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Pharmacological Properties of *Dianthus caryophyllus*: A Comprehensive Review of Its Therapeutic Potential

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ABSTRACT

The medicinal knowledge of herbal plants plays a crucial role in finding new sources of drugs. Finding novel medicine sources heavily relies on the therapeutic understanding of herbal plants. The Carnation (Dianthus Caryophyllus) is a plant commonly used in traditional folk medicine and an important member of the Caryophyllaceae family. In vitro and in vivo experimental models are frequently used to study the different applications of complete plant sections. The current study attempts to offer scientific evidence in favor of the pharmacological effects of the different phytoconstituents that have been separated from plants. Pharmacological experiments revealed that the various parts of the plant possessed anti-inflammatory, anti-cancer, antibacterial, antifungal, antiviral, insecticidal, repellent, antioxidant, and Reno-protecting qualities. Therefore, this review encompasses a thorough literature examination of Dianthus Caryophyllus's plant characteristics, traditional usage, chemical ingredients, and pharmacological activity.

Keywords: Carnation, Caryophyllaceae, Folk medicine, Phytoconstituents.

1. INTRODUCTION

One of the best often expanded cut flowers, ranking among the top 10 cut flowers worldwide, is the Dianthus caryophyllus (carnation) plant, which belongs to the Caryophyllaceae family [1]. The carnation, or Dianthus caryophyllus, is currently the second most popular flower worldwide. Carnations are commonly used to express feelings of love, interest, and distinction on significant events. Theophrastus's descriptions of Dios Anthos, the flower of the gods, are the source of the genus name [2]. Since the scent of carnations is similar to that of cloves, Linnaeus came up with the species name caryophyllus, which is derived from the genus of cloves. The ancient Greeks most likely gave the D. caryophyllus plant its name as a coronation flower [3].

More than 200 years of breeding have produced the trade carnations of today. Compared to their wild progenitors, carnations have a greater spectrum of colours, more prominent flowers, and sturdy stems. They also bloom all year round. Despite having larger flowers, tetraploids are less productive, so the majority of commercial cultivars are diploids [4]. Heart disease, cancer, Parkinson's disease, and Alzheimer's disease are among the many illnesses brought on by an overabundance of free radicals in the body, which harm healthy cells and tissues. Antioxidants are crucial for reducing the risk of cancer, slowing down the deteriorating process, and counteracting the harm caused by free radicals in the human body. There is minimal difference between various tissue segments in carnation research, which mostly concentrates on high extracts and particular volatile components. The medicinal properties of carnation extracts have an unclear underlying material basis, which restricts their potential for further development and use [5].

Medicinal plants and herbs are used by an increasing number of patients worldwide for medical purposes. Making informed decisions on their use will therefore benefit from methodological examination of their biological characteristics, safety, and restorative potential. According to recent assessments, plants generate a large number of secondary metabolites that are biosynthetically produced from primary metabolites and are a significant source of numerous medications [6]. Alkaloids, triterpenes, coumarins, cyanogenic glycoside, cyanidin, pelargonidin, the yellow isosalipurposide, essential oil, volatile oil, and a variety of phytoconstituents were found in Dianthus caryophyllus, according to a phytochemical investigation. The plant's anticancer, antibacterial, antifungal, antiviral, insecticidal and repellent, antioxidant, Reno-protective, analgesic, and anti-inflammatory properties were demonstrated by pharmacological investigations. Thus, the current review emphasizes chemical constituents and pharmacological effects Dianthus caryophyllus [7].

2. PLANT PROFILE

2.1 Synonyms:

Dianthus arbuscula Lindl, Dianthus arrectus Dumort, and Dianthus acinifolius Schur. Schur's Dianthus binatus Dianthus coronarius (L.) Brum's, Dianthus caryophyllus var. coronarius L., Link ex Spreng, Dianthus corsicus Schur, Dianthus kayserianus Costa Dianthus longicaulis [8].

2.2 Scientific classification:

Kingdom: Plantae **Infrakingdom:** Streptophyta **Clade:** Tracheophyta **Category:** Spermatophyta **Class:** Magnoliopsida superorder **Family:** Caryophyllaceae; **Order:** Caryophyllales **Genus:** Dianthus **species:** Caryophyllus [9][10].

2.3 Common names:

Arabic: Gronfel; Burmese: Zaw-hmwa-gyi; **English:** Border carnation, Carnation, Clove pink, Divine-flower, Gilly-flower; **French:** Oeillet, Oeillet des fleuristes; **German:** Garten-Nelke, Land-Nelke, Nelke; **Japanese:** Oranda-nadeshiko; **Spanish:** Clavel; **Swedish:** Trädgårdsnejlika [11].

2.4 Nativity:

The common name for Dianthus caryophyllus L. is "carnation," which comes from the Greek word "carnis," which meaning "freshly colored." Around the world, gardens are growing this variety of flowering decorative herb. The Pyrenees Mountains in France and Spain are home to this species, which is native to the Mediterranean region [12]. Italy, Spain, and the Netherlands are the main producers in Europe. Carnation blooms are brought to Europe from the Middle East, South America, and Africa. Originally from France and Italy, wild Dianthus caryophyllus is rare [13].

2.5 Ethno botany:

Only a small number of the approximately 320 species in the Dianthus genus have been identified as having therapeutic potential thus far. The traditional Chinese medical system is the main application for Dianthus spp. China uses Dianthus caryophyllus, D. chinensis, D. anabolics, and D. barbatus, whereas Africa uses D. basics, and China and Japan employ D. superbus for various ailments [14].

2.6 Description:

The plant is a glabrous, branching herb that can grow between 15 and 60 cm tall, either as an annual or perennial. Its leaves are linear-lanceolate with sharp tips, and may have ciliate edges at the base, or smooth borders. Flowers appear at the tips of branches, either singly or in clusters. The epicalyx consists of 4–6 broad, ovate, herbaceous scales, covering about one-fifth to one-fourth of the calyx tube's length, with abruptly mucronate tips. The cylindrical calyx tube is 20–30 mm long. There are five petals that are obovate-triangular in shape, with extended limbs, cuneate claws, and are pink-red or white, sometimes with darker centers, and glabrous [15][16].

2.7 Genome sequence:

Multiple next-generation multiplex sequencing platforms were used to sequence the entire genome of *Dianthus caryophyllus* L. cv. "Francesco." K-mer analysis revealed that non-redundant sequences accounted for 91% of the 622 Mb carnation genome, totaling 568,887,315 base pairs and 45,088 scaffolds. The analysis identified 13 rRNA genes, 92 snoRNA genes, 143 miRNA genes, and 1,050 tRNA genes within the assembled genome. Excluding those within transposable elements, 43,266 full and partial gene structures were identified for protein-coding genes [17].

3. TRADITIONAL USES

Carnations were used in perfumery. Usually, 500 kg of flowers provide 100g of oil [18]. It has long been used to treat wounds, gum and throat infections, and other ailments as a vermifuge, diaphoretic, cardiotonic, alexiteric, and for gastrointestinal problems. The plant has long been used to treat wounds, gastrointestinal problems, and other ailments in China, Japan, and Korea [19]. In Europe, herbal therapy has long been utilized to treat heart and mental health conditions. It has been discovered that carnation blooms possess nervine, stimulant, diaphoretic, antispasmodic, and alexiteric qualities. The herb has been used as a vermifuge in China [20].

Carnations have long been used as medicine and as spices. As an antibacterial, it relieves toothaches and also heals sneezing and eye disorders. Essential oil from carnations was utilized to boost memory and repair abilities. Oil was also used to cure wounds, reduce disorientation, and as an appetizer [21].

