophyllum* also shows anti-inflammatory properties. They have reported that the essential oil showed a stronger anti-inflammatory activity (49.54%) comparable to Indomethacin (42.29%), while those of 8-hydroxy cuminic acid and β-sitosterol were weaker.[22] The anti-inflammatory activity of the essential was also performed by using carrageenan-induced rat paw oedema model.[41] Salehi and other researchers in 2019 have reported that the ethanolic extracts of the seeds showed an anti-inflammatory effect against chronic inflammation induced by cotton pellet granuloma. The evidence presented above backs up the common use of these plants to treat pain and inflammation. Compounds derived from *Apium leptophyllum* have been examined for their anti-inflammatory properties in more recent research. Lutein, a naturally occurring flavone with a variety of biological activities, was found to have important anti-inflammatory activity in both acute and chronic inflammatory conditions.[18] Salehi and other researchers in 2019

have also reported anti-diabetic activity of *Apium leptophyllum* and showed that hexane extract of the seeds of *Apium leptophyllum* effectively reduced glucose, triglyceride levels and cholesterol in streptozotocin (STZ)-induced diabetic rats; it also increased HDL and serum insulin as compared to the negative diabetic rats.[18] *Apium leptophyllum* was found to be toxicity free and safe as no alterations were found in Hematological, biochemical and histopathological studies.[42]

Anti-diarrhoeal and Anti-asthamatic Properties

Apium leptophyllum have been reported to have anti-diarrheal and anti-asthmatic properties. The study for Anti-diarrheal properties of *Apium leptophyllum* was carried by Sahoo and other researchers in 2016. It was discovered that the flavonoid fraction of *Apium leptophyllum* fruit (FFALF) has anti-diarrheal qualities mediated by prevention of hyper secretion and gastrointestinal motility, confirming the plant's traditional use.[43] The anti-asthmatic properties of *Apium leptophyllum* were carried by Sahoo and other researchers to confirm the traditional assertion that the flavonoid fraction of *Apium leptophyllum* fruit (FFALF) has anti-asthmatic properties. Furthermore, in all of the animals, FFALF showed dose-dependent anti-asthmatic action. As a result, the FFALF was shown to have anti-asthmatic characteristics, most likely as a result of its membrane stabilizing properties, as well as lowering antibody formation and blocking antigen generated by histamine and acetylcholine.[35]

Anti-cancer Properties

Various studies have shown Anticancer potential of *Apium leptophyllum*. Helal and other coworkers in 2017 have evaluated anti-proliferative role of essential oil as well as1-nonadecanol, β-sitosterol, and 8-hydroxy cuminic acid on colorectal carcinoma (HCT-116), human hepatocellular carcinoma (HePG-2), human prostate carcinoma (PC-3) and mammary gland carcinoma (MCF-7) cell lines and found that, the essential oil and 8-hydroxy cuminic acid revealed the highest anti-proliferative activity against these cell lines.[23] Another study was carried out by Sahoo and other researchers in 2014 to demonstrate the chemopreventive potential of flavonoidal fractions of *Apium leptophyllum* fruits (FFALF) on Swiss mice. He reported that co-administration of FFALF reported significant activity against induced skin papilloma.[12] Another study was carried out by Ganesh and other researchers in 2019 to find *in-vitro* anti-proliferative potential of *Apium leptophyllum* against EAC Cell Lines. They used both aqueous and ethanolic extract to carry out anti- proliferative effect of *Apium leptophyllum*. The results revealed that ethanolic extract of *Apium leptophyllum* (EEAL) was more anti-cancerous against Ehrlich Ascites Carcinoma and was dose dependent. The Ethanolic extract showed 98.87% and Aqueous extract showed 87.32% and of cytotoxicity.[44] Phytochemicals present in *Apium leptophyllum* and the cancer against they are used are shown in Table 7.

CONCLUSION

Apium leptophyllum is an herbaceous plant and grows in various parts of the world. Different parts of the plants are rich in terms of vitamins, alkaloids, phenolics minerals and flavonoids which are responsible for its medicinal applications. Proven pharmacological activities (such as antioxidant activity, anti-inflammatory activity, antimicrobial activity, antiasthametic, antidiarroheal, antidiabetic and anticancer) of *Apium leptophyllum* would make it suitable to treat several diseases. Moreover, further extensive research investigations are needed to know the mechanism of action of *Apium leptophyllum* in treatment of various diseases and disorders thus can be utilized for the development of effective drug formulations for the well-being of humans.

