

## Nutritional and therapeutic importance of *Daucus carota*- A review

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**Abstract:-** Phytochemical analysis showed that the root of *Daucus carota* contained alkaloids, carbohydrates, chlorogenic acid, flavonoids, phenols, essential oil, terpenoid and coumarin. The nutritional analysis of carrot juice showed that the juice contained: protein  $1.067 \pm 0.058\%$ , crude fat  $0.367 \pm 0.089\%$ , crude fibre  $1.167 \pm 0.153\%$ , carbohydrates  $6.100 \pm 0.346\%$ , many vitamins and minerals. The pharmacological studies revealed that the plant possessed cytotoxic, antioxidant, antidiabetic, antimicrobial, smooth muscle relaxant, hypotensive effect and decrease intraocular pressure, gastro-protective, nephro-protective, hepato-protective, cardio-protective antidepressant memory enhancement, anti-inflammatory, reproductive, wound healing and hear induction and many other effects. The current review highlights the chemical constituents, nutritional and pharmacological effects of *Daucus carota*.

**Keywords:** constituents, nutritional, therapeutic, pharmacology *Daucus carota*.

### I. INTRODUCTION:

The World Health Organization (WHO) estimates that 80 percent of the world population, presently use herbal medicine for some aspect of primary health care [1]. Plant showed nutritional and therapeutic benefits including antimicrobial, antioxidant, anticancer, hypolipidemic, cardiovascular, central nervous, respiratory, immunological, anti-inflammatory, analgesic antipyretic and many other pharmacological effects [2-60]. Phytochemical analysis showed that the root of *Daucus carota* contained alkaloids, carbohydrates, chlorogenic acid, flavonoids, phenols, essential oil, terpenoid and coumarin. The nutritional analysis of carrot juice showed that the juice contained: protein  $1.067 \pm 0.058\%$ , crude fat  $0.367 \pm 0.089\%$ , crude fibre  $1.167 \pm 0.153\%$ , carbohydrates  $6.100 \pm 0.346\%$ , many vitamins and minerals. The pharmacological studies revealed that the plant possessed cytotoxic, antioxidant, antidiabetic, antimicrobial, smooth muscle relaxant, hypotensive effect and decrease intraocular pressure, gastro-protective, nephro-protective, hepato-protective, cardio-protective antidepressant memory enhancement, anti-inflammatory, reproductive, wound healing and hear induction and many other effects. The current review will highlight the chemical constituents, nutritional and pharmacological effects of *Daucus carota*.

### II. SYNONYMS:

*Carota sylvestris* (Mill.) Rupr., *Caucalis carnosa* Roth, *Caucalis carota* (L.) Crantz, *Caucalis daucus* Crantz, *Caucalis glabra* Forssk., *Daucus allionii* Link., *Daucus australis* Kotov, *Daucus blanchei* Reut., *Daucus carota* var. *brachycaulos* Reduron, *Daucus carota* f. *epurpuratus* Farw., *Daucus carota* f. *fischeri* Moldenke, *Daucus carota* f. *goodmanii* Moldenke, *Daucus carota* subsp. *hispidus* Masclef, *Daucus carota* var. *pseudocarota* (Rouy & E.G. Camus) Reduron, *Daucus carota* f. *roseus* Millsp., *Daucus carota* f. *roseus* Farw., *Daucus communis* Rouy & E. G. Camus, *Daucus communis* var. *pseudocarota* Rouy & E. G. Camus, *Daucus esculentus* Salisb., *Daucus exiguus* Steud., *Daucus gingidium* Georgi, *Daucus glaber* Opiz ex Celak., *Daucus heterophyllus* Raf., *Daucus kotovii* M. Hiroe, *Daucus levis* Raf., *Daucus marcidus* Timb.-Lagr., *Daucus maritimus* With., *Daucus montanus* Schmidt ex Nyman, *Daucus neglectus* Lowe, *Daucus officinalis* Gueldenst. ex Ledeb., *Daucus polygamus* Jacq. ex Nyman, *Daucus scariosus* Raf., *Daucus sciadophyllus* Raf., *Daucus strigosus* Raf., *Daucus sylvestris* Mill., *Daucus vulgaris* Neck., *Tiricta daucoides* Raf [61-62].

### III. TAXONOMIC CLASSIFICATION:

**Kingdom:** Plantae; **Division:** Magnoliophyta; **Class:** Equisetopsida, **Subclass:** Magnoliidae; **Superorder:** Asterales, **Order:** Apiales, **Family:** Apiaceae, **Genus:** *Daucus*, **Species:** *Daucus carota* [61-63].

### IV. COMMON NAMES:

**Arabic:** gazar; **Chinese:** hu luo bo; **English:** carrot; **French :** carotte; **German:** Karotte, Möhre, Mohrrübe; **India:** gajar; **Italian:** carota; **Japanese:** ninjin; **Korean:** danggeun, hongdangmu; **Portuguese:** cenoura; **Spanish:** zanahoria [62].

### Distribution:

Carrot is the one of the major vegetable crops cultivated worldwide. The domesticated types are divided into two groups: the Eastern or Asian carrots (var. *atrorubens*), with mainly purple and yellow roots; and the Western carrots (var. *sativus*) with mainly orange roots. Carrots were thought to be domesticated in Afghanistan as the primary centre of diversity and they were spread over Europe, Asia and the Mediterranean area, and the origin of western cultivated carrots were thought to be in the Asia Minor Centre, primarily Turkey [63]. It is now distributed in **Africa** (Algeria, Libya, Morocco, Tunisia); **Asia** ( Russian Federation, Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan, Afghanistan, Pakistan, Iran, Iraq, Palestine, Jordan, Lebanon, Syria, Turkey); **Europe** (Belarus, Estonia, Lithuania, Moldova, Russian Federation-European part, Ukraine, Austria, Belgium, Czech Republic, Germany, Hungary, Liechtenstein, Luxembourg, Netherlands, Poland, Slovakia, Switzerland, Denmark, Ireland, Norway, Sweden, United Kingdom, Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Greece, Italy, Macedonia, Montenegro, Romania, Serbia, Slovenia, France, Portugal, Spain) [62].

### Description:

The stems are erect and branched, generally about 2, feet high, tough and furrowed. Both stems and leaves are more or less clothed with stout, coarse hairs. The leaves are very finely divided, the lowest leaves considerably larger than the upper; their arrangement on the stem is alternate, and all the leaves embrace the stem with the sheathing base. The blossoms are densely clustered together in terminal umbels, or flattened heads, in which the flower-bearing stalks of the head all arise from one point in rays, each ray dividing to form a secondary umbel, or umbellule of white flowers, the outer ones of which are irregular and larger than the others. The flowers themselves are very small, but from their whiteness and number, they form a conspicuous head, nearly flat while in bloom, or slightly convex, as the seeds ripen, the umbels contract, the outer rays, which are to begin with 1 to 2 inches long, lengthening and curving inwards, so that the head forms a hollow cup hence one of the old popular names for the plant (Bird's Nest). The fruit is slightly flattened, with numerous bristles arranged in five rows. The ring of finely-divided and leaf-like bracts at the point where the umbel springs is a noticeable feature [64].

### Traditional uses:

*Daucus carota* was cultivated for the enlarged fleshy taproot, eaten as a raw vegetable or cooked in many dishes. Eaten sliced, diced, cut up, or shoe-stringed, carrots were used in many mixed vegetable combinations. They were sold in bunches, or canned, frozen, or dehydrated. They may be baked, sauteed, pickled, and glazed, or served in combination with meats, in stews, roasts, soups, meat loaf or curries. Roasted carrot was used as coffee substitutes. Essential oil was used to flavor liqueurs and perfumes. Seeds were aromatic, carminative, diuretic, emmenagogue, stimulant, and were used for dropsy, chronic dysentery, kidney ailments, worms, as aphrodisiac, nervine tonic, and for uterine pain. Roots were refrigerant and used in infusion for threadworm, as diuretic and eliminating uric acid [65-67]. The ethnobotanical uses of this species also included applications in the treatment of cough, diarrhea, dysentery, cancer, malaria, tumors, as an antiseptic, abortifacient, aphrodisiac, carminative, stimulant, stomachic and tonic [68]. *Daucus carota* was used by the Ancient Egyptians as a stimulant, carminative, diuretic, anthelmintic and as a decoction for infantile diarrhea [69].

**Parts used:** Roots, leaves and seeds [70].

### Physicochemical characteristics:

The physicochemical investigation of carrot seed oil revealed: relative density ( $d^{20}_{20}$ ):  $0.9811 \pm 0.0013$ , refractive index ( $n^{20}_D$ ):  $1.473 \pm 0.004$ , acidity (oleic,%):  $5.60 \pm 1.13$ , peroxide value (meq/kg):  $16.0 \pm 2.1$ , saponification number  $143.6 \pm 12.7$ , unsaponifiable matter: (g/kg)  $9.3 \pm 1.2$  [71]. The physical and chemical properties of carrot seed (dry matter basis) showed that: moisture %:  $6.41 \pm 0.87$ , crude protein %:  $25.19 \pm 1.13$ , crude oil %:  $7.89 \pm 0.68$ , crude fibre %:  $31.99 \pm 2.21$ , ash %:  $11.52 \pm 0.14$ , Total carbohydrate: %:  $52.3 \pm 2.13$ , HCl insoluble ash %:  $0.0056 \pm 0.0012$ , weight of 1000 seeds/ g:  $2.68 \pm 0.18$ , and essential oil yield %:  $1.01 \pm 0.02$  [72].

### Chemical constituents:

The nutritional analysis of carrot juice showed that the juice contained: moisture  $91.100\% \pm 0.265$ , protein  $1.067 \pm 0.058\%$ , ether extracts (crude fat)  $0.367 \pm 0.089\%$ , ash  $1.333 \pm 0.153\%$ , crude fibre  $1.167 \pm 0.153\%$ , carbohydrates  $6.100 \pm 0.346\%$ , specific gravity  $1.069 \pm 0.003$ , pH  $6.233 \pm 0.058$ , ascorbic acid (mg/100g)  $16.667 \pm 1.332$ ,  $Ca^{++}$  (mg/100g)  $55.000 \pm 0.000$ ,  $Fe^{++}$  (mg/100g)  $1.667 \pm 0.153$ ,  $PO_4$  (mg/100g)  $44.333 \pm 1.155$ , thiamine (mg/100g)  $0.057 \pm 0.006$ , niacin (mg/100mg)  $0.300 \pm 0.000$ , riboflavin  $0.100 \pm 0.000$  (mg/100g),  $\beta$ -carotene  $2730 \pm 43.589$ , colour (out of 10)  $2.000 \pm 0.000$  and vitamin A  $2805 \pm 6.532$ . The mineral analysis of carrot seed cultivated in Turkey showed that it contained (dry matter basis) (mg/kg): Al:  $23.31 \pm 2.17$ , B:  $0.306 \pm 0.073$ , Ca:  $164.11 \pm 31.02$ , Cr:  $0.086 \pm 0.011$ , Cu:  $0.06 \pm 0.01$ , Fe:  $8.21 \pm 0.93$ , K:  $180.55 \pm 37.36$ , Mg:  $15.48 \pm 1.61$ , Mn:  $0.403 \pm 0.083$ , Na:  $24.35 \pm 4.39$ , Ni:  $0.059 \pm 0.008$ , P:  $75.40 \pm 19.28$ , Se:  $0.005 \pm 0.001$ , V:  $0.184 \pm 0.038$  and Zn:  $0.281 \pm 0.061$  [71-73]. Phytochemical analysis of ethanol extract of *Daucus carota* roots

extracts showed that it contained alkaloids, carbohydrates, chlorogenic acid, flavonoids, phenols, terpenoid and coumarin [74]. Flavonols (quercetin, kaempferol, rutin or quercetin 3-rutinoside) and flavones (apigenin, luteolin and chrysin) were identified from different parts of carrot [75-77]. Furanocoumarin, 8-Methoxypsoralen and 5-methoxypsoralen (0.01-0.02 pg/g fresh weight) were isolated from the fresh plant. Their concentrations were increased in the diseased plant [78]. *Daucus carota* essential oil yields 3% for seeds and 2.1% for leaves. A total of 48 compounds were identified in *Daucus carota* essential oil of leaves, 46 in seeds essential oil. The essential oil from seeds was predominantly composed of oxygenated monoterpenes (66.08 %) and oxygenated sesquiterpenes (16.41%). The main components were geranyl acetate (52.45%), cedrene S (14.04%), and asarone (11.39%). The oil from leaves is mainly composed of hydrocarbon monoterpenes (64.59%) and hydrocarbon sesquiterpenes (22.18%),  $\alpha$ -pinene (27.44%), sabinene (25.34%), germacrene D (16.33%) [79]. Mojaba *et al.*, mentioned that the leaves of carrot (*Daucus carota* L. subsp. sativus (Hoffman.) Arcang. from Iran gave 0.2 % (v/w) essential oil. Ninety-one compounds were identified in the essential oil. The main class of the compounds was monoterpenes (30.0 %), sesquiterpenes (27.8 %) and phenyl propanes (26.4 %). The major constituents were trans-anethole (23.5 %) and myrcene (14.5 %) [80]. The changes occurring in the essential oil yield and chemical composition of *Daucus carota* L. subsp. sativus (Hoffm.) Arcang. during flowering and fruiting process were studied. The essential oil yield varied from 0.7% to 1.8% (v/w) during umbel ontogeny. The resulted essential oils contained 34 constituents, forming 94.5–97.9% of the total compositions. The essential oil composition was characterized by high proportions of monoterpenoids (35.9–81.3%) and sesquiterpenoids (15.1–62.0%). Major constituents of the essential oils were carotol (10.2–58.5%),  $\alpha$ -pinene (21.2–41.2%), myrcene (6.4–14.1%), limonene (4.4–12.7%), and sabinene (0.2–5.3%). The results obtained were of significance for determining the most favorable time for harvesting carrot umbels for better yield of quality essential oil [81]. The analysis of the essential oil of carrot cultivated in Turkey seed and edible seed oil showed that they contained 34 and 14 components, respectively. The major constituents of seed essential oil were carotol (66.78%), daucene (8.74%), (Z,Z)- $\alpha$ -farnesene (5.86%), germacrene D (2.34%), trans- $\alpha$ -bergamotene (2.41%),  $\beta$ -selinene (2.20%),  $\beta$ -bisabolene (1.90%), bicyclogermacrene (1.87%) and  $\beta$ -caryophyllene (1.10%) [72].

In studying the essential oils of the fruits of *Daucus carota* ssp. *maximus*, it revealed the presence of at least 19 components. The fruit essential oil consisted chiefly of phenylpropanoids (56.84%) and sesquiterpene hydrocarbons (40.79%), accompanied by relatively much smaller amounts of monoterpenes (1.33%) and oxygenated sesquiterpenes (1.04%). The leaf and stem oils revealed the presence of at least 40 (leaves) and 21 (stems) components. The leaf essential oil consisted chiefly of oxygenated sesquiterpenes and sesquiterpene hydrocarbons 51.20% and 25.25% of the oil composition respectively, as well as relatively smaller amounts of monoterpene hydrocarbons (6.31%), n-alkanes (4.55%), monoterpene alcohols (4.19%) and a straight chain aldehyde (3.22%). The stem oil was dominated by oxygenated sesquiterpenes (80.05%) accompanied by relatively small amounts of monoterpenes (10.07%) and sesquiterpene hydrocarbons (6.91%) [82].

The fatty acid composition of carrot seed oil cultivated in Turkey showed that it contained (mg/100g): palmitic:  $10.01 \pm 0.13$ , palmitoleic:  $0.64 \pm 0.02$ , stearic:  $2.41 \pm 0.06$ , oleic:  $0.17 \pm 0.01$ , linoleic:  $11.82 \pm 1.17$ , petroselinic:  $59.35 \pm 3.81$ , vaccenic:  $0.55 \pm 0.01$  and arachidic:  $0.81 \pm 0.03$  [72]. The essential oils of *Daucus carota* seeds from ten wild populations spread over northern Tunisia were characterized by a predominance of sesquiterpene hydrocarbons in most samples (22.63-89.93% of the total oil composition). The main volatile compounds identified were  $\beta$ -bisabolene (mean content of 39.33%), sabinene (8.53%), geranyl acetate (7.12%), and elemicin (6.26%). The volatile composition varied significantly across the populations, even for oils of populations harvested in similar areas [83]. The essential oil of the flowering and mature umbels with seeds of wild *Daucus carota* L. subsp. *carota* from two different sites in Tunisia, contained: eudesm-7(11)-en-4-ol (8.2 - 8.5%), carotol (3.5 - 5.2%), sabinene (12.0 - 14.5%),  $\alpha$ -selinene (7.4 - 8.6) and 11- $\alpha$ -(H)-himachal-4-en-1- $\beta$ -ol (12.7 - 17.4%), whereas the oils from Tunis were predominantly composed of elemicin (31.5 - 35.3%) and carotol (48.0 - 55.7%) as the main components [84]. The essential oil of *Daucus carota* subsp. *carota* from Portugal, composed of hydrocarbon monoterpenes (46.6%) and oxygenated monoterpenes (29.5%), with geranyl acetate (29.0%),  $\alpha$ -pinene (27.2%) and 11 $\alpha$ H-himachal-4-en-1 $\beta$ -ol (9.2%), being the main components [85]. The chemical composition of the essential oils from the fruits of *Daucus carota* var. *sativus* (yellow carrot) and var. *boissieri* (red carrot) was determined using GC/FID and GC/MS. 29 and 32 compounds were identified accounting for 96.58 and 96.72 % of the total detected components in the hydrodistilled yellow and red carrot oils, respectively. Yellow carrot fruit essential oil had a lower percentage of monoterpenes representing 2.24% and containing mainly  $\beta$ -pinene (0.52%) and  $\alpha$ -limonene (0.43%) and oxygenated monoterpenes represented 0.66% containing mainly linalool (0.34%). Red carrot fruit essential oil had higher percentage of monoterpenes representing 3.92% and containing mainly  $\beta$ -pinene (1.04%) and p-cymene (1.01%) and didn't contain any oxygenated monoterpenes. On the other hand, sesquiterpenes were presented in higher percentage in yellow carrot fruit essential oil, containing mainly carotol (66.7%),  $\beta$ -bisabolene (3.91%), trans- $\alpha$ -bergamotene (3.41%), germacrene (2.34%) and  $\alpha$ -curcumene (2.2%). Almost the same percentage and different pattern can be noticed for the red carrot fruit

essential oil [carotol (67.71%),  $\beta$ -bisabolene (7.66%), trans- $\beta$ -caryophyllene (4.79%) and trans- $\alpha$ -asarone (2.33%)]. Only n-nonanal as a non terpene compound was present in yellow carrot fruit essential oil (0.05%) [86]. Phytochemical investigation of the fruits of *Daucus carota* resulted in the isolation of a new sesquiterpene named as daucucarotol. It was the first example for a natural eudesmane sesquiterpene with a hydroxymethyl group located at a methine carbon rather than a usual quaternary carbon in the two fused six-membered ring systems [87]. Daucane-type sesquiterpenes such as trans-dauc-8-ene-4b-ol, trans-dauca-8,11-diene, dauca-5,8-diene, acora-4,9-diene, acora-4,10-diene, carotol, daucol and daucucarotol were isolated from *Daucus carota* [78, 87-89]. Ahmed *et al.*, isolated four sesquiterpenes daucane esters, one polyacetylene, one sesquiterpene coumarin, and sitosterol glucoside from the roots of the wild *Daucus carota* ssp *carota* [90]. Extracts of fresh roots and foliage of the garden carrot (*Daucus carota*) were analyzed for linear furocoumarins (psoralens) compared with standard psoralen, xanthotoxin, bergapten, isopimpinellin, heracleolin, and oxypeucedanin. Results showed that garden carrot (*Daucus carota*) does not contain these photosensitizing, photomutagenic, and photocarcinogenic chemicals or, if present, they occur at very low levels (0.5 ppm) [91-92]. Carotenoids were responsible for the yellow, orange, and red colors of carrots, while anthocyanins, a class of polyphenolic compounds, were responsible for the color of purple carrots. The main anthocyanins detected in two different black carrots (*Daucus carota* L. ssp. *sativus* var. *atrorubens* Alef L. ssp. *sativus* var. *atrorubens* Alef.) cultivars, associated with Antonina and Purple Haze varieties, from Cuevas Bajas (Málaga, Spain), were found to correspond to five cyanidin-based anthocyanins: cyanidin 3-xylosylglucosylgalactoside, cyanidin 3-xylosylgalactoside and the sinapic, ferulic and coumaric acids derivative of cyanidin 3-xylosylglucosylgalactoside. The anthocyanins present in the black carrots were essentially acylated and their levels were found to correspond to 25 and 50% of the total phenolic content for the purple Haze and Antonina varieties, respectively [93]. However, black carrot contained anthocyanin, the content of monomeric anthocyanins, values ranged between 1.5 and 17.7 mg/100 g fresh weight, the major anthocyanins isolated from black carrot (*Daucus carota* ssp. *sativus* var. *atrorubens* Alef.) was Cyanidin 3-xylosyl(glucosyl)galactosides acylated, with sinapic acid, ferulic acid, and coumaric acid. Cyanidin 3-xylosyl (sinapoyl glucosyl) galactoside was found to exhibit a lower visual detection threshold and a higher pH stability than cyanidin 3-xylosyl (feruloyl glucosyl) galactoside and cyanidin 3-xylosyl (coumaroyl glucosyl) galactoside [94]. Carrot roots were rich in carotenoids. Six carotenes ( $\alpha$ -,  $\beta$ -,  $\gamma$ -, and  $\zeta$ -carotenes,  $\beta$ -zeaxanthin, and lycopene) were separated from typical and dark orange carrots.  $\alpha$ - and  $\beta$ -carotene represented the major carotenoids accounting for 13-40% and 45-80% of the carotenoids in orange carrots [95-96]. Total phenolics of carrot varieties varied among the cultivars and ranged from 17.9 to 97.9 mg gallic acid equivalents (GAE)/100 g fresh weight [94]. Twelve polyphenolic compounds were isolated from 70 and 40% ethanolic extracts of wild *Daucus carota* included myricetin, chlorogenic acid, luteolin, apigenin, rutin, catechin, ferulic acid, p-coumaric acid, 3-hydroxybenzoic acid, hydroxybenzaldehyde, caffeic acid and cinnamic acid. Rutin represented the major component in both extracts [97]. The total phenol contents of leaves extract of Algerian wild carrot *Daucus carota* was (13.83 mg GAE/g) and of the seeds extract was (7.08 mg GAE/g) [79]. Average content of total polyphenols (mg/kg) in many carrot varieties was  $81.25 \pm 13.11$ -  $113.69 \pm 11.57$  mg/kg,  $\beta$ -carotenes (mg/kg)  $24.58 \pm 2.38$ -  $124.28 \pm 3.54$  and the average values of antioxidant activity (% inhibition) in carrot  $6.88 \pm 0.92$ -  $9.83 \pm 0.62$  [98]. Carrot roots of orange, red, yellow, white and purple color were freeze-dried and analyzed for phenolic content by Folin-Ciocalteu assay and UV/Vis assay. Carrots developing purple roots possessed on average 9 times more phenolics than roots of other colors. Furthermore, they were rich in anthocyanins that caused very high antiradical activity. Red carrots showed higher antioxidant activity than orange, yellow and white carrots and in the season of lower rainfall they accumulated higher amounts of phenolic compounds. Carrots of Asian origin belonging to Eastern gene pool were more often purple or red and richer in phenolics and had higher antiradical activity than those from the Western gene pool with orange roots [99]. Three flavones included luteolin, luteolin 3'-O-beta-D-glucopyranoside and luteolin 4'-O-beta-D-glucopyranoside were isolated from the methanol extract of *Daucus carota* seeds [68].

### Pharmacological effects:

#### Cytotoxic effects:

The effect of *Daucus carota* fraction, pentane/diethyl ether (50:50), on was investigated in lung, skin, breast and glioblastoma cancer cell motility and invasion. A pronounced decrease in cancer cell motility was observed in the 4 cell lines. The treatment also led to a decrease in cancer cell invasion and an increased cell adhesion. Additionally, the *Daucus carota* fraction decreased the activation of the p-GTPases Rac and CDC42, a finding which may partially explain the decrease in cell motility [100]. The cytotoxic effect of *Daucus carota* oil extract (DCOE) was studied in acute myeloid leukemia (AML) cells. All the AML cell lines tested were sensitive to the extract while peripheral mononuclear cells were not. It appeared that it produced effect via increase in cells positive for annexinV and for active caspases, indicating that DCOE induced apoptotic cell death in AML. Inhibition of the MAPK pathway decreased sensitivity of AML cells to DCOE, indicating that cytotoxicity may be dependent on its activity. The authors concluded that, DCOE induced selective apoptosis in

AML cells, possibly through a MAPK-dependent mechanism [101]. The chemopreventive effects of oil extract from *Daucus carota* umbels was investigated on 7,12-dimethyl benz(a)anthracene (DMBA)-induced skin papilloma in mice. The extract was administered to animals via gavage (0.02 ml of 100% oil), intraperitoneal (0.3 ml of 2% oil), and topical (0.2 ml of 5, 50, and 100% oil) routes for 20 weeks. Tumor appearance, incidence, yield, and volume were compared with those of a non-treated control group. Topical 100% treatment delayed tumor appearance, and inhibited tumor incidence and yield by 40 and 89%, respectively. Topical 50% treatment inhibited tumor incidence and yield by 30 and 83%, respectively, whereas the 5% treatment inhibited tumor yield by 36%. Tumor volume was decreased by 99, 91, and 70% following topical treatments with 100, 50, and 5% oil, respectively. Intraperitoneal treatment inhibited tumor yield by 43%, and decreased tumor volume by 85%, whereas gavage treatment showed minimal effects. Both intraperitoneal and topical treatment decreased infiltration and hyperplasia with an increase in the level of hyperkeratosis [102].

The major flavonoids isolated from the methanol extract of *Daucus carota* seeds (luteolin, luteolin 3'-O-beta-D-glucopyranoside and luteolin 4'-O-beta-D-glucopyranoside) were tested for cytotoxicity towards brine shrimp. The LD<sub>50</sub> value of luteolin was  $5.3 \times 10^{-2}$  mg/ml, and that of its 3'-O-glucoside and 4'-O-glucoside were > 1.0 mg/ml [68]. Falcarinol from carrots at concentrations above 10  $\mu$ M decreased cell proliferation of CaCo-2 cells after 48 and 72 h [103]. The effects of five fractions from carrot juice extract (CJE) [three polyacetylenes (falcarinol, falcarindiol and falcarindiol-3-acetate) and two carotenoids (beta-carotene and lutein)] were studied in human lymphoid leukaemia cell lines. Treatment of all three lymphoid leukaemia cell lines with the fraction from carrot extracts contained polyacetylenes and carotenoids showed that they were significantly cytotoxic. Treatments with purified polyacetylenes also induced apoptosis in a dose and time responsive manner. Falcarinol and falcarindiol-3-acetate isolated from *Daucus carota* were more cytotoxic than falcarindiol. In contrast, the carotenoids showed no significant effect on either apoptosis or cell proliferation in all investigated cells [104]. The effect of falcarinol was studied in the development of azoxymethane induced colon preneoplastic lesions in male rats. Feeding of rats with freeze-dried carrots containing 35  $\mu$ g falcarinol per gram, or the same dose of falcarinol, delayed the development of tumours and aberrant crypt foci following 18 weeks [105].

The effect of carrot juice extracts was studied in myeloid and lymphoid leukemia cell lines together with normal hematopoietic stem cells. Leukemia cell lines and nontumor control cells were treated with carrot juice extracts for up to 72 hours *in vitro*. Induction of apoptosis was investigated by using annexin V/propidium iodide staining followed by flow cytometric analysis, the results were confirmed by using 4'-6-diamidino-2-phenylindole morphology. Effects on cellular proliferation were investigated via cell cycle analysis and cell counts. Treatment of leukemia cell lines with carrot juice extract induced apoptosis and caused cell cycle arrest. Lymphoid cell lines were affected to a greater extent than were myeloid cell lines, while, normal hematopoietic stem cells were less sensitive than cancer cell lines [106]. The anticancer effect of *Daucus carota* oil extract fractions was studied on the human breast adenocarcinoma cell lines MDA-MB-231 and MCF-7. By using of WST assay, the pentane fraction (F1) and 1:1 pentane:diethyl ether fraction (F2) possessed the highest cytotoxicity against both cell lines. Flow cytometric analysis revealed that both fractions induced the accumulation of cells in the sub-G1 phase and increased apoptotic cell death and chromatin condensation. The increase in apoptosis in response to treatment was also apparent in the increase in BAX and the decrease in Bcl-2 levels as well as the proteolytic cleavage of both caspase-3 and PARP as revealed by Western blot. Treatment of MDA-MB-231 cells with either fraction also significantly reduced the level of phosphorylated Erk but did not show any effect on phosphorylated Akt [107].

The anticancer activity of the pentane fraction (F1) and the 1:1 pentane:diethyl ether fraction (F2) of the *Daucus carota* oil extract was evaluated against human colon adenocarcinoma cell lines (HT-29 and Caco-2). Treatment of cells with various concentrations of F1 or F2 fractions produced a dose-dependent inhibition of cell proliferation. Flow cytometric analysis indicated that both fractions induced sub-G1 phase accumulation and increased apoptotic cell death. Western blot revealed the activation of caspase-3, PARP cleavage, and a considerable increase in Bax and p53 levels, and a decrease in Bcl-2 level. Treatment of HT-29 cells with either fraction markedly decreased the levels of both phosphorylated Erk and Akt [108]. The *in vitro* anticancer activity of *Daucus carota* oil extract was evaluated on cell lines using the trypan blue exclusion method and the WST-1 cell proliferation assay. The anticancer activity of the oil extract was evaluated against human colon (HT-29, Caco-2) and breast (MCF-7, MDA-MB-231) cancer cell lines. Oil extract caused significant increase in cell death and decrease in cell proliferation. The effects of the oil on cell lines were time and dose-dependent [109]. In cytotoxic investigation of the essential oils from the fruits of *Daucus carota* var. sativus (yellow carrot) and var. boissieri (red carrot), a highest cytotoxic activity was observed against HepG-2 cell with IC<sub>50</sub> values ranging from 163-172  $\mu$ g/ml for both oils [86].

