Chemical and Biological Potential of *Ammi visnaga* (L.) Lam. and *Apium graveolens* L.: A Review (1963-2020)

Shereen S. T. Ahmed, John R. Fahim, Usama R. Abdelmohsen, Ashraf N. E. Hamed

1 Department of Pharmacognosy, Faculty of Pharmacy, Minia University, Minia 61519, Egypt.
2 Department of Pharmacognosy, Faculty of Pharmacy, Deraya University, New Minia 61111, Egypt.

Received: January 3, 2021; revised: June 17, 2021; accepted: June 26, 2021

Abstract

Medicinal plants have a vital role in our life, providing us with a variety of secondary metabolites with varied chemical structures and biological activities. *Ammi visnaga* (L.) Lam. and *Apium graveolens* L. are common traditional plant species that have long been used for the prevention and treatment of several health problems. Both *A. visnaga* and *A. graveolens* belong to the carrot family, Apiaceae (Umbelliferae) and showed different groups of natural compounds, such as coumarins, furanochromones, and essential oils. In view of that, the current review describes various classes of chemical constituents identified so far from these medicinal species, together with their valued pharmacological and therapeutic effects.

Key words

*Ammi visnaga*, *Apium graveolens*, Apiaceae (Umbelliferae), Natural products, Biological activities.

1. Introduction

Family Apiaceae (Umbelliferae) is a family of aromatic and flowering plants, known as celery, carrot or parsley family, or simply as umbellifers. It includes more than 3000–3750 species in 300–455 genera. Plants of this family are characterized by a heavy aromatic smell due to the presence of essential oils. The family Apiaceae consists of three subfamilies, namely Apioideae, Saniculoideae and Hydrocotyloideae; each is divided into tribes and subtribes [1-5]. The most common members of this family include *Anethum graveolens* L. (dill), *Anthriscus cerefolium* L. (chervil), *Angelica* spp. (angelsica), *Apium graveolens* L. (celery), *Carum carvi* L. (caraway), *Coriandrum sativum* L. (coriander), *Cuminum cyminum* L. (cumin), *Foeniculum vulgare* Mill. (fennel) and *Pimpinella anisum* L. (anise), ...etc. [2,3]. Apiaceae plants have been shown to possess different biological properties, including: antimicrobial, antitumor, hepatoprotective and apoptotic activities [2].

2. Results and discussion

2.1. *A. visnaga*

*A. visnaga* is widely distributed in North Africa, Europe, Atlantic Islands, southwestern Asia, North America and Eastern Mediterranean region [6]. The fruits of *A. visnaga* were used in the treatment of mild angina symptoms, mild obstruction of the respiratory tract in bronchial asthma, as a postoperative treatment for patients with renal calculi, for intestinal cramps, pain with menstruation and as a diuretic [6, 7].

2.1.1. Phytochemical review

*A. visnaga* contains several classes of secondary metabolites, noticed from the isolated groups of compounds, including furanochromones, coumarins, flavonoids and essential oil. A comprehensive list of the previously isolated compounds from *A. visnaga* is presented in Table 1 and Figure 1.

2.1.2. Biological review

2.1.2.1 Antimicrobial effects

The antimicrobial potential of both the ethanolic and aqueous extracts of *A. visnaga* fruits were tested against eight pathogenic micro-organisms; *Candida tropicalis*, *Leuconostoc mesenteroides*, *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Candida albicans* and *Pseudomonas aeruginosa* at different concentrations (0.05-50 mg/mL) by the plate-diffusion method. The ethanol extract demonstrated the highest activity against Gram-positive bacteria with a minimum inhibitory concentration (MIC) of 5 mg/mL for *E. faecalis*. In addition, the MIC value of the same extract against the Gram-negative bacteria, *E. coli* and *K. pneumonia* was 12.5 mg/mL [23].

The essential oil of *A. visnaga* fruits was also tested against *E. coli*, *E. coli* ATCC 25922, *S. aureus*, *S. aureus* ATCC 43300, *P. aeruginosa*, *P. aeruginosa* ATCC 27853, *Enterobacter aerogenes*, *K. pneumoniae* and *Morganella morganii*. The oil showed the highest activity against *E. coli*, *E. coli* ATCC 25922, *S. aureus* ATCC 43300 and *P. aeruginosa* ATCC 27853 as indicated by the inhibitory zones' diameters (29, 25 and 25 mm, respectively) [18].

2.1.2.2 Cardiovascular effects

*A. visnaga* seeds were reported to reduce the pain caused by the decrease in the heart blood flow due to its γ-pyrones components. Visnadin, visnagin and khellin have cardiovascular effects due to their calcium channel blocking properties [24-26].
| No. | Name                                      | Molecular weight | Molecular formula | Organ         | Ref. |
|-----|-------------------------------------------|------------------|-------------------|---------------|------|
|     | **A) γ-Pyrones (Furanochromones)**        |                  |                   |               |      |
| 1   | Khellinol                                 | 246.21           | C_{17}H_{20}O_{5} | Fruits        | [8]  |
| 2   | 4-Norvisnagin                             | 216.19           | C_{17}H_{20}O_{4} | Fruits        | [8]  |
| 3   | Visamminol [syn.: 1”-Deoxy (S) angelicain]| 276.28           | C_{17}H_{18}O_{5} | Fruits        | [8]  |
| 4   | Khellin                                   | 260.24           | C_{17}H_{20}O_{5} | Fruits        | [8]  |
| 5   | Visnagin                                  | 230.22           | C_{17}H_{20}O_{4} | Fruits        | [8]  |
| 6   | Ammiol                                    | 276.24           | C_{17}H_{20}O_{5} | Fruits        | [8]  |
| 7   | Khellol                                   | 246.21           | C_{17}H_{20}O_{5} | Fruits        | [8]  |
| 8   | Khellol-O-β-D-glucoside                   | 408.40           | C_{18}H_{20}O_{10} | Seeds        | [9]  |
| 9   | Ammiol-O-β-D-glucoside                    | 438.40           | C_{18}H_{20}O_{10} | Seeds        | [9]  |
| 10  | Pimolin                                   | 460.43           | C_{21}H_{20}O_{3} | Fruits        | [10] |
| 11  | Cimifugin                                 | 306.31           | C_{18}H_{20}O_{3} | Umbels       | [11] |
| 12  | Prim-O-β-D glucosyl cimifugin             | 468.45           | C_{22}H_{20}O_{11} | Umbels       | [11] |
|     | **B) Benzoferans**                        |                  |                   |               |      |
| 13  | Khellinone                                | 236.22           | C_{17}H_{20}O_{3} | Fruits        | [8]  |
| 14  | Visnaginone                               | 206.19           | C_{17}H_{20}O_{3} | Fruits        | [8]  |
|     | **C) Pyranocoumarins**                    |                  |                   |               |      |
| 15  | Samidin                                    | 386.40           | C_{17}H_{20}O_{5} | Fruits        | [12] |
| 16  | (9R,10R)-9-O-(3-Methylbutanoyl)-10-acetate| khellactone      | 388.41           | C_{17}H_{20}O_{5} | Fruits | [12] |
| 17  | Visnadine                                 | 388.41           | C_{17}H_{20}O_{5} | Fruits        | [6]  |
| 18  | Z-Khellactone-3-β-D-glucopyranoside       | 438.43           | C_{17}H_{20}O_{10} | Fruits       | [13] |
|     | **D) Furanocoumarins**                    |                  |                   |               |      |
| 19  | Xanthotoxin                               | 216.19           | C_{17}H_{20}O_{3} | Fruits        | [12] |
| 20  | Bergaptene                                | 216.19           | C_{17}H_{20}O_{3} | Fruits        | [12] |
| 21  | Psoralen                                  | 186.16           | C_{17}H_{20}O_{3} | Fruits        | [12] |
|     | **E) Flavonoids**                         |                  |                   |               |      |
| 22  | Rhamnazin                                 | 330.29           | C_{17}H_{20}O_{2} | Fruits        | [8]  |
| 23  | Isohamnetin                               | 316.26           | C_{17}H_{20}O_{2} | Fruits        | [8]  |
| 24  | Quercetin                                 | 302.23           | C_{17}H_{20}O_{2} | Aerial parts  | [14] |
| 25  | Rhamnetin                                 | 316.26           | C_{17}H_{20}O_{2} | Aerial parts  | [14] |
| 26  | Rhamnazin-3-O-β-D-glucopyranoside         | 478.40           | C_{22}H_{20}O_{12} | Aerial parts  | [14] |
| 27  | Isohamnetin-3-O-β-D-glucopyranoside       | 478.40           | C_{22}H_{20}O_{12} | Aerial parts  | [14] |
| 28  | Rhamnazin-3-O-β-D-glucopyranoside         | 492.43           | C_{22}H_{20}O_{12} | Aerial parts  | [14] |
| 29  | Isohamnetin-3-O-β-D-glucopyranoside       | 478.40           | C_{22}H_{20}O_{12} | Aerial parts  | [14] |
| 30  | Quercetin-3-O-rutinoside                  | 610.52           | C_{22}H_{20}O_{16} | Aerial parts  | [14] |
| 31  | Quercetin-3-O-β-D-glucopyranoside         | 464.40           | C_{22}H_{20}O_{12} | Aerial parts  | [14] |
| 32  | Isohamnetin-3-O-rutinoside                | 624.54           | C_{22}H_{20}O_{16} | Aerial parts  | [14] |
| 33  | Quercetin-7,3',3''-O-triglucopyranoside   | 788.66           | C_{22}H_{20}O_{32} | Aerial parts  | [14] |
| 34  | Kaempferol                                | 286.24           | C_{17}H_{20}O_{4} | Fruits        | [15] |
| 35  | Kaempferol-3-rutinoside                   | 594.52           | C_{22}H_{20}O_{13} | Leaves, flowers and fruits | [16] |
| 36  | Kaempferol-3-O-β-D-glucopyranoside        | 448.40           | C_{22}H_{20}O_{13} | Leaves, flowers and fruits | [16] |
| 37  | Apigenin                                  | 270.24           | C_{15}H_{10}O_{5} | Fruits        | [15] |
| 38  | Luteolin                                  | 286.24           | C_{15}H_{10}O_{6} | Fruits        | [15] |
| 39  | Chrysoeriol                               | 300.26           | C_{16}H_{10}O_{4} | Fruits        | [15] |
| 40  | Quercetin-3-sulfate                       | 382.30           | C_{16}H_{10}O_{6}S | Leaves, flowers and fruits | [16] |
| 41  | Rhamnetin-3-sulfate                       | 396.33           | C_{16}H_{10}O_{10}S | Leaves, flowers and fruits | [16] |
| 42  | Isohamnetin-3-sulfate                     | 394.31           | C_{16}H_{10}O_{6}S_{2} | Leaves, flowers and fruits | [16] |
| 43  | Genistin                                  | 432.40           | C_{21}H_{20}O_{10} | Leaves and roots | [17] |
| 44  | Sissoarin                                 | 446.40           | C_{22}H_{20}O_{10} | Leaves and roots | [17] |
| 45  | Isofermononetin                           | 268.26           | C_{16}H_{10}O_{4} | Leaves and roots | [17] |
| 46  | Fornomonetin                              | 268.26           | C_{16}H_{10}O_{4} | Leaves and roots | [17] |
| 47  | Prunetin                                  | 284.26           | C_{16}H_{10}O_{5} | Leaves and roots | [17] |
| 48  | Biochanin-A                               | 284.26           | C_{16}H_{10}O_{5} | Leaves and roots | [17] |
| 49  | Daidzein                                  | 254.24           | C_{15}H_{10}O_{4} | Leaves and roots | [17] |
| 50  | 4',6',7-Trihydroxyisoflavone             | 270.24           | C_{15}H_{10}O_{5} | Leaves and roots | [17] |
| No. | Name                        | Molecular weight | Molecular formula | Organ      | Ref. |
|-----|-----------------------------|------------------|-------------------|------------|------|
| 51  | α-Thujene                   | 136.23           | C_{10}H_{16}      | Aerial parts | [18] |
| 52  | 3-Methylpentenol            | 100.16           | C_{5}H_{10}O      | Aerial parts | [18] |
| 53  | β-Myrcene                   | 136.23           | C_{10}H_{16}      | Aerial parts | [18] |
| 54  | Isoctyl isobutyrate         | 144.21           | C_{8}H_{14}O_{2}  | Aerial parts | [18] |
| 55  | Butyl isobutyrate           | 144.21           | C_{8}H_{14}O_{2}  | Fruits     | [19] |
| 56  | Linalool                    | 154.25           | C_{10}H_{14}O_{2} | Aerial parts | [18] |
| 57  | 2,2-Dimethylbutanoic acid   | 116.16           | C_{12}H_{22}O_{2} | Aerial parts | [18] |
| 58  | α-Isophorone                | 138.21           | C_{9}H_{16}O      | Aerial parts | [18] |
| 59  | 2-Nonyne                    | 124.22           | C_{9}H_{18}      | Aerial parts | [18] |
| 60  | Bornyl acetate              | 196.29           | C_{10}H_{20}O_{2} | Aerial parts | [18] |
| 61  | Thymol                      | 150.22           | C_{10}H_{18}O_{2} | Aerial parts | [18] |
| 62  | Geranyl acetate             | 196.29           | C_{10}H_{20}O_{2} | Aerial parts | [18] |
| 63  | Lavandulyl acetate          | 196.29           | C_{10}H_{20}O_{2} | Aerial parts | [18] |
| 64  | Citronellyl propionate      | 212.33           | C_{10}H_{20}O_{2} | Aerial parts | [18] |
| 65  | Croweacin                   | 192.21           | C_{10}H_{20}O_{2} | Aerial parts | [18] |
| 66  | Neryl isobutanoate          | 224.34           | C_{10}H_{20}O_{2} | Aerial parts | [18] |
| 67  | α-Damascone                 | 192.30           | C_{10}H_{20}O_{2} | Aerial parts | [18] |
| 68  | (2Z,6E) Farnesal            | 220.35           | C_{10}H_{20}O_{2} | Aerial parts | [18] |
| 69  | Isoamyl-2-methylbutyrate    | 172.26           | C_{10}H_{20}O_{2} | Fruits     | [19] |
| 70  | α-Pinene                    | 136.23           | C_{10}H_{18}O_{2} | Whole plant | [19] |
| 71  | β-Pinene                    | 136.23           | C_{10}H_{18}O_{2} | Whole plant | [19] |
| 72  | α-Terpinene                 | 136.23           | C_{10}H_{18}O_{2} | Whole plant | [19] |
| 73  | Limonene                    | 136.23           | C_{10}H_{18}O_{2} | Whole plant | [19] |
| 74  | 3-Hexenyl isobutanoate      | 170.25           | C_{10}H_{18}O_{2} | Fresh aerial parts | [20] |
| 75  | Nerol                       | 154.25           | C_{10}H_{18}O_{2} | Fresh aerial parts | [21] |
| 76  | Hexanal                     | 100.16           | C_{6}H_{12}O      | Umbels     | [19] |
| 77  | Sabinenne                   | 136.23           | C_{10}H_{18}O_{2} | Umbels     | [19] |
| 78  | Tetracosanoic acid          | 368.64           | C_{24}H_{48}O_{2} | Aerial parts | [22] |
| 79  | Stearic acid                | 284.50           | C_{18}H_{36}O_{2} | Aerial parts | [22] |
| 80  | Petroselinic acid           | 282.50           | C_{18}H_{36}O_{2} | Fruits     | [22] |
| 81  | Arachidic acid              | 312.53           | C_{20}H_{40}O_{2} | Fruits     | [22] |
| 82  | β-Sitosterol                | 414.71           | C_{25}H_{50}O_{2} | Aerial parts | [22] |

**G) Coumestans**

| No. | Name              | Molecular weight | Molecular formula | Organ      | Ref.      |
|-----|-------------------|------------------|-------------------|------------|-----------|
| 83  | Coumestrol        | 268.22           | C_{15}H_{20}O_{5} | Leaves and roots | [17] |

Ahmed et al. | J. Adv. Biomed. & Pharm. Sci.
Figure 1: Chemical structures of the reported compounds from *A. visnaga*.
Figure 1: (continued).
Figure 1: (continued).
Figure 1: (continued).
They inhibit the contraction of vascular smooth muscles, causing dilatation of the peripheral and coronary vessels and stimulate coronary circulation [24,25]. Both the peripheral and coronary vasodilator properties were also found with visnagin, which has been used in angina pectoris as it leads to non-specific inhibition of the contractility of vascular smooth muscles [24,25]. Moreover, it has negative inotropic and chronotropic effects and aids in reducing peripheral vascular resistance [26]. It also causes a weak inhibition of the hydrolytic activity of phosphodiesterase (PDE) isozymes (PDE5, PDE4, PDE3, cyclic GMP activated PDE2 and PDE1). This inhibitory effect on cyclic nucleotide PDEs may be responsible for the vasodilatory action of visnagin at high concentrations [26]. The chloroform and methanol extracts (at 1 mg/mL) of *A. visnaga* fruits cause the contractions of the rabbit Guinea pig aorta *in vitro* [6]. The coronary blood flow increased in isolated Guinea pig hearts via visnadin at 60 and 120 μg/mL by 46 and 57%, respectively [6]. Visnadin (< 10 μM) was reported to cause inhibition of the contractions induced by the depolarization with 80 mM KCl or by CaCl2 in the KCl-depolarized aorta. Its inhibitory effects were not increased when the depolarization time was prolonged and was similar in aorta incubated in 5 or 40 mM KCl [27]. Samidin and khellol glucose were reported to exhibit positive inotropic effects on the heart [6]. Khellin was reported to increase HDL-cholesterol in normolipidemic subjects. It also reported having vasodilator, bronchodilator and spasmyloitic activities [24]. It has been developed in the treatment of angina pectoris as a bronchodilator and coronary medicine due to its peripheral and coronary function as a vasodilator [28]. Besides being such an antiasthmatic and vasodilator and also an important relaxant without influencing blood pressure [29]. The vasodilating features of *A. visnaga* are associated with the pyranocoumarin, visnadin and its two primary pyrones, khellin and visnagin. Khellin and visnadin have been shown to have antagonistic activity with calcium, which in turn results in vasodilating activities. It has been shown that visnadin exhibits both peripheral and coronary vasodilator activities and is also used to treat angina pectoris. It inhibits the contractions mediated by the entry of Ca2 + via L-type Ca2 + channels [27].

### 2.1.2.3 Prevention of kidney stone formation

Khellin is a spasmyloitic agent and visnagin also may decrease peripheral vascular resistance, which may make the stone to pass through the urinary tract easily. In an *in vitro* cell culture experimentation, khellin and visnagin exhibited preventive activity and decreased lactate dehydrogenase enzyme. Also, khellin and visnagin illustrated preventive effects *in vivo* through decreasing deposition of calcium oxalate crystals [6,30].

### 2.1.2.4 Treatment of vitiligo

Khellin has phototherapeutic activities like as those of the psoralens without the formation of detectable DNA mutations or phototoxic effects. It has therefore been used for the treatment of vitiligo [31]. A total of 36 patients suffering from different types of vitiligo underwent 6 months of treatment with a novel gel formulation of khellin (1%), based upon a water/2-propanol/propylene glycol (WPG) ternary system, caused repigmentation in 86.1% of the treated cases, as opposed to 66.6% in the placebo group [6,31].

#### 2.1.2.5 Antioxidant effects

*A. visnaga* has antioxidant activity [32,33]. The antioxidant effect of the butanolic extract of *A. visnaga* was determined via the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method. At a concentration of 200 μg/mL, the butanolic extract quenched the DPPH radical by 78.7% [6,34].

#### 2.1.2.6 Antidiabetic activities

In many cultures, such as those of Palestine, Morocco and the Sefrou region, *A. visnaga* is considered a popular antidiabetic agent [22,35-36]. An aqueous sample containing *A. visnaga* was shown to possess a substantial hypoglycemic effect when offered to both regular and streptozotocin rats with diabetes [22,37]. In addition, a decoction formulated from the *A. visnaga* fruits had the potential in normoglycemic rats to minimize blood glucose levels by 51% in comparison to a hypoglycemic agent (tolbutamide) [22,38].

#### 2.1.2.7 Anti-inflammatory activities

Visnagin decreases the expression of mRNA and the release of TNF-α, IL-1β and IFNγ. The anti-inflammatory activity of visnagin could be due to the inhibition of transcription factors, such as AP-1 and NFκB [22,39]. Visnagin also has a neuroprotective effect that is responsible for its anti-inflammatory activity [22].

