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THE PHARMACOLOGICAL IMPORTANCE OF *CENTAUREA CYANUS* - A REVIEW

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ABSTRACT

Chemical analysis of different parts of *Centaurea cyanus* revealed that the plant contained flavonoids**,** anthocyanins, phenilpropanic compounds, aromatic acids, phenolcarboxylic acids, amino acids, sugars, indole alkaloids**,** and it was rich in minerals and trace elements. The previous pharmacological studies showed that the plant possessed antibacterial, anti-inflammatory, neural, antioxidant, diuretic, gastro-protective and many other effects. This review will discuss the chemical constituents and pharmacological effects of *Centaurea cyanus*.

Key words: *Centaurea cyanus*, Pharmacology, Chemical constituents.

INTRODUCTION

During recent years, herbal medicine has become an increasingly scientifically based system of healing. Due to demands from both the public and medical establishments, studies leading to the scientific explanation of plant therapeutic capabilities are allowing this practice to gain increasing credibility and acceptance within the medical community [1-2]. The recent studies showed that the plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavors, fragrances, colors, pesticides and food additives [2-60]. Chemical analysis of different parts of *Centaurea cyanus* revealed that the plant contained flavonoids**,** anthocyanins, phenilpropanic compounds, aromatic acids, phenolcarboxylic acids, amino acids, sugars, indole alkaloids**,** and it was rich in minerals and trace elements. The previous pharmacological studies showed that the plant possessed antibacterial, anti-inflammatory, neural, antioxidant, diuretic, gastro-protective and many other effects. This review was designed to discuss the chemical constituents and pharmacological effects of *Centaurea cyanus*.

History and Nomenclature

In ancient Egypt, reproductions of cornflowers have been found dating back to the first half of the 4th millennium BC (Stone to Bronze Age). As a companion of cereal plants and probably also because of its similar colour to the blue lotus (Nymphaea coerulea), it soon became a symbol of life and fertility. It was even cultivated as a garden plant, portrayed, for instance, on wall friezes, and on wall and floor designs in houses and palaces of the Amarna period (1364–1347 BC). Often flower heads appeared on faience and glazed earthenware, which was also used for pendants of earrings, necklaces, and collars for ladies. From the 18th dynasty (from 1552 BC) until the Greek–Roman period, florists used cornflower heads for grave decorations. In the tomb of Tut-ankh-Amun, Howard Carter (in 1922) found wreaths and garlands of cornflowers together with petals of the blue lotus flower on the three coffins. Plants were given to the deceased to accompany him on his way, as an aid for reanimation. The scientific name of the genus, Centaurea was derived from the story of the centaur Chiron, Achilles adviser. According to Greek myth, Achilles was wounded with a poisoned arrow (by Herakles), and his wound was healed by applying cornflower plants. The species name cyanus was given because of the flowers vivid blue colour. The common name 'Cornflower' comes from the fact that the plant grows wild in the grain fields of southern Europe. In Christian symbolism, cornflower became a symbol of the Queen of Heaven, Mary, and Christ. The cornflower has also been used as a symbol of tenderness, of fidelity, and of reliability. Botticelli (15th century) decorated the garments of some of the figures in his paintings with a cornflower design Cornflower has also been used as a symbol of power and majesty such as in the tapestry called

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'Verdure of arms of Emperor Charles V. The two-headed eagle as the sign of the Habsburg Monarchy and the coat of arms is surrounded by various realistically-drawn plants, among them cornflower, with its tubular florets and characteristic bracts dominating the space [61-64].

When Napoleon forced Queen Louise of Prussia from Berlin, she hid her children in a cornfield and kept them entertained and quiet by weaving wreaths of cornflowers. One of her children, Wilheim, later became the emperor of Germany. Remembering his mother's bravery, he made the cornflower a national emblem of unity [64-65].

Taxonomic classification

Kingdom: Plantae, Phylum: Anthophyta, Class: Dicotyledoneae, Family: Asteraceae, Genus: Centaurea, Species: cyanus [2].

Common names: Centaurea, Bachelor's Buttons, Bluebonnet, Bluebottle, Blue Centaury, Cyani, Bluebow, Hurtsickle, Blue Cap and Cyani-flowers.

Distribution

The plant is a native of Europe and the Middle East, it is a garden flower in the United States, and now cultivated worldwide, it is spread all over Europe and Western Asia [66-68].

Description

Centaurea cyanus consists of stem, leaves, inflorescences, marginal and central flowers. Stem up to 3 mm in diameter, fistular, bright green, longitudinally furrowed, slightly pubescent. Leaves linear, a prominent central vein, both surfaces pubescent. The flowers are produced in flowerheads 1.5-3 cm diameter, with a ring of a few large, spreading ray florets surrounding a central cluster of disc florets. The ray florets up to 2 cm length, sterile, consist of fused petals with small 5-8 upper teeth. In the disc florets the petals are fused into a tube five apical lobes. They are bisexual, containing both fertile anthers and a fertile pistil. The bracts, 12-15 mm length, 5-9 mm width, enclosing the hard head of the flower are numerous, with tightly overlapping scales, each bordered by a fringe of brown teeth. Odour is faint, pleasantly aromatic [69].