#### **Antioxidant effect:**

The effects of a 3-week supplementation of the diet with carrot (15% dry matter) in antioxidant status was studied in rats. Carrot consumption improved the antioxidant status. It significantly decreased the urinary excretion of thiobarbituric acid reactive substances (TBARS), reduced the TBARS levels in heart, increased the vitamin E

plasmatic level and tended to increase the ferric reducing ability of plasma (FRAP) as compared to the controls. The carrot diet provided carotenoid antioxidants: 5.1 mg  $\beta$ -carotene, 1.6 mg  $\alpha$ -carotene and 0.25mg lutein per 100 g diet. The three carotenoids were detected in the plasma of the rats fed the carrot diet at 125, 41, 43 nmol/l concentrations respectively.  $\beta$ -Carotene was also detected in liver and heart [110]. Antioxidants and antioxidant capacity of seven colored carrots were studied. Antioxidant capacities of the hydrophilic and hydrophobic fractions were determined using 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and 2,2'-diphenyl-1-picrylhydrazyl (DPPH) methods. Five anthocyanins, chlorogenic acid, caffeic acid, and four carotenoids were quantified by HPLC. Anthocyanins were the major antioxidants in purple-yellow and purple-orange carrots, and chlorogenic acid was the major antioxidant in all carrots. Both the DPPH and ABTS assays showed that the hydrophilic extract had higher antioxidant capacity than the hydrophobic extract. Purple-yellow carrots had the highest antioxidant capacity, followed by purple-orange carrots, and the other carrots did not significantly differ [111]. The flavones isolated from the methanol extract of *Daucus carota* seeds (luteolin, luteolin 3'-O-beta-D-glucopyranoside and luteolin 4'-O-beta-D-glucopyranoside) were studied for antioxidant effects. Among these three flavones, luteolin showed the highest degree of free radical scavenging activity ( $RC_{50} = 4.3 \times 10^{-4}$  mg/ml) in the 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay [68]. Digested purple carrot extract exhibited intracellular ROS-inhibitory capacity, with 1mg/ml showing the ROS clearance of 18.4%. A 20.7% reduction in oxidative DNA damage due to colon mucosa cells' treatment with digested purple carrot extract was observed [112]. The *in vitro* antioxidant activity of *Daucus carota* oil extract (DCOE) was evaluated using 1,1-diphenyl-2-picryl hydrazyl free radical scavenging assay (DPPH), ferrous ion chelating assay (FIC) and the ferric reducing antioxidant power assay (FRAP). DCOE exhibited antioxidant activity in all assays. The FRAP value was  $164 \pm 5.5$   $\mu$ mol for  $FeSO_4$  /g, and the  $IC_{50}$  values for DPPH and FIC assays were  $2.1 \pm 0.03$  mg/ml and  $0.43 \pm 0.02$  mg/ml, respectively [109]. The antioxidant activity of the essential oils from the fruits of *Daucus carota* var. sativus (yellow carrot) and var. boissieri (red carrot) was investigated using DPPH. Both oils were able to reduce DPPH and to prevent the degradation of the deoxyribose sugar in a concentration dependent manner. Carrot oils showed promising scavenging activity of DPPH with an  $IC_{50}$  of 12.71 mg/ml and 14.15 mg/ml for the yellow and red carrot oils, respectively [86]. The antioxidant activity of wild *Daucus carota* extracts seed (70% and 40% ethanol) was investigated. The results indicated that the 70% ethanolic extract has a higher total phenol and flavonoid content than 40% ethanolic extract. The antioxidant activity of 70% ethanolic extract was  $86.88 \% \pm 3.018$ , whereas, the scavenging activity of 40% ethanolic extract was  $78.72\% \pm 3.276$  [97]. The n-Hexane, ethyl acetate, and methanol extracts of leaves of *Daucus carota* were examined for free radical scavenger activity using DPPH method. The compounds possessed antioxidant activity in the n-hexane extract was lutein. The compound at concentration of 0.616, 1.025, and 2.05 ppm had antioxidant activities of  $0.94 \pm 0.05$ ,  $18.53 \pm 0.15$  and  $49.07 \pm 0.86\%$ , respectively [113]. The antioxidant features of the black carrot extracts was appeared significantly higher than that of orange carrots, the recorded reducing capacity of two black carrots extracts was ( $86.4 \pm 8.0$  and  $182.0 \pm 27$   $\mu$ M TE/100 g fw) and the radical scavenging ability was ( $17.6 \pm 9.0$  and  $240.0 \pm 54.0$   $\mu$ M TE/100 g fw) [93]. High-carbohydrate, high-fat diet-fed rats developed hypertension, cardiac fibrosis, increased cardiac stiffness, endothelial dysfunction, impaired glucose tolerance, increased abdominal fat deposition, altered plasma lipid profile, liver fibrosis and increased plasma liver enzymes together with increased plasma markers of oxidative stress and inflammation as well as increased inflammatory cell infiltration. Purple carrot juice reversed all these parameters. Anthocyanins were responsible for the antioxidant and anti-inflammatory properties of purple carrot juice and improvement of glucose tolerance and maintaining cardiovascular and hepatic structure and function, while,  $\beta$ -carotene did not reduce oxidative stress, cardiac stiffness or hepatic fat deposition [114].

#### CNS effects:

The effects of ethanolic extract of *Daucus carota* seeds on cognitive functions, total serum cholesterol levels and brain cholinesterase activity were studied in mice. The ethanolic extract of *Daucus carota* seeds (DCE) was administered orally in three doses (100, 200, 400 mg/kg) for seven successive days to different groups of young and aged mice. Elevated plus maze and passive avoidance apparatus was used as exteroceptive behavioral models for testing memory. Diazepam-, scopolamine- and ageing-induced amnesia were used as interoceptive behavioral models. DCE (200, 400 mg/kg, po) showed significant improvement in memory scores of young and aged mice. The extent of memory improvement evoked by DCE was 23% at the dose of 200 mg/kg and 35% at the dose of 400 mg/kg in young mice using elevated plus maze. Significant improvements in memory scores were observed with the using passive avoidance apparatus and aged mice. DCE also reversed the amnesia induced by scopolamine (0.4 mg/kg, ip) and diazepam (1 mg/kg, ip). *Daucus carota* extract (200, 400 mg/kg, po) significantly reduced the brain acetylcholinesterase activity and cholesterol levels in young and aged mice. The extent of inhibition of brain cholinesterase activity evoked by DCE at the dose of 400 mg/kg was 22% in young and 19% in aged mice. There was a remarkable reduction in total cholesterol level as well, to the extent of 23% in young and 21% in aged animals with this dose of DCE [115]. The effects of *Daucus carota* seeds was evaluated in memory in rats. The ethanolic extract of *Daucus carota* (DCE) was administered orally in three doses (100, 200 and 400

mg/kg) for seven successive days to different groups of young and aged rats. Elevated plus-maze, Hebb-Williams maze and hexagonal swimming pool were used as exteroceptive behavioral models for testing memory. Diazepam-, scopolamine- and aging-induced amnesia were used as interoceptive behavioral models. DCE (200 and 400 mg/kg, po) induced significant improvement in memory of young and aged rats in elevated plus maze, Hebb Williams maze and hexagonal swimming pool. It also reversed the amnesia induced by scopolamine (0.4 mg/kg, ip) and diazepam (1mg/kg, ip). The results clearly indicated that *Daucus carota* seeds is a promising therapy to improve memory especially in management of Alzheimer patients [116]. The antidepressant potential of ethanol root extract of *Daucus carota* (DC) was studied in different animal models, forced swim test (FST), tail suspension test (TST), apomorphine induced hypothermia (AIH), reserpine induced hypothermia (RIH), 5-HTP potentiation of head twitches (HTPPH) in mice. Fluoxetine (25 mg/kg) was used as a standard drug in FST, TST and HTPPH models and desipramine (20 mg/kg) as a standard drug in AIH and RIH models. The antidepressant activity of DC (400 mg/kg) was comparable to that of standard drugs [117]. The seeds contained choline, and have been reported to inhibit brain cholinesterase activity, with a possibility to elevate the brain acetylcholine levels via increased synthesis of acetylcholine, which beneficial in cognitive dysfunctions [118-119].

