



## A Review on *Phyla nodiflora* Linn.: A Wild Wetland Medicinal Herb

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### ABSTRACT

*Phyla nodiflora* Linn. (Verbenaceae) is a small creeping herb, commonly known as Jalpapli. The plant is used to cure many problems. It is used for pain in knee joints, for lack of bowel movement, used in ulcers and boils, in swollen cervical glands. It is also used in gonorrhoea. The antibacterial activity of plant has also been traced. The plant has showed antibacterial activity against bacteria such as *E. coli*, *Pseudomonas*, *Staphylococcus*. *Phyla* has been the source of traditional medicines against diseases like liver disorders, dandruff control, indigestion in children etc. In this paper the plant has been reviewed for its phytochemistry, pharmacological studies and antimicrobial activity.

**Keywords:** *Phyla nodiflora*, verbenaceae, phytochemicals, flavonoids, sterols, pharmacological.

### INTRODUCTION

Plants are an essential component of the universe. After various observations and experimentations many medicinal plants were identified as source of important medicine.<sup>1</sup> Medicinal plants have been used since prehistoric period for the cure of various diseases. Since these are in common use by the local people and are of great importance that's why a lot of people are engaged in the trade of important medicinal herbs throughout the world. Especially, people living in villages have been using indigenous plants as medicine.

Knowledge of medicinal values of plants is recognized by almost every society on earth. The inhabitants of the remote places have good knowledge about the utilization of plants because of the non-availability of synthetic drugs. In addition, for the survival, they use the plant-based drugs growing nearby their villages. Based on their right or wrong experiences they discovered the therapeutic agents of these plants in particular diseases. These experiences are transferred from parents to offspring<sup>2</sup>.

Forests are the richest source of the medicinal plants. India is rich in its forest wealth. The medicinal plants have contributed lot in the development of the Indian system of medicine and India is a store house of genetic diversity of medicinal plant with the increasing acceptance of traditional medicine as an alternative form of health care. The screening of the medicinal plants for active compounds is very important. Traditional medicine based on plants has played a key role in the health care system of many countries little- India, China etc.<sup>3</sup> Herbal medicine is still the main stay of about 70- 80% of the world population stay on the herbal medicine.

*Phyla nodiflora* is the important member of the family verbenaceae showing a variety of medicinal uses. It can be the source of the indigenous medicine.

### Plant Name

*Phyla nodiflora* Linn.

### Local Name

Jal Papli

### Vernacular Names

English	:	Lippia, Frog fruit
Philippines	:	Busbusi, Chachahan
Thailand	:	Yaa Riet Pla
Hindi	:	Bukkan, Jalpapli
Sanskrit	:	Vasir Vasuka
Marathi	:	Ratolia Vakkan
Tamil	:	Poduthalai

**Synonyms:** *Lippia incisa*, *Lippia nodiflora*, *Lippia reptans* Kunth, *Phyla incisa* Small

### Classification

Kingdom	:	Plantae
Division	:	Magnoliophyta
Class	:	Magnoliopsida
Order	:	Lamiales
Family	:	Verbenaceae
Genus	:	<i>Phyla</i>
Species	:	<i>Nodiflora</i>

### Distribution

It is distributed in India, Sri Lanka, Ceylon, Baluchistan, South and Central America and Tropical Africa. It is native of California.

In India, it is found in the warmer parts including A.P., Karnataka, Kerala, and Maharashtra, some parts of



Rajasthan, Tamil Nadu, U.P. and W.B. It is common in wet places along bunds or irrigation canal edges and sliver banks.

### Habitat and ecology

*Phyla* grows best on bared ground in periodically moist sites (heavy rainfall, flooding or opening of springs) that also undergo periods of water stress<sup>4</sup> and with apparently poor soil structure. It is found mostly on high-moisture-holding clay to clay loams soils in floodplains or wetlands. *Lippia* is well adapted to moist clay soils in riverine and floodplain environments<sup>5-8</sup> and has been observed to grow most prolifically on sites which experience periodic flooding of short duration.<sup>9</sup> Flood plain catchments with summer rainfall and/or regular spring-summer flooding appear to be the most susceptible to lippia invasion.<sup>5</sup> The deep rooting system of lippia allows it to take advantage of intermittent rainfall faster than perennial pasture grasses as the clay soils maintain moisture to considerable depths.<sup>4</sup> It can inhabit lighter flood-free soils such as sandy loams found adjacent to floodplains<sup>9,5</sup> and has been observed growing on higher ridge country above wetter channel areas.<sup>10</sup> *Lippia* tolerates frequent and occasional inundation but it will also survive drier conditions by becoming dormant for sustained periods of time. Its tolerance towards inundation seems dependent on the length of time it is flooded and the turbidity of the water. It can tolerate extended periods of waterlogged soil. However four to eight weeks of turbid water inundation may be enough to kill most individuals and up to three months inundation may be intolerable.<sup>7</sup> The length of time that *Lippia* will survive dry conditions appears to be unknown. It is often referred to as being drought tolerant<sup>5,7</sup> and able to re-establish quickly when moist conditions return.<sup>5</sup> *Lippia* also appears to be quite frost hardy<sup>11</sup> as dormant nodes will re-shoot in warmer weather, following heavy frosts. Although lippia grows well in disturbed sites it will also grow in some relatively undisturbed sites. *Lippia* can over run a site in the complete absence of livestock as shown in its occurrence on roadsides, ungrazed reserves and lightly grazed woodlands.

### Botanical Description

*Phyla nodiflora* is one of the members of the family verbenaceae. There are about 34 genera in this family. Genus *Phyla* includes 21 scientific plant names of which 13 are accepted species name. *Phyla* is a fast-growing, mat-forming and prostrate perennial plant. When in competition with other species, it can grow to a height of 20-30 cm, and dominate other plants. Once dominance is established, lippia tends to become more prostrate and lower growing. Its life form is described as a running herb<sup>6</sup> and an aquatic herb.<sup>12</sup>

**Stems-** of *Phyla* are green to purple in colour when young and can become somewhat grey and woody with age. Young stems are 2-3 mm thick and can be between 30-95 cm long.

**Roots-** are produced from leaf axils along stems and consist of a central taproot; usually 50-60 cm in length, but thought to extend up to 2 m. An extensive fibrous root system extends from the taproot. *Lippia* also produces fibrous roots from some stem nodes.

**Leaves-** arise in pairs at stem nodes and are rounded (10-20 mm long and 3-7 mm wide), entire or bluntly toothed at the tip and narrow towards the petiole (2-5 mm) at the leaf base. Leaves can be somewhat canescent, that is, having a grayish green appearance due to a covering of fine hairs on their surface (hence the botanical name)

**Flowers** -White to purple flowers are produced in heads (10 mm in diameter) on long peduncles (15-45 mm) arising from leaf axils. As they mature, individual flowers become tubular at their bases, ending in a 2-lipped calyx and surrounded by longer broad overlapping bracts.<sup>9</sup> The lower lip (2-lobed and yellow towards the base) is twice as long as the upper lip (3-lobed).<sup>9</sup>

**Fruits** – 1-1.5 mm in diameter, release two tiny brown, oval, flattened seeds at maturity.

**Seeds** are barely visible to the naked eye.



Figure 1: Leaves of *Phyla nodiflora*

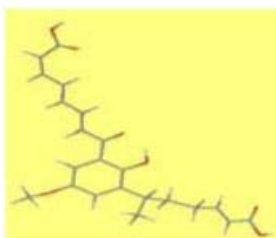


Figure 2: Inflorescence of *Phyla nodiflora*

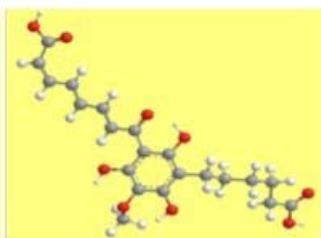
**PHYTOCHEMISTRY**

The plant is rich in many important medicinal useful compounds. The plant contains a variety of constituents such as triterpenoids, flavonoids, phenols, steroids, and many others. Among these flavonoids were the most commonly found. Nodifloretin (3),  $\beta$ -sitosterol glycoside and stigmasterol glycoside from the leaves of *L. nodiflora*.<sup>13</sup> Nodifloridin A (1) and Nodifloridin B(2) along with lactose, maltose, glucose, fructose, and xylose were isolated from the plant.<sup>14</sup> Two new flavone glycosides lippiflorin A (16) and lippiflorin B (17), along with the known compound nepetin and batalilfolin from the ethanol extract of *L. nodiflora*. were isolated.<sup>15</sup> From the flowers of *L. nodiflora*, two flavones glycosides, 6-hydroxyluteolin-7-O-apioside and luteolin-7-O-glucoside, and three flavones 6-hydroxyluteolin, nepetin, and batatifolin were isolated.<sup>16</sup> From the alcoholic extracts of *L. nodiflora*, two phenylpropanoid compounds acteoside (18) and 2'-O-acetyechinacoside and a flavone demethoxycentaureidin were isolated.<sup>17</sup> From *L. nodiflora*, twelve flavones sulfates Hispidulin 7-sulfate (4), Hispidulin 7,4'-disulfate (5), Jaceosidin 7,4'-disulfate (6), Nepetin 3',4'-disulfate (7), Nodifloretin 6,7-disulfate (8), 6-Hydroxyluteolin 6,7-disulfate(9), Nodifloretin 7-sulfate (10), 6-Hydroxyluteolin 6-sulfate(11), 6-Hydroxyluteolin 7-sulfate (12), Jaceosidin 7-sulfate(13), Nepetin 7-sulfate (14), and Hispidulin 4'-sulfate (15), along with the known compounds Nepetin, Hispidulin, and Jaceosidin.<sup>18</sup> Halleridone and Hallerone as their acetyl derivatives from the leaves of *L. nodiflora* were isolated.<sup>19</sup> From the methanolic extract of the aerial parts of *L. nodiflora*, a new triterpenoid lippiacin, a new steroid 4', 5'-dimethoxybenzoxystigmasterol along with the known stigmasterol and  $\beta$ -sitosterol [1, 6]. were isolated.<sup>20</sup>

[1]

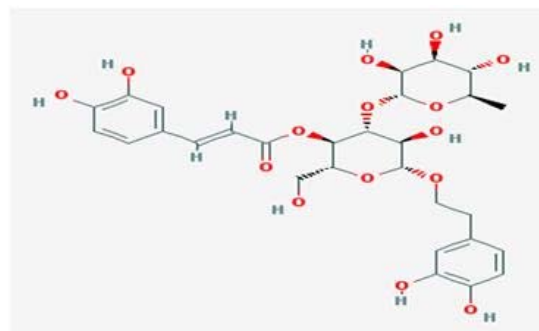


[2]



- (3) R1 = OH, R2 = OH, R3 = OH, R4 = OCH3  
 (4) R1 = OCH3, R2 = OSO3H, R3 = OH, R4 = H  
 (5) R1 = OCH3, R2 = OSO3H, R3 = OSO3H, R4 = H  
 (6) R1 = OCH3, R2 = OSO3H, R3 = OSO3H, R4 = OCH3  
 (7) R1 = OCH3, R2 = OH, R3 = OSO3H, R4 = OSO3H  
 (8) R1 = OSO3H, R2 = OSO3H, R3 = OH, R4 = OCH3  
 (9) R1 = OSO3H, R2 = OSO3H, R3 = OH, R4 = OH  
 (10) R1 = OH, R2 = OSO3H, R3 = OH, R4 = OCH3  
 (11) R1 = OSO3H, R2 = OH, R3 = OH, R4 = OH  
 (12) R1 = OH, R2 = OSO3H, R3 = OH, R4 = OH

- (13) R1 = OCH3, R2 = OSO3H, R3 = OH, R4 = OCH3  
 (14) R1 = OCH3, R2 = OSO3H, R3 = OH, R4 = OH  
 (15) R1 = OCH3, R2 = OH, R3 = OSO3H, R4 = H  
 (16) R1 = OH, R2 = O-L-arabinosyl, R3 = OH, R4 = OH  
 (17) R1 = OH, R2 = O-L-arabinosyl, R3 = OH, R4 = O-L-rhamnoside



(18)

The plant was fractionated several constituents from the *Phyla nodiflora* using multi component solvent systems; Hexane:Toluene:Ethyl acetate (2:1.5:0.5) for methanol extract and Hexane:Ethyl acetate (3:1) for chloroform and petroleum ether extract. Five different phenolic components were isolated and were compared using a HPTLC, among these extracts, the highest number of constituents were isolated from the butanol extract.<sup>21</sup> The molecular basis of a compound, cyclo pentane phenanthrenol, which exhibit anti inflammatory property was also given.<sup>22</sup> Nodifloretin-A, a new flavone was also discovered.<sup>23</sup> Chemical and biological investigations of medicinal herbs *Phyla nodiflora*, *Ruellia patula* and *Ruellia brittoniana* was done.<sup>24</sup> Steroidal constituent from the aerial parts of *Lippia nodiflora* Linn was also obtained.<sup>25</sup>

**Volatile constituents**

The extracts of *L. nodiflora* were steam-distilled afforded a mixture hydrocarbons and a mixture of oxygenates. In the hydrocarbon fraction, among the 14 constituents the major constituent was  $\beta$ -caryophyllene (20%). Among the oxygenated fraction 18 components were found to have concentrations greater than 0.5%, while 12 constituents were found to be in amounts less than 7%, while five components (1-octen-3-ol, phenethyl alcohol, linalool, p-cymen-8-ol, and methyl salicylate) were found to be in amounts between 10 to 20 percent of the total.<sup>26</sup>

**Antimicrobial activity**

The antimicrobial activities on *phyla nodiflora* was also seen.<sup>27</sup> The phytochemical and antimicrobial studies were also done.<sup>28</sup> The Indian medicinal plants were screened for their anti microbial activity.<sup>29</sup>

**Antibacterial activity**

The Methanolic extract of *Phyla nodiflora* had been evaluated for antibacterial (*S.aureus*, *M.luteus*, *P.mirabilis*). The anti microbial screening was performed

by agar diffusion method using a paper disc. The sterilized (autoclaved at 120°C for 30 min) medium was inoculated with the suspension of the micro organisms. The paper impregnated with the extracts (1000µg/ml) was placed on the solidified medium. The Petri dishes were pre incubated for one hour at room temperature and incubated at 37°C for 24hrs and 48 hrs for antibacterial and antifungal activity respectively. Gentamycin (1000µg/ml) used as a standard for anti bacterial. The ethanol extract showed significant antibacterial activity due to the presence of bio-active compounds when compared with petroleum - ether and aqueous extract.<sup>30</sup> The antibacterial activity against *E. coli*, *P.aeruginosa*, and *Staphylococcus aureus* was seen.<sup>31</sup> The antibacterial activity was seen in the essential oils of this plant.<sup>32</sup> The antibacterial activity was also shown by the methanolic extract of the seeds of *phyla nodiflora*.<sup>33</sup>

### Antifungal activity

The antifungal activity of crude extracts of *L.nodiflora* L. against the human pathogenic fungi was reported. The crude extract of various solvents of *Phyla nodiflora* had been screened for Antifungal activity against *Aspergillus niger*, *A. Flavus*, *Paecilomyces varioti*, *Microsporium gypseum*, *Trichophyton rubrum*. All crude extract had significant inhibition activity against most of the fungi. Ethanol extract had maximum inhibition activity (100 %) against tested organism as compared to aqueous (82.6%), Methanol (61 %), Ethyl acetate (87 %) extracts.<sup>34</sup> There are some terpenoids in *L nodiflora* composition, it shows antifungal activity.<sup>35</sup> High antifungal activity in *L rehmanii* due to presence of the oil content β-caryophyllene and β-caryophyllene oxide which were the major compounds that are present in *L. nodiflora* as sesquiterpenes.<sup>36</sup>

### Larvicidal Activity

The essential oils of the leaves of *Lippia alba*, *Lippia aff. gracilis*, *Lippia gracilis*, *Lippia microphylla* and *L. nodiflora* were tested for larvicidal activity against the instar larvae of *Aedes aegypti*. The higher larvicidal activity (LC50 = 26.3 µg/mL) was observed for the oil of *L. gracilis*, while appreciable activity was observed for the oil of *L.nodiflora*.<sup>37</sup>

## PHARMACOLOGICAL USES

### Skin problems

*Phyla* is used as the traditional medicine for the treatment of various skin diseases and used as folk cosmetics among the tribal communities of North-West Frontier Province, Pakistan.<sup>38</sup>

### Hepatoprotective and Antioxidant potential

The methanolic extract of *Lippia nodiflora* (MELN) has been evaluated for antioxidant activity and hepatoprotective effects in paracetamol induced liver injury (750mg/kg, b.w). MELN was administered orally for 7 days. The higher dose of MELN was found to be more effective than the lower dose in paracetamol induced liver damage. MELN produced significant

hepatoprotective effect by decreasing the activity of serum enzymes such as SGOT, SGPT, ALP bilirubin and lipid peroxidation. The MELN was found to be equivalent to that of standard silymarin 25mg/kg, thus the plant was found to be hepatoprotective probably due to the antioxidant potential on hepatocytes and the methanol extract of *L. nodiflora* for total phenolic content, indicated by the folin-ciocalteu phenol reagent was found to be 114.8 µg/mL total phenolics for 1 mg of the extract.<sup>39</sup>

### Antitumor activity

The methanolic extract of *Lippia nodiflora* has been evaluated for antitumor activity using Erlich's ascites carcinoma (EAC) bearing swiss albino mice. The mice were administered with the methanol extract at 200 and 400 mg/kg of body weight daily for nine days after 24 hours of tumor inoculation. The methanolic extract indicated significant ( $p < 0.001$ ) decrease in tumor volume, viable cell count and packed cell volume, the life span of the mice was also found to be increased. For the mice treated with the methanol extract the hematological profiles reverted to more/less normal levels, while the serum enzymes, total proteins and bilirubin were altered narrowly. The methanol extract increased the levels of reduced glutathione (GSH), catalase (CAT) and superoxide dismutase (SOD) and reduced the levels of lipid peroxidation. The plant was found to bear good antitumor activity, which was supposed to be due to the increased of antioxidant activity.<sup>40</sup>

### Anti-diuretic activity

The diuretic potential of methanol and aqueous extracts of the aerial parts was assessed in albino rats using *in-vivo* Lipschitz test model. The volumes of urine, urinary concentration of sodium and potassium ions were the parameters of the study. Furosemide was used as standard. The results indicate that methanol and aqueous extract at 500 mg/kg body weight shows a significant ( $p < 0.05$ ) increase in the urine volume and electrolyte excretion ( $p < 0.001$ ) when compared to control. Both the extracts show significant diuretic activity.<sup>41</sup>

### Anti-inflammatory activity

The crude methanol extract and the isolated compound of cyclopentano phenanthrenol from *L.nodiflora* were assessed for anti-inflammatory activity. Human peripheral blood mono nuclear cells were used as models to examine intracellular protein levels of pro-inflammatory mediators (MAPK and NF-KB) and the mitogen induced lymphocyte proliferation, cytokine mRNA expression (TNF-α, IL-1β and IL-6). The NO release levels, on treatment with the extract and the isolated compound were correlated with the underlying iNOS mRNA expression in the murine macrophage cell line RAW 264.7. In the cell line RT-PCR for COX-2, MMP2 and MMP9 were also conducted. As an *in vitro* model for the rat basophilic leukemia cell line RBL-2H3 was employed for PLA2 activity. The crude extract (20 µg/mL) and the isolated compound (10µg/mL) were used to assess the



activity. Cyclo-pentano phenanthrenol was found to inhibit TNF- $\alpha$ , IL-1 $\beta$  and IL-6 expression, prostaglandin biosynthesis via PLA2, NO release via iNOS suppression and COX-2 inhibition and the activation of intracellular targets, MAPK and NF-KB. Thus the compound was concluded to exhibit anti-inflammatory activity.<sup>42</sup> Anti inflammatory and anti neocptive activities of methanoic extract of *Lippia nodiflora* Linn was also seen.<sup>43</sup>

#### Antiuro lithiatic activity

The ethanolic extract of *Phyla nodiflora* Linn had been evaluated against calculi producing Diet induced urolithiasis.<sup>44</sup> *Phyla* was studied for its antiuro lithiatic activity against most common type of renal stones i.e. calcium oxalate type. Calcium oxalate urolithiasis was induced by administration of Gentamycin and calculi producing diet (5% ammonium oxalate in standard rat pellet feed). The extract was also assessed for effect on in vivo antioxidant parameters like lipid per oxidation, reduced glutathione, catalase in hyperoxaluric kidney and in vitro scavenging of nitric oxide and 2-diphenyl-2-picryl hydrazyl free radicals. Ethanolic extract of *P. nodiflora* exhibited significant effect in preventing calcium oxalate stone formation and also in dissolving the pre-formed calcium oxalate stones in the kidney along with significant effect on both in vitro and in vivo antioxidant parameters. The present study clearly demonstrates the antiuro lithiatic activity of *P. nodiflora* supporting the traditional claim.

#### Antidiabetic and Hypolipidaemic

The effect of methanol extract of *Lippia nodiflora* L. in Streptozotocin induced diabetic rats was reported.<sup>45</sup> The methanol extract of *Lippia nodiflora* at three dose levels were administered orally to Streptozotocin (STZ) (40mg/kg bw) induced diabetic rats for 15 days. The extract at three dose levels showed a significant increase in the liver, muscle glycogen and serum insulin level and a significant decrease in fasting blood glucose, glycosylated hemoglobin levels and serum marker enzyme levels. The total cholesterol and serum triglycerides levels were also significantly reduced and the high density lipoprotein level was significantly increased upon treatment with the *L. nodiflora* methanol extract. Histochemical study of pancreas also confirmed the biochemical findings. