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A Comprehensive Review on the Therapeutic Potential of *Calliandra haematocephala* Hassk (Red Powder Puff)

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Abstract:

In recent years, the interest and research in medicinal plants have increased in a great deal. *Calliandra haematocephala* is a flowering plant in the family Febaceae, it is commonly called as Red Powder Puff. It is usually cultivated in garden for ornamental purpose therefore it is also called as ornamental plant. A wide range of chemical compounds have been isolated, mainly flavanoids, polysaccharides, alkaloids, glycosides, saponin, steroids, tannins, terpenoids, carbohydrates and proteins. Traditionally it is used as antioxidant and blood purifier. Betulinic acid in *Calliandra haematocephala* is reported to be responsible for antitumor, anti HIV and antirotaviral activity. *Calliandra haematocephala* shows several characteristic pharmacological effects like Antibacterial,Antimicrobial, Antifungal, Gastroprotective, Immunoadjuvant, Antisickling, Antihelmintic, Antidiabetic etc. Hence the present article includes the detailed exploration of phytochemistry and therapeutic aspects of *Calliandra haematocephala* in an attempt to provide a direction for further research.

Keywords: *Calliandra haematocephala*, Ornamental plant, Phytochemistry, Therapeutic aspects.

Introduction:

Throughout human history, medicinal plants have been identified and utilised. A vast range of chemical compounds that are essential to many biological processes can be synthesised by plants.[1] An enormous variety of medications are derived from plants, making them valuable sources of medicine. Plants can be used safely, affordably and effectively for medicinal purposes and they are widely available.[2] The goal of using plants as sources of therapeutic agents is to isolate bioactive compounds for direct use as drugs such as digoxin, digitoxin, and morphine as well as produce bioactive compounds with novel or well-known structures as lead compounds for semisynthesis to produce patentable entities with higher activity or lower toxicity such as metformin, verpamil and amiodarone.[3] Likewise, there are 132 species in the genus *Calliandra*. Few of them are native to Asia or Africa; the majority originate from America.These species exhibit a wide range of pharmacological properties including antiulcerogenic, anticonvulsant, anti-inflammatory, and antimodulatory effects. *Calliandra* species are also utilised in the production of honey, pulp and paper, improved soil, and fodder.[4] Red powder puff, also known as *Calliandra haematocephala* (Hassk), is a species of flowering plant

belonging to the genus *Calliandra* in the family *Febaceae*.[5] Evergreen *Calliandra haematocephala* (Hassk) shrub with forked petiole or axis, smooth leaves, and balls of noticeable dark crimson stamens that resemble powder puffs. It is indigenous to America's tropical and subtropical regions.[6] Hasskarl's description of Calliandra haematocephala was based on specimens grown at the Java Botanic Garden.[5] Calliandra haematocephala is typically used for ornamental purposes in gardens.[4] Analysis using Gas Chromatography/Mass Spectroscopy (GC/MS) demonstrated the presence of methyl esters of fatty acids, triterpene (Lupeol), and sterols. The wide range of actions is caused by the high concentration of flavonoids and phenolic substances.[6] Research indicates that Calliandra haematocephala possesses antiulcerogenic, immunomodulatory, gastroprotective, anticonvulsant, and anti-inflammatory qualities. Because the floral extract has antioxidant properties, it is utilised worldwide as a tonic and blood purifier. Haemorrhoids are treated with its roots. The anticancer, anti-HIV, and anti-rotaviral properties of calliandra are said to be attributed to betulinic acid. It has been used historically as an antibacterial agent.[7]

Table 1: scientific classification of *Calliandra haematocephala*.

Binomial Name	*Calliandra haematocephala* (Hassk)
Common Name	Red Powder Puff
Kingdom	Plantae
Order	Fabales
Family	Febaceae
Genus	*Calliandra*
Species	*haematocephala*

Figure 1: plant of *Calliandra haematocephala*.