#### Antimicrobial effects:

Four sesquiterpenes daucane esters, one polyacetylene, one sesquiterpene coumarin, and sitosterol glucoside isolated from the roots of the wild *Daucus carota* ssp *carota*, showed a range of low antibacterial activities against four Gram positive (*Staphylococcus aureus*, *Streptomyces scabies*, *Bacillus subtilis* and *Bacillus cereus*) and two Gram negative species (*Pseudomonas aeruginosa* and *Escherichia coli*) as well as antifungal against *Fusarium oxysporum* and *Aspergillus niger* [90]. The flavones isolated from the methanol extract of *Daucus carota* seeds (luteolin, luteolin 3'-O-beta-D-glucopyranoside and luteolin 4'-O-beta-D-glucopyranoside) were evaluated for antibacterial effects. Both luteolin and its 4'-O-glucoside demonstrated bactericidal activity against *Staphylococcus aureus* and *Escherichia coli*, MIC =  $5.0 \times 10^{-2}$  -  $1.0 \times 10^{-1}$  mg/ml). Luteolin also demonstrated antibactericidal activity against *Bacillus cereus* and *Citrobacter freundii* (MIC =  $5.0 \times 10^{-2}$  mg/ml). Luteolin 3'-O-glucoside showed bactericidal activity against *Bacillus cereus* and *Lactobacillus plantarum* (MIC =  $2.5 \times 10^{-1}$  mg/ml and  $5 \times 10^{-1}$  mg/ml, respectively) [68]. The antimicrobial activity of the essential oils of the flowering and mature umbels with seeds of wild *Daucus carota* L. subsp. *carota* from two different sites in Tunisia, were assayed by using the broth dilution method on *Escherichia coli* ATCC 35218 and *Staphylococcus aureus* ATCC 43300, and clinical strains of *Candida albicans* and *C. tropicalis* 1011 RM. The MIC values obtained were all > 2.5% (v/v) [84]. The *in vitro* antimicrobial activity of essential oils of *Daucus carota* seeds was evaluated, using the disk-diffusion method, against one Gram-positive (*Staphylococcus aureus*) and two Gram-negative bacteria (*Escherichia coli* and *Salmonella typhimurium*), and a pathogenic yeast (*Candida albicans*). All tested essential oils exhibited antibacterial and antifungal activities against the assayed microorganisms [83]. The antimicrobial activity of the essential oil of *Daucus carota* subsp *carota* from Portugal was evaluated against several Gram positive and Gram negative bacteria, yeasts, dermatophytes, and *Aspergillus* strains. The results showed a significant activity towards Gram positive bacteria (MIC = 0.32–0.64 µl/ml), *Cryptococcus neoformans* (0.16 µl/ml), and dermatophytes (0.32–0.64 µl/ml). The inhibition of the germ tube formation and the effect of the oil on *Candida albicans* biofilms were also unveiled. The oil inhibited more than 50% of filamentation at concentrations as low as 0.04 µl/ml (MIC/128) and decreased both biofilm mass and cell viability [85]. The antimicrobial effect of wild *Daucus carota* extracts seed (70% and 40% ethanol) were examined against Gram positive (*Staphylococcus aureus* ATCC 6538-P, *Staphylococcus hyicus* – isolated from the soil, *Micrococcus luteus* – isolated from soil, cryptogamic culture of *Bacillus subtilis* ATCC 6633), Gram negative (*Pseudomonas aeruginosa* ATCC 9027, *Escherichia coli* ATCC 8739 and *Salmonella Abony CIP- 8039*, and *Acinetobacter johnsonii* – isolated from the environment, *Moellerella wisconsensis* – isolated from the environment) and fungi (*Candida albicans* ATCC 10231, *Candida utilis* Lia-01, *Saccharomyces cerevisia* ATCC 9763 and *Aspergillus brasiliensis* ATCC 16404). The extracts were active against bacteria, the MIC against 2 Gram positive bacteria was 1.56-3.125 mg/ml and against 3 strains of Gram negative bacteria was 3.125-12.50 mg/ml, whereas against 1 strain of yeast was 3.125-6.25 mg/ml [97]. The essential oil of wild *Daucus carota* aerial parts at the end of the flowering stage (DCEO) inhibited the growth of *Campylobacter jejuni*, *Campylobacter coli*, and *Campylobacter lari* strains, including one multidrug resistant *Campylobacter jejuni*. The molecules responsible for the antibacterial activity were identified as (E)-methylisoeugenol and elemicin [120]. A strongest antifungal activity was observed for carotol, the main sesquiterpenic compound in the carrot seed oil, it inhibited the radial growth of *Alternaria alternata* by 65% [121].

#### Gastroprotective effect:

The therapeutic potential of 50% ethanol extract from *Daucus carota* roots (EDC) was studied as antisecretory, gastroprotective, and antacid capacity using experimental rats. Assessment of EDC antisecretory and *in vivo* antacid capacities was carried out using a pyloric ligation induced ulcer model. The gastroprotective

effect was assessed with an absolute ethanol induced ulcer model. The integrity of gastric mucosa was evaluated using the estimation of glutathione and gastric mucus level and with histopathological examination of gastric mucosal cells. The effect of the extract on the liver was assessed by measuring serum biochemical parameters. The EDC significantly ( $P < 0.01-0.001$ ) reduced gastric lesions in both models. It also significantly ( $P < 0.05-0.001$ ) reduced the volume of gastric content, the total acidity was significantly ( $P < 0.05-0.001$ ) reduced with the doses of 100 and 200 mg/kg EDC. The mucus content and glutathione level increased significantly ( $P < 0.05$ ) in the absolute alcohol-induced ulcer. The EDC also showed *in vitro* antacid capacity. Histopathological studies further confirmed the effects of EDC by inhibiting congestion, edema, hemorrhage, and necrosis in gastric mucosa [122]. The anti peptic ulcer effects of the aqueous and methanolic extracts of *Daucus carota* umbels was investigated against ethanol induced gastric ulcer in rats. Aqueous and methanolic extracts showed significant protection against ethanol induced gastric ulcer with a curative ratio of 46.8 and 68.7%, at a dose of 250 mg/kg body weight, respectively [123]. The gastroprotective potential of the fresh juice extract of the roots of *Daucus carota* (200 and 400 mg/kg bw, orally) was studied in gastric ulcerations experimentally induced by pylorus ligation, aspirin and ethanol induced. The *Daucus carota* extracts were significantly decreased free acidity, total acidity and ulcer index, while it increased the pH and the mucus content as compared with control. The *Daucus carota* extract at a dose of 400 mg/kg produced 60.45, 56.80 and 43.51 % ulceration inhibition when the gastric ulceration were induced by pylorus ligation, aspirin and ethanol, respectively [124]. The gastroprotective effect of 4.08 g carrot juice administered by feeding tube was studied on the hydrochloric acid concentration in the stomach in aspirin-induced Wistar-strain rats. The result of carrot juice consumption together with aspirin shows a statistically significant reduction in HCl concentration in the stomach ( $P < 0.05$ ). The result was also significant when compared with Misoprostol [125].

