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REVIEW ARTICLE

Medicinal properties of celery seeds (*Apium graveolens* L.)

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ABSTRACT
Plant based traditional medicine system occupies a key role in treating various disease conditions. Medicinal plants are considered to be the backbone of herbal medicine as they contain several unique bioactive compounds. Herbal medicines have been used extensively in both tropical and subtropical places for curing and treating medical ailments. Herbal medicines are formulated using different parts of a plant. The active components present in different parts of the plant work synergistically to fight against several diseases. Celery (Apium graveolens; family Apiaceae) is used as a medicinal agent in Ayurveda and Unani medicine system. Scientific evidence indicates that leaf, stem, root and seed extracts of celery are reported to possess remarkable medicinal properties. Seeds are also important in human nutrition as they are a rich source of fatty acids, proteins, phytochemicals and micronutrients. Active compounds such as alkaloids, coumarins, flavonoids, glycosides, limonene, myrcene, phenols, phthalides, and steroids present in celery seeds are responsible for different medicinal properties. Medicinal properties of celery seeds include anticancer, antidiabetic, anti-hyperlipidemic, antioxidant, antimicrobial and anti-inflammatory activity. This review paper provides information on phytochemical constituents and medicinal properties of celery seeds that provide further research opportunities to unravel and exploit other unknown medicinal properties of celery seeds for the optimal benefit of mankind.
Key words: seeds, herbal medicine, *Apium graveolens*, bioactive compounds, therapeutic properties.

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INTRODUCTION

Plants produce a wide range of bioactive compounds. Dependence on plant based medicine is high among developing countries as it plays a major role in health care. Globally traditional medicine, especially herbal medicine is used for treating several disease conditions. Herbal medicine includes herbs, herbal preparation made using different parts of the plant and processed herbal products [1, 2]. Ecological diversity indicates India as a large repository of medicinal plants. In India, nearly three fourth of the population residing in rural areas rely on herbal therapy [3]. Celery, a native herb of Europe has a long history of use in Ayurveda and Unani medicinal system as a therapeutic agent for preventing cardiovascular diseases, decreasing blood pressure, as well as controlling blood glucose and lipid levels [4]. Celery which belongs to the family Apiaceae is called as Karafs in Arabs, Chin in Chinese, Celery in French, Sellerie in German, Apio in Spanish, Ajmoda in Urdu or Ajmod in India. It is commonly grown in developing countries such as Abyssinia, Algeria, Iran and India. In India, it is cultivated in north –western regions such as Amritsar, Haryana, Himalayan regions, Punjab and Uttar Pradesh [5]. High level of moisture and low temperature are required for growth of celery. Celery is predominantly cultivated in India, China and Egypt for its seed which is used as a flavoring agent. In India, nearly 40,000 tons of celery is produced every year of which 29, 250 tons are exported. There are three varieties of celery namely *Apium graveolens* var. *dulce* (blanched celery or simply celery) *Apium graveolens* var. rapaceum (edible rooted celery, celeriac or celery root) and *Apium graveolens* var. *secalinum* (leaf celery) [6, 7]. Celery (*Apium graveolens*) is a deciduous, erect, herbaceous binominal herb that has a shallow tap root system.

The stem is branched, hollow and succulent. The leaves are pinnate and the leaflets are ovate or sub orbicular that bear small white flowers. The fruit is a schizocarp and is slightly bitter in taste. The seeds are very small, dark brown in colour, ovoid to globose in shape and are used as a flavoring agent. Celery seeds have long been used in herbal therapy due to the presence of numerous bioactive compounds which work synergistically to fight against a number of common ailments. This review paper provides information on phytochemical constituents and medicinal properties of celery seeds.

Phytochemistry: Pharmacological and medicinal properties of plants products depend upon their chemical composition. Constituents of celery seeds include flavones, furanocoumarins, glycosides, phenolic compounds, steroids and trace elements [8]. Alkaloids, flavonoids, glycosides, steroids along with wide range of trace elements are present in seed extracts of *A. graveolens* [9, 10, 11]. A study by Al-Snafi on the phytochemical profile of celery seeds reported the presence of 16 other active components of which D limone (57.7%) and myrcene (18.7%) were present at a higher percentage. Apigenin, bergapten, caffeic acid, chlorogenic acid, isoimpinellin, ocimene and rutaretin are also present in celery seeds [12]. Other compounds present in celery seeds include gravebioside, isoimperatorin, osthenol, seslin, stigmasterol and umbelliferone [13]. Celery seeds are also rich in B complex vitamins [14, 15].

