

Ethnobotany, phytochemistry and pharmacology of *Biophytum sensitivum* DC

Abinash C. Bharati, Alakh N. Sahu

Department of Pharmaceutics, Institute of Technology, Banaras Hindu University, Varanasi, India

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ABSTRACT

Medicinal plants are widely being used by the traditional medical practitioners for curing various diseases in their day-to-day practice. *Biophytum sensitivum* DC (Oxalidaceae) is used as a traditional folk medicine in ailments such as inflammation, arthritis, wounds, tumors and burns, gonorrhoea, stomach ache, asthma, cough, degenerative joint disease, urinary calculi, diabetes, snake bite, amenorrhoea and dysmenorrhoea. It is a small, flowering, annual herb with sensitive leaves. It grows throughout tropical Africa and Asia, especially in Philippines and the hotter parts of India and Nepal. Phytochemical studies have shown that the major pharmacologically active constituents are amentoflavone and a polysaccharide fraction, BP100 III. Recent pharmacological study shows that it has antioxidant, immunomodulatory, anticancer, anti-inflammatory, chemoprotective, antidiabetic and wound healing potential. This review attempts to describe the ethnobotany, pharmacognosy, traditional uses, chemical constituents, and various pharmacologic activities and other aspects of *B. sensitivum*.

Key words: Amentoflavone, angiogenesis, *Biophytum sensitivum*, seismonasty

INTRODUCTION

Traditional medicines still remain the main resource for a large majority of people treating health problems. *Biophytum sensitivum* DC (Oxalidaceae) is a small, sensitive annual herb, growing throughout the tropical regions of South Asia, Africa and Madagascar. This “little tree plant” is known for its interesting characteristic similar to the touch-me-not plant. The medicinal plant is used traditionally in a number of ailments, such as joint pains, inflammations, fever, malaria, wounds, stomach ache, diabetes, gonorrhoea, tuberculosis, convulsion, thirst, tumor, burns, asthma, phthisis, snake bite, insomnia, arthralgia, arthritis, back pain, bone spur, bursitis, carpal tunnel syndrome, cervical spondylitis, degenerative joint disease, degenerative neck disease, fibromyalgia and leg cramps.^[1-3] It is commonly

known as Lajjaluka in Sanskrit, as it can be observed as inward curling of its leaves in response to touch stimuli. The Mukkutti (flowers) are significant for the people of Kerala, both for its medicinal and for its cultural and traditional values. During the national festival of Onam in Kerala, intricate and colorful arrangements of its flowers laid on the floor, called Pookalam, are made.

Generally, the whole plant is frequently used for medicinal purpose. But an ethnopharmacological survey of six medicinal plants in Mali and West Africa showed that most of the traditional preparations are made from leaves.^[4]

AYURVEDIC PROPERTIES

Rasa: Katu
Guna: Lakhu, Ruksha
Virya: Ushna^[5]

It is medicinally used in traditional Ayurvedic and Siddha systems. It is one of the auspicious herbs that constitute the group “Dasapushpam”, an Ayurvedic formulation.^[6] Ayurveda recommends its powder in gonorrhoeal infection and lithiasis and the decoction is advised for amenorrhoea and dysmenorrhoea. Powder with honey is indicated in Ayurveda for abnormal growths, glandular swellings, especially for hypothyroidism; grounded leaves with water show diuretic effect and relieve thirst in yellow fever. In Philippines, decoction of the leaves is used

Address for correspondence:

Mr. Alakh N. Sahu, Department of Pharmaceutics, Institute of Technology, Banaras Hindu University, Varanasi – 221005, India.
E-mail: ansahu.phe@itbhu.ac.in

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as an expectorant and in Java it is used for asthma. In Siddha system, the grounded leaves are given along with butter milk for diarrhea, grounded seeds are applied over wound and ulcer, the samoolam of this plant is mixed with honey and given for cough and chest congestion, and paste of the leaves is applied over burns and contusions.^[7] Mixture of powder with salt and red oil is eaten periodically for epilepsy in Cameroon.