#### **Nephroprotective and hepatoprotective effects:**

The renoprotective activity of *Daucus carota* root extract was studied in renal ischemia reperfusion injury in rats. Renal pedicles of rats were occluded for 45 minutes followed by 24 hours reperfusion. Six days prior to induction of I/R, groups of rats received petroleum ether extract, fractional methanolic extract and methanolic extract of *Daucus carota* root (250 and 500 mg/kg, orally). Renal ischemia reperfusion caused significant impairment of kidney function. Six day administration of *Daucus carota*, minimized this effect. Rats with renal I/R showed significantly decreased activity of superoxide dismutase, catalase, and reduced glutathione compared with the sham operated rats. These declining trends were significantly less in the group treated with petroleum ether, fractional methanolic and direct methanolic extract of *Daucus carota* root compared with those in I/R group. Renal I/R also produced a significant increase in malondialdehyde level, while pretreatment with *Daucus carota* extracts was associated with a significantly lower malondialdehyde level. Accordingly, *Daucus carota* extracts exerted renoprotective activity probably by the free radical scavenging activity [126]. The protective and curative potential of *Daucus carota* root extract was also investigated in renal ischemia reperfusion injury in rats. In protective and curative studies, 14 days prior and 14 days after the induction of ischemia/reperfusion (I/R), rats received petroleum ether extract (PEE 250 and 500 mg/kg), fractional methanol extract (FME 250 and 500 mg/kg) and direct methanol extract (DME 250 and 500 mg/kg) of *Daucus carota* root, orally, once daily. PEE at a dose of 500 mg/kg significantly ( $P < 0.001$ ) reduced the levels of serum creatinine (0.853-3.090 mg/dl), uric acid (1.300-3.500 mg/dl) and urea (58.26-132.00 mg/dl) compared to disease control. FME at a dose of 500 mg/kg body weight significantly ( $P < 0.001$ ) reduced the levels of serum creatinine (0.960-3.090 mg/dl), uric acid (1.700-3.500 mg/dl) and urea (77.17-132.00 mg/dl) compared to disease control. DME at a dose of 500 mg/kg body weight significantly ( $P < 0.001$ ) reduced the levels of serum creatinine (1.173-3.090 mg/dl), uric acid (2.267-3.500 mg/dl) and urea (84.75-132.00 mg/dl) compared to disease control [127]. The nephroprotective effects of ethanolic root extract of *Daucus carota* (200 and 400 mg/kg, po) was studied against gentamicin-induced nephrotoxicity in albino Wistar rats. Nephrotoxicity was induced in rats by intraperitoneal administration of gentamicin (100 mg/kg/day) for 8 days. Gentamicin intoxication induced elevated serum urea, BUN, uric acid, and creatinine levels which was found to be significantly ( $P < 0.01$ ) decreased in a dose-dependent manner in groups received *Daucus carota*. The nephroprotective effects of *Daucus carota* were further confirmed by histological observations [128]. The hepatoprotective and antioxidant activity of methanolic extract of *Daucus carota* seeds was studied in experimental rats. Oxidative stress were induced in rats by thioacetamide 100 mg/kg sc, in four groups of rats (two test, standard and toxic control). Two test groups received *Daucus carota* seeds extract (DCSE) at doses of 200 and 400 mg/kg. Standard group received silymarin (25 mg/kg) and toxic control received only thioacetamide. On the 8<sup>th</sup> day animals were sacrificed and liver enzyme, serum glutamic pyruvic transaminase (SGPT), serum glutamic-oxaloacetic transaminase (SGOT) and alkaline phosphatase (ALP) were estimated in blood serum and antioxidant enzyme, superoxide dismutase (SOD), catalase (CAT), glutathione reductase (GRD), glutathione peroxidase (GPX), glutathione-S-transferase (GST) and lipid peroxidation (LPO) were estimated in liver homogenate. A significant decrease in SGPT, SGOT and ALP levels was observed in all drug treated groups as compared to thioacetamide group ( $P < 0.001$ ), furthermore, significant ( $P < 0.001$ ) increase in SOD, CAT, GRD,



GPX and GST was observed in all drug treated groups as compared with thioacetamide group. However, a significant ( $P < 0.001$ ) reduction in LPO was observed as compared to toxic control group [129]. The effect of carrot extract on  $\text{CCl}_4$ -induced acute liver damage was evaluated in mice. The extracts significantly lowered the serum levels of glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, lactate dehydrogenase, alkaline phosphatase, sorbitol and glutamate dehydrogenase elevated by  $\text{CCl}_4$ -induction. Extract also decreased the elevated serum bilirubin and urea. The increased activities of hepatic 5'-nucleotidase, acid phosphatase, acid ribonuclease and decreased levels of succinic dehydrogenase, glucose-6-phosphatase and cytochrome P-450 produced by  $\text{CCl}_4$  were reversed by the extract in a dose-responsive way [130].

The hepatoprotective effect of kaempferol (100 and 200 mg/kg bw) isolated from *Daucus carota* leaves was tested in paracetamol induced liver damage of albino rats. Paracetamol induced significant ( $P < 0.05$ ) increase in liver enzymes along with hepatic necrosis and visible disarrangements in hepatic tissues. Oral treatment with kaempferol reversed all the serum and liver parameters, dose-dependently [131].

#### **Cardiovascular effects:**

Ethanol extract of *Daucus carota* at the dose of 10–100 mg/kg caused a dose-dependent fall in systolic and diastolic arterial blood pressure in normotensive anesthetized rats. These effects were not blocked by atropine (1 mg/kg). Pretreatment with *Daucus carota* did not alter the pressor response to norepinephrine indicating that, cardiovascular effects of *Daucus carota* were independent of cholinergic or adrenergic receptors involvement. In spontaneously beating guinea-pig paired atria, *Daucus carota* induced a concentration-dependent decrease in force and rate of atrial contractions. In rabbit thoracic aorta, *Daucus carota* caused inhibition of  $\text{K}^+$ -induced contractions [132]. Fractionation of aerial parts of *Daucus carota* resulted in the isolation of two coumarin glycosides coded as DC-2 and DC-3. Intravenous administration (1-10mg/kg) of these compounds caused a dose-dependent fall in arterial blood pressure in normotensive anaesthetised rats, Both compounds caused dose-dependent (10-200 pg/ml) inhibitory effect on spontaneously beating guinea pig atria as well as on the  $\text{K}^+$ -induced contractions of rabbit aorta. The results indicated that DC-2 and DC-3 acting through blockade of calcium channels, the effect which may be responsible for the blood pressure lowering effect of the compounds observed in the *in vivo* studies [133]. Aqueous extract of *Daucus carota* tubers were investigated for inotropic and cardioprotective effects by measuring various biochemical parameters at the test doses of 250 and 500 mg/kg. Isoproterenol (5.25 mg/kg and 8.5 mg/kg) was administered subcutaneously on 29<sup>th</sup> and 30<sup>th</sup> day respectively in order to induce myocardial infarction. Cardiac tonicity was estimated by evaluating  $\text{Na}^+\text{K}^+$ -ATPase,  $\text{Mg}^{2+}$ -ATPase and  $\text{Ca}^{2+}$ -ATPase levels in heart. The levels of  $\text{Na}^+\text{K}^+$ -ATPase and  $\text{Mg}^{2+}$ -ATPase were decreased and that of  $\text{Ca}^{2+}$ -ATPase was increased in extract-treated group significantly ( $P < 0.001$ ). Cardioprotection was assessed by estimating serum aspartate transaminase, alanine transaminase, lipid peroxidase, and lactate dehydrogenase levels and cardiac total protein, lipid peroxidase, and lactate dehydrogenase. The levels altered by isoproterenol were restored significantly by the administration of the extract [134]. High-carbohydrate, high-fat diet-fed rats developed hypertension, cardiac fibrosis, increased cardiac stiffness, endothelial dysfunction, impaired glucose tolerance, increased abdominal fat deposition, altered plasma lipid profile, liver fibrosis and increased plasma liver enzymes together with increased plasma markers of oxidative stress and inflammation as well as increased inflammatory cell infiltration. Purple carrot juice reversed all these parameters [114]. The effects of a 3-week supplementation of the diet with carrot (15% dry matter) in lipid metabolism was studied in rats. A significant decrease of cholesterol level in liver (–44%;  $p = 0.0007$ ) was observed together with a reduction of the level of liver triglycerides (–40%;  $P = 0.0005$ ). Fecal total steroids excretion increased by 30% upon feeding the carrot diet as compared to the control. The secretion of bile acids was maintained, whereas the cholesterol apparent absorption was reduced in rats fed carrot diet [110].

#### **Antidiabetic effect:**

A dichloromethane (DCM) extract of carrot roots stimulated insulin-dependent glucose uptake (GU) in adipocytes in a dose dependent manner. Bioassay-guided fractionation of the DCM extract resulted in the isolation of the polyacetylenes faltarinol and faltarindiol. Both polyacetylenes were significantly stimulated basal and/or insulin-dependent GU in 3T3-L1 adipocytes and porcine myotube cell cultures in a dose-dependent manner. Faltarindiol increased peroxisome proliferator-activated receptor (PPAR) $\gamma$ -mediated transactivation significantly at concentrations of 3, 10 and 30  $\mu\text{M}$ , while PPAR $\gamma$ -mediated transactivation by faltarinol was only observed at 10  $\mu\text{M}$ . Faltarindiol was linked to the ligand binding domain of PPAR $\gamma$  with higher affinity than faltarinol, both polyacetylenes exhibited characteristics of PPAR $\gamma$  partial agonists. Faltarinol was shown to inhibit adipocyte differentiation as evident by gene expression studies and Oil Red O staining, whereas faltarindiol did not inhibit adipocyte differentiation, which indicated that these polyacetylenes showed different modes of action [135].