Traditional uses

Externally it is used as an anti-inflammatory and astringent herb for eye ailments and skin cleansing. An eye wash made with cornflower blossoms is used for conjunctivitis and blepharitis as well as to relieve strained, tired or puffy eyes. Blue blossoms infused in water have both curative and calming action for nervous disorders. Eye wash is reputed to strengthen weak eyes. Traditionally it is said to work best on blue eyes. The dried flowers are antipruritic, antitussive, astringent, weakly diuretic, emmenagogue, ophthalmic, very mildly purgative, and tonic. An infusion can be used in the treatment of dropsy, constipation, or as a mouthwash for ulcers and bleeding gums. This infusion is also taken as a bitter tonic and stimulant, improving the digestion and possibly supporting the liver as well as improving resistance to infections. Water distilled from the marginal flowers was formerly in repute as a remedy for weak eyes and a soothing lotion for conjunctivitis. The seeds are used as a mild laxative for children. Cornflower leaves are used to create a cleansing facial steam for dry sensitive skin. A decoction of the leaves is antirheumatic [66, 70-72].

Part used medicinally: Flowers.

Chemical constituents

Various flavonoids were isolated from *Centaurea cyanus* including apigenin-4'-O-(6-O-malonil-glucoside)-7-O-glucuronide, apigenin-4-O-glucoside, apigenin-7-O-glucoside (cosmosiin), apigenin-7-O apio- glucoside (apiin), methyl-apigenin and methyl-vitexin, cyanidin-3-O-succinyl-glucoside- 5-O-glucoside (centaurocyanin), cyanidin-3,5-diglucoside (cyaniding), 5-methoxy-apigenine (hispidulin), quercetin-3-O-gluco- rhamnoside (rutoside), rhamnetin, isorhamnetin, isorhamnetin-7-O-glucoside, naringenin, kaempferol-glycosides, luteolin-glycosides, quercetin, naringin, naringenin-7-O-gluco-rhamnoside, quercetin-3-glucorhamnoside, apigenin-7-glucoside, quercetin-7-glucoside, quercetin -3-glucoside, apigenin-8-C-glucoside, aringenine, caffeic, chlorogenic, neochlorogenic acids and umbeliferone [67, 73-75].

It was also contained aromatic acids including phenyl carboxylic acid derivates such as: *cis* and *trans*-caffeic acids, protocatechic and chlorogenic acids, *p*-hidroxibenzoic, *p*-coumaric, vanilic, syringic, ferulic, salicilic and benzoic acids, as well as *cis/trans*-sinapic acids or *o/p*-hidroxiphenylacetic acids [76].

The plant also contained amino acids, sugars (glucose, fructose, zaharose, raffinose) [67], and coumarins (scopoletin, umbelliferone) [77].

In studying the phenolcarboxylic acids content of the flowers, it appeared that they contained 23 acids: chlorogenic, cis- and trans-caffeic, p-hydroxybenzoic, p-coumaric, vanillic, syringic, ferulic, salicylic, p-hydroxy-phenylacetic, o-hydroxyphenylacetic, benzoic, cis- and trans-sinapic and other less known phenolcarboxylic acids [78].

Analysis of a methanol extract of the seeds of *Centaurea cyanus* gave four indole alkaloids: moschamine, cis-moschamine, centcyamine and cis-centcyamine [79].

Centaurea cyanus also contained at least two compounds (Centaur X_1 and X_2) related to decadiene-1,9-triyne-3,5,7; and at least two compounds (Centaur Y_1 and Y_2) related to octatetraene-1,3,5,7 [80].

Qualitative studies performed on the tinctures and crude aqueous, ethanol and acetone extracts of *Centaurea cyanus* raw material (flower head and aerial part) revealed the superiority of crude extracts and acetone extract for isolation of polyphenols (quercetin, apigenin and caffeic acid derivates) [81].

However, the total of phenilpropanic compounds, flavonoids and anthocyanins was determined in *Centaurea cyanus.* The highest concentration of flavonoids were determined in purple flowers (0.21 – 0.22%), next in the pink flowers (0.19%) and the lowest in blue flowers.

Anthocyanins highest concentration was found in purple (1.36-3.63%), in blue (0.24-0.67%) and in pink flowers and inflorescences (0.07-0.23%). In purple inflorescences, the concentration of phenilpropanic compounds is higher (0.36%) than in blue inflorescences (0.15%), but in aerial parts with purple inflorescences is lowest (0.24%) than in aerial parts with blue inflorescences (0.31%) [70]. *Centaurea cyanus* also contained K-5.75%, Ca-2,46%, Mg-0.27%, Na-0.02%, Fe-0,0175, Mn-0.0061% and Zn-0.0052%. Selective plant extract have been shown as containing: K, Ca, Mg, Na, Fe, Mn and Zn [67].

