PHYTOCHEMICAL AND PHARMACOLOGICAL OVERVIEW OF CELOSIA CRISTATA AND FUTURE PERSPECTIVE AS POTENTIAL PHYTOTHERAPEUTIC AGENT

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ABSTRACT
Medicinal plants are the Nature’s gift to human beings to help them pursue a disease-free healthy life. Plants are a valuable source of a lot of secondary metabolites. *Celosia cristata* is a member of the genus Celosia and is commonly known as cockscomb, since the flower looks like the head on a rooster (cock). The plants are hardy and resistant to most diseases and grow equally well indoors or out, though the perfect place is one with no shade and a well drained soil, as the plant are susceptible to fungal diseases. The plant is used frequently as an ornamental plant indoors. Their leaves and flowers can be used as vegetables. Cockscomb flowers are also known as Wool Flowers or Brain Celosia, suggestive of a highly colored brain. The flowers belong to the amaranth family, Amaranthaceae. The Celosia plant is an annual dicotyledon. The recent studies showed that the plant exerted a wide range of pharmacological activities. The chemical constituents and pharmacological activities of *Celosia cristata* were presented in this review.

KEYWORDS: Secondary metabolites, *Celosia cristata*, Pharmacological activities, Chemical constituent etc.

1. INTRODUCTION
1.1. Description
They are annual plants of tropical origin and are herbaceous meaning they lack a woody stem. They grow well in both humid and arid conditions and their flowers can last for up to 8 weeks.[1] A high number of seeds can be produced by each flower, up to 1,500 per gram or 43,000 per ounce. The plant often grows up to 30 cm (1 ft) in height, though many are smaller. The leaves are either green or bronze/maroon, depending upon the cultivar. The flower can be broken into three parts: their spikes, plumes and crests vary from one another but have standard commonalities they are usually brightly colored, usually red, yellow, pink, or orange, though other colours can be present. In some instances, a variety of colours are present in hybrids.

Fig 1: *Celosia cristata* flowering plant.
1.2. Scientific classification

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<tr>
<th>Kingdom</th>
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<td>C. cristata</td>
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<td>Binomial name</td>
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2. CULTIVATION

The plants are hardy and can be grown easily from the seeds. Since the plants are of tropic origin, they thrive in areas with tropical climate. However, they can also be grown in summer months in the colder climate. The plants being annual plants, grow for only about one fourth of a year. A soil temperature of about 16 °C (60 °F)[2] is ideal for growth. The plants are relatively easy to grow and care for, having few insects that feed on them. Mites, though, are known to feed on the plants. The plants are also susceptible to leaf spotting, root rot and root strangulation.[3] However the former two can be prevented by avoiding a damp soil and the latter by frequent weeding. Also wetting the leaf and flowers should be avoided as they can lead to fungal diseases.

3. PROPAGATION OF HERB

Seed - sow early to mid spring in a warm greenhouse. Germination should take place within 2 weeks. When large enough to handle, prick the seedlings out into individual pots and plant them out after the last expected frosts. Consideration giving them some protection, such as a cloche, until they are growing away strongly.[3]

4. PHYTOCONSTITUENTS

To study the chemical constituents of Celosia cristata Solvent extraction, silica gel column chromatography, Sephadex LH-20 and recrystallization were used for the isolation and purification of the constituents. The structures of the extracts were identified on the basis of spectral analysis, such as UV, IR, 1H-NMR, 13C-NMR and MS. Results showed: From the EtOH extract of Celosia cristata, 6 compounds were isolated and identified as 4-hydroxyphenethyl alcohol (1), kaempferol (2), quercetin (3), β-sitosterol (4), 2-hydroxyoctadecanoic acid (5), stigmasterol (6). 1,4-6 compounds are isolated from Celosia cristata for the first time.[4]