HABITAT

It is found in wetlands, plains of tropical Africa and Asia, mainly Philippines, and normally grows in shade of trees, at a low and medium altitude and is distributed throughout the hotter parts of India, Nepal, Thailand, Malaysia, Indonesia and Sri Lanka.^[8] *B. sensitivum* is easily propagated from seeds. It thrives on rich soil that is slightly acidic in pH. The plants grow in damp soil. Watering in winter has to be reduced, but the soil should not be allowed to dry. It requires a temperature of 16°C–29°C and medium humidity. Flowering occurs from August to January.^[9]

Synonyms

Common name: Life plant, little tree plant, sensitive plant

French: *allehya*

Bengali: Jhalai

Hindi: Lajalu, Lajjaalu, Lakshmana, Zarer

Indo-China: Chua me

Kannada: Haramuni, Jalapushpa

Malayalam: Mukkutti

Marathi: Jharera, Lajwanti, Lahanmulaka

Sanskrit: Jhullipuspa, Lajjaluka, Panktipatra, Pitapushpa, Vipareetalajjaalu

Tamil: Nilaccurunki, Tintaanaalee

Telugu: Attapatti, Chumi, Jala pupa^[10]

Taxonomical classification

Kingdom: Plantae

Phylum: Tracheophyta

Class: Magnoliopsida

Order: Oxalidales

Family: Oxalidaceae

Genus: *Biophytum*

Species: *sensitivum*

Botanical name: *Biophytum sensitivum* (L.) DC^[11]

BOTANICAL DESCRIPTION

It is an annual herb which looks like a miniature palm, with unbranched, erect, glabrous or hairy stems from 2.5 to 25 cm. Leaves are sensitive, pinnately compound, crowded into rosette on top of stem, and 5–12 cm long, with 6–12 pairs of leaflets. The leaflets are opposite, petiole is short, gradually increases in size upward, being 1.5 cm long, oblong and apiculate at apex. Flowers are dimorphic, 8 mm across yellow peduncle, many, and up to 10 cm long. Sepals are 5, lanceolate, imbricate, and acute with parallel nerves. Petals are 5, yellow with red marking,

connate into salver shaped corolla and much exceeding the sepals, lobes rounded. The fruit is a capsule which is ellipsoid, apiculate, slightly exceeding the sepals. Seeds are ovoid and transversely striate. Stamens are 10, distinct filament free, the five inner ones are longer and styles are five.^[8,12] The fundamental vascular structure of both stem and petiole consists of a circle of collateral bundles, and is often accompanied externally by a sclerenchymatous ring in pericycle. As the name of family implies, oxalic acid is very common in tissue, where it is believed to occur in the form of dissolved potassium oxalate crystals as well as being secreted as calcium oxalate, usually in the form of small solitary cubical and crystal cell. These cells accompany and form sheath to the vascular bundles of the vein in *B. sensitivum*. Leaflets are usually dorsiventral having glandular hair, stalk of varying lengths and unicellular heads. Stomata are rubiacious with at least one and sometimes two subsidiary cells parallel to the pore. Vascular bundles of the vein are provided with enlarged terminal tracheids. The TS of stem shows pericycle bounded by composite and more or less continuous ring of sclerenchyma.^[13]