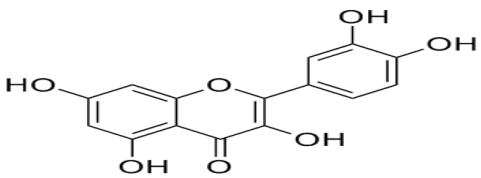
Figure 2: flower of *Callindra haematocephala*.

Figure 3: leaves of *Calliandra haematocephala*.

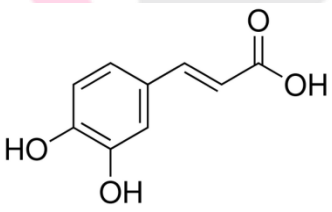
Figure 4: budding.

Phytochemistry:

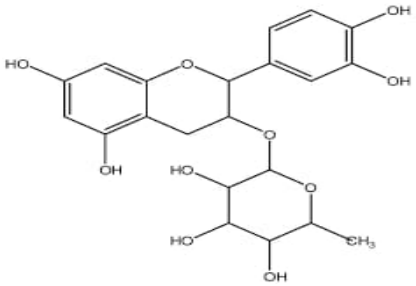
Major phytochemical categories found in various plant components include phenolic chemicals, flavanoids, polysaccharides, alkaloids, glycosides, triterpenes,[9] saponins,[10] steroids, tannins, terpenoids, carbohydrates and proteins.[8] Plants that possess betulinic acid are known for their anticancer, anti-HIV and anti-rotaviral properties. The extract's phenolics, saponins and flavonoids have the ability to scavenge free radicals, which is why it is utilized for hepatoprotection and possesses antioxidant action.[11] The leaves of *Calliandra haematocephala* are said to contain a variety of imino acids including pipecolic acid(A non protein amino acid), trans-4 and trans-5-hydroxypipecolic acid, trans-cis-4,5-dihydroxypipecolic acid and trans-4-acetylaminopipecolic acid.[12] Other Chemical components from acetidin fraction of *Calliandra haematocephala* include p-hydroxybenzoic acid, betulinic acid, caffeic acid, protocatechuic acid, astilbin and neo-isoastilbin. A portion of the substances also produced lupeol.[8] Six flavonoids and one phenolic acid were isolated from aerial parts as well as volatile constituents of fresh aerial parts were extracted.[13] There were sixty-four compounds found accounting for 93.32% of the plant's total volatiles. Consisting of 72.34% and 20.98% respectively, were the oxygenated and non-oxygenated molecules. Various flavonoid and phenolic phytochemicals such as quercetin, gallic acid, caffeic acid and sinapic acid, have been identified. [14] From the leaves and stem of *Calliandra haematocephala* Hassk (*Fabaceae*), three novel acylated quercetin rhomboids have been isolated, and their structures have been established as quercetin 200-O-caffeate, quercetin 300-O-gallate and quercetin 200,300-di-O-gallate. Additionally, 17 recognized substances were identified as myricetin 3-O-β-D-$^4C_1$-glucopyranoside, quercetin, caffeic acid, gallic acid and methyl gallate, myricetin 3-O-(600-O-galloyl)-β-D-glucopyranoside, afzelin and isoquercitrin, myricitrin 200-O-gallate, afzelin 200-O-gallate, myricitrin 300-O-gallate, quercetin 200-O-gallate, and 1,2,3,4,6-penta-O-galloyl- β-D-$^4C_1$-glucopyranose, myricitrin 200,300-di-O-gallate and quercetin 3-O-methyl ether, myricitrin, afzelin 300-O-gallate.[15] Procyanidin-type condensed tannins with a low degree of galloylation made up the majority of the twig, procyanidin-type condensed tannins with a high level of galloylation made up the leaf, and procyanidin-type condensed tannins with no galloylation made up the majority of the stem bark. Furthermore, compared to synthetic antioxidant BHA, all of the produced condensed tannins demonstrated significantly greater antioxidant activities, with leaf showing the highest activity, followed by twig and stem bark. Therefore, it is possible to hypothesize that the quantity of hydroxyl groups on the B-ring and the degree of 3-O-galloylation in condensed tannins may be significant factors in the antioxidant activities of these compounds, and that various sections of *Calliandra haematocephala* may offer natural antioxidant sources.[20] Catechin-3-O-rhamnoside was separated from the bark's ethyl acetate extract and shown a range of antibacterial activities. Hexane fraction analysis resulted in the separation of lupeol and a combination of sterols. β-sitosterol, dodecanoic acid and lupeol are also identified in extract.[13] Three flavonoid glycosides, quercetin-3-O-rhamnopyranoside, keampferol-3-O-(2"-O-galloyl)-rhamnopyranoside and myricetin-3-O-(2",3"-di-O-galloyl)-rhamnopyranoside, were identified along with three flavonoid aglycones, quercetin, kaempferol and myricetin.[14]



