

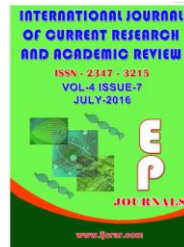


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***Biophytum sensitivum* Chemical Constituents and Medicinal Properties: A Review**

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KEYWORDS

Biophytum sensitivum, phytochemical, phytoconstituents.

A B S T R A C T

World is rich in knowledge with a wide diversity of medicinal plants which provide people with traditional healing methods for diseases in general healthcare area. *Biophytum sensitivum* is a plant with various medicinal properties such as analgesic, anti-pyretic, anti-inflammatory, immunomodulatory, antitumor, antidiabetic, antioxidant, antibacterial, antihypertensive, chemoprotective, radioprotective, antifertility and anti-asthmatic. This review study provides an extensive detail about the phytochemical, pharmacological and folkloric uses of *Biophytum sensitivum*. It has been used indigenously in the field of Ayurveda, Sidhha and Unani for many decades. Various parts of the plant has the presence of variety of phytoconstituents such as flavonoids, saponins, tannins, terpenes, steroids, amino acids, essential oil, polysaccharides and pectin.

Introduction

The genus *Biophytum* is a member of the family Oxalidaceae and distributed in tropical Asia, Africa, America and the Philippines. In India, nine species of *Biophytum* are prominently found and out of these, three species viz. *Biophytum sensitivum* DC. Syn. *Oxalis sensitivum* Linn., *Biophytum reinwardtii* Edgew and *Biophytum umbraculum* Welw. Syn. *Biophytum petersianum* Klotzsch are reported to have ethnomedicinal potential. *Biophytum sensitivum* (L.) DC (*B. sensitivum*), commonly known as 'Life plant', is a mesophytic under-shrub growing in slightly moist places. The plant is

distributed up to an altitude of 1,800 m and is available during the rainy season in moist shady places (Warrier *et al.*, 2014). The plant is traditionally used for centuries in the treatment of various health ailments. It is an important medicinal plant in the Indian traditional system of medicine like Ayurveda (The wealth of India, 1988). It is extensively used for its wide therapeutic potential such as analgesic, anti-pyretic, anti-inflammatory, immunomodulatory, antitumor, antidiabetic, antioxidant, antibacterial, antihypertensive, chemoprotective, radioprotective, antifertility and anti-asthmatic.

Description

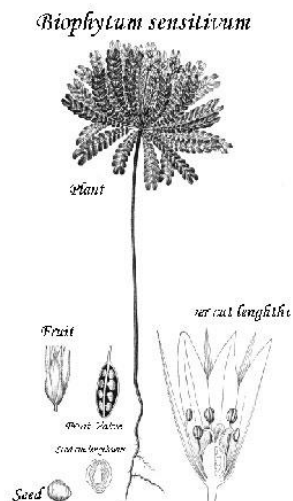
It is a small plant, rarely exceeds 2.5-20 cm in height and form an unbranched woody erect stem. All leaves grow on the top of the stem. Leaves are abruptly pinnate, sensitive, 3.8-12.7 cm long and are made of 8-17 pairs of leaflets. Leaflets are opposite, 1 cm long, terminal pairs the largest and pairs becoming smaller downwards. Flowers are dimorphic, 8 mm across, yellow and crowded at apices of the peducles. The sepals are lanceolate, 7 mm long with parallel nerves. Corolla is much exceeding the sepals. Lobes are rounded and spreading. Style is nearly glabrous. Fruits are ellipsoid capsule. Seeds are prominently ridges and transversely striated. The plant has been observed flowering and fruiting in the month of September to December (CSIR, 2004; Pullaiah, 2006).



