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BIOPHYTUM SENSITIVUM DC.: A REVIEW

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ABSTRACT: *Biophytum sensitivum* DC. (Family - Oxalidaceae), commonly known as "Lajjalu" in Northern India, is an annual herb that grows at the foothills of the Himalayas. It is an indigenous medicine, used against "Madhumeha" (Diabetes mellitus) apart from being used as tonic, stimulant, and in the treatment of stomach ache, asthma, insomnia, convulsions, cramps, chest-complaints, inflammations, tumours and chronic skin diseases. It has been scientifically screened for various pharmacological activities such as anti-tumour, antipyretic, immunomodulatory, antidiabetic, antiulcer, radio-protective, larvicidal, antibacterial and antioxidant. Phytochemical investigations showed the presence of flavonoids and phenolic compounds as the major constituents. The present work attempts to compile a review on macroscopic characteristics, chemical constituents, pharmacological reports, clinical studies, formulations and patents listed for this plant. The data has been collected from major databases like Chemical Abstracts, Medicinal and Aromatic Plants Abstracts, PubMed, Scirus, Science Direct, and other online and electronic databases' which has then been systematically collated for a holistic review about *Biophytum sensitivum*.

INTRODUCTION: The nature has blessed us with numerous "gifts" in this world. The plants are one of them, which form the basis of life and give us not only food and shelter but also the medicine to alleviate ailments, relieve pain and for longevity. According to W.H.O. about 75-80% of the world population, mainly in the developing countries still use plant based medicines for primary health care.

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Many of the currently available drugs were derived directly or indirectly from phytochemicals [1]. India has a rich heritage of usage of medicinal plants in the Ayurvedic, Siddha and Unani systems. The country has about 15000 medicinal plants that include 7000 plants used in Ayurveda, 700 in Unani, 600 in Siddha, 450 in Homeopathy and 30 in modern medicines [2].

1. *Biophytum* Genus: *Biophytum* is a genus of about 50 species of annual and perennial herbaceous plants distributed in tropical Asia, Africa, America and Philippines. In India, nine species are found and out of these only three species *viz.*, *Biophytum sensitivum* DC. (*Syn Biophytum petersianum* Klotzsch.), *B. reinwardtii*

Edgew. and *B. umbraculum* Welw. are reported to have ethnomedicinal properties [3]. *B. sensitivum* (Family - Oxalidaceae) commonly known as 'Nagbeli' and "Lajjalu", is an annual herb that grows at the foothills of the Himalayas, around the inner Tarai region (east of Koshi river) in Eastern Nepal [4].

2. Traditional Uses of *Biophytum sensitivum*: In Ayurveda, it is a tonic, stimulant and used in the treatment of stomach ache, diabetes and asthma. It is also used in insomnia, convulsions, cramps, chest-complaints, inflammations, tumours, chronic skin diseases. Pounded plants are given in insomnia [5]. The decoction of the root is given in fever, gonorrhoea and lithiasis. The leaves are diuretic, astringent and antiseptic. Decoction of leaves is used as an expectorant and is given in asthma and phthisis. Paste of the leaf is applied to wounds and cuts to stop bleeding. The powdered seeds are applied to wounds, and (with butter) to abscesses to promote suppuration [6]. The crushed whole plant is used in chronic skin troubles. It is eaten to induce sterility in man. It is a folk medicine against "Madhumeha" (Diabetes mellitus), particularly in Eastern Nepal [7, 8]. 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 [9]. *B. sensitivum* is one of the plants used against snake envenomation. The whole part of plant is used to counteract the snake venom activity [10]. It is one of the auspicious herbs that constitute the group "Dasapushpam", which comprise ten potential herbs which are culturally and medicinally significant to the people of Kerala in India [11]. During the last few decades, extensive research has been carried out to elucidate the chemistry, biological activities, and medicinal applications of *B. sensitivum*, it has been proved to be revolutionary therapeutic plant to combat life threatening diseases.

3. Distribution and Propagation: It is a common weed distributed in wet lands (mostly plains) of tropical Africa, Asia and India, and is found normally in the shade of trees and shrubs, in grasslands, at low and medium altitudes. It is commonly known as by various vernacular names such as Lajjalu (Hindi), Sensitive Plant (English), Mukkutti (Malayalam), Alambusha, Jalapushpa, Panktipatra, Pitapushpa (Sanskrit), Nilaccurunki, Tintanali (Tamil), Jhalai (Bengali), Hara Muni Jalapushp (Kannada), Jharera, Lajwanti (Marathi), Attapatti, Chumi, Jala (Telugu) and Alleluya (French) [12]. It is easily propagated through seeds**.** Seeds are propelled away from the plant by built up tension from when they dry and sown in a mixture of moist peat and sand, after sowing it is covered with a transparent cover to increase humidity. It requires bright indirect sunlight to partial shade, medium humidity and 16 °C to 29 °C temperature, moist soil and water soluble fertilizers during growth season [13].

4. Morphological Description of the Plant: It is an annual herb which looks like a miniature palm, with unbranched, erect, glabrous or hairy stems from 2.5 to 25cm**.**

4.1. Leaves: Leaves are green in color, peripinnate, 3.7-12.7cm long, crowded into a rosette on the top of the stem; leaflets 6-15 pairs, oblong, very variable in size, 6-12 mm long [5, 13]. The remarkable feature of leaflets is their ability to fold together representing an extreme form of "sleep movement" which is exhibited by a lot of members in this family. When applying pressure, tapping or damaging them they fold together in a few seconds. This plant also displays this behavior when the light drops at night. This ability is not restricted to the leaves; the peduncle which carries the flowers has the same ability and also drops at night [14].

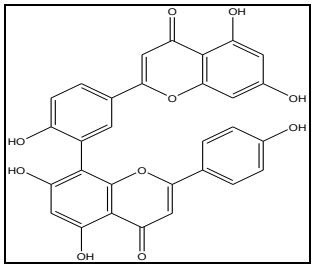
4.2. Flowers: Flowers are dimorphic, normally yellow, white or orange with a red / orange streak in the center of each of the 5 petals on long peduncles of various lengths; petals usually twice as long as the sepals, capsules elliptic, shining [13, 15]. The flowers are many, and crowded at the apices of the numerous peduncles. The sepals are subulate-lanceolate, striate, and about 7 millimeters long. Interesting feature of flowers of this plant is heterostyly. Heterostyly in *B. sensitivum* is responsible for 3 flower morphs. The three morphs (tristylous) each have a stable difference in pistil- and stamen length. The fruit is a capsule which is ellipsoid, apiculate, slightly exceeding the sepals. Seeds are ovoid and transversely striate [14].

5. Regeneration of *Biophytum sensitivum*: *B. sensitivum* has been studied for the potential of regeneration by callus culture and micro-propagation techniques [16]. Microprapagation of leaf and shoot tip explants in MS medium containing 0.05mg l-1 TDZ and 1mg l-1 BAP results in formation of 14 shoots. The *in vitro* regenerated plants from the callus obtained from shoot tip and leaf explants were hardened, transferred to the field, established well and found normal. It is reported the regeneration of the plant through direct and indirect organogenesis and somatic embryogenesis using MS medium supplemented with 2, 4-D or NAA in combination with BAP induced callusing in stem, inflorescence tip and flower bud explants. Eighty percent of the root plantlets and ninety percent of the somatic embryo derived plantlets survived on soil medium [17].

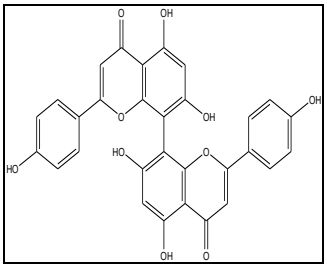
6. Chemical Constituents: The whole plant contains various chemical constituents like phenolic and polyphenolic compounds, saponin, essential oil, polysaccharides and pectin. The main constituent was found to be amentoflavone. Amentoflavone was quantified by reversed phase high performance liquid chromatography (RP-HPLC) in methanolic extract of roots, stems and leaves and the contents were estimated to be 0.26% in roots, 0.33% in stems, and 0.012% in leaves [18]. High-performance thin layer chromatographic (HPTLC) method has been developed for estimation of amentoflavone and was validated for precision (intra- and inter-day), repeatability, and accuracy were 0.52-1.36% [19]. Various chemical constituents of *B. sensitivum* have been summarized in **Table 1**.

TABLE 1: REPORTS ON ISOLATED PHYTOCONSTITUENTS FROM *B. SENSITIVUM*

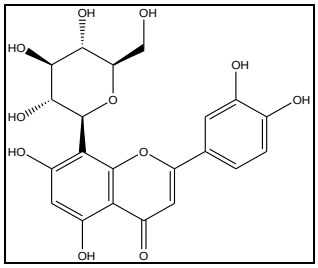
Plant Part / Extract	Isolated Compounds
Aerial parts	Amentoflavone and Cupressoflavone (bioflavone) [20, 21]
	Polysaccharide, BP100 III, which is composed of galacturonic acid and rhamnose [22, 23]
	Luteolin-7-methyl ether, isoorientin and 3-methoxyluteolin 7-O-glucoside (Flavonoids) [20]
	4-caffeoylquinic acid and 5-caffeoylquinic acid [21]
Leaves	Orientin, isoorientin, isovitexin, isoorientin 7-O-glucoside, isoorientin 2-O-rhamnoside [24, 25]
Roots	(–)-epicatechin [21]
Whole plant / Essential oil	1, 4-dimethoxy benzene, 1, 2-dimethoxy benzene, 2-methoxy-4-methyl phenol, (Z)-linalool oxide, (*E*)-linalool oxide, linalyl acetate, 1-octen-3-ol and isophorone [26]



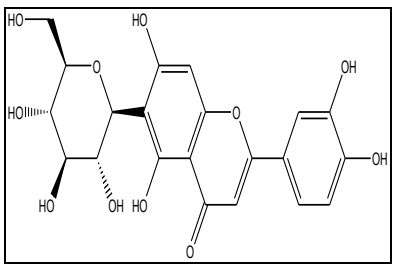
Amentoflavone



Cupressuflavone



Orientin



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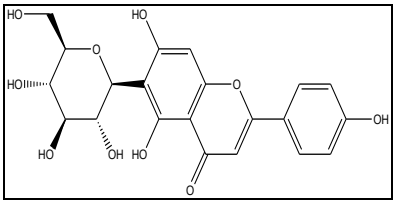

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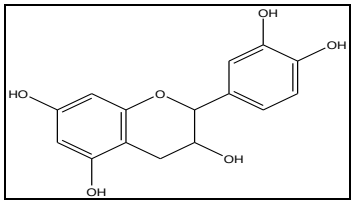
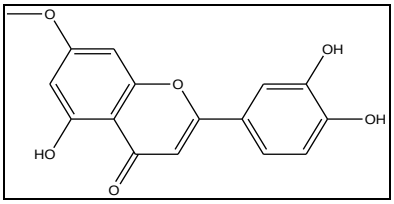
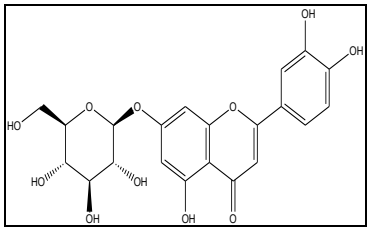