ACKNOWLEDGEMENT

Authors are thankful to the Central Library and Departmental Library (Department of Zoology) of Baba Ghulam Shah Badshah University for providing access to different journals and books for writing this article.

Funding source

Authors are thankful to UGC for providing Start up Research Grant to Dr. Mohd Salim Reshi (No. F.30-441/2018(BSR), dated 22-05-2018).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

WHO: World Health Organization; **API:** Ayurvedic Pharmacopoeia of India; **UNESCO:** United Nations Educational Scientific and Cultural Organization; **USDA:** United States Department of Agriculture; **DPPH:** 2, 2-diphenyl-1-picrylhydrazyl; **H_2O_2:** Hydrogen peroxide radical scavenging; **GC-MS:** Gas chromatography Mass spectroscopy; **FTIR:** Fourier transform infrared spectroscopy; **NMR:** Nuclear magnetic Resonance; **IC_{50}:** Half-maximal inhibitory concentration; **FFALF:** Flavonoidal fractions of *Apium leptophyllum* fruits; **BGSBU:** Baba Ghulam Shah Badshah University; **UGC:** University Grants Commission; **ROS:** Reactive oxygen species; **%:** Percentage; **µg/ml:** Micro-gram/mili-litre.

Authors' Contribution

M.S.R: Conceptualization, supervision, project administration, resources, funding acquisition, writing—review and editing, **T.A.S:** Conceptualization, methodology, writing—original draft preparation, **S.Y.G:** Writing—original draft preparation; All

authors have read and agreed to the published version of the manuscript.

SUMMARY

- *Apium leptophyllum* belongs to the family *Apiaceae (Umbelliferae)* and is commonly known as Ajmoda.
- The phytochemical screening of Apium plants has quantitatively demonstrated the presence of carbohydrates, alkaloids, glycosides, flavonoids, saponins and steroids, tannins and the active compounds thymol and coumarins are present.
- *Apium leptophyllum* shows strong antioxidant activities by inhibiting DPPH, hydroxyl, nitric oxide and superoxide radicals.
- *Apium leptophyllum* had shown various pharmacological properties viz anti-microbial, anti-fungal, anti-diarrhoeal, anti-asthmatic, anti- diabetic, anti-inflammatory and anticancer properties.

REFERENCES

1. Tene V, Malagon O, Finzi PV, Vidari G, Armijos C, Zaragoza T. An ethanobotanical survey of medicinal plants used in Loja and Zamora-Chinchipe, Ecuador. J Ethnogr Pharmacol. 2007;111(1):63-81.
2. Xie JH, Jin ML, Morris GA, Zha XQ, Chen HQ, Yi Y, *et al*. Advances on bioactive polysaccharides from medicinal plants. Crit Rev Food Sci Nutr. 2016;56; Suppl 1:S60-84. doi: 10.1080/10408398.2015.1069255, PMID 26463231.
3. UNESCO [report]; 1996.
4. Cowan MM. Plant products as antimicrobial agents. Clin Microbiol Rev. 1999;12(4):564-82. doi: 10.1128/CMR.12.4.564, PMID 10515903.
5. Nascimento GGF, Locatelli J, Freitas PC, Silva GL. Antibacterial activity of plant extracts and phytochemicals on antibiotic-resistant bacteria. Braz J Microbiol. 2000;31(4):247-56. doi: 10.1590/S1517-83822000000400003.
6. Kala CP, Dhyani PP, Sajwan BS. Developing the medicinal plants sector in northern India: Challenges and opportunities. J Ethnobiol Ethnomed. 2006;2(1):32. doi: 10.1186/1746-4269-2-32.
7. The ayurvedic pharmacopoeia of India (API), 2007, Government of India, Ministry of Health and Family Welfare, Department of Ayush. Ajamoda (Frt).
8. Boulos L. Flora of Egypt checklist revised.al-Hadara publishing. Cairo, (Egypt). 2009.
9. Barboza GE, Cantero JJ, Núñez C, Ariza Espinar L, Pacciaroni ADV. Medicinal plants: A general review and a phytochemical and ethnopharmacological screening of the native Argentine Flora. 2009.
10. Asamenew G, Tadesse S, Asres K, Mazumder A, Bucar F. A study on the composition, antimicrobial and antioxidant activities of the leaf essential oil of *Apium leptophylum* (Pers.) Benth. growing in Ethiopia. Ethiop Pharm J. 2008;26.
11. Himanshu BS, Bhattamisra SK, Biswas UK, Sagar R. Estimation of total phenolics and flavonoidal contents as well as *in vitro* antioxidant potential of *Apium leptophyllum* Pers. Herba Pol. 2013;59(3):37-50. doi: 10.2478/hepo-2013-0015.
12. Sahoo HB, Santani DD, Sagar R. Chemopreventive potential of *Apium leptophyllum* (Pers.) against DMBA induced skin carcinogenesis model by modulatory influence on biochemical and antioxidant biomarkers in Swiss mice. Indian J Pharmacol. 2014;46(5):531-7. doi: 10.4103/0253-7613.140587, PMID 25298584.
13. Umadevi I, Daniel M. Phenolics of some fruit spices of the Apiaceae. Natl Acad Sci Lett. 1990;13(12):439-41.
14. Atal CK, Sharma BR, Qadry SMJS. Coumarins from *Trachyspermum roxburghianum* and *Apium leptophyllum*. Indian J Pharmacol. 1973.
15. Banerjee SK, Singh K. A novel acid from *Apium leptophyllum*. J Indian Counc Chem. 1995;11:39-41.
16. Sherif AE. Pharmacognostical study of certain plants belonging to the family Apiaceae. Int J Innov Res Sci Eng Technol. 2013, A thesis submitted in partial inhibitory effect of polyherbal formulation on alpha-amylase;2:4556-65.
17. Saraswathy, Amala, Vidhya. Identification of the botanical sources and TLC/HPTLC pattern of 'ajamoda' in trade. J Pharmacogn Phytochem. 2013.
18. Salehi B, Venditti A, Frezza C, Yücetepe A, Altuntas Ü, Uluata S, *et al*. *Apium* plants: Beyond simple food and phyto pharmacological applications. Appl Sci. 2019;9(17):3547. doi: 10.3390/app9173547.
19. Ganesh MS, Radhika J, Yuvarani S. preliminary phytochemical screening and *in-vitro* antioxidant potential of different extracts of *Apium leptophyllum* pers. Int Res J Pharm. 2019;10(8):91-5. doi: 10.7897/2230-8407.1008251.
20. Park RJ, Sutherland MD. Some constituents of. *Apium leptophyllum* (DC) F. Muell. Aust J Chem. 1969;22(2):495-6. doi: 10.1071/CH9690495.
21. Silva B, Gilberto AA, Luiz B. Essential oils of *Apium leptophyllum*. Rev Bras Farmacol. 1971;52:15-20.
22. Helal IE, Galala AA, Saad HEA, Halim AF. Chemical composition and α-amylase inhibitory activity of *Apium leptophyllum* essential oils. J Am Sci. 2015;11(4).
23. Helal IE, Galala AA, Saad HEA, Halim AF. Bioactive constituents from *Apium leptophyllum* Fruits. J Pharm Res Int. 2017;14(3):1-8. doi: 10.9734/BJPR/2016/30289.
24. Sahoo HB, Patro SK, Sagar R, Santani DD. Mutagenic evaluation and spectroscopic characterization of flavonoidal fraction of *Apium leptophyllum* (Pers.) fruit. Int J Nutr Pharmacol Neurol Dis. 2015;5(2):82. doi: 10.4103/2231-0738.153798.
25. Lupoli F, Vannocci T, Longo G, Niccolai N, Pastore A. The role of oxidative stress in Friedreich's ataxia. FEBS Lett. 2018;592(5):718-27. doi: 10.1002/1873-3468.12928, PMID 29197070.
26. Landrault N, Poucheret P, Ravel P, Gasc F, Cros G, Teissedre PL. Antioxidant capacities and phenolics levels of French wines from different varieties and vintages. J Agric Food Chem. 2001;49(7):3341-8. doi: 10.1021/jf010128f, PMID 11453773.
27. Srinivasan RMJN, Chandrasekar MJN, Nanjan MJ, Suresh B. Antioxidant activity of *Caesalpinia digyna* root. J Ethnopharmacol. 2007;113(2):284-91. doi: 10.1016/j.jep.2007.06.006, PMID 17686593.
28. Packer L, Rimbach G, Virgili F. Antioxidant activity and biologic properties of a procyanidin-rich extract from pine (*Pinus maritima*) bark, pycnogenol. Free Radic Biol Med. 1999;27(5-6):704-24. doi: 10.1016/s0891-5849(99)00090-8, PMID 10490291.
29. Hazra B, Biswas S, Mandal N. Antioxidant and free radical scavenging activity of *Spondias pinnata*. BMC Complement Altern Med. 2008m;8(1):63-4. doi: 10.1186/1472-6882-8-63.
30. Lee K, Shibamoto T. Antioxidant activities of volatile components isolated from Eucalyptus species. J Sci Food Agric. 2001;81(15):1573-9. doi: 10.1002/jsfa.980.
31. Kim HJ, Chen F, Wu C, Wang X, Chung HY, Jin Z. Evaluation of antioxidant activity of Australian tea tree (*Melaleuca alternifolia*) oil and its components. J Agric Food Chem. 2004;52(10):2849-54. doi: 10.1021/jf035377d, PMID 15137824.
32. Shukla S, Mehta A, Bajpai VK, Shukla S. *In vitro* antioxidant activity and total phenolic content of ethanolic leaf extract of *Stevia rebaudiana* Bert. Food Chem Toxicol. 2009;47(9):2338-43. doi: 10.1016/j.fct.2009.06.024, PMID 19540900.
33. Shahriar S. Akhter, Ismail Hossain, MD, Aminul HAQUE and Ahmed Bhuiyan. J Med Plants Res. 2012. Evaluation of *In vitro* antioxidant activity of bark extracts of *Terminalia arjuna*:5286-98.