Flower of *Biophytum sensitivum*



Whole plant of *Biophytum sensitivum*



Different parts of *Biophytum sensitivum*

Taxonomical classification (Pullaiah, 2006)

Kingdom: Plantae
 Phylum: Tracheophyta
 Class: Magnoliposida
 Order: Oxalidales
 Family: Oxalidaceae
 Genus: *Biophytum*
 Species: *sensitivum*
 Botanical name: *Biophytum sensitivum* (L.) DC

Vernacular names (Editorial Committee of the Flora of Taiwan, 1993)

Common name: Life plant, little tree plant, sensitive plant
 French: *alleluia*
 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

Physiochemical analysis (Kumaratunga, 2003)

Extractable Matter

Crushed, air dried plant material (about 4 g) was weighed to a glass-stoppered conical flask. Solvent (100 mL) was added, weighed, shaken well and allowed to stand for 1h. It was then boiled for 1 h and cooled. The weight was readjusted with specified solvent and filtered. Filtrate (25 mL) was taken, solvent was evaporated and oven dried at 105 °C for 6 h, cooled in a desiccator and weighed.

Total Ash

Crushed, air dried plant material (about 4 g) was weighed to a previously ignited crucible. The material was ignited by gradually increasing the temperature to 550°C until it was free from carbon. The crucible was cooled and weighed

Acid Insoluble Ash

Hydrochloric acid (25 mL, cone. -70 g/L) was added to the crucible containing total ash, covered with a watch glass and boiled gently for 5min. The insoluble matter was collected on an ashless filter paper and washed with hot water until the filtrate was neutral. The filter paper containing the insoluble matter was transferred to the original crucible and ignited to a constant weight.

Water Soluble Ash

Water (25 mL) was added to the crucible containing total ash, covered with a watch glass and boiled gently for 5min. The insoluble matter was collected on an ashless filter paper and washed with hot water. The filter paper containing the insoluble matter

was transferred to the original crucible and ignited for 15 min. at a temperature not exceeding 450 °C. Water soluble ash is the calculated difference in weight between the total ash and the residue remaining after treatment of the total ash with water. Moisture content of the samples was estimated and all the calculations were done on dry weight basis.

Phytochemistry (Abinash *et al.*, 2012)

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 with minute amount of cupressoflavone.

Other than amentoflavone, the flavonols present were luteolin 7-methyl ether, isoorientin, 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*. Further isolation and quantification of C-glycosyl flavones and proanthocynidin from the plant showed the presence of isoorientin, orientin, isovitexin, isoorientin 7-O-glucoside, isoorientin 2''-O-rhamnoside in methanolic extract of the leaves. From the roots, (-)-epicatechin and epicatechin-(4 β -8)-epicatechin (proanthocynidin B2) were isolated and the highest amount of C-glycosyl flavones was found in leaves. 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%) and 2-methoxy-4-methyl phenol (3.5%), the monoterpenes (Z)-linalool oxide (8.1%) , (E)-linalool oxide (5.2%), linalyl acetate (3.4%) , 1-octen-3-ol (9.5%), isophorone (3.1%), and

69 minor compounds. The water extract of aerial parts 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.

Medicinal Uses

The study revealed the insulinotropic effect of *Biophytum sensitivum*. The anti-inflammatory activity of aqueous and methanol extracts of aerial parts and roots were studied in the carrageenin-induced rat paw oedema model. All the extracts except the methanol extracts of aerial parts exhibited anti-inflammatory activity. Apart from this, mostly in ayurveda, this is a tonic, stimulant and in the treatment of stomach ache, diabetes and asthma. It is also used in insomnia, convulsions, cramps, chest-complaints, inflammations, tumors, chronic skin diseases.

Uses as folklore medicine (Council of Scientific and Industrial Research, 1988; CSIR, 2004; Kirtikar *et al.*, 2005)

The whole plant is dried, powdered and given internally to cattle to stop excessive salivation. In the Philippines, the powdered seeds are used as vulnerary and along with butter they are applied to abscesses to promote suppuration. The crushed whole plant is used in chronic skin troubles and is also eaten to induce sterility in man. A decoction of the leaves is given in asthma and phthisis. The plant is also used in chest complaints, insomnia and convulsious cramps and inflammatory tumors. The plant decoction is used in amenorrhoea and dysmenorrhoea and its powder for the gonorrhoeal infection and lithiasis.

Activity studies

Analgesic activity and Anti-pyretic activity (Chatterjee *et al.*, 2008)

The analgesic activity of methanolic extract of *Biophytum sensitivum* showed analgesic effect by Tail flick method at the doses of 100 and 200 mg/kg in mice. The analgesic activity in respective doses was found to be 54.93% and 67.91% against acetic acid induced writhing in mice.

It was concluded that methanolic extract showed significant increase in activity at higher dose. The anti-pyretic activity of methanolic extract of *Biophytum sensitivum* was tested against yeast induced pyrexia in rats. The results showed that the rats treated with plant extract at the dose of 100 and 200 mg/kg showed significant decrease in body temperature and also this decrease is dose dependent.

Anti-inflammatory activity

The methanolic extract of whole plant of *B. sensitivum* was reported to have significant anti-inflammatory activity at the dose of 100 and 200 mg/kg in the carrageenin-induced, histamine-induced and dextran-induced paw oedema model in the rats (Jachak *et al.*, 1999). Anti-inflammatory activity of aqueous extracts of aerial parts and roots, methanol extract of aerial parts and ultrafiltration fractions of a methanol extract of roots of *B. sensitivum* were also evaluated in the carrageenin-induced rat paw edema. All the fractions except the methanol extract of aerial parts inhibited the formation of carrageenin-induced paw edema (Sekhar *et al.*, 2012).

Amentoflavone and procyanidines isolated from the *B. sensitivum* has been reported to possess *in vivo* anti-inflammatory activity and to inhibit COX when tested *in vitro*. Amentoflavone has been reported to downregulates COX-2 expression with concomitant inhibition of NF- κ B/DNA binding activity with inhibition of

degradation of I κ B α and NF- κ B translocation into the nucleus in TNF α -activated A549 cells (Guruvayoorappan *et al.*, 2007).

Immunomodulatory activity

The methanolic extract of *B. sensitivum* increased the total WBC count and number of bone marrow cells. It is concluded that *B. sensitivum* has stimulatory effect on haematopoietic system, differentiation of stem cells and humoral arm of immune system. It is also found that the methanolic extract of *B. sensitivum* stimulates the immune cell system in Ehrlich ascites tumor bearing BALB/c mice, leading to potentiation of immune cell proliferation and NK cell mediated tumor lysis (Inngjerdingen *et al.*, 2008). The pectic polysaccharide (BP1002) obtained from a hot water extract of the aerial parts of *B. sensitivum* is reported to have ability to activate macrophages and dendrite cells (Gronhaug *et al.*, 2011). The pectin polysaccharide (BP11) from the aerial parts of *B. sensitivum* and its fragments (BP11.1 and BP11.2) expressed immunomodulating activity against Peyer's patch immune competent cells and macrophages (Guruvayoorappan *et al.*, 2008).

Antitumor activity (Guruvayoorappan *et al.*, 2007; Inngjerdingen *et al.*, 2008; Gronhaug *et al.*, 2007)

The methanolic extract of *B. sensitivum* found to inhibit the growth of solid tumor induced by Dalton's lymphoma ascites (DLA) cells and ascites tumor induced by Ehrlich ascites carcinoma (EAC) cells. The extract was 100% toxic at a concentration of 0.5 mg/ml to both DLA and EAC cells. It was also found to be cytotoxic towards L929 cells in culture at a concentration of 0.1 mg/ml.

Methanolic extract of *B. sensitivum* have reported to produce apoptotic effect by regulating bcl-2, Caspase-3 and p53 genes in B16F-10 cells and regulates nitric oxide and proinflammatory cytokine production in B16F-10 cells, TAMs and peritoneal macrophages. Amentoflavone isolated from the *B. sensitivum* found to augments lymphocyte proliferation, natural killer cell and antibody dependant cellular cytotoxicity through enhanced production of IL-2 and IFN- γ and restrained serum sialic acid and gamma glutamyl transpeptidase production in Ehrlich ascites carcinoma cells bearing mice.

The aqueous extract of *B. sensitivum* leaves also found to inhibit the tumor volume, viable cell count and enhancement of survival time of DLA bearing mice. It is concluded that aqueous extract of *B. sensitivum* leaves has significant anti-tumor activity.

Antiangiogenic activity (Guruvayoorappan *et al.*, 2007)

Amentoflavone isolated from *B. sensitivum* reported to inhibit tumor directed angiogenesis by disrupting the integrity of endothelial cells and by altering the endogenous factors such as IL-1 β , IL-6, TNF- α , GM-CSF and VEGF that are required for the process of neovascularization. This antiangiogenic activity of amentoflavone is responsible for inhibition of tumor growth and metastasis.