The effect of the methanol extract of *Daucus carota* (wild carrot) seeds (100, 200 and 300 mg/kg bw orally for 6 days), was studied on the serum levels of lipids and biochemical indices of kidney and liver function in streptozocin-induced diabetic (type 1) rats. Administration of *Daucus carota* seeds extract in diabetic rats for six

days, at all doses, significantly decreased serum levels of total cholesterol, triglycerides and creatinine. Furthermore, oral administration of extract (200 and 300 mg/kg) significantly decreased serum levels of Low density lipoprotein cholesterol, aspartate amino transferase and urea. Also, extract (300 mg/kg) decreased serum level of alanine aminotransferase ( $P < 0.05$ ) [136].

#### **Antiinflammatory effects:**

The anti-inflammatory effects of the aqueous and methanolic extracts of *Daucus carota* umbels was studied in acute and chronic inflammation in rats. In acute inflammation, the aqueous and methanolic extracts produced maximum anti-inflammatory activity at doses of 400 and 140 mg/kg body weight with 90.9 and 58.6 % inhibition, respectively. In chronic inflammation, the same doses showed maximum anti-inflammatory activity with 58 and 44.1 % inhibition, respectively [123]. The essential oil of *Daucus carota* subsp *carota* from Portugal, exhibited some anti-inflammatory potential by decreasing nitric oxide production around 20% in LPS-stimulated macrophages, without decreasing macrophages viability [85]. The ethanolic extract of *Daucus carota* seeds was investigated for anti-inflammatory and analgesic activity at the doses of 100, 200 and 400 mg/kg bw, orally. Carrageenan-, histamine- and serotonin-induced paw edema were used to study the effect of extract in acute inflammatory model, while, formaldehyde-induced arthritis was employed as a chronic model in rats. The acetic acid-induced writhing response and formalin-induced paw licking time in the early and late phases of mice were used to assess analgesic activity. The higher doses of the extract (200 and 400 mg/kg, po) inhibiting carrageenan, histamine and serotonin-induced paw edema as well as formaldehyde-induced arthritis successfully. The extract (200 and 400 mg/kg, po) also significantly attenuated the writhing responses induced by an intraperitoneal injection of acetic acid and late phase of pain response induced by a subplantar injection of formalin in mice [137]. *Daucus carota* seed extracts were investigated as Cyclooxygenase (COX) enzymes inhibitor. Compounds, 2,4,5-trimethoxybenzaldehyde, oleic acid, trans-asarone and geraniol were isolated from seed extract. They showed 3.32, 45.32, 46.15, and 3.15% of prostaglandin H endoperoxide synthase-I (COX-I) inhibitory activity and 52.69, 68.41, 64.39 and 0% prostaglandin H endoperoxide synthase-II (COX-II) inhibitory activity, respectively at 100 mg/ml. Compound 2,4,5-trimethoxy benzaldehyde showed selectivity towards COX-II enzyme inhibition at 100 µg/ml [138].

#### **Effects on reproductive systems:**

The petroleum ether extract and fraction 5 (fatty acids) of carrot seeds arrested the normal estrus cycle of adult mouse and reduced the weight of ovaries significantly. The cholesterol and ascorbic acid content in ovaries were significantly elevated by the extract and fraction 5 of carrot seeds. A significant inhibition of delta 5,3-beta-hydroxy steroid dehydrogenase and glucose-6-phosphate dehydrogenase (the two key enzymes involved in ovarian steroidogenesis) were also recorded in mouse ovaries after 15 days of treatment [139].

The petroleum ether, alcoholic, and aqueous extracts of *Daucus carota* were evaluated for their possible antiovarulatory activity in rabbits with copper-induced ovulation. All extracts inhibited ovulation in 40%, or less, of the animals [140]. The influence of carrot seed extract (CSE) on spermatogenesis, number and motility of sperms in cauda epididymis was studied in male rats. Administration of CSE caused a significant increase in cauda epididymis sperm reserve compared with the control ( $28.2 \pm 1.8 \times 10^6$  vs.  $45.1 \pm 2.0, \times 10^6$ ). The extract also protected testis from the gentamicin-induced necrosis. The CSE administration caused about 3.5-times increase in the LH levels even in spite of receiving 5 mg/kg/day gentamicin with no significant effect on FSH levels. The testosterone concentrations in the group received 400 mg/kg CSE were 30% and 83% higher than its levels in the control and gentamicin treated group, respectively. Accordingly, CSE can overcome reproductive toxicity of gentamicin and induces spermatogenesis probably through the elevation of testosterone levels [141].

The alcoholic extract of *Daucus carota* seed was administered at different doses ranging from 50 to 250 mg/kg bw after coitus showed a significant dose dependent antifertility effect. The administration of the extract at a lower dose showed anti-implantational activity, whereas higher doses caused fetal resorption. The main effect of the extract appeared to be an abortifacient activity. At higher dose levels, the extract demonstrated an estrogenic nature with a prolonged estrous phase, whereas lower doses showed an antiestrogenic nature and an increase in the percentage duration of the diestrous phase of the estrous cycle. The extract produced neither progestational nor antiprogesterational effects [142].

#### **Wound healing effect:**

The soft paraffin based cream containing 1%, 2% and 4% w/w of ethanolic extract of *Daucus carota* (EEDC) root was formulated and evaluated in wound healing activity on excision and incision wound models. Animals treated with topical EEDC cream formulation (1%, 2% and 4% w/w) showed significance decrease in wound area, epithelization period and scar width whereas, the rate of wound contraction was significantly increased ( $P < 0.01$ ,  $P < 0.001$  and  $P < 0.001$  respectively) as compared to control group animals in excision wound model. In incision wound model there was significant increase ( $P < 0.01$  and  $P < 0.001$ ) in tensile strength,

hydroxyproline and protein content of animals treated with topical EEDC cream formulation (2% and 4% w/w, respectively). Ethanolic extract of *Daucus carota* root cream when applied topically did not show any sign and symptoms of skin irritation [143].

#### **Effect on smooth muscles:**

A nitrogen containing tertiary base isolated from the seeds of *Daucus carota*, the base and its bromide have been studied on smooth muscles of ileum, uterus, blood vessels and trachea of different species of animals. The tertiary base possessed papaverine like nonspecific smooth muscle relaxant and spasmolytic activity, but its activity was found to be about one-tenth of that of papaverine [144].

#### **Effect on intraocular pressure:**

In normotensive rabbits, topical application of *Daucus carota* seed extract at the concentration of 0.3, 0.6 and 1.2% resulted in mean intraocular pressure (IOP) reduction of 19.33, 23.20 and 25.61% respectively. No significant difference was observed between the change in IOP in 0.6 and 1.2% extract treated groups, 0.6% concentration was chosen for further evaluation in rabbits with experimentally elevated IOP. In water loaded rabbits, maximum mean IOP reduction with 0.6% extract was 29.39%, which was comparable to pilocarpine [145].

#### **Hair induction effect:**

Animal studies were carried out by application of standardized *Daucus carota* extract in gel formulation to the shaved dorsal skin of albino rats, then histomorphometric analysis was employed to study induction of the hair follicle cycle. The effect of extract on the telogen to anagen transition, the protein expression levels of  $\beta$ -catenin in hair follicles were determined by immunohistochemistry. The results showed that petroleum ether *Daucus carota* extract promoted hair growth by inducing the anagen phase. The histomorphometric analysis data indicated that topical application of the extract in gel form induced an earlier anagen phase and prolonged the mature anagen phase, in contrast to control and 1% minoxidil treated group. Results also revealed an increase in both the numbers and size of hair follicles of the extract treated group. Moreover, the immunohistochemical analysis revealed earlier induction of  $\beta$ -catenin in hair follicles of the extract-treated group, compared to the control group [146].

## **V. CONCLUSION**

The current review discussed the chemical constituents, nutritional, pharmacological, and therapeutic effects of different parts of *Daucus carota* to be utilized in medical practice as a result of its safety and effectiveness.

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