#### 2.1.2.8 Cytotoxic activities

The cytotoxicity of khellin was measured against four cancer cell lines: MCF-7 (breast cancer), MKN-45 (gastric cancer), HEp-2 (larynx cancer) and HT-29 (colorectal cancer). The findings were, however, not positive and the substance did not demonstrate any cytotoxic activity against the four cell lines at the tested concentrations [22,40]. Nevertheless, khellin exhibited mild to moderate activity against the hepatocellular carcinoma cell line [41]. An ethanolic extract of *A. visnaga* exhibited cytotoxic activity on cervical cancer and breast cancer cell lines [22,42]. Further research was performed into the cytotoxic activity of isolated khellin and visnagin against Hep-G2 (liver carcinoma), HCT 116 (colon carcinoma), Hela (cervical carcinoma), MCF7 (breast carcinoma) and Hep-G2 (liver carcinoma); the findings exhibited the cytotoxic activity of both khellin and visnagin against the Hep-G2 cell line [22,43].

#### 2.1.2.9 Hair loss

The topical use of *A. visnaga* was tested for hair loss. A lotion consisting of visnadin and other components leading to enhancement in local microcirculatory flow [22,44].
2.1.2.10 Antimutagenic effects

In *Salmonella typhimurium* T98, khellin exhibited inhibitory effects of the mutagenicity of two promutagens benzo[a]pyrenes, 2-aminofluorene and 2-aminoanthracene, while visnagin illustrated a greater toxic effect. The total extract of the fruits of *A. visnaga* displayed a higher inhibition ability against 2-aminoanthracene, 1-hitropyrene and daunomycin than khellin alone. This was attributed to the presence of additional inhibitors such as coumarins or due to the synergistic effect of different compounds [22,45].

2.1.2.11 Immunostimulatory activities

Immunostimulatory effects were detected by *A. visnaga* total and protein extracts. Extracts were evaluated on splenocyte using an MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay with or without concanavalin-A (Con-A) stimulation, a mitogenic agent used as a positive control agent [46].

2.1.2.12 Larvicideal and insecticideal activities

Both larvicidal and insecticidal features of *A. visnaga* have been investigated and the khellin toxicity was examined against *Oncopeltus fasciatus* (Hemiptera) and *Aedes aegypti* (Diptera) larvae, where high activity was observed [22,48]. Khellin and visnagin may therefore be used for the production of new botanical acaricides [49]. *A. visnaga* fruit ethanolic extract caused inhibition of the lipid content in the haemolymph of nymphs and adults [50], while *A. visnaga* n-butanolic extract caused inhibition to glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) activity in the haemolymph [51].

2.1.2.13 Herbicideal activities

*A. visnaga* dichloromethane extract exhibited herbicidal activity. Khellin and visnagin were responsible for their herbicidal effect [22,52].

2.2 *A. graveolens*

*A. graveolens* (Apiaceae) is widely distributed in Italy, Sweden, Egypt, Algeria and Ethiopia [53]. It consists of three varieties that are classified according to the part of the plant consumed [54]: *A. graveolens* var. *dulce*; commonly known as celery, *A. graveolens* var. *rapaceum*; commonly known as celeriac or root celery and *A. graveolens* var. *secalinum*; commonly known as smallage or leaf celery. Celery is an important source of minerals, vitamins and amino acids. It has many different uses such as sedative, stimulant, carminative, laxative, antispasmodic, anthelmintic, diuretic, urinary antiseptic, emmenagogue and aphrodisiac [53,55].

2.2.1 Phytochemical review

*A. graveolens* contained various classes of secondary metabolites, noticed from the isolated groups of compounds including: flavonoids, coumarins, furanocoumarins, isobenzofurans, sesquiuterpenes, phthalides and miscellaneous [55]. A comprehensive list of the previously isolated compounds from *A. graveolens* is presented in (Table 2 and Figure 2).

2.2.2 Biological review

2.2.2.1 Anticancer activities

Celery seed oil (CSO) is a source of anticancer phytochemicals. When, CSO (300 mg/kg, p.o.) was given to rats for four weeks after DENA-induced hepatocellular carcinoma (diethyl nitrosamine) (HCC), its increased caspase-3 expression and decreased PCNA expression, suggesting both apoptotic and anti-proliferative activity, respectively. CSO uses anti-mutagenic, anti-inflammatory and proapoptotic pathways to exert its anticancer effect [53].

2.2.2.2 Antibacterial activities

The essential oil of celery displayed strong inhibitory activities against *E. coli* and moderate inhibition against *S. aureus* and *P. aeruginosa* [77].

2.2.2.3 Antiulcerogenic activities

Evaluation of the antiulcerogenic activity in rats was done by using the HCl/EtOH method. Inhibition of gastric lesions by extracts of *A. graveolens* was dose-dependent for both seeds and aerial parts by (51–95%) and (53–76%), respectively. The methanolic and aqueous extracts at 300 mg/kg caused inhibition of gastric lesions, which was similar to that induced by omeprazole (94%) [77].

2.2.2.4 Hypolipidemic effects

Ethanol seed extract of *A. graveolens* showed a decrease of serum total cholesterol, low-density lipoprotein cholesterol, triglycerides and significant increase in high-density lipoprotein cholesterol in the treated groups. The oral administration of ethanol seed extract of *A. graveolens* showed good hypolipidemic effects. The results agreed to the traditional use of *A. graveolens* in the treatment of hyperlipidemia [78].

2.2.2.5. Antihypertensive effects

Administration of the methanolic, hexanoic and aqueous-ethanolic celery seeds extracts was used to demonstrate their effects on blood pressure and heart rate using spironolactone as a guide. The findings showed that in hypertensive rats, they decreased blood pressure and increased heart rate, but they had no effect on normotensive rats. At 300 mg/kg, each celery seed extract resulted in a decrease in blood pressure of 38, 24 and 23 mmHg and an increase in heart rate of 60, 25 and 27 beats/min, respectively [79].

3. Conclusion

Several classes of secondary metabolites isolated from different parts of *A. visnaga* including furanochromones, furanocoumarins, pyranocoumarins, flavonoids and essential oil, where flavonoids and essential oil are the most common investigated classes, while others need more attention from the researchers. Fruits and aerial parts were investigated. Therefore, other parts need further investigation.
### Table 2: A list of previously isolated compounds from *A. graveolens*.

| No. | Name                                                      | Molecular weight | Molecular formula | Organ               | Ref.  |
|-----|-----------------------------------------------------------|------------------|-------------------|---------------------|-------|
| A)  | **Flavonoids**                                            |                  |                   |                     |       |
| 1   | Luteolin                                                  | 286.24           | C_{19}H_{10}O_{6} | Leaves              | [56, 57] |
| 2   | Kaempferol                                                | 286.24           | C_{19}H_{10}O_{6} | Leaves              | [57]   |
| 3   | Apinan                                                   | 564.50           | C_{29}H_{20}O_{14}| Leaves              | [58]   |
| 4   | Luteolin-7-O-β-D-apiosyl-(1→2)-β-D-glucopyranoside       | 580.49           | C_{32}H_{28}O_{15}| Leaves              | [59]   |
| 5   | Luteolin-7-O-β-D-glucopyranoside                         | 448.38           | C_{29}H_{18}O_{11}| Leaves              | [59]   |
| 6   | Luteolin-7-O-[β-D-apiosyl (1→2)-[6-O-malonyl]]-β-D-glucopyranoside | 666.54           | C_{29}H_{20}O_{18}| Leaves              | [59]   |
| 7   | Chrysoselin-7-O-β-D-apiosyl (1→2)-β-D-glucopyranoside    | 594.52           | C_{27}H_{20}O_{15}| Leaves              | [59]   |
| 8   | Apigenin-7-O-β-D-glucopyranoside [syn.: Apigetrin]        | 432.40           | C_{21}H_{16}O_{10}| Leaves              | [60]   |
| 9   | Apigenin-7-O-β-D-apiosyl-(1→2)-β-D-glucopyranoside       | 564.49           | C_{24}H_{20}O_{14}| Leaves              | [59]   |
| 10  | Apigenin-7-O-[β-D-apiosyl (1→2)-[6-O-malonyl]]-β-D-glucopyranoside | 650.54           | C_{29}H_{20}O_{17}| Leaves              | [59]   |
| B)  | **Coumarins and furocoumarins**                          |                  |                   |                     |       |
| 11  | Apionetin                                                 | 244.24           | C_{14}H_{12}O_{4} | Seeds               | [61]   |
| 12  | Apionetin-O-β-D-glucopyranoside                          | 406.38           | C_{20}H_{20}O_{9} | Seeds               | [61]   |
| 13  | Bergapten                                                 | 216.19           | C_{12}H_{14}O_{2} | Seeds               | [61]   |
| 14  | Isopimpinellin                                            | 246.21           | C_{16}H_{16}O_{5} | Seeds               | [61]   |
| 15  | 8-Hydroxy-5-methoxysoralene                              | 232.19           | C_{12}H_{16}O_{3} | Seeds               | [61]   |
| 16  | 5-Methoxy-8-O-β-D-glucosyloxysoralene                    | 394.33           | C_{21}H_{20}O_{10}| Seeds               | [61]   |
| 17  | Isorutarin                                                | 424.4            | C_{20}H_{18}O_{10}| Seeds               | [61]   |
| 18  | Vellein                                                   | 392.40           | C_{18}H_{16}O_{8} | Seeds               | [61]   |
| 19  | Celerin                                                   | 260.28           | C_{14}H_{12}O_{4} | Seeds               | [62]   |
| 20  | 4,9-Dihydroxy-7H-furo[3,2-g][1] benzopyran-7-one-4-methylether-9-O-β-D-glucopyranoside | 394.33           | C_{18}H_{20}O_{10}| Seeds               | [63]   |
| 21  | 7,8-Dihydroxy-6-(3-methyl-2-butenyl)-2H-1-benzopyran-2-one-8-methylether | 260.29           | C_{14}H_{16}O_{4} | Seeds               | [64]   |
| 22  | (1'S,2'S)-2-(1,2-Dihydroxy-1-methylethyl)-2,3-dihydro-7H-furo[3,2-g][1] benzopyran-one | 262.26           | C_{14}H_{16}O_{5} | Seeds               | [64]   |
| 23  | Ostheno                                                   | 230.26           | C_{12}H_{16}O_{3} | Seeds               | [61]   |
| 24  | Celereci                                                  | 262.26           | C_{14}H_{16}O_{5} | Seeds               | [61]   |
| C)  | **Isobenzofurans**                                        |                  |                   |                     |       |
| 25  | 3-Butylhexahydro-1(3H)-isobenzofuranone                   | 196.29           | C_{12}H_{12}O_{2} | Leaves and stalks   | [65]   |
| 26  | (3R,3αR,7αS)-3-Butylhexahydro-1(3H) isobenzofuranone     | 196.29           | C_{12}H_{12}O_{2} | Leaves and stalks   | [65]   |
| 27  | (3α,3αS,7αR) 7,7α-Didehydro-3-butylhexahydro-1(3H) isobenzofuranone | 194.27           | C_{12}H_{12}O_{2} | Leaves and stalks   | [66]   |
| 28  | (3α,3αR,7αS)-3'S-β-D-Glucopyranosyloxy, 7,7α-didehydrobutylhexahydro-1(3H) isobenzofuranone | 372.41           | C_{16}H_{22}O_{8} | Leaves and stalks   | [65]   |
| 29  | (Z)-4,5,6,7-Tetrahydro-3-butylidene-1(3H) isobenzofuranone | 192.25           | C_{12}H_{12}O_{2} | Leaves and stalks   | [65]   |
| 30  | (E) 3S,4,5,8-Tetrahydro-3-butylidene-1(3H) isobenzofuranone | 192.25           | C_{12}H_{12}O_{2} | Leaves and stalks   | [65]   |
| 31  | Senkyunolide-J [syn.: (E) 3S,4,5,6,7,8-Hexahydro, 6R,7R-dihydroxy-3-butylidene-1(3H) isobenzofuranone] | 226.27           | C_{12}H_{12}O_{4} | Leaves and stalks   | [65]   |
| 32  | Senkyunolide-N [syn.: (E) 3S,4,5,6,7,8-Hexahydro-6S,7S-dihydroxy-3-butylidene-1(3H) isobenzofuranone] | 226.27           | C_{12}H_{12}O_{4} | Leaves and stalks   | [65]   |
| 33  | (S) 3-Butyl-1(3H) isobenzofuranone                        | 190.24           | C_{12}H_{12}O_{2} | Leaves and stalks   | [66]   |
| 34  | 3α,4-Dihydro-3-(3-methylbutylidene)-1(3H) isobenzofuranone | 204.26           | C_{12}H_{12}O_{2} | Leaves and stalks   | [67]   |
| 35  | 3-(3-Hydroxybutyl)-1(3H)-isobenzofuranone-O-β-D-glucopyranoside | 368.38           | C_{12}H_{12}O_{8} | Leaves and stalks   | [67]   |
| 36  | 3-(3-Hydroxybutyl)-1(3H)-isobenzofuranone-O-[β-D-apiosyl-(1→2)-β-D-glucopyranoside] | 500.49           | C_{25}H_{22}O_{12}| Leaves and stalks   | [67]   |
| 37  | 3-(3-Methylbutylidene)-1(3H)-isobenzofuranone             | 202.25           | C_{12}H_{12}O_{2} | Leaves and stalks   | [68]   |
| No. | Name                                                                 | Molecular weight | Molecular formula | Organ    | Ref. |
|-----|----------------------------------------------------------------------|------------------|-------------------|----------|------|
| 38  | β-Selinene                                                           | 204.35           | C19H24            | Seeds    | [57] |
| 39  | α-Selinene                                                           | 204.35           | C19H24            | Seeds    | [57] |
| 40  | σ-Selinene                                                           | 202.34           | C19H22            | Seeds    | [57] |
| 41  | γ-Selinene                                                           | 204.35           | C19H24            | Seeds    | [57] |
| 42  | (1β,4β,4,14-Epoxy-1,11-eudesmanediol-11-O-β-D-glucopyranoside        | 416.51           | C21H26O8          | Seeds    | [68] |
| 43  | (1β,4α,7αH)-1,4,11-Eudesmanetriol-11-O-β-D-glucopyranoside           | 418.52           | C21H26O8          | Seeds    | [68] |
| 44  | (1β,2α)-4(15)-Eudesmene-1,2,11-triil-11-O-β-D-glucopyranoside         | 416.51           | C21H26O8          | Seeds    | [68] |
| 45  | 1β-(4(15)-Eudesmene-1,11,14-triil-11-O-β-D-glucopyranoside           | 416.51           | C21H26O8          | Seeds    | [68] |
| 46  | Sedanonic acid [syn.: 1-(1-Carboxycyclohex-1-en-6-yl) pentan-l-one]    | 210.27           | C13H18O3          | Leaves   | [69, 70] |
| 47  | 1-(3-Carboxycyclohex-1-en-2-yl) pentan-l-ol                          | 198.26           | C13H18O3          | Leaves   | [69, 70] |
| 48  | Sedanonic anhydride                                                 | 192.25           | C13H16O2          | Leaves   | [69, 70] |
| 49  | Sedanolic acid [syn.: 1-(3-Carboxycyclohex-2"n-4-yl) pentan-l-ol]     | 198.26           | C13H18O3          | Leaves   | [69, 70] |
| 50  | Sedanolide [syn.: (3-Butyl-5,6,7,7a-tetrahydrophthalide]              | 194.27           | C13H18O2          | Leaves   | [69, 70] |
| 51  | 3-Isobutylidene-3a,4,5,6-tetrahydrophthalide                         | 192.25           | C13H18O2          | Leaves   | [69, 70] |
| 52  | 2-Deoxybrassinolide                                                 | 464.70           | C26H24O11         | Seeds    | [71] |
| 53  | Anthriscinol methyl ether                                           | 222.24           | C12H16O4          | Seeds    | [61] |
| 54  | Limonene                                                            | 136.23           | C10H16            | Leaves   | [62] |
| 55  | p-Coumaric acid                                                     | 164.16           | C9H6O3            | Leaves   | [72] |
| 56  | Caffeic acid                                                        | 180.16           | C9H6O4            | Leaves   | [72] |
| 57  | Ferulic acid                                                       | 194.18           | C10H16O4          | Leaves   | [72] |
| 58  | Chlorogenic acid                                                    | 354.31           | C18H16O9          | Leaves   | [59] |
| 59  | Junipediol A 8-0-β-D-glucoside [syn: 2-(3,4 Dihydroxyphenyl)-3'-methyl ether-1,3-propanediol 1-O-β-D-glucopyranoside] | 360.36           | C18H18O2          | Seeds    | [73] |
| 60  | Junipediol A 4-0-β-D-glucopyranoside [syn: 2-(3,4-Dihydroxyphenyl)-3'-methyl ether-1,3-propanediol 4'-O-β-D-glucopyranoside] | 360.36           | C18H18O2          | Seeds    | [68] |
| 61  | Falcariindol [syn: (3R,85,9Z)-4,6-Diyne-3,8-diol-1,9-heptadecadiene] | 260.40           | C12H24O2          | Roots    | [74] |
| 62  | (3R,85,9Z)-4,6-Diyne-3,8-diol-8-methyl ether-1,9 heptadecadiene       | 274.40           | C12H24O2          | Roots    | [74] |
| 63  | 3-Methyl ether-4,5-methylenedioxy benzoic acid                      | 196.16           | C9H18O2           | Seeds    | [75] |
| 64  | (R)3-Methyl-5-propyl-2-cyclohexen-1-one                             | 152.23           | C10H16O           | Leaves   | [76] |