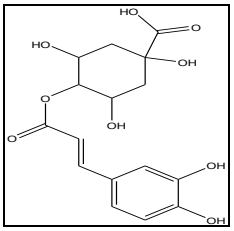
(-)- epicatechin



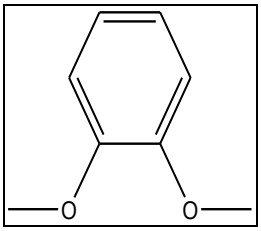
Luteolin-7-methyl ether



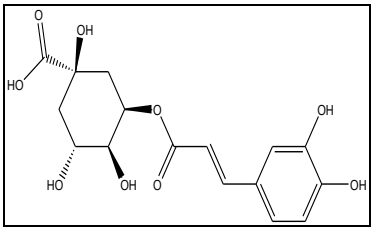
Luteolin-7-o-glucoside



4-caffeoylquinic acid



1, 2-dimethoxy benzene



5-caffeoylquinic acid

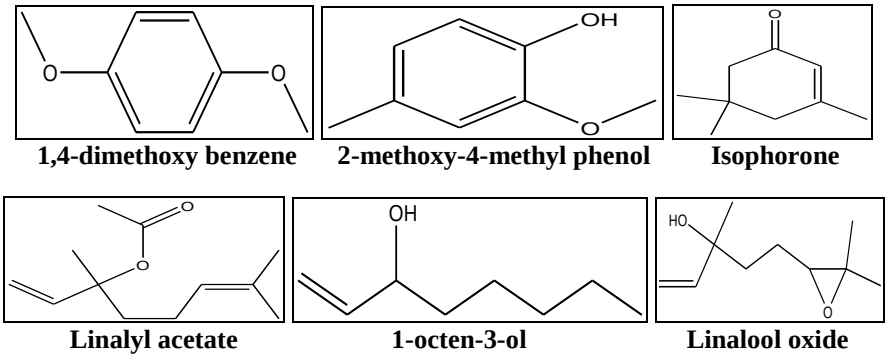


FIG. 1: CHEMICAL STRUCTURES OF IMPORTANT CONSTITUENTS OF *BIOPHYTUM SENSITIVUM*

7. Pharmacological Reports: The plant has been screened for a number of pharmacological activities. It has been reported to exhibit anti-tumor, antipyretic, immunomodulatory, anti-diabetic, antiulcer, radioprotective, larvicidal and antioxidant activities. Reported pharmacological activities of *B. sensitivum* have been summarized in **Table 2**.

TABLE 2: PHARMACOLOGICAL ACTIVITIES OF *BIOPHYTUM SENSITIVUM*

Activity	Plant part / Extract / Fraction / Isolate	Dose / Animals / organisms used	Experimental Model	Mechanism of action / Result
Anti-tumour	Leaves / WE	100 and 200 mg/kg for 28 days / Swiss albino mice	Solid tumour by Dalton's Ascitic Lymphoma	Decreased the tumor volume and viable cell count there by increasing the life span of DAL [27]
	Whole plant / ME	0.1 mg/ml in L929 cell culture and 500 µ/dose/animal / BALB/c mice	Dalton's ascites lymphoma and Ehrlich ascites carcinoma cells	Inhibit the solid tumor development in mice induced with DAL cells and increase the lifespan of mice bearing Ehrlich ascites carcinoma tumors by 93.3%. Also reduced GSH, GGT and NO levels in ascites tumor bearing animals [28]
Apoptotic Effect	Whole plant / ME	10 µ/mL in B16F-10 melanoma cells	B16F-10 melanoma cells	Inhibit production of NO and proinflammatory cytokines such as interleukin-1beta, interleukin-6, GMCSF, tumor necrosis factor-alpha in B16F-10 cells, tumor-associated macrophages, and peritoneal macrophages and induces apoptosis in B16F-10 melanoma cells [29]
	Amentoflavone (biflavonoid)	10 µ/mL in B16F-10 melanoma cells	B16F-10 melanoma cells	It stimulates apoptosis by regulating bcl-2, Caspase-3 and p53 genes in B16F-10 melanoma cells and regulates nitric oxide and proinflammatory cytokine production in B16F-10 cells, TAMs and peritoneal macrophages [30]
Anti-angiogenic activity	Whole Plant / ME	50 mg/kg in B16-F10 melanoma cell-induced capillary formation in C57BL/6 mice	B16F-10 melanoma cells	Significantly inhibited the tumor directed capillary formation induced by melanoma cells and antiangiogenic activity is exerted through its cytokine modulation activity and inhibitory activity against VEGF mRNA expression [31]
	Leaf / Acetone extract	Fertilized eggs of gallus	Chick chorioallantoic membrane (CAM) assay *in vivo*	Prevented signaling of angiogenesis from epithelial cells and significantly inhibited development of capillary networks in CAM and has potential anti-angiogenic property [32]
Chemo protective effect	Whole plant / ME	Swiss albino mice	Cyclophosphamide (CTX) induced toxicity	Significantly increased the total WBC count, bone marrow cellularity and alpha-esterase positive cells compared to control mice treated with CTX alone. Also reduced CTX induced intestinal damage and level of the pro-inflammatory cytokine, TNF-alpha, and increased the levels of cytokines IFN-gamma, IL-2 and GM-CSF [33]
Anti-metastatic effects	Whole plant / ME	Lung tissue of C57BL/6 mice	B16F-10 melanoma cells	Exhibited antimetastatic effects through the inhibition of invasion and motility by regulating the expression of MMPs, prolyl hydoxylase, lysyl oxidase, nm23 gene, ERK-1, ERK-2, STAT-1, and proinflammatory cytokines [34]