4. CHEMICAL CONSTITUENTS

Triterpenes, alkaloids, coumarins, cyanogenic glycoside, cyanidin, pelargonidin, the yellow isosalipurposide, essential oil, volatile oil, and numerous other chemical components were found in Dianthus caryophyllus, according to a phytochemical investigation [22]. The primary components responsible for the color of carnation blooms were yellow isosalipurposide, cyanidin, and pelargonidin [23]. 100g of oil is produced from 500kg of flowers. The carnation flowers' (Dianthus caryophyllus) chemical makeup and essential oil were assessed. Gas chromatography-mass spectrometry (GC-MS) identified twelve volatiles as the key constituents of carnation flower oil [18]. Eugenol, hexyl benzoate, hexenyl benzoate, benzyl benzoate, benzoin, nootkatone, benzyl salicylate, m-cresyl phenyl acetate, hexadecanoic acid, eicosene, and phenyl ethyl alcohol were the main constituents. When the plant was treated with 200 ppm stigmasterol, the amount of benzyl benzoate increased significantly, from 12.62 to 45.04 percent. The treatment with 50 ppm stigmasterol and 400 ppm putrescine produced the most notable change in eugenol, from 21.48 to 33.54% [24]. Four chemical groups were present in the oil of Dianthus caryophyllus cultivated in Egypt that was extracted using an organic solvent: Pcymene 3.32%, limonene 4.91, β-pinene 3.11%, and phellandrene 3.52% are monoterpene hydrocarbons; oxygenated monoterpene is 26.71% (elemol 5.51%, citronellol 1.11%, bornyl acetate 3.12%, eugenol 15.29%, methyl eugenol 1.68%); sesquterpene hydrocarbons are 12.83% (ϒ-cadinene 4.12%, calamene 8.71%), and various other compounds are 20.97% (benzyl benzoate 14.12%, benzyl salicylate 6.85%). Apigenin-C-glycoside, kaempferol 3-O-β-dglucopyranosyl-(1→2), and three other flavonoids[α-l-rhamnopyranosyl-(1→6)] -O--kaemp-ferol 3-O-[α-lrhamnopyranosyl-(1→6)] and -β-d-glucopyranosideIn nine distinct carnation cultivars—America, Esperia, Harem, Miledy, Raggio di Sole, Roland, Rosa Antico, Tempest, and Tiepolo—-β-d-glu-copyranoside was identified as the primary flavonoid component. The composition of phenol analysis was investigated in vitro and in vivo on healthy and Fusarium oxysporum-inoculated Dianthus caryophyllus tissues. Flavonol glycoside peltatoside (3-[6-O-(alpha-L-arabinopyranosyl)-beta-D-glucopyranosyl] quercetin), flavone datiscetin (3, 5, 7, 2'-tetrahydroxyflavone), and two benzoic acid derivatives, protocatechuic acid (3, 4-dihydroxybenzoic acid) and vanillic acid (4-hydroxy-3-methoxybenzoic acid) were extracted from the plant. A phenolic compound called kaempferide triglycoside was extracted from carnation cultivars that were resistant to Fusarium. The petals of deep pink and red-purple flower cultivars of Dianthus caryophyllus were used to produce 3,5-Di-O-(beta-glucopyranosyl) cyanidin 6''-O-4,6'''-O-1-cyclic malate and its cyanidin equivalent, 3,5-di-O- Dianthus caryophyllus yielded a large number of Dianthramide, all of which were determined to be amides between a cinnamic acid (p-coumaric) moiety and either an anthranilic acid moiety (anthranilic, 4-hydroxyanthranilic, 4-methoxyanthranilic) or a benzoic acid (benzoic, salicylic, βresorcylic, 4-methoxysalicylic). However, in comparison to dianthalexin and dianthramides A and B, the quantities of these dianthramides were negligible [26]. An antiviral protein that was extracted from carnations contained lysine ϵ-groups, which gave it its antiviral properties. None of the 14 amino acids produced by acid hydrolysis included sulfur [27]. Proteins called dianthin 30 and 32 were separated from Diathus caryophyllus leaves and purified by chromatography on CM-cellulose. Pelargonidin 6''-O-4, 6''-O-1-cyclic malate (beta-glucopyranosyl) [25]. It was discovered that the molecular weight of dianthin 30 was 29 500, whereas the molecular weight of dianthin 32 was 31 700. Mannose is one of the glycoproteins found in both dianthus [28]. Esterified polysaccharides, benzoic, p-hydroxybenzoic, vanillic, Trans p-coumaric, cis and Trans ferulic, 3-methoxy-4-hydroxy-n-chlorophenyl propionic, and (in significant quantities) dihydroferulic acid were all present in healthy Dianthus caryophyllus stems. The amounts of these phenolic acids were impacted by fungal infection, which also caused the formation of two different kinds of anthranilic acid derivatives that contained 2, 2′-dicarboxy-5, 5′-dihydroxy-N, N-diphenylamine and dianthramides [29]. Nonetheless, the chemical makeup of fresh and ensiled carnation is as follows: lignin 10.7 and 9.5; cellulose 28.2 and 28.3; hemicellulose 6.2 and 6.3; ether extract 3.1 and 3.4; nitrogen free extract 50.5 and 47.0; crude fiber 25.3 and 28.1; ash 9.1 and 10.9; neutral detergent fiber 43.2 and 44.3; acid detergent fiber 37.0 and 38.0; lignin 22.1 and 23.4%; dry matter 90.8 and 89.0; crude protein 11.1 and 10.5; ether extract 3.1 and 3.4 [30].