Seismonasty

Biophytum shows nastic movement in leaves in response to touch, contact with foreign body, drop of rain, wind, vibration, heat and closes its leaflets and the movement is independent of direction of the stimulus. Degree of movement varies according to intensity of stimulus applied. When the leaf apex of sensitive plant is touched lightly, only a few pairs of leaflets close up, and when roughly touched, all the leaflets react in the same way from the apex downward. The pulvinus is a motor structure consisting of a rod of sclerenchyma surrounded by collenchymas. In its extended position, the cells of the entire collenchymas are distended with water, and on receiving the action potential signal by touch, the cells in the lower half of the pulvinus respond by expelling potassium and chlorine ions and taking up calcium ions. This results in an osmotic gradient that draws water out of the affected cells. The lower pulvinus cells temporarily shrink due to water loss. This forces the entire structure to curve down in the manner of a fan. In this contracted position, the pulvinus no longer functions as a support and the petiole droops.^[14,15] In addition, botanists have discovered signaling molecule called turgorin which is thought to be a new class of phytohormone regulating all the leaf movements by controlling the turgor of plant cells. The turgorin molecule contains a strongly acidic, free sulfuric acid group and it was found that diluted sulfuric acid induced leaf closing as strongly as turgorin. Hence, it was concluded that the leaf-closing activity of turgorin is due to the strong acidity of its sulfuric acid group.^[16]

PHYTOCONSTITUENTS

Phytochemical studies of *B. sensitivum* showed that it contains a number of phenolic and polyphenolic compounds, saponin, essential oil, polysaccharides and pectin. The main bioactive constituents found are bioflavonoid, amentoflavone [Figure 1] with minute amount of cupressoflavone. Quantification of amentoflavone by reversed phase high performance liquid

chromatography (HPLC) in methanolic extract of roots, stems and leaves revealed the amounts to be 0.26% in roots, 0.33% in stems, and 0.012% in leaves. Aqueous extract showed much smaller quantities of these phytoconstituents.^[17] Other than amentoflavone, the flavonols present were luteolin 7-methyl ether, isoorientin [Figure 2], 3'-methoxyluteolin 7-O-glucoside, as well as two acids, 4-caffeoylquinic acid and 5-caffeoylquinic acid, that were isolated from aerial parts of *B. sensitivum*.^[18] Further isolation and quantification of C-glycosyl flavones and proanthocyanidin from the plant showed the presence of isoorientin, orientin [Figure 3], isovitexin [Figure 4], isoorientin 7-O-glucoside, isoorientin 2''-O-rhamnoside in methanolic extract of the leaves. From the roots, (-)-epicatechin [Figure 5] and epicatechin-(4 β -8)-epicatechin (proanthocyanidin B2) were isolated and the highest amount of C-glycosyl flavones was found in leaves.^[19] The essential oil of air-dried *B. sensitivum* was investigated by gas chromatography-spectroscopy (GC-FID and GC-MS) and was found to contain mainly 1,4-dimethoxy benzene (24.9%), 1,2-dimethoxy benzene (10.6%) [Figure 6] and 2-methoxy-4-methyl phenol [Figure 7] (3.5%), the monoterpenes (*Z*)-linalool oxide (8.1%) [Figure 8], (*E*)-linalool oxide (5.2%),