**E) Phthalides**

| No. | Name                                                                 | Molecular weight | Molecular formula | Organ    | Ref. |
|-----|----------------------------------------------------------------------|------------------|-------------------|----------|------|

**F) Miscellaneous**
Figure 2: Chemical structures of the previously isolated compounds from *A. graveolens*. 
Figure 2: (continued).
Figure 2: (continued).
Figure 2: (continued).
Also, many biological studies have been conducted on A. visnaga and resulted in having antimicrobial, anti-diabetic, anti-inflammatory, cytotoxic, antinutagenic, immunostimulatory, larvicidal, insecticidal, herbicidal and cardiovascular effects. Also, it causes the prevention of kidney stone formation and it has a role in the treatment of vitiligo. On the other hand, A. graveolens is rich in many compounds as flavonoids, coumarins, furanocoumarins, isobenzofurans, sesquiterpenes, phthalides and miscellaneous. Coumarins, isobenzofurans and flavonoids are the most commonly investigated. Leaves and seeds were investigated. Therefore, other parts need further investigation. As well, the effectiveness of A. graveolens has been proven as an anticancer, antibacterial, antiulcerogenic, hypolipidemic and anti hypertensive effects.

Conflict of interests

The authors declare that there is no conflict of interests regarding this review.

Oridc

Shereen Ahmed https://orcid.org/0000-0002-4864-9154
John Fahim https://orcid.org/0000-0002-2425-0819
Usama Ramadan Abdelmohsen https://orcid.org/0000-0002-1014-6922
Ashraf E. N. Hamed https://orcid.org/0000-0003-2230-9909

References

[1] Downie SR, Katz-Downie DS, Watson MF. A phylogeny of the flowering plant family Apiaceae based on chloroplast DNA RPL16 and rpoe1 intron sequences: towards a suprageneric classification of subfamily Apiioideae. American Journal of Botany. 2000;87(2):273-92.
[2] Amini MS, Joharchi MR. Ethnobotanical knowledge of Apiaceae family in Iran: A review. Avicenna Journal of Phytomedicine. 2016;6(6):621-35.
[3] Sahebkar A, Iranshahi M. Biological activities of essential oils from the genus Ferula (Apiaceae), Asian Biomedicine. 2010;4(6):835-47.
[4] Christova-Bagdasarian VL, Bagdasarian KS, Atanassova MS. Phenolic compounds and antioxidant capacity in bulgarian plans (dry seeds). Journal of Essential Oil Bearing Plants. 2013;212(1):57-65.
[5] Jimenez Mejias P, Vargas P. Taxonomy of the tribe Apieae (Apiaceae) revisited as revealed by molecular phylogenies and morphological characters. Phytotaxa. 2015;212(1):57-79.
[6] Al-Snafi AE. Chemical constituents and pharmacological activities of Ammi majus and Ammi visnaga; a review. International Journal of Pharmacy and Industrial Research. 2013;3(3):257-65.
[7] WHO. WHO monographs on selected medicinal plants. WHO Library Cataloguing in Publication Data. 2007;23:32-3.
[8] Abou-Mustafa EA, Salih NM, Elgamal MHA, Shalaby NMM, Eissa N, El-Dyb M. A further contribution to the γ-pyrene constituents of Ammi visnaga fruits. Planta Medica. 1990;56(1):134.
[9] Tjarks LW, Spencer GF, Seest EP. Isolation and 1H and 13C NMR of ammiol and kheltol glucosides. Journal of Natural Products.1989;52(3):635-46.
[10] Elgamal MHA, Shalaby NMM, El-Hagrasy AM, El-Mounayri JS, Simon A, Duddeck H. A further contribution to some gamma-pyrene constituents of Ammi visnaga. Fitosintesis. 1998;9:549-50.
[11] Sellami HKN, Apolitano A, Masullo M, Smiti S, Piacenti S, Pizzà C. Influence of growing conditions on metabolite profile of Ammi visnaga umbels with special reference to bioactive furanochromones and pyranocoumarins. Phytochemistry. 2013;95:197-206.
[12] Winderl B, Schaiger S, Gandzera M. Fast and improved separation of major coumarins in Ammi visnaga (L.) Lam. by supercritical fluid chromatography. Journal of Separation Science. 2016;39(20):4042-8.
[13] Sonnemann HE, J.M. Eisenheim N, Frömming KK. Isolation and characterization of an angular-type dihydroxyaromacoumaringlycoside from the fruits of Ammi visnaga (L.) Lam. (Apiaceae). Zeitschrift für Naturforschung C. 1995;50(9-10):729-31.
[14] Bencheaier R, Khettab H, Kabouche A, Kabouche Z, Iay M. Flavonoids and antioxidant activity of Ammi visnaga L. (Apiaceae). Records of Natural Products. 2011;5(1):52-5.
[15] Mabrouk SS, El-Shayeb NM. Inhibition of aflatoxin production in Aspergillus flavus by natural coumarins and chromones. World Journal of Microbiology and Biotechnology. 1992(8):60/2.
[16] Harborne JB, King L. Flavonoid sulphaes in the Unbeiflora. Biochemical Systematics and Ecology. 1976;4(2):111-5.
[17] Abdulmanea K, Prakudina EA, Lankov P, Vaníčková L, Koblovková R, Zelený V, Lapčík O. Immunochemical and HPLC identification of isoflavonoids in the Apiaceae family. Biochemical Systematics and Ecology. 2012;45:237-43.
[18] Khalifah A, Labed A, Semra Z, Ali kaki B, Kabouche A, Touzani R, Kabouche Z. Antibacterial activity and chemical composition of the essential oil of Ammi visnaga L. (Apiaceae) from Constantine, Algeria. International Journal of Medicinal and Aromatic Plants. 2011;1(3):302-5.
[19] Khadra A, El Mouki R, Mgues K, Araujo ME. Variability of two essential oils of Ammi visnaga (L.) Lam. a traditional Tunisian medicinal plant. Journal of Medicinal Plants Research. 2011;5(20):5079-82.
[20] Soro KN, Sabri L, Amali S, Khabbal Y, Zair T. Chemical composition of Moroccan Ammi visnaga L. (Lam.) and antibacterial activity of its essential oil against extended-spectrum beta-lactamase-producing and not producing bacteria. Compost Biores. 2015;13(3):168-75.
[21] Feirouz B, Salima KG. Antibacterial activity and chemical composition of Ammi visnaga L. essential oil collected from Boumerdes (Algeria) during three periods of the plant growth. Journal of Essential Oil-Bearing Plants. 2014;17(6):1317-28.
[22] Khalil N, Bishr M, Desouky S, Salama O. Ammi visnaga L., A Potential Medicinal Plant: A Review. Molecules. 2020;25(2):301-18.
[23] Ghareeb AM, Zedan TH, Gharbi LA. Antibacterial and antifungal activities of Ammi visnaga extracts against pathogenic microorganisms. Iraq Journal of Science. 2011;52(1):30-6.
[24] Hashim I, Jan A, Marwat KB, Khan MA. Phytochemistry and medicinal properties of Ammi visnaga (Apiaceae). Pakistan Journal of Botany. 2014;46(3):861-7.
[25] Alam S, Anjum N, Akhtar J, Bashir F. Pharmacological investigations on khella- (Ammi visnaga L.). World Journal of Pharmaceutical Research. 2016;5(13):212-24.
[26] Duarte J, Torres AL, Zarzuelo A. Cardiovascular effects of visnagin on rats. Planta Medica. 2000;66(1):35-9.
[27] Duarte J, Vallejo I, Pérez-Vizcaino F, Jiménez R, Zarzuelo A, Tamargo J. Effects of visnadin on rat isolated vascular smooth muscles. Planta Medica. 1997;63(3):233-6.
[28] Balandin MF, Kinghorn AD, Farnsworth NR. Plant-Derived Natural Products in Drug Discovery and Development. In Human Medicinal Agents from Plants; American Chemical Society; Washington, DC, USA. 1993;534:2-12.
[29] Al-Snafi AE. A review of a medicinal plants with broncho-dilatory effect Part 1. Scholars Academic Journal of Pharmacy. 2015;5(7):297-304.
[30] Vanachayangkul P, Ammi visnaga L, for prevention of urolithiasis, Doctor of Philosophy. University of Florida, 2008.
[31] Orecchia G, Sangalli G, Gazzani G, Giordano C, Gilio M. Cardiovascular effects of visnagin in lipopolysaccharide-(LPS) stimulated BV-2 murine microglia cells. Analytical and Bioanalytical Electrochemistry. 2018;7(13):212-24.
[32] Mansouri L, Ahmadi H, Maghrani M, Eddouks M. Hypoglycemic effect of aqueous extract of Ammi visnaga L. (Amaranthaceae) on diabetic rats. Archives of Pharmacal Research. 2002;25(2):301-4.
[33] Mansouri L, Ahmadi H, Maghrani M, Eddouks M. Hypoglycemic effect of aqueous extract of Ammi visnaga L. (Amaranthaceae) on diabetic rats. World Journal of Pharmaceutical Research. 2011;1(3):168-75.
[34] Usama Ramadan Abdelmohsen https://orcid.org/0000-0002-1014-6922
[35] Shereen Ahmed https://orcid.org/0000-0002-4864-9154
[36] John Fahim https://orcid.org/0000-0002-2425-0819
[37] Asghar E. N. Hamed https://orcid.org/0000-0003-2230-9909
[38] Amini MS, Joharchi MR. Ethnobotanical knowledge of Apiaceae family in Iran: A review. Avicenna Journal of Phytomedicine. 2016;6(6):621-35.
[39] Al-Snafi AE. A review of a medicinal plants with broncho-dilatory effect Part 1. Scholars Academic Journal of Pharmacy. 2015;5(7):297-304.
[40] Mansouri L, Ahmadi H, Maghrani M, Eddouks M. Hypoglycemic effect of aqueous extract of Ammi visnaga L. (Amaranthaceae) on diabetic rats. Archives of Pharmacal Research. 2002;25(2):301-4.
Ateya AM, Abou-Hashem M, El-Sayed Z, Abbas F. Biological activity of the Egyptian medicinal plants: part 4 cytotoxicity of 50 Egyptian plants and species against hepatocellular carcinoma. Journal of Ethnomedicine. 2014;1:56-63.

Patel H, Nematzi N, Shrivati A. Cytotoxic activity effects of Ammi visnaga extract on Hela and MCF7 cancer cell lines. Journal of Animal Biology. 2013;7(2):25-33.

Beltagy AM, Beltagy DM. Chemical composition of Ammi visnaga L. and new cytotoxic activity of its constituents khellin and visnagin. Journal of Pharmaceutical Sciences and Research. 2015;7(6):285-291.

Curri SB Bombardelli E. Pharmaceutical compositions having activity on the cutaneous microcirculation. United States patent US. 1993;176(5):919-23.

Schimner O, Rauch P. Inhibition of metabolic activation of the promutagens, benzo [a] pyrene, 2-aminofluorene and 2-aminoanthracene by furanochromones in Salmomella typhimurium. Mutagenesis. 1998;13(4):385-9.

Daoudi A, Aarab L, Abdel-Sattar E. Screening of immunomodulatory activity of total and proteolytic extracts of some Moroccan medicinal plants. Toxicology and Industrial Health. 2013;29(3):245-53.

Bhagavathula AS, Al-Khatib AJ, Elnour AA, Al Kalbani NM, Shehab A. Ammi visnaga in treatment of urolithiasis and hyperglycemia. Pharmacognosy Research. 2015;7(4):397-400.

Maleck M, Santos FC, Serdeiro MT, Guimarães AF, Ferreira B, Gunaydin K. Almeida AP Khellin: A furanochromone with toxicity against Oncopeltus fasciatus (Hemiptera) and Aedes aegypti (Diptera). Journal of Natural Pharmaceuticals. 2013;4(1):32-6.

Pavela R. Acaricidal properties of extracts and major furanochromones from the seeds of Ammi visnaga Linn. against Tetranychus urticae Koch. Industrial Crops and Products. 2015;67:108-13.

Ghoneim K, Al-Daly A, Amer M, Mohammad A, Khadrawy F, Mahmoud MA. Effects of Ammi visnaga L. (Apiaceae) extracts on the main metabolites in haemolymph and fat bodies of Schistocerca gregaria (Forskal) (Orthoptera: Acraeidae). Journal of Advances in Zoology. 2014;1(1):11-23.

Ghoneim K, Al-Daly A, Khadrawy F, Amer M, Mahmoud MA. Efficacy of the toothpick weed Ammi visnaga L. (Apiaceae) fruit extracts on transaminase activity in certain tissues of Schistocerca gregaria (Forskal) (Orthoptera: Acraeidae). International Journal of Entomology Research. 2016;15(19):28-38.

Travaini ML, Sosa GM, Cecarelli EA, Walter H, Cantrell CL, Carrillo NJ, Dayan FE, Meepagala KM, Duke SO. Khellin and visnagin, furanochromones from Ammi visnaga (L.) Lam., as potential bioherbicides. Journal of Agricultural and Food Chemistry. 2016;64(50):9475-87.

Ahmedy O. Study of the anticancer potential of celery seed oil against chemically induced hepatocellular carcinoma in rats: a mechanistic approach. Al-azhar Journal of Pharmaceutical Sciences. 2016;53(1):14-28.

Quiros CF. Cerey: Apium graveolens L. In Genetic Improvement of Vegetable Crops. 1993:523-34.

Al-Asmari AK, Athar MT, Kadasah SG. An updated phytopharmacological review on medicinal plant of Arab region: Apium graveolens Linn. Pharmacognosy Reviews. 2017;11(21):13-8.

Han D, Row KH. Determination of luteolin and apigenin in celery using ultrasonic-assisted extraction based on aqueous solution of ionic liquid coupled with HPLC quantification. Journal of the Science of Food and Agriculture. 2011;91(15):2888-92.

Kooti W, Daraei N. A review of the antioxidant activity of celery (Apium graveolens L). Journal of Evidence-Based Complementary & Alternative Medicine. 2017;22(4):1029-34.

Mencherini T, Cau A, Bianco G, Loggia RD, Aquino RP. An extract of Apium graveolens var. dulce leaves: structure of the major constituent, apin and its anti-inflammatory properties. Journal of Pharmacy and Pharmacology. 2007;59(6):891-7.

Liu G, Zhuang L, Song D, Lu C, Xu X. Isolation, purification and aminofluorene and 2-aminodihydrophthalides from celery, Celeriac and fennel. The Journal of Organic Chemistry. 1963;28(4):985-7.

Kitajima J, Ishikawa T, Sato H. Polar constituents of celery seed. Phytochemistry. 2003;64(5):1003-11.

Collin HA, Isaac S. Apium graveolens L. (Celery). In: In Vitro Culture and the Production of Flavors. Medicinal and Aromatic Plants III, Book series (Agriculture). 1991:15:73-94.

Bjeldanes LF, Kim IS. Phthalide components of celery essential oil. The Journal of Organic Chemistry. 1977;42(13):2333-5.

Fujoka S, Sakurai A. Brassinosteroids. Natural Product Reports. 1997;14(1):1-10.

Yao Y, Sang W, Zhou M, Ren G. Phenolic composition and antioxidant activities of 11 celery cultivars. Journal of Food Science. 2010;75(1):9-13.

Simaratanamongkol A, Umkhera H, Noguchi H, Panichayaparakaran P. Identification of a new angiotensin-converting enzyme (ACE) inhibitor from Thai edible plants. Food Chemistry. 2014;165:92-7.

Zulorn C, Joher K, Ganzae M, Schubert B, Sigmund EM, Mader J, Greil R, Ellmerer EP, Stuppner H. Polycyclelenses from the Apiceae Vegetables Carrot, Celery, Fennel, Parsley and Parsnip and Their Cytotoxic Activities. Journal of Agricultural and Food Chemistry. 2005;53(7):2518-23.

Hussain MT, Ahmed G, Jahan N, Adiba M. Unani description of Tukhme Karaf (Seeds of Apium graveolens Linn) and its Scientific reports. International Research Journal of Biological Sciences. 2013;2(11):88-93.

Wilson CW. Relative recovery and identification of carbonyl compounds from celery essential oil. Journal of Food Science. 1970;35(6):766-8.

Baanaou S, Boufira I, Mahmoud A, Boukell K, Marougui B, Boughattas NA. Antiulcerogenic and antibacterial activities of Apium graveolens essential oil and extract. Natural Product Research. 2013;27(12):1075-83.

Mansi K, Abushoffa AM, Disi A, Abujarba T. Hypolipidemic effects of seed extract of celery (Apium graveolens) in rats. Pharmacognosy Magazine. 2009;5(20):301-5.

Moghadam MH, Imenshahidi M, Mohajeri SA. Anti hypertensive effect of celery seed on rat blood pressure in chronic administration. Journal of Medicinal Food. 2013;16(6):558-63.

butylohexahydrophthalide stereoisomers in celery, celeriac and fennel. Journal of Agricultural and Food Chemistry. 1997;45(12):4554-7.

Kurobayashi Y, Kouno E, Fujita A, Morimitsu Y, Kubota K. Potent Odorants Characterize the aroma quality of leaves and stalks in raw and boiled Celery. Bioscience, Biotechnology and Biochemistry. 2006;70(4):958-65.

Gold H, Wilson CW. Alkylidene phthalides and dihydrophthalides from Celery. The Journal of Organic Chemistry. 1963;28(4):985-7.