The preliminary phytochemical analysis on the extracts of Celosia cristata showed the presence flavonoids, mucilages, phenolic compounds & tannins, saponins, triterpenoids, alkaloids, carbohydrates, proteins, amino acids, gums and steroids.[5] The plant contained betain, and several sterols. The inflorescence contained amaranthin, isoamarantin, celosianin and isocelosianin. The seeds contain 10.1-12.8% of protein and yield 7.2-7.9% fatty oil. The plant also contained choline esters of hyaluronic acid.[6,7] Six compounds were isolated from the ethanolic extract of Celosia cristata and identified as 4-hydroxyphenethyl alcohol, kaempferol, quercetin, β-sitosterol, 2-hydroxy octadecanoic acid and stigmasterol.[8]

The analysis of Celosia cristata L. Showed that the protein content in dried samples is about 19.40%, 24.60% and 27.04% in the inflorescence, leaf and stalk and seed respectively. These proteins are rich in all kinds of amino acid; many kinds of vitamins such as B1, B2, C, E and beta-carotene are in high content and dietary fiber and inorganic elements are abundant, the amount of fat in seed is about 10.1%.[9] The total polyphenols, flavonoids and tannin contents of methanolic extracts on the cockscome flowers were 6.80, 2.34 and 6.23mg/g extract residue, respectively.[10] Cochliophilin A (5-hydroxy-6, 7-methylenedioxyflavone) as a host specific attractant towards zoospores of Aphanomyces cochlioides was isolated from Celosia cristata, that is susceptible to the pathogen. Its content in Celosia seedlings was quantified as 1.4 µg/g fresh weight. A new iso flavone, cristatein (5-hydroxy-6-hydroxymethyl -7,2 0 -dimethoxyisoflavone, 2) and five known flavonoids were also identified.[11,12]

The changes of flavonoid compounds in Flos Celosiae cristatae were determined after carbonizing processed. Among the ten batches of processing samples, these compounds were not determined in two batches, but were found in the other eight batches, with the content of kaempferol as 0.002 -0.025% and isorhamnetin as 0.001 - 0.011%.[13] Five saponin, cristatain, celosin A, celosin B, celosin C and celosin D were isolated from the seeds of Celosia cristata.[14] A new triterpenoid saponin, semenoside A, was isolated from Semen Celosia cristatae.[15] Two glycoproteins, CCP-25 and CCP-27 were purified from the leaves of Celosia cristata [16]. However, eighteen compounds were isolated and fifteen compounds were identified, they were p-hydroxyphenylethanol, kaempferol, quercetin, cristatain, celosin A, celosin B, celosin, sphingosine, β-sitosterol, stearic acid, stigmasterol, daucosterol, palmitin acid and n-hexacosonic acid.[17]

5. TRADITIONAL USES OF CELOSIA HERB[18]

I. Celosia, also known as wool flowers and cockscomb, is a member of the amaranth family and originated from the native regions of Asia and Africa. The leaves and the young shoots can be cooked and eaten as a vegetable.
II. The leaves also have a soft texture and a mild spinach-like taste. They are also pepped up with such things as hot pepper, garlic, fresh lime and red palm oil and eaten as a side dish.

III. This impressive botanical is used to treat uterine bleeding, bloody stool and bleeding haemorrhoids. Indeed, every part of the celosia plant occupies a valued niche in the world of natural healing.

IV. The flowers bring diarrhoea under control while the leaves are used as dressings for boils and sores. The seeds ease stresses centered within the chest and they are also rendered into poultices applied to broken bones.

V. Celosias are one of the most eye-catching tender annuals to grow in the garden, with the three types of Celosia being easily distinguishable from one another: plumes, crests, or spikes.

VI. Recent studies have shown that an extract from Celosia used as an alcohol solution may help heal burns and wounds faster.

VII. It has also been used in the past for skin sores, eruptions and mouth sores. It is not proven to speed up healing yet but studies are still being conducted to determine if it can be used for medicinal purposes.

VIII. It is also not unheard of for the plant to be used to treat problems with the eye as well.

IX. Flower tops have been used for amenorrhoea, dysentery, spitting up blood, haemorrhoids, leucorrhoea, and atypical uterine bleeding.

X. As a parasiticide it is very effective against Trichomonas, a 20% extract can cause the Trichomonas to disappear in 15 minutes. The seed is hypotensive and ophthalmic.