	Amentoflavone / (biflavonoid)	50 mg/kg for 10 days/ lung tissue of C57BL/6 mice	B16F-10 melanoma cells	Inhibited tumor metastasis through a regulatory mechanism involving MMP-2, MMP-9, prolyl hydroxylase, lysyl oxidase, VEGF, ERK-1, ERK-2, STAT-1, NM23 and Icytokines in lung tissues [35]
Immuno-modulatory Effect in cancer	Whole plant / ME	0.1 mg/ml in L929 cell culture and 500 µ/dose/animal/ BALB/c mice	Dalton's lymphoma ascites and Ehrlich ascites carcinoma cells	Increased the total WBC count and bone marrow cell count and also enhanced the differentiation of stem cells by increasing the presence of γ-esterase-positive bone marrow cells and have stimulatory effect on the humoral arm of the immune system and production of immune cells by increasing weight of spleen and thymus [36]
	Whole plant / ME	BALB/c mice	Ehrlich ascites carcinoma cells	Significantly enhanced the proliferation of splenocytes, thymocytes, bone marrow cells and natural killer cell activity [34]
Antioxidant Activity	Whole plant / ME	BALB/c mice	*In vitro* Models (Lipid peroxidation scavenge superoxide radicals and NO) and *in vivo* Model	Inhibited lipid peroxidation and scavenge superoxide radicals; and in vivo inhibited Phorbol-12-myristrate-13-acetate-induced superoxide radical generation in macrophages and significant increase in catalase activity, Glutathione-S-transferase, GSH, Glutathione reductase and decrease in glutathione peroxidase [37]
	Whole plant / ME	25 to 900 µg/ml	*In vitro* DPPH radical scavenging activity	Maximum percentage inhibition about 43.96 at concentration of 110.46 µg/ml and the reducing capabilities were found to be in dose dependent manner [38]
	Whole plant / PE, CE, ME and WE	-	*In vitro* DPPH radical scavenging activity , Phosphomolybdenum assay	Significant of maximum free radical scavenging activity was exerted by acetone and methanol extracts [39]
Antidiabetic Activity	Leaves / ME	Rabbit	Alloxan induced diabetes	Significant hypoglycaemic effect (possibly due to pancreatic beta-cell stimulating action) [40]
	Leaves / ME	Rabbit	Non-diabetic and alloxan-diabetes	Insulinotropic effect may be mediated through stimulating the synthesis/release of insulin from the beta cells of Langerhans [41]
	Leaves / WE	200 mg/kg bo for 28 days Adult male wistar rats	Normal and STZ NAD induced diabetic	Significant antidiabetic activity [42]
	Whole plant / ME and WE	200 mg/kg bo albino wistar rats	Alloxan induced diabetes	Significant hypoglycaemic activity [43]
Antibacterial and Antifungal Activity	Leaves / PE, CE, ME and acetone extract	*B. subtilis, S. aureus, Strep. pneumonia, K. pneumoniae, Salm. typhi, P. vulgaris*, and *E. coli*	Agar well diffusion method	Methanol and acetone extracts showed significant antibacterial activity [44]
	Whole plant / PE, CE, ME and WE	*E. coli, K. pneumonia, P. aeruginosa, S. aureus, S. viridians.*	Disc diffusion method	Significant activity against UTI pathogens [45]
	Leaves / Acetone extract	*A. fumigatus, A. niger, C. neoformans*	Disc diffusion method	Significant antifungal activity [46]
Antihyperten-sive and Calcium antagonistic activity	Whole plant / Hydroalcoholic extract	1 mg /ml /kg bo/ Wistar rats	Isolated wistar rat tissue (aorta rings)	Non-competitively antagonized calcium chloride and high-K+-induced aorta contractions in a concentration-dependent manner, have significant hypotensive effect which may result from inhibition of calcium influx *via* both voltage- and receptor-operated calcium channels [47]
Anti-inflammatory activity	Aerial parts / ME and WE	Wistar rats	Carrageenin induced rat paw oedema	Water extract showed significant activity [48]
	Whole plant / ME	100 and 200 mg/kg / Wistar rats	Carrageenin-induced, histamine-induced and dextran-induced paw oedema	Significant anti-inflammatory activity [49]
	Amentoflavone / Roots	10 and 50 mM of amentoflavone	*In vitro*	IC_{50} value -12.4 mM and selective inhibitor of cycloxygenase (COX)-1 catalyzed prostaglandin biosynthesis [50]
Radio-protective Effect	Whole plant / ME	50 mg/kg b.wt Swiss albino Mice	Gamma irradiation Model (6 Gy/animal)	Reduced the levels of alkaline phosphatase (ALP), glutamate pyruvate transaminase (GPT) and lipid peroxide (LPO) levels, and enhanced glutathione

				(GSH) content in liver and intestinal mucosa and radioprotective effect is mediated through immunomodulation as well as sequential induction of IL-1beta, GM-CSF and IFN-gamma [51]
Hypo-cholesterolemic Effect	Leaves / WE	200 mg/kg body weight/day for 28 days/ Male albino mice	Cholesterol induced hypercholesterolemia	Significant hypocholesterolemic effect by improving all the parameters of lipid profile like VLDL/LDL [52]
Anti-pyretic effect	Whole plant / ME	Wistar rats/ 100 and 200 mg/kg bo	Yeast-induced pyrexia in rats	Significant antipyretic property and considerably reduces the febrile response in rats [49]
Analgesic activity	Whole plant / ME	100 and 200 mg/kg	Tail flick method and acetic acid induced writhing method	Significant analgesic activity [49]
Larvicida activity	Leaves / Acetone extract	10, 15 and 25 mg/l	*Aedes aegypti* mosquito	Effective larvicidal, pupicidal and also interfered with the normal development and emergence of adult mosquitoes [53]
	Whole plant / ME	50, 100, 150, 200 and 250 mg/l	*Culex quinquefasciatus*	Moderate Larvicidal activity against *Culex quinquefasciatus* with LC_{50}=215.34 mg/ml
Antifertility Activity	Whole plant / CE, ME and n-butanol extracts	400 mg/kg/	Female wistar albino rats	Methanol extract exhibited maximum (100%) antifertility activity and the activity was reversible on withdrawal of the treatment of the extract [54]
Hypolipidemic and Antiobesity Activity	Stems / Ethyl acetate and ME	200 and 400mg/Kg bo/ Adult albino rats	High fat diet induced rats	Both extracts significantly reduced the elevated levels of (TC), (TG), LDL-cholesterol and VLDL-cholesterol, AST and ALT and elevate the decreased level of HDL-cholesterol and possess good hypolipidemic and anti-obesity activity but ethylacetate extract was found to be more active than methanol extract [55]
Antiepiletic activity	Leaves / ME	50, 100 and 200 mg/kg p.o. / Wistar rats	MES test and PTZ induced seizures	Significantly and dose-dependently reduced the duration of tonic hind limb extension in both experimental models and also delayed the onset of tonic-clonic convulsions induced by pentylenetetrazol in mice [56]
Anti-urolithiatic activity	Whole plant / ME	100, 200, and 400 mg/kg bo for 7 days/ Male wistar albino rats	Zinc disc implantation induced urolithiasis	Significantly prevent the formation of urinary stones and the possible mechanism underlying this effect is mediated collectively through diuretic, antioxidant and anti-inflammatory effects of the plant [57]
Anti-ulcer Activity	Leaves / ME	250mg/kg body weight Wistar albino rats	Aspirin induced models	Showed significant anti-ulcer property, and it may be due to the presence of tannins [58]
Wound Healing property	Aerial parts / ME	1g and 2g for 15 days Wistar strain albino rats	Excision wound Model	Significant wound healing activity and showed higher rate of wound contraction, increased level of Hydroxy proline, hexosamine content, super dismutase, ascorbic acid and decreased lipid [59]

PE, CE, ME and WE represents Petroleum ether, Chroloform, Methanol and Water extract.
B. subtilis, S. aureus, Strep.pneumonia, K.pneumoniae, Salm. typhi, P. vulgaris, and *E. coli, A. fumigatus, A. niger* and *C. neoformans* represents *Bacillus subtilis, Staphylococcus aureus, Streptococcus pneumonia, Klebsiella pneumoniae, Salmonella typhi, Proteus vulgaris, Escherichia coli, Aspergillus fumigatus, Aspergillus niger* and *Candida neoformans* respectively.

8. Toxicity Studies: Acute toxicity of *B. sensitivum* extracts was studied in rodents. The aqueous extract of leaves of the plant was studied and found non-toxic at the dose levels of 100, 200 and 300 mg/kg body weight by oral route in mice [27]. 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 [49]. The median lethal dose (LD_{50}) of the hexane, chloroform, ethyl acetate, n-butanol and ethanol extracts of the plant were found to be greater than 1g/kg when administered by intraperitoneal route to rats [54].

9. Clinical Studies: *Biophytum sensitivum* is used in the treatment of diabetes in the Ayurvedic system of medicines. Traditionally it is said to have a insulin like compound. The mechanism of action is not well understood but appears to have insulin-tropic properties. Clinical studies have been reported on the formulation containing *B. sensitivum* [60]. DB14201 has been marketed since 2002 under Ayurvedic license issued by Drug Controller of the State of Kerala, under the trade name Diabedrink. It is a combination of 16 herbs used in Ayurveda.

It contains *Zizyphus jujube, Terminalia chebula, Mangifera indica, Emblicao-fficinalis, Embelia ribes, Curcuma longa, Aerva lanata, Syzygium cumini, Coscinium fenestratum, Salacia Oblonga, Cyclea peltata, Biophytum sensitivum, Strychnos potatorum, Cyperus rotundus, Vetiveria zizanioides,* and *Centella asiatica* as ingredients. Subject blinded, placebo controlled, randomized clinical studies have been repoted on 30 patients suffering from Type 2 Diabetes in the ages of 29-71 of both gender which were on single oral hypoglycemic agent Glibenclamide, since more than three months but with inadequately controlled blood sugar levels (FBS level >120 mg/dl and/ or PPBS levels >200 mg/dl) on the day of recruitment.

The study period for each subject was 90 days with a follow-up of 15 days thereafter. The entire evaluation was completed in 11 months. It is reported that the herbal formulation DB14201 is safe in T2DM patients when administered along with glibenclamide and improves the effectiveness of glibenclamide in offering better glycemic control. It also provides significant improvement in fasting and post prandial blood sugar levels in comparison to addition of placebo and also significantly reduces HbA1c levels.

10. Formuations of *Biophytum sensitivum*: Herbal creams and gels were prepared by incorporating the dry methanolic extract of whole plant of *B. sensitivum* into emulsifying cream and aqueous washable gel base. It was evaluated for *in vitro* antibacterial efficacy against four different bacterial strains (*Salmonella typhi*, *Staphylococcus aureus, Escherichia coli* and *Bacillus subtillis*) using the agar well diffusion method. The results showed that *B. sensitivum* has high potential as antibacterial agent when formulated as cream and gel for topical use [61]. An optimized tablet formulation was prepared of *B. sensitivum* using the dried whole plant methanolic extract.

It was evaluated for their antioxidative properties *in vitro* based on their total flavonoid content (TFC) against a standard flavonoid, Quercetin and also *in vivo* for antidiabetic activity in Streptozotocin (STZ) induced diabetic rats against Glibenclimide, an antidiabetic drug. The drug exhibited antioxidant and antidiabetic properties of the formulation [62].

11. Patent Related to *Biophytum sensitivum*: Herbal formulation comprising of extracts from selected Indian medicinal plants *Zizyphus jujube, Terminalia chebula, Mangifera indica, Emblicao-fficinalis, Embelia ribes, Curcuma longa, Aerva lanata, Syzygium cumini, Coscinium fenestratum, Salacia Oblonga, Cyclea peltata, Biophytum sensitivum, Strychnos potatorum, Cyperus rotundus, Vetiveria zizanioides,* and *Centella asiatica* as ingredients used for prevention and treatment of diabetes and associated complications has been patented [63].

CONCLUSION: Traditionally the parts of the plant have been known to possess a wide spectrum of medicinal properties namely antiseptic properties, including positive effects in variety of skin infections and in the treatment of diabetes. Antibacterial, antifungal and antidiabetic activities have been proved by the scientific research work. *Biophytum sensitivum* is widely prescribed for the treatment of diabetes in Ayurvedic system of Medicine. The whole plant is also used traditionally in the treatment of various ailments.

The plant has been evaluated exhaustively for various pharmacological activities and reported to possess anti-inflammatory, antipyretic, antimicrobial, antiobesity, antioxidant, anti-diabetic, anti-fungal, anti-cancer, larvicidal, anti-obesity, anti-hypertensive, antiepileptic, wound healing and antifertility activities.

No systematic work has been carried out to isolate bioactive constituents responsible for afore-mentioned bioactivities. The plant contains phytoconstituents like flavonoids, steroids, phenolic compounds but till now only nineteen phytoconstituents have been isolated. Amongst these constituents, only flavonoids (amentoflavone) have been suggested to possess most of pharmacological activities. These observations suggest that detailed investigations are needed with a view to isolate bioactive constituents, and to standardize the plant on the basis of isolated bioactive markers. Only one formulation containing *B. sensitivum* as one of the ingredients has been patented which is used in the treatment of diabetes and diabetic complications. It has been found to be safe in a toxicity studies.

Clinical studies on 30 type 2 diabetic patients have been conducted to observe antidiabetic potential of the plant showed beneficial effects in diabetic patients. Finally, it is concluded that *B. sensitivum* is the source of plenty of bioactive constituents which has the potential to be developed as efficacious and safer drugs.

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REFERENCES:

1. Grover JK, Yadev S and Vats V: Medicinal plants of India with antidiabetic potential. J Ethnopharmacol 2002; 1: 81-100.
2. Das JS: The largest genetic paradise of India lacks biotechnological implementation. Curr Sci 2008; 94: 558-559.
3. The Wealth of India: A Dictionary of Indian Raw Materials and Industrial Products (Raw materials) Revised Edition, Council of Scientific and Industrial Research, New Delhi, India 1988; 6: 151-152.
4. Warrier PK, Nambiar VPK and Ramankutty C: Indian Medicinal Plants-A Compendium of 500 Species. Orient Longman Publishers, India 1: 1994.
5. The wealth of India: A Dictionary of Indian Raw Materials and Industrial Products (Raw materials) First Supplement Series, National Institute of Science Communication and Information Resources, Council for Scientific and Industrial Research, New Delhi, India 2004.
6. Kirtikar KR and Basu BD: Indian Medicinal Plants, Dehradun, International Book Distributor 1: 2005.
7. Puri D, Baral N and Upadhyaya BP: Indigenous plant remedies in Nepal used in heart diseases. J Nepal Med Assoc 1997; 36: 334–337.
8. Pant PC and Joshi MC: Studies on some controversial indigenous herbal drugs based on ethnobotanical research. A review. J Res Educ Indian Med 1993; 12: 19–29.
9. Sri KT, Ushasri S, Shalemu RM, Yamini NP and Anjaneyulu P: *Biophytum sensitivum* DC – An overview. Int J Pharmacol Screen Methods 2013; 3(2): 69-79.
10. Gomes A, Das R, Sarkhel S, Mishra R, Mukherjee S and Bhattacharya S: Herbs and Herbal constituents active against snake bite. Indian J Exp Biol 2010; 48(9): 865–78.
11. Varghese KJ, Anila J, Nagalekshmi R, Resiya S and Jiny JS: Dasapushpam: The traditional uses and the therapeutic potential of ten sacred plants of Kerala state in India 2010; 1(10): 50-59.
12. Tseng-Chieng H and Guojia KW: Flora of Taiwan, Editorial committee of the Flora of Taiwan, 2nd edition 1993.
13. Pullaiah T: Encyclopedia of World Medicinal Plants, Regency Publication, New Delhi 2006.
14. Dutta AC and Dutta TC: Botany for Degree Students, 6th edition, Oxford University Press, Oxford 1997; 724.
15. Pawar T and Vyawahare NS: Phytochemical and pharmacological profile of *Biophytum sensitivum* (L) DC. Int J Pharm Pharm Sci 2014; 6(11): 18-22.
16. Viji MO: Micropropagation of *Biophytum sensitivum* from leaf and shoot explants. VISTAS 2014; 3(1): 152-155.
17. Shivaana MB, Vasanthakumari MM and Mangala MC: Regeneration of *Biophytum sensititum* DC. by organogenesis and somatic embryogenesis. Indian J Biotechnol 2009; 8: 127-131.
18. Bucar F, Jachak SM, Noreem Y, Kartnig T, Perera P, Bohlin L and Schubert ZM: Amentoflavone from *Biophytum sensitivum* and its effect on COX-1/COX-2 catalysed prostaglandin biosynthesis. Planta Med 1998; 64(4): 373-4.
19. Ravishankara MN, Pillai DA, Padh H and Rajani M: A Sensitive HPTLC method for estimation of amentoflavone, a bioactive principle from *Biophytum sensitivum* (Linn.) DC. and *Putranjiva roxburghii* Wall. JPC 2003; 16(3): 3-6.
20. Yun LL and Wan YW: Chemical constituents of *Biophytum sensitivum*. J Chinese Pharm Sci 2003; 55(1): 71-75.
21. Bucar F, Jachak SM, Noreem Y, Karting T, Perera P and Bohlin L: Catalysed prostaglandin M. Amentoflavone from *Biophytum sensitivum* and its effect on COX-1/COX-2 biosynthesis. Planta Med 1998; 64(4): 373-374.
22. Inngjerdingen M, Inngjerdingen KT, Patel TR, Allen S, Chen X and Rolstad B: Pectic polysaccharides from *Biophytum petersianum* Klotzsch and their activation of macrophages and dendritic cells. Glycobiology 2008; 18(12): 1074-1084.
23. Inngjerdingen KT, Coulibaly A, Diallo D, Michaelsen TE and Paulsen BS: A Complement Fixing Polysaccharide from *Biophytum petersianum* Klotzsch, a medicinal plant from Mali, West Africa. Biomacromolecules 2006; 7(1): 48-53.
24. Bucar FS, Jachak M, Kartnig TH, Noreen Y, Bohlin L and Schubert ZM: Phenolic Compounds of *Biophytum sensitivum* and their Activities on COX Catalyzed Prostaglandin biosynthesis. International Symposium of Bioassay Methods in Natural Product Research and Drug Development, Swedish Academy of Pharmaceutical Sciences, Uppsala University, Uppsala, Sweden 1997, 49.
25. Bucar F, Jachak SM, Kartnig T and Schubert ZM: Phenolic compounds from *Biophytum sensitivum*. Pharmazie 1998; 53(3): 651-653.
26. Leopold J, Gerhard B, Andrea W, Mohamed SP and Beena J: Medicinally used plants from India: Analysis of the essential oil of air-dried *Biophytum sensitivum* (L.) DC. Scientica Pharmaceutica 2004; 72(1): 87-96.
27. Bhaskar VH and Rajalakshmi V: Anti-tumour activity of aqueous extract of *Biophytum sensitivum* Linn. Biological Research 2010; 3(1): 76-80.
28. Guruvayoorappan C and Kuttan G. Immunomodulatory and anti-tumour activity of *Biophytum sensitivum* extract. Asian Pac J Cancer Prev 2007; 8 (1):27-32.
29. Guruvayoorappan Cand Kuttan G: Apoptotic effect of *Biophytum sensitivum* on B16F-10 cells and its regulatory effects on nitric oxide and cytokine production on tumor-associated macrophages. Integr Cancer Ther 2007; 6: 373-380.
30. Guruvayoorappan C and Kuttan G: Amentoflavone stimulates apoptosis in B16F-10 melanoma cells by regulating bcl-2, p53 as well as caspase-3 genes and regulates the nitric oxide as well as proinflammatory cytokine production in B16F-10 melanoma cells, tumor associated macrophages and peritoneal macrophages. J Exp Ther Oncol 2008; 7(3): 207-218.
31. Guruvayoorappan C and Kuttan G: Anti-angiogenic effect of *Biophytum sensitivum* is exerted through its cytokine