5. PHARMACOLOGICAL EFFECTS

5.1 Anticancer effect:

Kaempferide triglyceride, extracted from *Dianthus caryophyllus*, was effective in inhibiting the growth of both native and estrogen receptor β-overexpressing colon cancer cells through a mechanism independent of ligand binding to estrogen receptors. By raising the proportion of cells in the G0/G1 phase, it had an impact on the HCT8 cell cycle's advancement. In cells overexpressing estrogen receptor β, it boosted the levels of two key antioxidant proteins, superoxide dismutase type 2 (SOD2) and metallothionein type 2 (MT2A). The biological effects of kaempferide triglyceride were further investigated by using elevated levels of estrogen receptor β. In a colon cancer xenograft model, the combined treatment of dianthin with EGF and saponin SO-1861 was assessed. Human colon cancer cells HCT116, HER14, and NIH3T3, all overexpressing the EGF receptor, were used to assess real-time in vitro cytotoxicity. In the xenograft model, dianthin along with EGF (0.35 µg/treatment) and SO-1861 (30 µg/treatment) were administered to tumor-bearing animals and HCT116 cells. Tumor progression was tracked using (18) F-2-fluor-2-deoxy-d-glucose, small animal PET, and x-ray computed tomography. The in vivo results showed a significant reduction in tumor volume and glycolytic activity in the treated group (over 95% reduction; $P < 0.05$), while the in vitro data demonstrated strong receptor specificity [32].

5.2 Anti-bacterial effect:

Aqueous and methanol extracts of D. caryophyllus aerial parts exhibit antagonistic activity against Helicobacter pylori, a key causative agent of peptic ulcer disease and chronic active gastritis, and are associated with stomach cancer. The whole plant extract of D. caryophyllus exhibits antibacterial action against Klebsiella pneumonia, Bordetella bronchiseptica, and Staphylococcus epidermidis. Eugenol and thymol, two antibacterial constituents were isolated from dried carnation buds, exhibit antagonistic action against Proteus mirabilis and E. coli, two gram-negative bacteria, with a minimum inhibitory concentration (MIC) of 7.8 μg mL1. However, the antibiotic activity was 15.6 μg mLG1 for the three strains of gram-positive bacteria, Bacillus cereus, Listeria monocytogenes, and Staphylococcus aureus. The plant pathogens Bacillus subtilis, B. cereus, and Xanthomonas ssp [33].

5.3 Antifungal effect:

When tested against pathogenic fungi that cause Fusarium wilt, Fusarium oxysporum f. sp. dianthus pathotypes, the kaempferide triglyceride and other flavonoid glycoside analogues isolated from D. caryophyllus showed antagonistic activity against the same [34].

5.4 Antiviral effect:

The antiviral properties of Dianthus caryophyllus crude extract were evaluated against hepatitis A virus-27 (HAV-27) and herpes simplex virus-1 (HSV-1). Using the plaque infectivity count test, a non-toxic dose of Dianthus caryophyllus seed extract (20 μg/ml) to both Vero and HepG2 cells demonstrated strong antiviral efficacy against HSV-1 and HAV-27. The extract had no discernible impact on either adsorption or the phases of virus replication. The antiviral activity of two medicinal medications—acyclovir and amantadine, which are employed as controls for HSV-1 and HAV-MBB, respectively—has been compared to that of the seed extract under study. The findings demonstrated that the seed extract's inhibitory activity against the same viruses was significantly greater than that of manufactured pharmaceutical medications. [35] *Dianthus caryophyllus* produced an antiviral protein with lysine ϵ-groups, which are responsible for its antiviral activity. Acid hydrolysis of the protein yielded 14 amino acids, none of which contained sulphur. After incubation with four proteolytic enzymes, the protein's viral inhibitory effect remained unaffected. The protein did not possess ribonuclease (RNase) activity and could not prevent the RNA breakdown caused by pancreatic RNase. However, it protected *Nicotiana glutens L.* from infection by both the intact tobacco mosaic virus (TMV) and the RNA derived from it. The authors suggested that the protein's ϵ-amino groups competed for critical host binding sites with similar groups in the TMV and specific amino groups in the RNA, which are important during the early stages of virus infection. [27].

5.5 Insecticidal and repellent effect:

Dianthus caryophyllus essential oils were tested for their larvicidal properties against Culex pipiens mosquito larvae in their late third to early fourth instars. With an LC50 value greater than 50 mg/l, the essential oils of Dianthus caryophyllus also demonstrated moderate larvicidal activity. With LC50 values of 18.28, 16.56, and 23.03 mg/l, respectively, eugenol, (E)-anethole, and α-terpinyl acetate were the most poisonous of the pure components [36]. The essential oil extracted from carnation (Dianthus caryophyllum) flowers has a strong deterrent impact on yellow fever mosquitoes (Aedes aegypti) and ticks (Ixodes ricinus nymphs). The most effective repellent component was discovered to be phenoxyethanol [37].

5.6 Antioxidant effect:

The DPPH assay method was used to examine the carnation flowers' volatile oil scavenging ability. Although the entire plant had a scavenging effect, the maximum scavenging activity was observed when 400 ppm stigma sterol was added [24].

5.7 Reno protective effect:

Rats were utilized to investigate the protective effects of Dianthus caryophyllus extract against renal failure induced by gentamicin. The 96% ethanol extract of *Dianthus caryophyllus* demonstrated the ability to prevent nephrotoxicity and enzyme changes caused by gentamicin. This protective effect may be linked to the antioxidant properties of the extract. [38].

5.8 Analgesic effect:

Although Dianthus caryophyllus's analgesic qualities are not well established in the scientific literature, a few research and traditional applications indicate the plant may have some potential for pain relief. Flavonoids, alkaloids, and phenolic acids are among the plant's constituents that have been shown to have modest analgesic effects through potential modulation of pain pathways. Carnation extracts or infusions have been utilized in traditional medicine to treat common ailments like headaches and muscle soreness. These effects are probably brought on by these substances' anti-inflammatory and antioxidant qualities, which may help lessen the root causes of pain [39].

5.9 Anti-inflammatory effect:

Flavonoids, phenolic acids, and alkaloids are among the bioactive substances found in Dianthus caryophyllus. These substances are well-known for their antioxidant and anti-inflammatory qualities. By preventing the synthesis of pro-inflammatory cytokines and inflammatory response-related enzymes including cyclooxygenase (COX) and lipoxygenase (LOX), flavonoids in particular might modify inflammatory pathways. The phytochemical profile and indirect research on related species point to possible anti-inflammatory properties, despite the lack of direct proof regarding Dianthus caryophyllus's anti-inflammatory activities. Flavonoids and phenolic acids, among other bioactive substances found in the plant, are known to reduce oxidative stress and affect important inflammatory pathways like COX-2, iNOS, and NF-κB. To completely confirm its effectiveness and identify the best dosage and application techniques for therapeutic use, more clinical research is required [39].

6. CONTRAINDICATIONS AND SIDE EFFECTS

It is not recommended for nursing mothers or pregnant women to use D. caryophyllus. Since it was a potent spice, children younger than two years old should not be given it. People with high blood pressure must also avoid using it. Carnations can be used to treat gastritis and ulcers, but only in modest amounts [21]. Dianthus caryophyllus exposure at work can cause asthmatic and allergy symptoms. Along with 15 patients with allergic asthma who were not exposed to carnations and 15 healthy carnation workers who served as control subjects, a total of 16 participants were examined in the indoor D. caryophyllus growing with symptoms during exposition time. 15 out of 16 patients had positive results from the skin prick test using carnation extract, whereas all control participants had negative results. Thirteen out of sixteen individuals had positive results from the nasal provocation test using carnation extract. The RAST and nasal provocation findings showed a substantial correlation ($P<0.01$). In almost all patients, immunoblotting of sera from 13 patients revealed two large IgE-binding fractions of 34 and 35 kd, which may constitute the primary allergen [40]. There were some unfavourable complications with eugenol. Consuming eugenol can result in metabolic acidosis, respiratory syndrome, and a corrosive effect. Eugenol can lead to disseminated intravascular coagulation, protein and blood toxicity, low blood sugar, and liver failure in infants. Eugenol has been shown in animal studies to induce anorexia and gastroenteritis [41,42].

7. CONCLUSION

The plant profile, chemical components, pharmacological effects, and traditional applications of Dianthus caryophyllus as a beneficial herbal remedy are highlighted in the current review due to its efficacy and safety. One of the most common herbs in the cut flower trade is Dianthus caryophyllus. In addition to its significance in floriculture, it is a highly useful medicinal plant. In China, Japan, and Korea, the plant is traditionally used to cure wounds, gastrointestinal disorders, and other illnesses. Plants are also utilized to treat various illnesses in Egypt and certain African nations. Plants are also utilized to treat various illnesses in Egypt and certain African nations. Recent pharmacological research has also examined the plant's anti-inflammatory, analgesic, antiviral, antifungal, anticancer, and analgesic properties. Since these qualities of plants are linked to some of the worst diseases in human civilization, it was necessary to estimate further and test the anticancer, antiviral, and anti-insecticide qualities of the plant. Additional research on medication development from plant extracts and their constituents of D. caryophyllus should be conducted due to the plant's numerous beneficial biological activities and traditional medicinal significance.

Conflict of Interest: No conflict

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