Nativity, Phytochemistry, Ethnobotany and Pharmacology of *Dianthus caryophyllus*

Satish Chandra, D.S. Rawat, Dinesh Chandra and Jyotsna Rastogi

Department of Biological Sciences, College of Basic Science and Humanities, Govind Ballabh Pant University of Agriculture and Technology Pantnagar, Pantnagar, 263145, Uttarakhand, India

*Corresponding Author: Satish Chandra, Department of Biological Sciences, College of Basic Science and Humanities Govind Ballabh Pant University of Agriculture and Technology Pantnagar, Pantnagar, 263145, Uttarakhand, India*

**ABSTRACT**

*Dianthus caryophyllus* L. (carnation) is an important cut flower in trade. This plant traditionally used in China, Japan and Korea in the treatment of wounds and gastro-intestinal disorder and various other ailments. In recent pharmacological studies plant tested for anticancer, antiviral, antibacterial, antifungal and anti-insecticide activities. Kaempferide triglycoside a phenolic compound from plant exhibit anticancer properties against colon cancer cell lines and also show antifungal properties against *Fusarium* wilt causative pathogenic fungi. Plant extract possesses antibacterial properties against *Helicobacter pylori*, *Pseudomonas* spp. and *Bacillus* spp. The seeds extract of *D. caryophyllus* exhibit potent antiviral activity against HIV, herpes simplex virus-1 (HSV-1) and hepatitis A virus-27 (HAV-27). Essential oil extracted from flowers of carnation shows arthropods repellent and larvicidal activity.

**Key words:** Anticancer, antibacterial, Caryophyllaceae, *Dianthus*, traditional medicine

**INTRODUCTION**

*Dianthus* L. is annual or perennial herb belongs to Angiosperm’s family Caryophyllaceae, subfamily Caryophyllideae and tribe Caryophyllideae (Bittrich, 1993). Etymologically *Dianthus* is made up of two Greek words “Dis” (should be Dios), means the principal deity (Jupiter of the Romans) and “Anthos” means flower. The name of the genus was coined by Linnaeus because of the beautiful garden flower carnation (Shishkin, 1970). The genus *Dianthus* is famous for beautiful flowers and the most demanding in cut flower trade. The genus represented by about 320 species widespread in North temperate regions, mostly in Asia and Europe and especially in the Mediterranean region, few species occur in Africa and America (Ghazanfar, 1986; Rabeler *et al.*, 2005; Mabberley, 2008). *Dianthus* is famous for pink, red or both with white mosaic coloured flowers.

There are several reviews have been published providing information about different medicinal plants of family Caryophyllaceae and their biomedical properties. But all the published reviews (Sharma and Arora, 2012; Mamadalieva *et al.*, 2014; Nono *et al.*, 2014; Chandra and Rawat, 2015) did not focused on Phytochemistry, nativity and ethnobotanical aspects of *Dianthus caryophyllus*. Collective information about medicinal importance, biochemistry and pharmacological properties is lacking till date. The present review is aim to fill this knowledge gap.

**Nativity:** *Dianthus caryophyllus* L. is widely known as Carnation derived from Greek word “Carnis” which means fresh coloured. This species is famous flowering ornamental herb cultivated
in gardens throughout the world. This species is native of Mediterranean area and grows wild in Pyrenees Mountains of France and Spain (Cumio, 2013).

**Taxonomy:** Taxonomically *D. caryophyllus* belongs to genus *Dianthus* subgenus *Caryophyllum* Ser. and section *Leiopetali* Boiss (Shishkin, 1970). *Dianthus caryophyllus* is annual or perennial, 15-60 cm long, branched, glabrous herb. Leaves are linear lanceolate, apex acute, margin smooth or ciliate at base. Flowers are solitary or in clusters at tips of branches. Epicalyx scales are 4-6 in number, broad-ovate, abruptly mucronate at apex, herbaceous, appressed to calyx, covering one fifth to one quarter the length of calyx tube. Calyx tube is cylindrical, 20-30 mm long. Petals are 5, limb exerted, triangular obovate, toothed at apex, auricle absent, pink-red or white, sometimes spotted with darker centers, claw cuneate, glabrous. Stamens are 10 (5 epipetalous+5 alternipetalous). Ovary is ovoid- elongate, style-2. Seed are numerous, black, peltate, with facial hilum; embryo straight (Shishkin, 1970; Ghazanfar, 1986). The gametophytic chromosome number in *D. caryophyllus* is 15 and sporophytic chromosome number (2n) is 30 (Van Loon and Jong, 1978; Chen et al., 2003).