Antimetastatic activity

Amentoflavone isolated from *B. sensitivum* reduced experimental tumor metastasis at the dose of 50 mg/kg for 10 consecutive days in C57BL/6 mice injected with B16F-10 melanoma cells (Guruvayoorappan *et al.*, 2008).

Amentoflavone found to produce antimetastatic effect by altering proinflammatory cytokine production and inhibiting the activation and nuclear translocation of p6, p50, c-Rel subunits of nuclear factor-kappaB, and other transcription factors such as c-fos, activated transcription factor-2, and cyclic adenosine monophosphate response element binding protein in B16F-10 melanoma cells (Guruvayoorappan *et al.*, 2008).

Hypoglycaemic activity (Puri *et al.*, 1998; Puri *et al.*, 2001; Puri *et al.*, 2008; Ananda *et al.*, 2012)

The aqueous solution of *B. sensitivum* leaf extract was administered to rabbits at the dose of 200 mg/kg to study its effect on alloxan-induced diabetes. There was significant improvement in the glycaemic state in the subdiabetic and mild diabetic rabbits only. The results indicated that the *B. sensitivum* has hypoglycaemic effect mediated through pancreatic beta-cell stimulating action. The mild hypoglycemic activity of crude extract of *B. sensitivum* was also demonstrated in the obese glucose-intolerant rabbits at the dose of 200 mg/kg.

Effect of oral administration of aqueous solution of *B. sensitivum* leaf extract at the dose of 200 mg/kg for 28 days was studied in normal and streptozotocin-nicotinamide-induced diabetic rats. The *B. sensitivum* leaf extract treatment significantly reduced the blood glucose and glycosylated haemoglobin levels and significantly increased the total haemoglobin, plasma insulin and liver glycogen levels in diabetic rats. It also increased the hexokinase activity and decreased glucose-6-phosphatase, fructose-1,6-bisphosphatase activities in diabetic rats. The results indicate that aqueous solution of *B. sensitivum* leaf extract possesses significant antidiabetic activity.

Anti-bacterial activity (Natarajan *et al.*, 2010)

The methanol, chloroform, acetone and petroleum ether extracts of leaves of *B. sensitivum* showed antibacterial activity against *B. subtilis*, *S. aureus*, *S. pneumonia*, *K. pneumonia*, *S. typhi*, *P. vulgaris* and *E. coli* by agar well diffusion method in the range of 7-25 mm. The acetone extracts showed remarkable anti-bacterial activity against *B. subtilis*. The extracts from the leaves exhibited considerable and variable inhibitory effects against most of the tested microorganism.

Antioxidant activity (Guruvayoorappan *et al.*, 2006)

B. sensitivum extract was found to scavenge superoxide radicals, hydroxyl radicals and inhibited *in vitro* lipid peroxidation at concentrations of 50, 95 and 20 µg/ml (IC₅₀) respectively. The extract also scavenged nitric oxide (IC₅₀ = 100 µg/ml). The extract found to induce the dose-dependent scavenging of nitric oxide in culture.

Intraperitoneal administration of *B. sensitivum* extract inhibited superoxide generation in macrophages *in vivo* in mice. The extract also produced significant increase in catalase activity, glutathione, glutathione-S-transferase and glutathione reductase. The levels of glutathione peroxidase decreased after administration of *B. sensitivum* extract. These results indicate that *B. sensitivum* extract has significant antioxidant activity both *in vitro* and *in vivo*.

Antihypertensive activity (Titrikou *et al.*, 2007)

The whole plant extract of *B. sensitivum* is reported to possess antihypertensive

potential on guinea pig and rat model. The extract non-competitively antagonized calcium chloride and high-K⁺-induced contraction of isolated rat aorta in a concentration-dependant manner.

The extract also found to inhibit noradrenaline-induced contractions of aorta. These results strongly indicate that antihypertensive effect of *B. sensitivum* results from inhibition of calcium influx via both voltage and receptor operated calcium channels.