MEDICINAL PROPERTIES OF CELERY SEEDS

Anticancer property: Globally, cancer is the second leading causative factor of death after cardiovascular diseases. The role of natural products in treating and preventing cancer is remarkable. Apigenin, flavonoids, tannins, phenolic compounds, d-limonene, selinene, luteolin, linolenic acid, psoralen, oleic acid and perillyl alcohol present in celery seeds exhibit anticancer activity [16, 17]. Research indicates that phenolic acids such as p-coumaric acid, ferulic acid and caffeic acid present in celery seeds significantly contribute to anticancer activity [18].Celery seed extracts have anticancer activities and growth inhibition on various cancer cell lines including acute lymphoblastic leukemia cell line (CEM-C7H2), glioma cell line (C6), breast cancer cell line (MCF-7), human neuroblastoma cells (SH-SY5Y) and cervical carcinoma cells [19, 20, 21, 22]. Jumaily evaluated the anticancer effect of aqueous, ethanol and hexane seed extracts of *A. graveolens* on two cell lines namely RD and L20B using different concentrations (6.25, 12.5, 25, 50, 100 and 200µg/mL). Hexane extract showed the maximum anticancer activity at a concentration of 100 and 200 µg/mL. Phthalides present in celery seeds contribute to anticancer activity [23].

Celery seeds exhibit anticancer activity through different mechanisms such as

- By blocking the metabolic activation of mutagens or by binding to the target sites to prevent binding of mutagens [24].
- By inhibiting the action of phosphotidyl inosit-3 kinase enzyme (PI3K) [25].
- Through induction of p53 expression, which result in cell cycle arrest and apoptosis [26].
- By increasing the activity of glutathione S-transferase (GST). Glutathione S-tranferase detoxifies carcinogens, blocks inflammatory reaction, decreases oxidative stress and inhibits the action of xenobiotics [27, 28, 29, 30].

Antidiabetic activity: Current curative treatment available for diabetes is associated with shortcomings such as metabolic alterations, undesirable side effects and higher rates of secondary failure. On the other hand, use of herbal extract ensures similar effectiveness with minimum side effects. Results of animal experimental studies have demonstrated the use of celery seeds as a hypoglycemic agent. Al-Shwilly, reported that oral administration of 60 mg/kg n-butanol seed extract of *A. graveolens* to rats for a period of 15 days resulted in proliferation of pancreatic beta-cells and reduction in glucose levels [31]. Another study by Ismael reported that oral administration of n-butanol seed extract of *Apium graveolens* for 21 days to rats, not only decreased blood glucose levels, but at the same time drastically reduced malondialdehyde (MDA) concentration and increased glutathione (GSH) concentration [32]. In a study by Niaz *et al* it was found that administration of alcoholic seed extract of *A. graveolens* (400mg/kg) to diabetic rats brought about significant reduction in blood glucose levels and increase in the insulin levels [33].Tashakori *et al* investigated the hypoglycemic effect of hexane seed extract of *A.graveolens* on streptozotocin induced diabetic rats. There was a significant decrease in glucose, triglycerides and cholesterol levels ($p<0.0001$). Histopathological reports showed that rats which received celery seed extract had less atrophy, necrosis and inflammation when compared to the control group [34]. Celery seeds unveil its antidiabetic activity in different ways such as increasing secretion of insulin, proliferation of β-cells and increasing the oxidative capability which enables the tissues to utilize glucose [35]. Seed extract of *A. graveolens* decreases oxidative stress, prevents lipid peroxidation and preserves pancreatic beta-cell integrity [36]. Aldose reductase is an enzyme which catalyzes the reduction of glucose to sorbitol. Unlike glucose, sorbitol cannot diffuse out of the cell membrane. Excess accumulation of sorbitol is responsible for development of micro complications that are associated with type 2 diabetes mellitus.

Apigenin present in celery seeds prevents reduction of glucose to sorbitol by inhibiting the action of aldose reductase [37].

Antihypertensive property: Retention of excessive fluid and poor flexibility of blood vessels lead to increased blood pressure known as hypertension. 3n – butylphthalide (NBP) present in celery seeds functions as a hypotensive agent by acting as a diuretic agent, as a vasodilator and by impacting the production of prostaglandins. Results of animal studies report that components such as NBP, apigenin, D-limonene, linalool, desanenolide, sedanolide present in celery seeds act as a hypotensive agent. Tsi and Tan investigated the hypotensive and vasorelaxant effect of NBP present in seed extract of *A. graveolens* on hypertensive rats. The results showed that celery seeds exhibited antihypertensive effect by acting as calcium channel blockers that inhibit the flow of calcium ions across the membranes of smooth muscle cells [38]. Ko *et al* documented that apigenin present in celery seeds exhibited hypotensive effect by inhibiting Ca^{2+} influx through voltage and lignin gated calcium channels [39]. Linalool, another active component present in celery seeds decreased blood pressure and improved the antioxidant status [40]. Hassanpour *et al* investigated the antihypertensive effect of hexane, methanol and aqueous ethanolic seed extract s of *A. graveolens* in deoxycorticosterone acetate–induced hypertensive rats. The results showed that administration of 300mg/kg of hexane, methanol, and aqueous-ethanolic extracts to hypertensive rats showed 38, 24, and 23mmHg reduction in blood pressure. HPLC analysis indicated that NBP present in hexane extract was 3.7 and 4 times greater than methanol and aqueous-ethanolic extracts [41]. A similar trend of results was reported by Tashakori et al [42]. The authors of the study evaluated the antihypertensive effect of aqueous, hexane and methanol seed extracts of *A. graveolens* in hypertensive rats. Hexane extract showed significantly stronger activity in lowering systolic and diastolic blood pressure. HPLC analysis showed that NBP level was high in hexane extract. The study highlighted that the vasorelaxant effect of celery seed was due to negative and positive chronotropic effects that occurred through blocking of Ca^{2+} in cardiac muscle cells. Celery seed extract not only improves blood flow but also prevents stroke, protects the brain and enhances energy production [43, 44].

Antihyperlipidemic activity: Hypolipidemic effect of celery seeds have been investigated in animal studies [45, 46]. Oral administration of ethanolic seed extract of *A.graveolens* at a dosage of 213 and 425 mg/kg for 60 days showed a significant decrease in serum total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), and significant increase ($p<0.05$) in high-density lipoprotein cholesterol (HDL-C) levels [47]. Similarly, another study by Ahmed *et al* also proved the antihyperlipidemic effect of celery seeds [48]. Celery seed decreases lipid levels by inhibiting hepatic cholesterol biosynthesis, increasing fecal bile acid excretion, enhancing the activity of plasma lecithin cholesterol acyltransferase and reducing lipid absorption in the intestine [49]. 3n butylphthalide present in celery also exhibits antioxidant activity and inhibitory effect on topoisomerase enzyme [50].

Antioxidant property: Free radicals or reactive oxygen species are produced in the body when cells use oxygen to generate energy from cellular redox process [51].These free radicals occupy a key role in the etiology of degenerative diseases by damaging DNA, proteins and lipids [52]. Antioxidants are compounds that interact, stabilize and protect cells from damage caused by free radicals. Antioxidants present in nature may be either exogenous or endogenous. The endogenous antioxidants can be classified as enzymatic and non-enzymatic. There has been a global shift towards the use of natural substances present in medicinal plants as therapeutic antioxidants. Research studies have evidenced that celery seed extract acts as a strong antioxidant agent due to its ability to scavenge free radicals [53]. Phytochemicals such as flavonoids, alkaloids and phenolic compounds present in celery seeds interfere with the metabolism of oxidative agent either by scavenging the free radicals or by impairing the microsomal enzymatic system needed for this metabolism [54, 55]. Superoxide dismutase (SOD) and catalase (CAT) are the two major scavenging enzymes that remove toxic free radicals. Al-Sa'aidi *et al* evaluated the antioxidant activity of n-butanol seed extract of *A. graveolens* in streptozotocin induced mature male rats. Administration of n-butanol seed extract of *A. graveolens* increased the action of superoxide dismutase, catalase and glutathione reductase [36]. Glutathione reductase, a major non-protein thiol, plays a vital role in the cellular antioxidant defense system as it scavenges the free radicals produced in the body [56]. A study by Yaser *et al* reported that methanolic seed extract of *A. graveolens* scavenged free radicals [57].

Antimicrobial activity: A number of plant derived compounds are found to exhibit antimicrobial activity against various pathogenic bacterial and fungal strains. Celery seeds inhibit the growth of pathogenic bacterial strains such as *Campylobacter jejuni*, *Escherichia coli*, *Listeria monocytogenes* and *Salmonella enterica* [58]. Shanmugapriya and Ushadevi reported antibacterial potential of seed extract of *A. graveolens* against urinary pathogens particularly *Escherichia coli* and *Pseudomonas aeruginosa* [59]. Oil and seed extracts of *A. graveolens* and *Coriandrum sativum* were tested for antibacterial activity against five bacterial strains. Oil and seed extracts of *A. graveolens* exhibited antibacterial activity against gram

positive and gram negative bacterial strains [60]. Sedanolide and senkyunolides present in seed extracts of *A. graveloens* inhibit the growth of fungal strains such as *Candida albicans*, *Candida kruseii, Candida parapsilasis*, *Caenorhabditis elegans* and *Panagrellus redivivus* [61].

Gastrointestinal effect: Celery seeds have been used in treating gut diseases, relieving abdominal pain, flatulence and visceral spasms [62].These effects have been claimed to be related to the phthalide constituents of celery seeds [63]. Experimental studies on rodents have proved anti-inflammatory effect and antiulcer property of seed extract of *A. graveolens* [64, 65]. A phthalide dimer isolated from the alcoholic extract of *A. graveolens* (A-CSE) inhibited the action of *Helicobacter pylori* which is a causative factor for peptic ulcer [66].

CONCLUSION AND FUTURE PERSPECTIVE

Results of numerous *in vitro* and *in vivo* studies (animal models) have highlighted the anticancer, antidiabetic, antihypertensive, antihyperlipidemic, antioxidant, antimicrobial and anti-inflammatory effect of celery seeds. Though celery seeds are reported to have several therapeutic properties, randomized clinical controlled trials are required to confirm the role of celery seeds in treating of several chronic illness and infections. In addition, research studies focusing on role of celery seeds in treating liver diseases, gout, arthritis, and urinary tract infections can be studied using *in vitro* and *in vivo* studies for the optimal benefit of mankind.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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