Review Article

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A REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL ASPECTS OF *CAESALPINIA PULCHERRIMA*

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ABSTRACT
Herbal medicine has become a popular form of healthcare. Even though several differences exist between herbal and conventional pharmacological treatments, herbal medicine can be tested for efficacy using conventional trial methodology. Several specific herbal extracts have been demonstrated to be efficacious for specific conditions. Even though the public is often misled to believe that all natural treatments are inherently safe, herbal medicines do carry risks. Ultimately, we need to know which herbal remedies do more harm than good for which condition. Because of the current popularity of herbal medicine, research in this area should be intensified *Caesalpinia pulcherrima*, a plant widely used in the traditional medicinal systems of India has been reported to possess antibacterial, anti-inflammatory, antioxidant, anticancer and immunosuppressive activities. This review highlights some of the phytochemical and pharmacological aspects of the plant which has been searched during their detailed study.
KEYWORDS: Phytochemical, Pharmacological, *Caesalpinia pulcherrima*

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INTRODUCTION

Caesalpinia pulcherrima (Caesalpiniaceae) is a small thorny tree, 6-9m in height and 15-25 cm in diameter with a few prickly branches. It is commonly known as Patag. In English known as *C. pulcherrima* wood, Brazil wood. The tree grows wild, in mountains and is cultivated in the gardens for its large panicles of yellow flowers. The tree was formerly cultivated in South-East Asia for the red dye, obtained from its heartwood[1], *C. pulcherrima* is distributed in Tamilnadu. Kerala, Karnataka, Andra Pradesh and West Bangal[2]. The leaves of C. pulcherrima are compound, with 8-12 pairs of oblong leaflets and small prickles. Flowers are yellow in terminal and axillary panicles, fruits are woody pods, sub compressed with a hard recurved short beak. Seed are 3-4, yellowish-brown. Wood is orange-red, hard, very heavy (wt, 1.073 kg/m3 , air dry), straight-grained with a fine texture[3]. No comprehensive review article on both the chemical and biological aspects of *C. pulcherrima* has appeared so far. Hence, an attempt was made by us to enumerate the phytochemical and pharmacological aspects in this article.

THERAPEUTIC USES

The wood is bitter, dry, sour, cooling; cure "Vata", biliouness, fever, delirium, ulcers, strangury, urinary concentration and blood complaints. It is considered astringent and sedative. It is useful in vitiated conditions of pitta. An infusion of the wood is a powerful astringent and emmenagogue. It is used in atonic diarrhea and dysentery, and its paste in rheumatism, hemorrhages and to treat wounds. Hot aqueous extract and chloroform extract of wood exhibited inhibitory action on cyclic AMP phosphodiesterase. The methanolic extract of the *C. pulcherrima* lignum showed sleep time-elongation effect in mice and significant anti-hypercholestermic activity. Brazilin dye is reported to have anti-inflammatory activity[4] . The trunk wood possesses antibacterial, demulcent and haemostatic properties. It is used in contusion, wounds, dysmenorrhoea, colic furnuculosis, impetigo, leucorrhoea and anemia. "The plant is one of the ingredients of an indigenous drug 'Lukol' which is administered orally for the treatment of non-specific leucorrhoea"[5].

PHYTOCHEMICAL CONSTITUENTS

The wood is reported to contain a glycoside containing ß-amyrin, glucose and the free amino acids: alanin,

aspartic acid, glycine, praline, valin, leucine, threonine; free sugars: lactose, galactose, 2-deoxyribose and glucose also present[6,7]. Heartwood contains several aromatic compounds, brazilin, C. pulcherrimachalcone, Caesalpin J, Caesalpin P. proto, C. pulcherrimain A, protoC. pulcherrimain B, homoisoflavonoids ß-sitosterol and presence of monohydroxybrazilin and benzyl dihydrobenzofuran derivatives is also reported in the lignum. It also contains C. pulcherrimaol, epiC. pulcherrimaol, 3'-deoxyC. pulcherrimaol, 3'-0- methylC. pulcherrimaol, 3'-0-methylepiC. pulcherrimaol, 3'-0-methylbrazilin, 4-0-methylepiC. pulcherrimaol, C. pulcherrimaon ß, 3- deoxyC. pulcherrimaone ß, 3'-deoxyC. pulcherrimaone ß and dibenzoxocin derivative, 10-0-methyl-protoC. pulcherrimaion ß. Presence of 4,4'-dihydroxy-2'-methoxychalcone, 8- methoxy-bonducellin, quercetin, rhamnetic and ombuin is also reported[8]. Three new homoisoflavonoids, 7-hydroxy-3-(4'-hydroxy-benzylidene)-chroman-4-one, 3,7-dihydroxy-3-(4'-hydroxy-benzyl)-chroman-4-one and 3,4,7-trihydroxy-3-(4'-hydroxy-benzyl)-chroman were isolated form the dried heartwood together with he known compounds 4,4'-dihydroxy-2'-methoxychalcone, 8-methoxybonducellin, quercetin, rhamnetin and ombuin [9]. A novel lactone, brazilide A has been isolated from an oriental crude drug, the heartwood of *C. pulcherrima* and its structure was established by spectroscopic analysis and X-ray crystallography [10]. Dong Seon Kion et al reported the 1H and 13C NMR signals of brazilein. Two new aromatic compounds structurally related to brazilin were isolated and identified from the heartwood .they possessed antihypercholesteremic activity[11]. A novel dimeric methanodibenzoxocinone, named neoC. pulcherrimaone A possessing a unique unprecedented novel carbon framework, has been isolated from the heartwood and its structure was elucidated on the basis of spectroscopic analysis. NeoC. pulcherrimaone competitively inhibited xanthine oxidase in a concentration –dependent manner. A novel biogenetically exclusive benzindenopyran, with a new carbon framework, neoprotoC. pulcherrimain and a new compound protoC. pulcherrimain A dimethyl acetal, were isolated together with protoC. pulcherrimain E-2, neoC. pulcherrimaone A and previously reported phenolic compound[12]. The woody part contains brazilin and brazilein. These are the main constituents of brazilwood were studied by vibrational spectroscopic study[13]. Dong Seon, Kion et al reported the 1H and 13C NMR signals of brazilein 14%. The sterol mixture (campesterol 11.2 . stigmasterol 18.9% and ß-sitosterol 69.9%), brazilin, brazilein. C. pulcherrimain E isolated from *C. pulcherrima* heartwood[14,15]. An essential oil consisting of D-aphellandrene, oscimene tannin gallic acid and saponin[16]. The pods contain 40% tannins[17]. The essential oil with a pleasant odour is found in the leaves. The oil contains d-a-phellandrene and oscimene[18,19]. The seeds contain 7% protein. The amino acids present in the seed-protein are: alanine, cystine, glycine, isoleucine, lysine, threonone, trypophan and valine. Petroleum ether extract of seeds give orange colored fixed oil (18%). The fatty acid content: capric, lauric, myristic, myristoplalmatic, palmitic, palmitoleic, oleic, linoleic, linolenicv and arachidic acids. The fixd oil is a potential ingredient of paints[20]. Two compounds were such as tetraacetylbrazilin and protoC. pulcherrimain isolated from the stem of *C. pulcherrima*[21], C. pulcherrimachalcone is isolated from *C. pulcherrima* . The proposed biosynthetic precursor of brazilin[22], Beak.NI et al reported that C. pulcherrimachalcon and brazilin were isolated from ethyl acetate extract of wood of *C. pulcherrima*[23]. Two compounds were isolated from *C. pulcherrima* L by multiple steps of column chromatography and thin layer chromatography. Structures of the two compounds were determined by spectroscopic methods[24] as 1',4'- dihydro-spiro[benzofuran-3(2H),3'-[3H-2]benzopyran]- 1',6',6',7'-tetrol and 3-[[4,5-dihydroxy-2(hydroxymethyl)phenyl]-methyl]-2,3-dihydro-3,6 benzofuran diol,homo isoflavonoids, 4-O-methylC. pulcherrimaol, protoC. pulcherrimain A, brazilin and caeasalpin J, isolated from *C. pulcherrima*[25]. Isolation of the red dye using both conventional and newly developed microwave method was carried out by Badami.S et al. The conventional heating of 2 h provided 0.656 +/- 0.049 g of the dye and by microwave heating at 540 W for 20 min, the yield obtained was 0.747 +/- 0.047 g [26]. Natural red dyes in old Indian textiles are evaluated by thin-layer chromatographic systems[27]. Phenolic compounds mainly included phenolic acids, flavonoid, tannins, coumarins, lignans, quinones, stilbenes, and curcuminoids are isolated from different traditional medicines including *C. pulcherrima*[28].

PHARMACOLOGICAL ACTIVITIES

Antioxidant Activity

Antioxidant activity of *C. pulcherrima* heartwood was studied both by in vitro and in vivo models. The ethyl aceate, methanol and water extracts exhibited strong antioxidant activity as evidenced by the low IC_{50} values in both 1,1-diphenyl-2-picryl hydrazyl (DPPH) and nitric oxide methods. Administration of the successive methanol and water extracts at 50 and 100 mg/kg body weight given for 4 days priors to carbon tetrachloride (CCl4) treatment caused a significant increase in the level of superoxide dismutase (SOD) and catalase and a

significant decease in the level of thiobarbituric acid reactive substances (TBARS), when compared to CCl4 treated control in both liver and kidney. These changes observed at 100 mg/kg body weight treatment were comparable to those observed for standard vit E at 50 mg/kg treatment[29]. Ethyl acetate extracts of *C. pulcherrima* show the antioxidant activity[30]. Brazilin is an antioxidative substance and it has a protective effect on the BrCCl3-induced depression of microsomal calcium sequestration activity[31].

Anticancer Activity

The chloroform extract of *C. pulcherrima* induces cell death in head and neck cancer cell. The viability of HNSCC4 and HNSCC31 cells (head and neck cancer cell lines) was noticeably decrease compared to that of HaCat cell (control group) in the presence of chloroform extract. Exposure to the chloroform extract of *C. pulcherrima* resulted in an increase in the sub-G1 phase of the cell cycle and condensation and shrinkage of nuclei in the HNSCC4 and HNSCC31 cells. The levels of P 53 and P 21 WAF1/CIP1 were also increased in the HNSCC4 and HNSCC31 cells. It indicate that chloroform extract of *C. pulcherrima* may increased cell death in the HNSCC4 and HNSCC31 cells, which is linked to increased cellular levels of P 53 and P 21 WAF1/CIP1[32]. Anticancer effect of methanol extract on oral carcinoma (KB) and osteosarcoma (HOS) cells were investigated. It seems that the anticancer effect is at least partially due to telomerase inhibitory effect. Dichloromethane, n-hexane and ethyl acetate fractions were screened for anticancer activity, from these the highest anticancer activity was found in dichloromethane fraction which had IC50 value of 4.4 and >4.0 ug/ml against oral carcinoma (KB) cells and osteosarcoma (HOS) cells, respectively[33]. An ethyl acetate extract of the heartwood of *C. pulcherrima* exhibited potent DNA strand –scission activity[34].

Anti-inflammatory Activity

C. pulcherrima show anti-inflammatory activity by inhibition of prostaglandin biosynthesis and nitric oxide production[35]. Brazilin has been known as a natural red pigment. It exhibited the inhibitory effect on lipopolysaccharide (LPS) - stimulated NO production in dose dependent manner. It suggests that suppressive effect of isoform of nitric oxide synthase gene expression by brazilin might provide one possible mechanism for its anti-inflammatory and cancer chemopreventive activity [36]. Brazilin forms a complex with Cu (II) in the presence as well as the absence of DNA. The Cu (II) – brazilin complex exhibited the strand cleavage activity for the pBR322 supercoiled DNA, converting supercoiled forms to nicked form. The presence of various scavengers for the oxygen species suppresses or reduces the cleavage activity of the complex, indicating that the DNA cleavage is oxidative [37]. Administration of brazilein after onset of cerebral ischemia reperfusion can reduce the brain infraction area and improve the neurological score. The mechanism underlying the action were investigated and attributed to the anti-inflammatory effect of brazilein[38].

Immunosuppressive Activity

Heartwood of *C. pulcherrima* has been used in Chinese medicines for treating a variety of immune-mediated pathology and inflammatory disease. Brazilein and ethanol extract could distinctly inhibit the proliferation of T lymphocyte stimulated by Concanavalin A (Con A) and the proliferation of B lymphocyte stimulated by lipopolysaccharides (LPS) and brazilein could suppress mice humoral immune response by plaque forming cell (PFC) test. Brazilein can induce apoptosis in mice spleen lymphocytes by flow cytometry analysis and DNA fragmentation assay, which may be one of the pathway that brazilein inhibited immune-competence of mice lymphocytes[39].

Antidiabetic Activity

Brazilein, active component of *C. pulcherrima* wood, decreases blood glucose in diabetic animals. Brazilein inhibits hepatic Gluconeogenesis by elevating the F-2, 6-BP level in hepatocytes, possibly by elevating cellular F-6-P/H-6-P levels and PFK-2 activity. Increased pyruvate kinase activity may also play a role in the antigluconeogenic action of braziline[40].

Antimicrobial Activity

Antimicrobial activity of *C. pulcherrima* against clinical isolate of methicillin resistant staphylococcus aureus (MRSA) and effect of *C. pulcherrima* extract on the invasion of MRSA to human mucosal fibroblasts (HMFs) was studied. Chloroform, n-butanol, methanol and aqueous extracts showed antimicrobial activity against standerd methicillin-sensitive staphylococcus aureus as well as MRSA[41]. In dilution method methanol extract markedly lowered the minimal inhibitory concentration (MICs) of ampicillin and oxacillin against MRSA. Here methanol extract may have antimicrobial activity and the potential to restore the effectiveness of ß-lactum antibiotics against MRSA and inhibit the MRSA invasion to HMFs. *C. pulcherrima* also shows the antibacterial activity[42].

Vasorelaxing Effect

Methanolic extract and two purified compounds (brazilin and hematoxylin) from *C. pulcherrima* were examined for their relaxant effects in isolated rat thoracic aorta. The methanolic extract significantly and dose dependently relaxed the a-receptor against phenylphrine-

precontracted aortic rings, without affecting passive tension of these vessels. Removal of the vascular endothelium, inhibition of nitric oxide (NO) synthase with 0.1 mM Nw -nitro-L-arginine and of cGMP biosynthesis with 10 µM Methylene blue abolished the vasorelaxant effect of the herbal extract at doses up to 30 µg/mi. similar vasorelaxant effects were observed with brazilin and hematoxylin[43]. The vasorelaxant activity of *C. pulcherrima* was investigated in isolated rat aorta and human umbilical vein endothelial calls.Brazilin induces vasorelaxation by the increasing intracellular Ca(2+) concentration in endothelial cells of blood vessels and hence activating Ca(2+)/calmodulin-dependent NO synthesis. The NO is released and then transferred into smooth muscle cells to activate guanylyl cyclase and increase cGMP content, resulting in vasorelaxation[44].

Antiproliferative Activity

Methanol, methanol-water (1:1) and water extract of *C. pulcherrima* showed selective activity against human cervixHeLa adenocarcinoma, human lung A549 adenocarcinoma, murine colon 26-L5 carcinoma, murine Lewis lung carcinoma (LLC) and murine B16-BL6 melanoma cells. Characteristic morphological change and DNA fragmentation indicated the antiproliferative activity to be due to the induction of apoptosis[45].

Antiplatelet Activity

Brazilin, the major component of *C. pulcherrima* was reported to show antiplatelet activity through the inhibition of phospholipase A2 (PLA2) activity and the increase in intracellular free Ca 2+ concentration ([Ca 2+ [i), its derivatives such as BRX-018, 6aS,cis)-Malonic acid 3-acetoxy-6a9-bis-(2-methoxycarbonyl-acetoxy)- 6,6a,7,11b-etrahydro-indeno[2,1-c]chromen-10-ylester methyl ester, was confirmed as one of the potential antiplatelet agents. Its antiplatelet activity may be based on the inhibitory mechanisms on TXA2 synthesis in stimulated platelets[46]

Analgesic Activity

The ethanol extract of heartwood and three crude fractions (petroleum ether (60-80°c), diethyl ether and ethyl acetate) were subjected to pharmacological screening for analgesic activity using acetic acid-induced writhing in albino mice. The ethanol extract of heartwood and three crude fractions were found to show peripheral analgesic activity[47].

Acaricidal Activity

Acaricidal effect of material derived from *C. pulcherrima* heartwood against Dermatophagoides farinae and Dermatophagoides pteronyssinus were assessed and compared with those evidenced by commercial benzyl benzoate and DEET. The LD (50) values of the methanol extracts were 6.31 and 5.44 µg/cm (3) against D. ferinae and D. pteronyssinus, respectively. Furthermore, the ethyl acetate fraction derived from the methanol extract was approximetly 8.71 more toxic than DEET against D. farinea and 4.73 time more toxic against D. pteronyssinus. From ethyl acetate fraction juglone (5—hydroxy-1, 4-naphthoquinone) was isolated. This indicated that the acaricidal activity of *C. pulcherrima* heartwood is due to the effects of juglone. Accordingly, juglone should prove to be quite useful as a potential control agent, lead compound and house dust mite indicator[48].

Miscellaneous

C. pulcherrima wood promotes blood circulation and removes blood stasis and cause subsidence of swelling and relieves pain. 5-hydroxy-1, 4-naphthoquinone isolated from heartwood of *C. pulcherrima*, when it is tested with Clostridium perfringens, it produced the strong (+++) inhibition at 5 and 2 mg/disk and moderate (++) inhibition at 1, 0.5 and 0.25 mg/disk. Furthermore this isolate revealed a weak (+) growth inhibition against Lactobacillus casei at 5 and 2 mg/disk. It indicates that hydroxyl fractional group of naphthoquinone seems to be required for selective growth-inhibiting activity against C. perfrings. Accordingly the compound derived from *C. pulcherrima* heartwood could be useful as a preventive agent against diseases caused by C. perfringens. *C. pulcherrima* extract from a study of screened. Chinese herbal medicines were found to be a potent agent for the inactivation of human sperm in vitro. Exposure of sperm from healthy donors to this agent showed remarkably reduced sperm motility. The antimotility effect of *C. pulcherrima* is concentration-dependent and about 2.5 mg/ ml is required to reduce motility to 50% the control medium (EC50). This result suggests that this traditional Chinese herbal medicine possesses an antimotility effect on human sperm in vitro and has the potential of becoming in the future a new and acceptable male oral contraceptive. Brazilin show the effect on glucose transport into isolated rat epididymal adipocytes. It may increase glucose transport by recruitment of GLUT4 from intracellular pools to the plasma membrane of adipocytes via the activation of PI3-kinase[51]. Brazilin increased [3H] 2-deoxyglucose uptake in isolated rat epididymal adipocytes. The fact that calcium may be required for the stimulatory effects of insulin on glucose transport suggests that brazilin might also require calcium for its glucose transport-stimulating action. Therefore maintenance of the intracellular calcium concentration, rather than an increase in it, may be essential for the stimulatory action of brazilin on glucose transport[49].

CONCLUSION

Caesalpinia pulcherrima may be considered as a valuable plant in both ayurvedic and modern drug development areas of its versatile medicinal uses. Emphasis has been laid on the pharmacological activity of brazilin and brazilein.

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