**Genome sequence:** The whole-genome of *Dianthus caryophyllus* L. cv. 'Francesco' was sequence by using combinations of different new-generation multiplex sequencing platforms. The total length of the non-redundant sequences was 568887315 bp, consisting of 45088 scaffolds, which covered 91% of the 622 Mb carnation genome as per estimated by k-mer analysis. A total of 13, 92, 143 and 1050 genes were identified for rRNAs, snoRNA, miRNA and tRNAs, respectively, in the assembled genomic sequences. For protein-encoding genes, 43266 complete and partial gene structures excluding those in transposable elements were deduced (Yagi et al., 2014).

**Phytochemistry:** Flower colour is controlled by mainly two pigment molecules, carotenoids and flavonoids. Carotenoids are terpenes derived from isoprene units, while flavonoids are phenolic compounds derived from amino acid phenylalanine. Carotenoids impart colours ranging from yellow to orange, while flavonoids produce blue, red, pink or violet colours. Anthocyanins are the most widespread group of pigmented flavonoids that stored in the vacuoles. Anthocyanins are glycosides that contain sugar in basic flavonoids skeleton. Without sugar anthocyanins are known as anthocyanidins. There are three main categories of anthocyanins that contribute to flower colour, delphinidins produce blue or purple colour, cyanidins produce red colour and pelargonidins that produce pink or brick red colour in the flower. Carnation lacks delphinidins and hence, does not produce blue coloured flower naturally (Zuker et al., 2002; Yagi et al., 2014). Flower colour and fragrance act as signal for pollinators. Fragrance present in flowers mainly due to fatty acid derivatives, terpenes and nitrogen containing compounds. Fragrance of *D. caryophyllus* is mainly due to presence of eugenol, β-caryophyllene and benzoic acid derivatives (Zuker et al., 2002). Same types of compounds are also present in scent of other *Dianthus* spp. flowers (Jurgens et al., 2003).

Saponins are steroid or triterpene glycosides, possess both lipid soluble (steroid or triterpene) and water soluble (sugar) element in one molecule. Such characteristics of saponins gives them detergent like properties and they form soapy lather when shaken with water (Vincken et al., 2007). Saponins are widely distributed in higher plants and classified on the basis of their aglycone or sapogenin skeleton into two groups. The first group consists of the steroidal saponins and second group consists of the triterpenoid saponins. The steroidal saponins are mainly found in monocotyledons while, triterpenoid saponins occur mainly in the dicotyledons (Sparg et al., 2004;
Man et al., 2010). Triterpene saponins are present in the family Caryophyllaceae (Bottger and Melzig, 2011). In *D. caryophyllus* quillaic acid (Fig. 1) acts as aglyconic component of saponins with one (monodesmosidic) or two (bisdemosidic) sugar chains (Gumnicka and Oleszek, 1998; Bottger and Melzig, 2011). The phytoecdysteroids mimics insect molting hormone ecdysteroids and strongly interfere with metamorphosis of insects at all development stages. Phytoecdysteroids are present in a wide variety of ferns, gymnosperms and angiosperms. Presence of phytoecdysteroids in *D. caryophyllus* is still to evaluate but, present in other species of *Dianthus* genus (Zibareva et al., 2003; Zibareva, 2009).

A new phenolic compound Kaempferide triglycoside (Fig. 1) isolated from *Fusarium* wilt resistant varieties of *D. caryophyllus* (Curir et al., 2001; Ardila et al., 2013). Kaempferide triglycoside synthesized from amino acid Phenylalanine. Phenylalanine converted to cinnamic acid by the action of phenylalanine ammonia lyases enzyme. Cinnamic acid condenses with acetate units to form the cinnamoyl structure of the flavonoids (Batra and Sharma, 2013). One molecule of 4-coumaryl-CoA with three molecules of malonyl-CoA form chalcones by the action of chalcone synthase enzyme. Furthermore, chalcone isomerase enzymes catalyses the two-step condensation and produces a colourless flavanone named naringenin. The oxidation of the naringenin by flavanone 3-hydroxylase yields the dihydrokaempferol (Petrussa et al., 2013). Dihydrokaempferol by enzyme flavonol synthase converted to kaempferol. Subsequently flavonoid 4’-O-methyl transferase enzyme transfer methyl group to kaempferol and transformed to kaempferide. Further, flavonoid 3-O-glucosyl transferase catalyses the transfer of glucose moiety to kampferide and kaempferide 3-O-glucoside is formed (Ishikura and Yang, 1994; Curir et al., 2003). In the last steps of kaempferide triglycoside biosynthesis two more glucose are added to and kaempferide 3-O-glucoside but the exact mechanism have not been elucidated yet (Fig. 2).