34. Hajaji El H, Lachkar N, Alaoui K, Cherrah Y, Farah A, Ennabili A, El Bali B, *et al*. 2010, Antioxidant properties and total phenolic content of three varieties of Carob tree leaves from Morocco. Records of Natural Products; 4 suppl 4:193-204.
35. Sahoo HB, Sagar R, Patro G, Panda M, Sahoo SK, Priyadarshini D. Pharmacological evaluation of *Apium leptophyllum* (Pers.) on bronchial asthma. J Pharm Bioallied Sci. 2016;8(4):341-5. doi: 10.4103/0975-7406.199343, PMID 28216960.
36. Khare CP. Indian medicinal plants: An illustrated dictionary. 1st ed. New Delhi: Springer Science+Business Media; 2008.
37. Abdel-Aziz E. GC/MS and antimicrobial Activity of volatile oil of *Apium leptophyllum* (Benth.). Zagazig J Pharm Sci. 1992;1(1):55-9. doi: 10.21608/zjps.1992.189020.
38. Smith PB. Staphylococcal infections. In: Balows A, Hausler WJ Jr, editors, Diagnostic procedures for bacterial, mycotic and parasitic infections. 6th ed. Washington: American Public Health Association Inc. 1981. p. 587-60.
39. Kariba RM, Siboe GM, Dossaji SF. *In vitro* antifungal activity of *Schizozygia coffaeoids* Bail. (Apocyanaceae). J Ethnopharmacol. 2001;74(1):41-4. doi: 10.1016/s0378-8741(00)00337-8, PMID 11137346.
40. Edziri H, Ammar S, Souad L, Mahjoub MA, Mastouri M, Aouni M, *et al*. *In vitro* evaluation of antimicrobial and antioxidant activities of some Tunisian vegetables. S Afr J Bot. 2012;78:252-6. doi: 10.1016/j.sajb.2011.09.012.
41. Winter CA, Risley EA, Nuss GW. Carrageenan induced edema in hind paw of the rat as an assay for anti-inflammatory drugs. Proc Soc Exp Biol Med. 1962;111(3):544-7. doi: 10.3181/00379727-111-27849.
42. Radhika J, Radhika J. Acute toxicity study of ethanolic extract of *Apium leptophyllum* pers in swiss albino mice. Int J Res Pharm Sci. 2019;10(4):3750-4. doi: 10.26452/ijrps.v10i4.1764.
43. Sahoo HB, Sagar R, Kumar A, Bhaiji A, Bhattamishra SK. Antidiarrhoeal investigation of *Apium leptophyllum* (Pers.) by modulation of Na+ K+ ATPase, nitrous oxide and intestinal transit in rats. Biomed J. 2016;39(6):376-81. doi: 10.1016/j.bj.2016.11.003, PMID 28043416.
44. Ganesh MS, Yuvarani S, Radhika J. *In-vitro* Cytotoxic Effect of *Apium leptophyllum* Against EAC Cell Lines. International Journal of Pharmacy and Biological Sciences-IJPBSTM. 2019;9(3):429-32.
45. Sahoo CR, Paidesetty SK, Padhy RN. The recent development of thymol derivative as a promising pharmacological scaffold. Drug Dev Res. 2021;82(8):1079-95. doi: 10.1002/ddr.21848, PMID 34164828.
46. Guo Y, Baschieri A, Amorati R, Valgimigli L. Synergic antioxidant activity of γ-terpinene with phenols and polyphenols enabled by hydroperoxyl radicals. Food Chem. 2021;345:128468. doi: 10.1016/j.foodchem.2020.128468, PMID 33341300.
47. Cetin H, Cilek JE, Oz E, Aydin L, Deveci O, Yanikoglu A. Acaricidal activity of *Satureja Thymbra* L. essential oil and its major components, carvacrol and γ-terpinene against