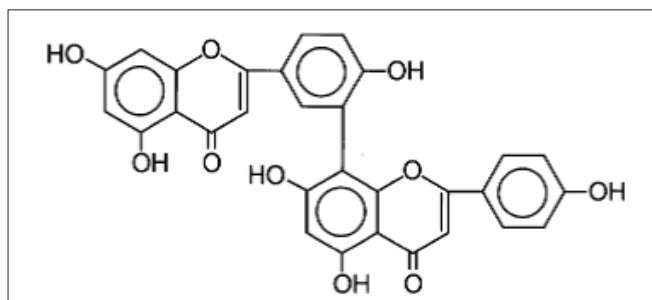


Figure 1: Amentoflavone

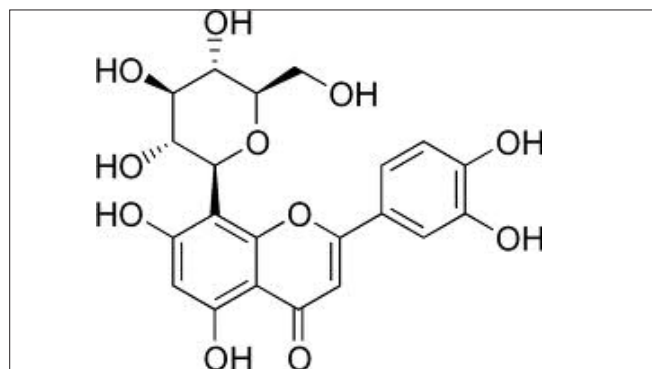


Figure 3: Orientin

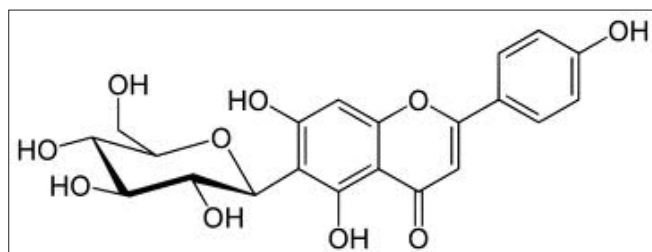


Figure 5: Epicatechin

linalyl acetate (3.4%) [Figure 9], 1-octen-3-ol (9.5%), isophorone (3.1%), and 69 minor compounds.^[20] The water extract of aerial parts [Figure 10] contains a bioactive polysaccharide, BP100 III, major part of which is composed of galacturonic acid and rhamnose, with branches being present on both the rhamnose and galacturonic acid residues.^[21]

Chemical structures of some important constituents of *Biophytum sensitivum*

Pharmacological activities

Biochemical and pharmacological research has shown *B. sensitivum* to possess a number of potential pharmacological activities which are summarized below.

Antioxidant activity

B. sensitivum has significant antioxidant activity both *in vitro* and *in vivo*. An extract of *B. sensitivum* was found to scavenge superoxide radicals generated by the photoreduction of riboflavin and hydroxyl radicals generated by the Fenton reaction and inhibited *in vitro* lipid peroxidation at concentrations of 50, 95, and 20 mg/ml [50% inhibition (IC₅₀)], respectively. The drug also scavenged nitric oxide (NO; IC₅₀ = 100 mg/ml). The extract also induced the dose-dependent scavenging of NO in culture. Intraperitoneal administration of *Biophytum*