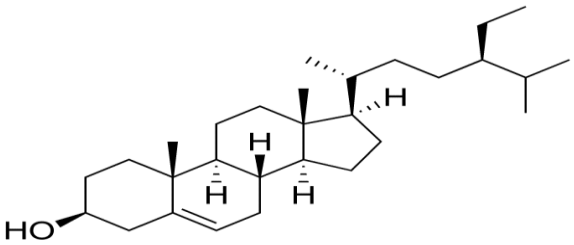
Quercetin



Caffeic acid

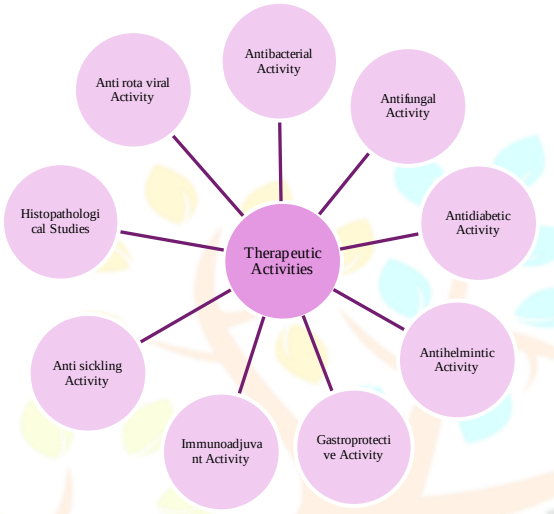


Catechin-3-O-rhamnoside



Beta sitosterol

TherapeuticActivities:



Antibacterial Activity:

According to the research, silver nanoparticles obtained from Callindra haematocephala leaf extract have antibacterial properties against E. coli. Gallic acid in the leaf extract is an important component in the production of silver nanoparticles, giving them antibacterial properties. Additionally, p-hydroxybenzoic acid, caffeic acid, protocatechuic acid, astilbine, neoisoastilbine, and catechin-3-O-rhamnoside were isolated from the bark of Callindra haematocephala by visible chromatographic methods. This drug exhibits a wide range of antimicrobial activity.In another study, an extract from the flowers of the Callindra haematocephala plant was tested in vitro and was found to be more active against Gram-positive Staphylococcus aureus.All doses of ethanolic extract of Callindra haematocephala leaves inhibited Gram-positive and Gram-negative bacteria. It is particularly effective against Pseudomonas aeruginosa; It also shows activity against Shigella flexneri, Bacillus subtilis, Micrococcus spp., Serratia marcescens and Salmonella typhi.Antibacterial properties of ethanolic extract of Callindra haematocephala, antibacterial properties of leaves against Gram-positive and Gram-negative bacteria and potential for adjuvant protection against nosocomial infections.[7]

Antifungal Activity:

Out of the six hundred fungus species that can cause infections, the primary pathogens linked to severe systemic infections are Aspergillusniger, Penicillumchrysogenum, Rizopusmicroporus, Trichodermaviride, and Candida albicans. There has been a recent rise in the number of immunocompromised patients who have died from fatal disseminated infections caused by pathogenic yeast Candida albicans (mucocutaneous infections, meningitis, endocarditis, and osteomyelitis) and other fungal species Aspergillusniger (bronchopulmonaryaspergillosis), Penicillumchrysogenum (necrotizing oesophagitis), Rizopusmicroporus (nosocomial infections), and Trichophytumrubrum (athlete's foot. A few antifungal medications and multidrug resistant strains of the disease increased the incidence and prevalence of diseases ranging from moderate to serious and potentially fatal, including aspergillosis, mucormycosis, candidiasis, and cryptococcosis. The intricate biological makeup of drug resistance mechanisms that have been acquired limits the available treatment options, which ultimately impacts patient care.Important antifungal medications such as azoles, terbinafine, and polyene antibiotics mostly target ergosterol, whereas the more recently developed, effective

medication echinocandins inhibits the peculiar β-1.3-glycan found in fungus cell walls. But these antifungal medications that are specific have higher negative effects.Plants generate secondary metabolites inducibly or constitutively to defend against pathogens that affect humans and animals. The biological activity of flavonoids, tannins, and alkaloids—the constitutive first-class metabolites of phenols—against microbes are stronger. Research has demonstrated that bioactive phenolic compounds obtained from plants exhibit antifungal and antioxidant properties.However, it's also thought that tannins and saponins have strong fungicidal effects and are toxic to harmful fungus species.Significant antifungal activity against infectious, life-threatening infections was demonstrated by Calliandra haematocephala leaves. Therefore, it may work in concert with synthetic antifungal medications to treat mild to severe fungal infections that pose a serious risk to human health.[6]

Antidiabetic Activity:

The critical component of glycemic management and a predictor of both micro- and macrovascular problems in diabetes mellitus is postprandial hyperglycemia. Medicines that lower postprandial hyperglycemia and block the enzymes alpha-amylase and alpha-glucosidase may be a unique treatment for this metabolic condition. These medications prevent the intestinal absorption of simple glucose and its conversion from postprandial starch. Furthermore, alpha glucosidase inhibitors enhance the release of glucoregulatory hormone glucagon-like peptide-1 (GLP-1) into the bloodstream, further contributing to the reduction of glucose levels.As a result, they function well as GLP-1 analogs and are important therapeutic interventions for Type 2 diabetes. When treating newly diagnosed Type 2 diabetes, acarbose, miglitol, and voglibose are used as adjuvants together with metformin and sulfonylureas to suppress the postprandial surge. However, these synthetic inhibitors have more gastrointestinal adverse effects.Increased lipid peroxidation in diabetes modifies lipid metabolism and causes important structural alterations. Long-term hyperglycemia raises the generation of reactive oxygen species, which causes lipid peroxidation and subsequent vascular problems.Bioactive phytochemicals derived from plants are known to lower hyperglycemia and have antidiabetic potential. Therefore, using plants' dual antioxidant and antidiabetic qualities could be a cutting-edge way to avoid the consequences of diabetes.Flavonoids, in particular isoquercitrin, delay stomach emptying, stimulate the expression of glucose transporter 4 in skeletal muscles, and improve insulin sensitivity by inhibiting sodium-dependent glucose uptake in the intestinal mucosa through sodium-dependent glucose transporter-1.[17]

Antihelmintic Activity:

Although piperazine citrate is probably very efficient against pinworms and round worms, it has also been shown to be effective against earth worms. A commercial product (piperazine citrate syrup made by Glaxo Smith Kline Pharmaceutical Limited) was utilized since crude piperazine citrate was not available. Therefore, there may be a small risk of slight differences in the outcome. The early investigation has shown remarkable antihelmintic activity.[10]

Gastroprotective Activity:

Through the measurement of acute stomach lesions caused by acidified ethanol, antiulcerogenic activity was assessed. Three months old, 25 to 35 g male Swiss mice were divided into groups of five and given oral injections of either butanolic extract (100 mg/kg) or the reference compound cimetidine (100 mg/kg) dissolved in vehicle as the positive control after a 24-hour fast. To produce stomach lesions, 200 µl of an acidified ethanol solution (0.3 M HCl/EtOH) was given orally to all animals one hour after the treatments. After giving the ulcerogenic substance to the animals for one hour, the animals were killed, and the stomachs were taken out, opened along the greater curvature, and rinsed with physiological saline to assess the extent of lesion damage. A computerised image analysis method was used to assess the extent of injury to the stomach mucosa from digital images. The ulcer index is defined as the proportion of the overall lesion area (hemorrhagic lesions) to the stomach's total surface area. However, the butanolic extract showed less activity than the reference compound at the same dosage (50% of inhibition at 100 mg/kg). By calculating the proportion of the injured region compared to the control group, the severity of stomach ulcers was measured. The outcomes show that the butanolic extract of C. Haematocephala has gastroprotective properties. This is likely due to its ability to

disrupt the ulcerogenic pathway by reducing or synthesising prostaglandins, which are one of the elements that contribute to gastric cytoprotection.[4]

Immunoadjuvant Activity:

A group of male Swiss mice, aged three months, received two weekly subcutaneous injections of either 100 µl saline (SAL) as the control group or 100 µg ovalbumin (OVA) combined with 100 µg of each adjuvant dissolved in 100 µl of saline as the vehicle. A week following the second vaccination, thicknesses were measured following a subcutaneous challenge with 100 µg OVA in 100 µl saline. The increase in the right footpad was used to measure delayed type hypersensitivity (DTH) reactions. Using a dial gauge that was spring-loaded, the thickness of the footpad was measured prior to 24, 48, and 72 hours after injection. The controls involved injecting 100 µl of saline into each animal's left hind footpad. The ovalbumin-specific responses were calculated by deducting the control mice's immune response to the OVA challenge**.** Aerial part of Calliandra Haematocephala contains saponin and it is important for biological properties. The cellular responses that support complement factor fixation and the release of specific cytokines, like interleukin (IL)-2 and interferon (IFN), as well as the humoral response, which causes increased circulation and secretion of antibodies and cytokines, like IL-4, IL-5, IL-6, and IL-10, are two ways that saponins' immunoadjuvant action can be seen. It justifies the butanolic extract of the calliandra haematocephala plant having an immunoadjuvant activity.[4]

Anti sickling Activity:

Mutant haemoglobin genes inherited from both parents cause sickle cell disease, a common genetic ailment. This condition is caused by a point mutation in the haemoglobin β-globin chain, which results in the hydrophobic amino acid valine replacing the hydrophilic amino acid glutamic acid at position six. Anaemia and crisis are the outcomes of sickle cell disease. The chemical constituents of ethanolic extract of Calliandra Haematocephala contain polyhydroxyl constituents like Gallic acid, methyl gallate, myricetin, quercetin, myricetin 3O-â-D-4C1-glucopyranoside, afzelin, isoquercetin, myricetin 3-O-(6''-O-galloyl)-â-Dglucopyranoside, myricetin 2''-O-gallate, quercetin 2''-O-gallate, afzelin 2''-O-gallate, myricetin 3''-O gallate,afzelin 3''-O-gallate, 1,2,3,4,6-penta-O-galloyl-â-D- 4C1glucopyranose, myricetin 2'',3''-di-O-gallate, quercetin 3- O-methyl ether. Because of these chemical constituents, this plant is highly oxygenated. The antisickling activity that has been observed may be attributed to the presence of these chemicals in Calliandra haematocephala. The antisickling ability of the plant may possibly be attributed to the presence of gallic acid, as studies have shown that this acid can shield human cells from oxidative damage. This suggests that there might be a lot of promise for the callliandra Haematocephala in treating sickle cell disease.[18]

Histopathological studies:

Hepatosis (non-inflammatory disorders), cirrhosis (a degenerative disorder that causes liver fibrosis), and acute or chronic hepatitis (inflammatory liver diseases) are the three categories of liver diseases that continue to be a global health concern. Unfortunately, the best courses of action for liver illnesses remain debatable since traditional or synthetic medications are often ineffective and can have dangerous side effects. Many of the medications on the market have direct or indirect plant-based origins. Because of their efficacy, potential for little adverse effects throughout therapy, and affordable price. A histological analysis of the control group's rat liver revealed the hepatic lobules, which are the structural units of the liver, to have a normal structure. Each lobule is made up of blood sinusoids and hepatocyte cords. Rats administered CCl4 twice a week for two weeks in a row had their liver examined, and findings included fatty alterations, congestion of the central vein, necrosis connected to inflammatory infiltration surrounding the vein, and disruption of the hepatic lobule's structure. The study's demonstrate that an alcoholic leaf extract of Calliandra haematocephala was useful in preventing rats' liver damage caused by CCl4, and it may also have some bearing on the hepatoprotective effect. Pure saponins or total saponins have the potential to show antihepatotoxic activity. Furthermore, histological investigations supported the idea that the plant's high concentration of phenolic and flavonoids, which have the ability to scavenge free radicals, inhibit lipid peroxidation, and boost antioxidant activity, could be responsible for the hepatoprotective effect. The outcomes showed that an alcohol leaf extract from Calliandra haematocephala might be utilised as a hepatoprotective agent.[13]

Anti rota viral activity:

The anti rota viral activities of C. haematocephala extracts at non-cytotoxic concentrations were found in varying degrees of potency, with the methanol extract demonstrating the strongest protection against Rota Viral infection compared to the other extracts. The therapeutic index ranged from 1.3 to 32, and the reduction in virus titer varied from 0.25 log10 TCID50 to 5.75 log10 TCID50. In-vivo, oral administration of the methanol extract at 50 mg and 100 mg/kg/day significantly decreased mortality, virus titers, duration and severity, and the small intestine lesion in Rota Viral-infected mice treated with methanol extract compared to those infected mice not receiving treatment.[19]

Other Activities:

- An amino acid that was extracted from Calliandra haematocephala leaves exhibits insecticidal properties against Spodopterafrugiperda.[13]
- Calliandra haematocephala has antimalarial action in its root bark.[20]
- Stronger antioxidant activity was shown by condensed tanin that was separated from Calliandra haematocephala leaves, twigs, and stem bark.[16]
- Glycosides, flavonoids, and terpenoids are present in the Calliandra haematocephala leaf extract prepared via ethyl acetate. The amount of antioxidants in wound tissues is greatly increased by this extract. Calliandrahaematocephala's antioxidant system may have a healing effect.[21]
- Calliandrahaematocephala's bark and leaves include compounds including myricetin and quercetin, which have been shown to have potent radical scavenging abilities.[21]
- Proteins, carbohydrates, steroids, flavonoids, glycosides, phenolics, saponins, alkaloids, tannins, and lipids are all present in Calliandra haematocephala leaf extract. There is more antibacterial action in flavonoids.[11]

Conclusion:

This review gives an account of the knowledge on the morphology, phytochemistry and pharmacological aspects of *Calliandra haematocephala* (Hassk). Several alkaloids, glycosides, phenolic compounds, flavanoids and tannins have been reported to present in different parts of *Calliandra haematocephala* (Hassk). Every part of this plant and it's principle active constituents like quarcetin, betulinic acid has gained importance for its different pharmacological activities. The pharmacological studies so far have been performed in-vitro and in-vivo. The most important pharmacological properties of this plant include gastroprotective, antidiabetic, antihelmintic, antimicrobial, immunoadjuvant, anti-sickling, antifungal, etc. Traditionally, it's different parts are used in folk medicines as anti-tumor, anti-oxidant, anti-malarial and astringent. It is also used as a blood purifier. Thus, the data and studies presented in this review will help in new product planning and R & D.

Conflicts of Interest:

There are no conflicts of interest and disclosures regarding the manuscript.

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