adult *Hyalomma marginatum* (Acari: Ixodidae). Vet Parasitol. 2010;170(3-4):287-90. doi: 10.1016/j.vetpar.2010.02.031, PMID 20303667.

48. Aligiannis N, Kalpoutzakis E, Mitaku S, Chinou IB. Composition and antimicrobial activity of the essential oils of two Origanum species. J Agric Food Chem. 2001;49(9):4168-70. doi: 10.1021/jf001494m, PMID 11559104.
49. Vajs J, Steiner I, Brozovic A, Pevec A, Ambriovic-Ristov A, Matkovic M, *et al*. The 1, 3-diaryltriazenido (p-cymene) ruthenium (II). J Inorg Biochem. 2015;153:42-8. doi: 10.1016/j.jinorgbio.2015.09.005, PMID 26409161.
50. Weiss A, Berndsen RH, Dubois M, Müller C, Schibli R, Griffioen AW, *et al*. *In vivo* antitumor activity of the organometallic ruthenium (II)-arene complex [Ru (η 6-p-cymene) Cl 2 (pta)](RAPTA-C) in human ovarian and colorectal carcinomas. Chem Sci. 2014;5(12):4742-8.
51. Wang D, Wang Q, Li S, Xu Y, Wang X, Wang C. Carvacrol methyl ether, a compound from the essential oil of *Gardenia Jasminoides* fruits, exhibits antioxidant effects in the deep-frying of Chinese Youmotou using sunflower oil. LWT. 2020;128:109502. doi: 10.1016/j.lwt.2020.109502.
52. Ben Arfa A, Combes S, Preziosi-Belloy L, Gontard N, Chalier P. Antimicrobial activity of carvacrol related to its chemical structure. Lett Appl Microbiol. 2006;43(2):149-54. doi: 10.1111/j.1472-765X.2006.01938.x, PMID 16869897.
53. Rivas da Silva AC, Lopes PM, Barros de Azevedo MM, Costa DC, Alviano CS, Alviano DS. Biological activities of a-pinene and β-pinene enantiomers. Molecules. 2012;17(6):6305-16. doi: 10.3390/molecules17066305, PMID 22634841
54. Kazemi M. Phytochemical composition, antioxidant, anti-inflammatory and antimicrobial activity of *Nigella sativa* L. essential oil. J Essent Oil Bear Plants. 2014;17(5):1002-11. doi: 10.1080/0972060X.2014.914857.
55. Goren AC, Bilsel G, Bilsel M, Demir H, Kocabas EE. Analysis of essential oil of *Coridothymus capitatus* (L.) and its antibacterial and antifungal activity. Z Naturforsch C J Biosci. 2003;58(9-10):687-90. doi: 10.1515/znc-2003-9-1016, PMID 14577632.
56. Singh HP, Batish DR, Kaur S, Arora K, Kohli RK. α-Pinene inhibits growth and induces oxidative stress in roots. Ann Bot. 2006;98(6):1261-9. doi: 10.1093/aob/mcl213, PMID 17028297.
57. Wongkattiya N, Sanguansermsri P, Fraser IH, Sanguansermsri D. Antibacterial activity of cuminaldehyde on food-borne pathogens, the bioactive component of essential oil from *Cuminum cyminum* L. collected in Thailand. J Complement Integr Med. 2019;16(4). doi: 10.1515/jcim-2018-0195, PMID 31129652.
58. Wang H, Liu Y. Chemical composition and antibacterial activity of essential oils from different parts of *Litsea cubeba*. Chem Biodivers. 2010;7(1):229-35. doi: 10.1002/cbdv.200800349, PMID 20087994.
59. Montanari RM, Barbosa LCA, Demuner AJ, Silva CJ, Carvalho LS, Andrade NJ. Chemical composition and antibacterial activity of essential oils from Verbenaceae species: Alternative sources of (E)-caryophyllene and germacrene-D. Quim Nova. 2011;34(9):1550-5. doi: 10.1590/S0100-40422011000900013.
60. Judžentiene A, Budiene J. Mugwort (*Artemisia vulgaris* L.) essential oils rich in germacrene D, and their toxic activity. J Essent Oil Res. 2021;33(3):256-64. doi: 10.1080/10412905.2020.1857854.
61. Sowmya S, Perumal PC, Ravi S, Anusooriya P, Shanmughavel P, Murugesh E, *et al*. 1-Pentacosanol isolated from stem ethanolic extract of *Cayratia trifolia* (L.) is A potential target for prostate cancer-*in silico* approach. Jordan J Biol Sci. 2021;14(2).
62. Sugano M, Morioka H, Ikeda I. A comparison of hypocholesterolemic activity of β-sitosterol and β-sitostanol in rats. J Nutr. 1977;107(11):2011-9. doi: 10.1093/jn/107.11.2011, PMID 908959.
63. Loizou S, Lekakis I, Chrousos GP, Moutsatsou P. β-sitosterol exhibits anti-inflammatory activity in human aortic endothelial cells. Mol Nutr Food Res. 2010;54(4):551-8. doi: 10.1002/mnfr.200900012, PMID 19937850.
64. Toledo CR, Pereira VV, Dourado LFN, Paiva MRB, Silva-Cunha A. Corosolic acid: Antiangiogenic activity and safety of intravitreal injection in rats eyes. Doc Ophthalmol. 2019;138(3):181-94. doi: 10.1007/s10633-019-09682-x, PMID 30809742.
65. Choudhury D, Ganguli A, Dastidar DG, Acharya BR, Das A, Chakrabarti G. Apigenin shows synergistic anticancer activity with curcumin by binding at different sites of tubulin. Biochimie. 2013;95(6):1297-309. doi: 10.1016/j.biochi.2013.02.010, PMID 23485682.
66. Imran M, Aslam Gondal T, Atif M, Shahbaz M, Batool Qaisarani T, Hanif Mughal M, *et al*. Apigenin as an anticancer agent. Phytother Res. 2020;34(8):1812-28. doi: 10.1002/ptr.6647, PMID 32059077.
67. Lu J, Papp LV, Fang J, Rodriguez-Nieto S, Zhivotovsky B, Holmgren A. Inhibition of mammalian thioredoxin reductase by some flavonoids: Implications for myricetin and quercetin anticancer activity. Cancer Res. 2006;66(8):4410-8. doi: 10.1158/0008-5472.CAN-05-3310, PMID 16618767.
68. Ahn KS, Hahm MS, Park EJ, Lee HK, Kim IH. Corosolic acid isolated from the fruit of *Crataegus pinnatifida* var. psilosa is a protein kinase C inhibitor as well as a cytotoxic agent. Planta Med. 1998;64(5):468-70. doi: 10.1055/s-2006-957487, PMID 9690354.
69. Fujiwara Y, Takaishi K, Nakao J, Ikeda T, Katabuchi H, Takeya M, *et al*. Corosolic acid enhances the antitumor effects of chemotherapy on epithelial ovarian cancer by inhibiting signal transducer and activator of transcription 3 signaling. Oncol Lett. 2013;6(6):1619-23. doi: 10.3892/ol.2013.1591, PMID 24260055.

Cite this article: Sheikh TA, Ganie SY, Reshi MS. Phytochemistry, Pharmacological Properties and Medicinal uses of *Apium leptophyllum*: A Review. Pharmacog Rev. 2023;17(33):135-43.