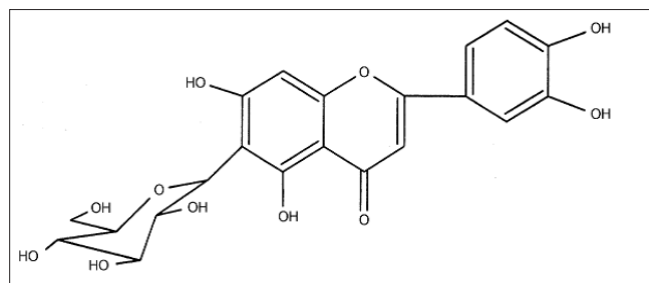


Figure 2: Isoorientin

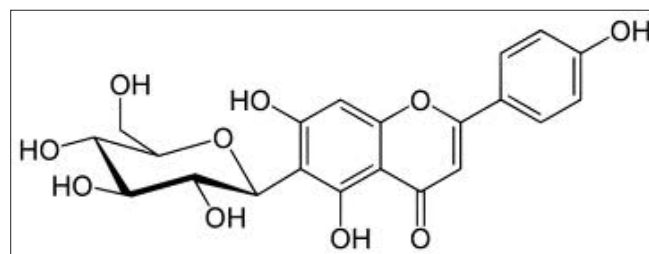


Figure 4: Vitexin

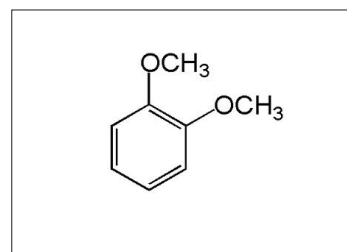


Figure 6: 1,2 dimethoxy benzene

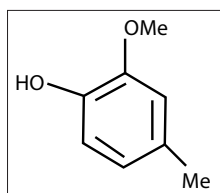


Figure 7: 2-methoxy 4-methyl phenol

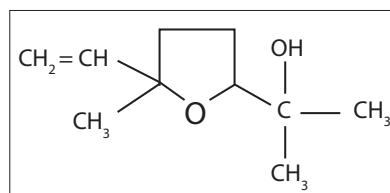


Figure 8: Linalool oxide

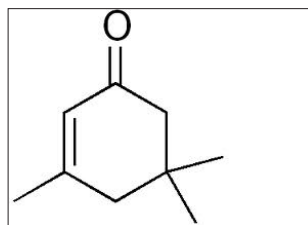


Figure 9: Linalyl acetate

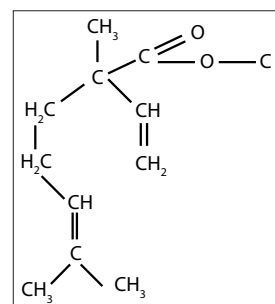


Figure 10: Isophorone

extract inhibited superoxide generation in macrophages *in vivo*. The administration of *B. sensitivum* to mice significantly increased the catalase activity. The extract produced a significant increase in glutathione levels in blood and liver. The levels of glutathione-*S*-transferase and glutathione reductase increased and that of glutathione peroxidase decreased after administering the *Biophytum* extract.^[22]

Anti-inflammatory activity

Amentoflavone (I3', I18-biapiogenin) was isolated from the roots of *B. sensitivum* DC (Oxalidaceae) and proved to be a selective inhibitor of cyclooxygenase (COX)-1 catalyzed prostaglandin biosynthesis when tested *in vitro*, with an IC₅₀ value of 12.4 mM (standard: indomethacin, IC₅₀ = 1.1 mM).^[17] The dose-dependent study indicated that prostaglandin E₂ (PGE₂) production was inhibited both at 10 and 50 mM concentrations of amentoflavone by 52 and 55.5%, respectively. Inhibitory effects of amentoflavone on PGE₂ biosynthesis and on NO production were associated with COX-2 and iNOS mRNA expression, by a rise in NO and corresponding enzyme.^[23] A comparative study was done in the carrageenan-induced rat paw edema model. It was found that the aqueous extract had maximum edema inhibition in comparison to the methanolic extract of root and aerial part.^[24]

Antidiabetic activity

B. sensitivum shows hypoglycemic activity. In alloxan-diabetic rabbits, initial dose–response studies showed that a dose of 200 mg/kg body weight (b.wt.) was optimum for hypoglycemia. A single administration of this dose to 16-h fasted non-diabetic rabbits brought about a 16.1% fall in fasting plasma glucose (FPG) level at the end of 1 h and 2 h, and the hypoglycemic effect persisted at the end of 6 h (13.8% fall). The study also showed rise in serum insulin levels in the treated animals, suggesting a pancreatic mode of action (i.e. insulinotropic effect) of *B. sensitivum*.^[25] Hypoglycemic effect was studied in the alloxan diabetic male rabbits of different severities: subdiabetic (alloxan recovered; AR), mild diabetic (MD) and severely diabetic (SD). Following single dose administration, there was fall in 1 h and

2.5 h glucose values by 25.9% and 27.4%, respectively, in the subdiabetic rabbits, and by 36.9% and 37.7%, respectively, in the mild diabetic rabbits.^[26]

Anti-angiogenic activity

Amentoflavone from *B. sensitivum* at nontoxic concentrations (0.05–0.2 mg/ml) showed significant inhibition of proliferation, migration, and tube formation of endothelial cells, which are the key events in the process of angiogenesis. *In vivo* studies in C57BL/6 mice showed remarkable inhibition (52.9%) of tumor-directed capillary formation and also controlled the production of various factors such as interleukin (IL)-1 β , IL-6, tumor necrosis factor (TNF)- α , granulocyte macrophage-colony stimulating factor (GM-CSF), and vascular endothelial growth factor (VEGF) involved in angiogenesis, thus resulting in anti-angiogenic effect by disrupting the integrity of endothelial cells.^[27]