**Ethnobotany:** Although, *Dianthus* genus possesses about 320 species but only few of them evaluated for medicinal properties till date. *Dianthus* spp. are mainly used in traditional Chinese medicinal system. *Dianthus caryophyllus, D. chinensis, D. anatolicus, D. barbatus* are used in china, while *D. basuticus* used in Africa and *D. superbus* used in China and Japan for different ailments. Different *Dianthus* species and their medicinal properties are summarised in Table 1.
Fig. 2: Biosynthesis of kaempferide triglycoside

Table 1: Medicinal properties of different Dianthus species

| Plant name     | Common name | Part use  | Medicinal properties/uses                                                                 | References                   |
|----------------|-------------|-----------|------------------------------------------------------------------------------------------|------------------------------|
| *Dianthus anatolicus* Boiss | Anatolian pink | Whole plant | It is used as general tonic and as an antipyretic in intermittent fever                    | Pullaiah (2006) and Hooper and Field (1937) |
| *Dianthus barbatus* L. | Sweet Williams | Whole plant | It is used as alternative of *D. chinensis* L.                                           | Bown (1995)                  |
| *Dianthus basuticus* Burtt Dav | Lesotho carnation | Root | The decoction used for cleansing of blood, flatulency and fertility in bulls               | Moteete and Van Wyk (2011)  |
| *Dianthus caryophyllus* L. | Carnation    | Flower buds | Used in the treatment of wounds, throat and gum infections, cardiotoxic, diaphoretic, vermifuge gastro-intestinal disorder and alexiteric  | Al-Rawi and Chakravarty (1988) and Mohammed and Al Bayati (2009) |
| *Dianthus chinensis* L. | Pink         | Whole plant | Used in the treatment of menostasis, gonorrhoea, cough, emmenagogue and diuretic          | Bown (1995) and WHO (1998)   |
| *Dianthus superbus* L. | Fringed pink | Whole plant | Used in the treatment of asthma, carbuncles and anti-inflammatory agent in the treatment of urinary infections | Lopez-Exposito et al. (2011) and Shin et al. (2012) |

Pharmacological properties

Anticancer activity: Kaempferide triglycoside a glycosylated flavonol isolated from *D. caryophyllus* exhibit human colon cancer cell line inhibitory properties due to induced over expression of estrogen receptor β (ER-β). This glycosylated flavonol exhibit its effect on the proliferation of colon cancer cells by not conventional inhibiting over expressing estrogen receptor β by a mechanism mediated by ligand binding to estrogen receptor; rather it affects HCT8 cell cycle progression by increased antioxidant enzymes production in estrogen receptor β over expressing cells and then increasing the G0/G1 cell fraction (Martineti et al., 2010). The results conclude, kaempferide triglycoside in dose-dependent manner is able to inhibit cell growth and DNA replication. kaempferide triglycoside possibly induced cell growth inhibition due to push cells into G0/G1 starvation and to increase the expression levels of two superoxide dismutase type 2 (SOD1) and metallothionein type 2 (MT2A) proteins the important antioxidant proteins (Martineti et al., 2010).

Moreover, the antioxidant proteins metallothionein (MT) control over cellular Zn metabolism by affecting Zn ions binding and releasing through-SH groups. The MT regulates Zn-containing proteins, enzymes (e.g., proapoptotic proteins, transcription factors (TFIIA) antioxidant factors, Zn finger proteins and Cu Zn-superoxide dismutase (Cu Zn-SOD) which are essential for multiple
intra cellular cell fate and signalling pathways. The Zn-containing MT work as tumor inhibitory proteins, which are important for optimum activity and stability of p53 by supplying Zn to it (Pedersen et al., 2009). Subsequently, activated p53 arrest cell cycle at G1 phase and prevent further DNA replication. Another antioxidant proteins superoxide dismutase (SOD) catalyse dismutation of superoxide into hydrogen peroxide and oxygen, by doing so act as important factor in antioxidant defence mechanism in nearly all cells exposed to oxygen (Khan et al., 2010). As a downstream mediator of the senescence-associated tumor suppression, SOD-2 effect in the inhibition of tumor and its growth in prostate epithelial cell lines and human breast cells by acting mac25/insulin-like growth factor binding-protein related protein-1 (IGFBP-rP1) (Plymate et al., 2003). Moreover, the exact mechanism of kaempferide triglycoside induced cell growth inhibition is not elucidated yet, perhaps SOD works in the same manner discussed above.

**Anti-bacterial activity:** Aqueous and methanol extract of aerial parts of *D. caryophyllus* show antagonistic activity against *Helicobacter pyloria* major etiological agent of chronic active gastritis and peptic ulcerdisease and is linked to gastric carcinoma (Castillo-Juarez et al., 2009). Whole plant extract of *D. caryophyllus* show antibacterial activity against *Bordetella bronchiseptica*, *Staphylococcus epidermidis* and *Klebsiella pneumonia* (Bonjar, 2004). Two antibacterial compound thymol and eugenol extracted from dried carnation bud show antagonistic activity against gram-negative bacteria *Escherichia coli* and *Proteus mirabilis* with MIC (minimum inhibitory concentration) value of 7.8 μg mL⁻¹. While, for the three strains of gram-positive bacteria *Bacillus cereus*, *Listeria monocytogenes* and *Staphylococcus aureus* the antibiotic activity was with MIC value of 15.6 μg mL⁻¹ (Mohammed and Al-Bayati, 2009). Some *Pseudomonas* spp. and *Bacillus* spp. isolated from the rhizosphere of *D. caryophyllus* also show antagonistic activity against some the plant pathogens *Bacillus subtilis*, *B. cereus* and *Xanthomona* ssp. (Sharma and Kaur, 2010).

**Antiviral properties:** The two Dianthin antiviral proteins (DAP 30 and DAP 32) extracted from the seeds *D. caryophyllus* exhibit anti HIV (Human immunodeficiency virus) activity. These proteins act as Ribosome-Inactivating Proteins (RIP) and suppress translation process of viral proteins (Lee-Huang et al., 1994; De Clercq, 2000; Desai et al., 2009). Seed extract of carnation also show potent antiviral activity against herpes simplex virus-1 (HSV-1) and hepatitis A virus-27 (HAV-27) (Barakat et al., 2010). The sap of the carnation suppress local lesion development of Tobacco Mosaic Virus (TMV) on *Nicotiana glutinosa* L. (Ragetli and Weintraub, 1962).

**Antifungal properties:** The kaempferide triglycoside and other flavonoid glycoside analogues isolate from *D. caryophyllus* were tested against Fusarium wilt causative pathogenic fungi *Fusarium oxysporum* f. sp. dianthi pathotypes and exhibited antagonistic activity against the same (Curir et al., 2001; Galeotti et al., 2008).

**Insecticide properties:** The essential oil of *D. caryophyllus* was evaluated for its larvicidal properties against the mosquito *Culex pipiens* and revealed moderate larvicidal activity. This mosquito is vector of Japanese encephalitis, meningitis, urticarial diseases and West Nile Virus (Kimbaris et al., 2012). Essential oil of carnation also possesses repellent property against ticks (*Ixodes ricinus*) and yellow fever mosquitoes (*Aedes aegypti*). In the carnation oil the major components for repellency are phenethyl alcohol, β-citronellol, cinnamyl alcohol, eugenol and coumarin along with minor amounts of α-pinene and geraniol (Tunon et al., 2006).
CONCLUSION

*Dianthus caryophyllus* is an important herb in cut flower trade. Apart from its floricultural importance, it is also a valuable plant of medicine. The plant traditionally used in China, Japan and Korea in the treatment of wounds and gastro-intestinal disorder and various other ailments. Plant also used in some African countries and Egypt in treatment of various ailments. In recent pharmacological studies plant also tested for anticancer, antiviral, antibacterial, antifungal and anti-insecticide activities. Among these properties the anticancer, antiviral and anti-insecticide properties of plant needed to be further evaluated and tested, as all these properties of plant related to some worst diseases of human society. Due to various promising biomedical activities and traditional medicinal importance, further studied should be carried out on drug development from plant extracts and their constituents of the *D. caryophyllus*.

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