XI. Celosia seed is able to clear liver fire, which makes it an ideal herb for syndromes of hyperactivity of liver-yang, for example hypertension.

6. PHARMACOLOGICAL ACTIVITY

6.1. Haemostatic effect

Five days after mice were given decoction of Flos Celosiae cristatae with the dosage of 17g/kg, they were compared with a control group. It emerged that the bleeding time (BT) was shortened greatly (P<0.01). Seven days after rabbits were given the same decoction with the dosage of 1.7g/kg, it was found that the coagulation time (CT), prothrombin time (PT) and plasma recovery (PRT) were shortened (P<0.05), and the euglobulin lysis time (ELT) was markedly shortened (P<0.01) in comparison with control.[19]

6.2. Hepatoprotective activity

A new triterpenoid saponin, semenoside A, was isolated from Semen Celosia cristatae. The hepatoprotective activity of semenoside A with an oral dose of 1.0, 2.0 and 4.0mg/kg, respectively, were investigated by carbon tetrachloride (CCL₄)-induced hepatotoxicity in mice. The results indicated that it had significant hepatoprotective effects (p < 0.01).[20] Cristatain saponin exhibited significant hepatoprotective effect on carbon tetrachloride (CCL₄) and N, N-dimethylformamide (DMF)-induced hepatotoxicity in mice, which were evidenced by significant decreases in the values of asparate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) of serum and histopathological examinations compared to controls.[21]

The antioxidant potential and protective effects of Celosia cristata L. (Family: Amaranthaceae) flower (CCF) extracts on tert-butyl-hydroperoxide (t-BHP)-induced oxidative damage in the hepatocytes of Chang cells and rat livers was studied. In vitro, CCF extracts exhibited protective effect through their radical scavenging ability to enhance cell viability, prevent reactive oxygen species (ROS) generation and inhibit mitochondrial membrane depolarisation in t-BHP-induced hepatotoxicity in Chang cells. In vivo, oral feeding of CCF (100mg and 500 mg/kg of body weight) to rats for five consecutive days before a single dose of t-BHP (2mmol/kg, i.p.) showed a significant (p<0.05) protective effect by lowering serum levels of glutamate oxaloacetate transaminase (GOT) and glutamate pyruvate transaminase (GPT). The extract decreased the hepatic levels of lipid peroxidation (MDA) and serum
level of triglyceride (TG) against t-BHP-induced oxidative stress. The histopathological hepatic lesions induced by administration of CCl4 were remarkably ameliorated by cristatina. Furthermore, it appeared that luteolin display hepatoprotective property in CCl4 induced liver injury in mice.

6.3. Cytotoxicity
The Cytotoxicity of water and organic solvent extracts were determined in the fibroblast cells Cos7 and in four cancer cell lines: HeLa, HepG2, SK-Hep1 and LS 174T. The aqueous extracts were also screened against BVDV and HBV, whereas organic solvent extracts were assayed on T. brucei. IC50 of the water extracts against Cos7, HeLa, HepG2, SK-Hep1 and LS 174T were 263.9, 2773.5, 200, 180 and >200 μg/ml respectively. IC50 of CH2Cl2 extracts against HeLa and Cos 7 were 472.0 and 136.0 μg/ml, while IC50 of MeOH extracts against same cell lines, were 499.8 and 77.2 respectively.

6.4. Antioxidant effects
The anti-oxidant and anti-aging activity of Celosia cristata were studied. Celosia cristata L. ethanol extract had anti-oxidant activity in a dose-dependent manner in 1-diphenyl-2-picryl-hydrazyl (DPPH) radical scavenging. Ethanol extract had anti-oxidant activity in a dose-dependent manner. Silica dose-dependently increased the intracellular ROS generation in RAW 264.7 cells. Celosia cristata L. ethanol extract showed anti-aging effects, the hyaluronidase inhibitory effects and elastase activity inhibitory effects were relatively strong, which suggesting the Celosia cristata L. ethanol extract might be used as hydration and anti-wrinkle agents.

The antioxidant compounds and antioxidant activities of the methanolic extracts and solvent fractions from cockscomb flowers were studied. To determine the antioxidant compounds in the methanolic extract and solvent fractions, the total polyphenol, flavonoid and tannin were measured by spectrophotometric methods. These were evaluated for antioxidative activities by DPPH and ABTS radical scavenging activities. The total polyphenol, flavonoids and tannin contents of methanolic extracts on the cockscomb flowers were 6.80, 2.34 and 6.23mg/g extract residue, respectively. The DPPH and ABTS radical scavenging activities of the methanolic extracts on the cockscomb flowers were 52.43 and 107.01mg Trolox equivalent antioxidant capacity per g extract residue, respectively.

The antioxidant activity test of Celosia cristata antiviral proteins (CCP-25 and CCP-27) using ferric reducing antioxidant power (FRAP) assay in vitro indicated that these proteins are strong antioxidants. The increase in activities of redox-enzymes such as peroxidase, catalase and polyphenol oxidase on tobacco mosaic virus (TMV) inoculation of test plants was inhibited when plants were treated with CCP-25 before TMV inoculation. The activity of phenylalanine ammonia lyase, involved in biosynthesis of antioxidative compounds was also inhibited.

6.5. Adipogenic effect
The in vitro the capacity of a Celosia cristata extracts to impact the adipogenic potential of nativehuman adipose tissue progenitor cells, i.e. commitment and differentiation towards adipogenic lineage, was evaluated. Native adipose tissue progenitor cells were isolated by immunoselection/depletion approaches from human subcutaneous adipose tissues. Two distinct cell culture conditions were used to assess the effect of Celosia cristata extract on commitment and differentiation of progenitor cells. Cells were cultured either in differentiation medium for 10 days in the presence/absence of Celosia cristata extracts to study the impact on differentiation or first cultured in a commitment-inducing medium, with or without Celosia cristata extract, for 48 h and then cultured 10 days in differentiation medium to assess the impact on commitment. In both experimental series, the fate of progenitor cells was studied by quantification of lipids and by determining the expression of key genes involved in adipogenesis. The Results showed that Celosia cristata extract reduces lipid content of progenitor cells undergoing differentiation. This reduction correlates with a reduced expression of C/EBPα. When progenitor cells are placed in commitment-inducing conditions, Celosia cristata extract induces a more potent reduction of lipid content. This reduction correlates with a decrease in the expression levels of master genes involved in adipogenesis: the genes of transcription factors PPARγ2 and C/EBPα as well as marker genes coding for LPL and GPDH.

6.6. Antimicrobial and anthelmintic profile
Celosia cristata flowers showed antioxidant properties and antimicrobial effect. It also had sun protection effects. The antimicrobial properties of ethanolic, methanolic and other solvent extracts of Celosia cristata L. was evaluated against microorganisms, Staphylococcus aureus, Bacillus subtilis, Salmonella typhimurium, Escherichia coli, Pseudomonas aeruginosa and Candida albicans. The minimal inhibitory concentration (MIC) values of the extracts against animal pathogenic bacteria and yeast were assessed using the broth microdilution methods. Results showed that different extracts differed clearly in their antimicrobial activities. MIC values in the range of 0.125 to 1mg/ml hexane fraction of methanolic and ethanolic extracts exhibited good activity against Staphylococcus aureus (0.125mg/ml), Bacillus subtiliss (0.5mg/ml) and Candida albicans (1mg/ml) and dichloromethane fraction showed similar results. Preinoculation treatment with Celosia cristata leaf extract prevented lesion production by sunnhemp rosette virus, tobacco mosaic virus and potato virus X in several local lesion hosts. The extract inhibited lesion formation only in treated areas and did not act on the virus directly, but only via the host. The persistence of inhibitory activity in
test hosts for up to 6 days indicates that the site of virus attachment is blocked semipermanently.\[31\]

Two N-terminally blocked antiviral glycoproteins, CCP-25 and CCP-27 were purified from the leaves of *Celosia cristata*. Study the anti-BVDV toxicity on EBrT cells, anti-BVDV protection in EBrT cells and anti-HBV effect in Hep G2, showed that the plant had no anti-BVDV toxicity on EBrT cells, anti-BVDV protection in EBrT cells, but it had anti-HBV effect in Hep G2 in high concentration.

An antiviral protein named CCP-27 was purifield from the leaves of *Celosia cristata* at the post-flowering stage by anion-exchange, cation-exchange and gel-filtration chromatography. It exhibited resistance against sunnhemp rosette virus in its test host Cymoposis tetragonoloba. It also exhibited deoxyribonuclease activity against supercoiled pBluescript SK+ plasmid DNA. It was found to nick supercoiled DNA into nicked circular form at lower protein concentration followed by nicked to linear form conversion at higher protein concentration. CCP-27 also possesses strong ribonuclease activity against Torula yeast RNA. Two antiviral glycoproteins, active against mechanical transmission of two tomo virus, tobacco mosaic virus and sunnhemp rosette virus and citrus ring spot virus (ungrouped), were purified from the dried leaves of *Celosia cristata*. These proteins, called CCP-25 and CCP-27, have M(r) 25 and 27 kDa. Their concentration was found to vary between the pre-flowering and post-flowering stages of *C. cristata* 90% lesion formation at a concentration of 20-30 µg ml(-1). They were resistant to proteases in the native state, but were readily digested when denatured. Both of them imparted actinomycin D sensitive resistance by inhibiting local lesions on Nicotiana tabacum cv. Samsun NN by tobacco mosaic virus. Their application, individually, also resulted in high resistance in systemic hosts to sunnhemp rosette virus and citrus ring spot virus.\[32\]

Antiviral protein and antioxidant activity: Proteins CCP-25 and CCP-27 isolated from *Celosia cristata* leaves studied for correlation between its antiviral and antioxidant activity. Antiviral proteins showed strong antioxidant activity through increases in activity of redox enzymes such as peroxidase, catalase and polyphenyl oxidase. It was evaluated using ferric reducing antioxidant power assay.\[33\]

The chloroform, methanol and aqueous extract of *Celosia cristata* leaves (100 mg/ml and 200 mg/ml) were used to determine the parasitism and mortality of earthworms (used as it shows resemblance with intestinal roundworm parasites anatomically and physiologically) in comparison with alendazole (100 mg/ml and 200 mg/ml). Worms placed in both aqueous and methanol extracts of *C. cristata* showed significant paralysis and leads mortality in dose dependent manner. Chloroform extract showed no significant activity against the worms. The results revealed that the aqueous extract had higher significant anthelmintic activity than methanol extract.\[34\]

6.7. Other pharmacological actions

*Celosia cristata* was considered as one of the herbal therapy acting as antitussive.\[35\] Choline esters of hyaluronic acid from the plant, when fed to rats, showed antiluc and gastro-protective effect. The plant prevented fluoride toxicity, the food supplemented with calcium can reduce the effect of high fluoride, and the food supplemented with both calcium and *Celosia cristata* extracts is better. The water extract of *Celosia cristata* could enhance immune function of mice. *Celosia cristata* could strengthen the mouse endurance and increase the deposit of muscle glycogen and hepatic glycogen. The ethanol extract of *Celosia cristata* possesses the actions of lowering lipids and MDA and may prevent fatty liver. The water extract of *Celosia cristata* exhibits a killing effect on Trichomonas vaginalis. *Celosia cristata* injection exhibits obvious effect of inducing abortion in second trimester on pregnant mice, guinea pig and rabbit.\[36\]

CONCLUSION

The recent studies displayed that *Celosia cristata* possessed a wide range of therapeutic activities which were proved that this plant have a potential regenerator capacity of various cells, antiproliferative activity, antimicrobial potentiality, adipogenic potentiality, cytotoxic potential. The wide range of therapeutic potentialities of *Celosia cristata* are mainly due to the presence of various bioactive molecules in flowers, roots, stems, leaves and herbs. This review was innovating the further reconstructing the new biomolecules with potential pharmacological activity of Celosia cristata.

REFERENCES

2. “Celosia Flower”. Archived from the original on 2011-08-09.
3. “Flowers Gallery”.