Anticancer effect

Amentoflavone at a concentration of 10 mg/ml significantly ($P < 0.001$) inhibited NO and proinflammatory cytokine (IL-1 β , IL-6, GM-CSF and TNF- α) production in B16F-10 cells, tumor-associated macrophages (TAMs) and peritoneal macrophages. Further study showed that amentoflavone stimulates apoptosis by regulating *bcl-2*, *caspase-3* and *p53* genes in B16F-10 melanoma cells.^[28] In a recent study by Guruvayoorappan on amentoflavone treatment, it was found to significantly lower the number of lung nodules ($P < 0.001$) and markedly decrease the mRNA expression of MMP-2, MMP-9, prolylhydroxylase, lysyl oxidase, VEGF, extracellular regulated kinase (ERK)-1, ERK-2, TNF- α , IL-1b, IL-6, and GM-CSF in lung tissues.^[29] *B. sensitivum* treatment significantly reduced lung tumor nodule formation, accompanied by reduced lung collagen hydroxyproline, hexosamine, and uronic acid levels, and downregulated the expression of matrix metalloprotease-2 and -9 and at the same time upregulated the lung tissue inhibitor

of metalloprotease-1 and -2 expression.^[30]

Chemoprotective effect

An alcoholic extract of *B. sensitivum* was studied against cyclophosphamide (CTX) induced toxicity in mice. Intraperitoneal (IP) administration of the extract with CTX significantly increased the total WBC count (3356 ± 236 cells/cm²), bone marrow cellularity (15.6 ± 0.42 cells/femur) and α -esterase positive cells (846 ± 30 cells) when compared to control mice treated with CTX alone and also increased the relative organ weight of the spleen and thymus. Further histopathologic analysis of the small intestine also suggested that *B. sensitivum* could reduce CTX-induced intestinal damage.^[31]

Immunomodulatory effect

Administration of *B. sensitivum* extract (500 mg/dose/animal) could inhibit the solid tumor development in mice induced with DLA cells and increase the lifespan of mice bearing Ehrlich ascites carcinoma tumors by 93.3%. The treatment significantly decreased the glutathione level (GSH), serum glutamyl transpeptidase (GGT) activity, and NO level and increased the WBC count, bone marrow cellularity and beta-esterase positive cell.^[32] In another study, the methanol extract of *B. sensitivum* regulated the production of IL-1 β , TNF- α , IL-6, and NO *in vitro* and *in vivo*. The extract inhibited the production of NO and proinflammatory cytokines in lipopolysaccharide (LPS) or concanavalin (Con) A-stimulated primary macrophages.^[33]

Radioprotective

The radioprotective effect of methanolic extract of was studied using *in vivo* mice models. They were exposed to whole body gamma irradiation (6 Gy/animal) after treatment with *B. sensitivum* (50 mg/kg b.wt.), which was followed by estimation that showed reduced levels of alkaline phosphatase (ALP), glutamate pyruvate transaminase (GPT) and lipid peroxide (LPO) levels, and enhanced glutathione (GSH) content in liver and intestinal mucosa.^[34]

Wound healing

Water extract of *B. sensitivum* has been traditionally used for wound healing and immunomodulatory activity. Recent study has shown that the aqueous extract of aerial part has the polysaccharide fraction, BP100 III, and has a monosaccharide composition typical of pectic substances, that exhibits potent dose-dependent complement fixing activity. The highest molecular weight fraction of BP 100 III is BP 100 III.1 which has more potent activity in the complement test system than the native polymer, while the two lower molecular weight fractions are less active than the native polymer. The major part of the BP100 III.1 consists of galacturonic acid and rhamnose sugar having additional arabinogalactan type II in polymer.

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