Antifertility activity

Ethanol, ethyl acetate, chloroform and n-butanol extracts of whole plant of *B. sensitivum* were studied for the antifertility potential at the dose of 400 mg/kg in female Wistar albino rats. All the extracts inhibited pregnancy with a significant reduction in number of implants as compared to control animals. The ethanolic extract exhibited maximum (100%) antifertility activity. The activity was reversible on withdrawal of the treatment of the extract.

Chemoprotective activity

Intraperitoneal administration of alcoholic extract of *Biophytum sensitivum* increased the total WBC count, bone marrow cellularity, alpha-esterase positive cells and weight of lymphoid organs in mice with cyclophosphamide induced toxicity. The extract treatment found to restore GSH in liver and intestinal mucosa, serum and liver ALP, GPT and lipid peroxidation.

The *B. sensitivum* extract reduced the level of the pro-inflammatory cytokine, TNF- α and increased the levels of cytokines IFN- γ , IL-2 and GM-CSF in cyclophosphamide treated mice. It was concluded that *Biophytum sensitivum* has significant

protective activity against cyclophosphamide induced toxicity (Guruvayoorappan *et al.*, 2007).

Radioprotective activity

Methanolic extract of *B. sensitivum* was found to enhance immunity as well as stimulate production of IL-1 β , IFN- γ and GM-CSF at the dose of 50 mg/kg in mice exposed to whole body gamma irradiation. It is concluded that *B. sensitivum* extract provides protection against radiation-induced hemopoietic damage (Guruvayoorappan *et al.*, 2008).

Larvicidal activity

Acetone extract of leaves of *B. sensitivum* was found to be effective larvicidal, pupicidal and also interfered with the normal development and emergence of adult mosquitoes at the concentration of 10, 15 and 25 mg/L on *Aedes aegypti* mosquito in a dose dependant manner. It is concluded that *B. sensitivum* is having an excellent potential as Larvicidal agent against *A. aegypti* strain (Shivakumar *et al.*, 2012).

Complement fixing activity

The aqueous extract of aerial part has the polysaccharide fraction, BP100 III, and has a monosaccharide composition typical for pectic substances, that exhibits potent dose-dependent complement fixating activity. The fractions of BP 100 III were prepared by the *endo*- α -D-(1 \rightarrow 4)-polygalacturonase degradation. The highest molecular weight fraction is BP 100 III.1 which has more potent activity in the complement test system than the native polymer which consists of galacturonic acid and rhamnose sugar having additional arabinogalactan type II in polymer (Inngjerdigen *et al.*, 2006).

Anti-fungal activity

The acetone extract of leaves of *B. sensitivum* had significant antifungal activity. The leaf extract of *B. sensitivum* inhibited the growth of fungal pathogens *A. fumigatus*, *A. niger*, *C. neoformans* and *Norcardia* sp. in disc method (Vijayan *et al.*, 2010).

Hypocholesterolemic effect

The oral administration of the water extract of leaves of *B. sensitivum* to hypercholesterolemic rabbits at the dose of 200 mg/kg restored the lipid profile near to normal level. It is concluded that *B. sensitivum* has significant hypocholesterolemic effect (Puri *et al.*, 2003).

Safety and toxicity profile

Acute toxicity of *B. sensitivum* extracts were studied in rodents. The methanolic extract of the *B. sensitivum* whole plant is well tolerated up to an oral dose of 4000 mg/kg of body weight as no mortality was observed within a period of 24 h. The aqueous extract of leaves of the plant is studied and found non-toxic at the dose levels of 100, 200 and 300 mg/kg body weight by oral route in mice. The median lethal dose (LD₅₀) of the hexane, chloroform, ethyl acetate, n-butanol and ethanol extracts of the plant were found to be greater than 1 mg/kg when administered by intraperitoneal route to rats.

Conclusion

Biophytum sensitivum used for its wide therapeutic potential such as analgesic, anti-pyretic, anti-inflammatory, immunomodulatory, antitumor, antidiabetic, antioxidant, antibacterial, antihypertensive, chemoprotective, radioprotective,

antifertility and anti-asthmatic. It possess potential to treat different ailments and still needs to be explored for various pharmacological activity. The future aspects of the plant can be anti asthmatic as it contains many of the phytochemicals and work has not been performed yet.

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