modulation activity and inhibitory activity against VEGF mRNA expression, endothelial cell migration and capillary tube formation. J Exp Ther Oncol 2007; 6(3): 241-250.
32. Manisha M and Ghanshyam GPG: Effects of the *Biophytum sensitivum* (L.) DC leaf extracts on anti-angiogenic properties by chorioallantoic membrane (CAM) assay. Int J Pure App Biosci 2015; 3(6): 183-191.
33. Guruvayoorappan C and Kuttan G: Evaluation of chemoprotective effect of *Biophytum sensitivum* (L.) DC extract against cyclophosphamide induced toxicity in Swiss albino mice. Drug Metabol Drug Interact 2007; 22(2-3): 131-150.
34. Guruvayoorappan C and Kuttan G: Anti-metastatic effect of *Biophytum sensitivum* is exerted through its cytokine and immunomodulatory activity and its regulatory effect on the activation and nuclear translocation of transcription factors in B16F-10 melanoma cells. J Exp Ther and Oncol 2008; 7(1): 49-63.
35. Guruvayoorappan C and Kuttan G: Amentoflavone inhibits experimental tumor metastasis through a regulatory mechanism involving MMP-2, MMP-9, prolyl hydroxylase, lysyl oxidase, VEGF, ERK-1, ERK-2, STAT-1, NM23 and cytokines in lung tissues of C57BL/6 mice. Immunopharmacol Immunotoxicol 2008; 30(4): 711-727.
36. Guruvayoorappan C and Kuttan G: Effect of *Biophytum sensitivum* on cell-mediated immune response in mice. Immunopharmacol Immunotoxicol 2007; 29(2): 337-350.
37. Guruvayoorappan C, Afira AH and Kuttan G: Antioxidant potential of *Biophytum sensitivum* extract *in vitro* and *in vivo*. J Basic Clin Physiol Pharmacol 2006; 17(4): 255-267.
38. Pallab K, Tapan KB, Pal KT and Ramen K: Estimation of total flavonoids content (tfc) and anti oxidant activities of methanolic whole plant extract of *Biophytum sensitivum* Linn. J Drug Del Ther 2013; 3(4): 33-37.
39. Johnson M, Shibila T, Revathy I, Utchimahali M and Ramesh M: Biopotency of *Biophytum sensitivum* DC. Res Pharm 2015; 5(1): 42-48.
40. Puri D and Baral N: Hypoglycemic effect of *Biophytum sensitivum* in the alloxan diabetic rabbits. Indian J Physiol Pharmacol 1998; 42(3): 401-406.
41. Puri D: The insulintropic activity of a Nepalese medicinal plant *Biophytum sensitivum*: Preliminary experimental study. J Ethnopharmacol 2001; 78(1): 89-93.
42. Ananda PK, Kumarappan CT, Sunil C and Kalaichelvan VK: Effect of *Biophytum sensitivum* on streptozotocin and nicotinamide-induced diabetic rats. Asian Pac J Trop Biomed 2012; 2(1): 31-35.
43. Moumita M, Bandyopadhyay D, Pramanik K, Chandra C and Tapan K: Antihyperglycemic activity of *Biophytum sensitivum* (L.) DC in alloxan diabetic rats, Orient Pharm Exp Med 2007; 7 (4): 418-425.
44. Natarajan D, Shivakumar MS and Srinivasan R: Antibacterial activity of leaf extract of *Biophytum sensitivum* (L.) DC. J Pharm Sci Res. 2010; 2: 717-720.
45. Jagadeesan S, Natarajan V and Vijayan Rajitha E: Antibacterial activity of selective plant extracts against urinary tract infection causing organisms. J Microbiol Biotechnol Res 2013; 3(3): 1-5.
46. Vijayan MN, Barreto I, Dessai S, Dhuri S, D' Silva R and Rodrigues A: Antimicrobial activity of ten common herbs, commonly known as 'Dashapushpam' from Kerala, India. Afr J Microbiol Res 2010; 4(22): 2357-2362.
47. Titrikou S, Eklu GK, Mouzou A, Aklikokou K and Gbeassor M: Calcium antagonistic activity of *Biophytum Petersianum* on vascular smooth muscles of wistar rat. Iranian J Pharmacol Ther 2007; 6(2): 185-189.
48. Jachak SM, Bucar F and Kartnig T: Anti-inflammatory activity of extracts *Biophytum sensitivum* in carrageen-induced rat paw oedema. Phytother Res 1999; 13(1): 73-74.
49. Chatterjee TK, Mishra M, Pramanik KC and Bandyopadhyay D: Evaluation of anti-inflammatory, antipyretic and analgesic properties of *Biophytum sensitivum*. Indian Drugs 2008; 45(2): 123-131.
50. Banerjee T, Van der VA and Ziboh VA: Down regulation of COX-2 and iNOS by amentoflavone and quercetin in A549 human lung adenocarcinoma cell line. Prostaglandins Leukot Essent Fatty Acids 2002; 66(5-6): 485-492.
51. Guruvayoorappan C and Kuttan G: Protective effect of *Biophytum sensitivum* (L.) DC on radiation-induced damage in mice. Immunopharmacol Immunotoxicol 2008; 30(4): 815-835.
52. Puri D: Hypocholesterolemic effect of *Biophytum sensitivum* leaf water extract. Pharm Biol 2003; 41(4): 253-258.
53. Shivakumar MS, Srinivasan R and Natarajan D: Bioefficacy of *Biophytum sensitivum* (L.) leaf extracts against dengue mosquito vector *Aedes aegypti* (L.) Res J Pharm Chem Biol Sci 2012; 3(3): 885-892.
54. Johnson DB, Kumar DC, Arunkanth KR, Giles D, Gopal M and Hubert VG: Antifertility activity of *Biophytum sensitivum*. Indian Drugs. 2003; 40(9): 523-525.
55. Rajanikant TK, Nagesh S and Senthilkumar KL: Evaluation of Hypolipidemic and anti-obesity activities of *Biophytum sensitivum* Linn extracts on high fat diet induced hyperlipidemic rats. Int J Pharm Chem Biol Sci 2015; 5(1): 357-360.
56. Kumar KS, Karunakar K, Jarinabanu T, Jameela T and Ragavendhra P: Antiepileptic activity of ethanolic extract of *Biophytum sensitivum* (L.) DC. in animal models. Int J Curr Res Acad Rev 2015; 3(7): 23-30.
57. Pawar AT and Niraj SV: Anti-urolithiatic activity of standardized extract of *Biophytum sensitivum* against zinc disc implantation induced urolithiasis in rats. J Adv Pharm Technol Res 2015; 6(4): 176-182.
58. Anindya B, Rashid MH, Rahman A and Pal TK: Screening of ethanolic extract of *Biophytum sensitivum* DC leaves on peptic ulcer induced by aspirin in wistar albino rats. Int J Pharm Phytopharm Res 2014; 3(6): 418-422.
59. Saritha B and Brindha P: Wound healing potential of *Biophytum sensitivum* (L.) DC: An ayurvedic drug. J Chem Pharm Res 2015; 7(3): 87-94.
60. Krishnan G and Gopalakrishna P: Pharmacological Integration: Adjunct effect of Db14201, A new herbal formulation developed based on ayurvedic principles, when co-administered with Glibenclamide: Results of a placebo-controlled trial. AGEMS 2015; 2(1): 2-10.
61. Pal TK, Dutta D, Banerjee R and Maity S: Formulation and evaluation of antimicrobial topical semisolid dosage form containing whole plant extract of *Biophytum sensitivum*. J Pharm Res 2013; 6(7): 641.
62. Pal TK, Kalita P, Burman TK, Chatterjee TK and Maity S: Formulation and evaluation of antidiabetic tablet containing whole plant extract of *Biophytum sensitivum* on the basis of total flavonoid content. World J Pharm Res 2007; 2(4): 986-1007.
63. Krishnan GG: Herbal formulation for prevention and treatment of diabetes and associated complications. United States patent application 2012; 8163312 B2.

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