Pharmacological effects

Antibacterial effect

The drug has an antibacterial effect in vitro (centaurocyanin), but only for the aerial parts of the plant without the flowers [66].

The water, ethanol and ethyl acetate extract of *Centaurea cyanus* were tested against *Agrobacterium radiobacter* var. *tumefaciens*, *Bacillus subtilis*, *Erwinia carotovora*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Ps. fluorescens*, *Sarcina lutea* and *Staphylococcus aureus*, in a concentration of 5, 10, and 15mg/disc. The water and ethanol extracts showed moderate activity against *Staphylococcus aureus* only [82].

Anti-inflammatory effect

Centaurea cyanus flower-heads had anti-inflammatory properties as shown by different pharmacological experiments including inhibition of carrageenan, zymosan and croton oil-induced edemas, inhibition of plasma hemolytic activity, and/or induction of anaphylatoxin activity [71].

Moschamine a safflomide-type phenylpropenoic acid amide found in *Centaurea cyanus* was a very potent COX-I inhibitor, it inhibited COX-I by 58% ($p < 0.012$) at the concentration of 0.1 µ mol /l [83].

Antiserotonin effect

Moschamine a safflomide-type phenylpropenoic acid amide found in *Centaurea cyanus*, was tested as antiserotoninergic agent. At the concentration of 10 µ mol /l, moschamine was able to inhibit forskolin-stimulated cAMP formation by 25% ($p < 0.015$), *via* inhibiting serotonin receptors in the OK cells. The inhibition was repressed by two 5-HT1 antagonists (Nan-190 and spiperone), suggesting that moschamine may suppress cAMP formation *via* binding to 5-HT1 receptors in the cells [83].

Antioxidant effect

Antioxidant activity of this selective plant extract obtained from *Centaurea cyanus* have been measured *in vitro,* using chemiluminescence's method – system luminol/H_2O_2. High antioxidant activity was exerted by *Centaurea cyanus*, similar to that produced by commercial *Camellia sinensis* (green tea) [67].

Gastroprotective effect

Pharmacological studies carried out on *Wistar* rats with stress-induced ulcer shown a very gastro-protective activity (protection percents over 80%) of the *Centaurea cyanus* extract [67]. The gastroprotective effects of *Centaurea cyanus* L. (herba) polysaccharides (P) and polyphenols (A) fractions was studied in stress-induced rat ulcer model. *In vivo* pharmacological studies revealed high influence of PA product (500 mg/kg) on deep, moderate and superficial gastric mucosal lesions, greater than that of chemical reference, Ranitidine. polyphenols fractions was proven more effective than Ranitidine in opposing the emergence of deep necrotic lesions only, suggesting the ability of polysaccharides compounds to consolidate gastric mucous layer as well as their certain tendency for cooperation with polyphenols fractions [84].

Diuretic effect

The effect of cornflower water extract was compared with hydrochlorothiazide on diuresis, Na^+ and K^+ excretion, and the changes in the prostaglandin E2 and kinins levels in the plasma of experimental rat's plasma. In hydrochlorothiazide receiving rats, the volume of urine excreted two and four hours after the administration of the drug was by 18% and 17%, respectively, higher as compared to the rats that were given cornflower water extract ($P<0.05$). The diuretic effect of cornflower water extract was noted in the animal group receiving this extract as compared to the control group: after two hours, the volume of urine excreted increased from 2.03±0.03 ml to 2.44±0.04 ml, and after four hours from 3.88±0.07 ml to 5.35±0.1 ml. Administration of hydrochlorothiazide under the load of salts and water resulted in a higher excretion of sodium and potassium as compared to the effect of cornflower water extract. The highest prostaglandin levels were found in the plasma of the animals receiving hydrochlorothiazide. Under the load of salts and water, a 13% and 15% increase in the amount of prostaglandins observed in the animals given cornflower water extract compared to the control animals respectively ($P<0.05$). The greatest increase in the amount of kinins was found in the groups of animals that given hydrochlorothiazide under the load of salts and water (14% and 22%, respectively). Kinin levels did not differ significantly between the control group and the groups receiving cornflower water extract [85].

Toxicity and adverse effects

Health risks or side effects following the proper administration of designated therapeutic dosages are not recorded. The drug possesses a weak sensitization potential [66].

Dose

Cornflower is rarely used today. Occasionally, it is used as an inactive ingredient in tea mixtures. The infusion is prepared by adding 1 gm of drug per cup. The infusion was taken several times daily [66]. As a tincture**,** it was used as 6-12 drops in juice, water, under the tongue or as desired. May be taken 3 times daily [68].

Conclusion

This review discussed the chemical constituents and pharmacological effects of *Centaurea cyanus* to enhance further pharmacological studies and clinical uses of the plant as a result of effectiveness and safety.

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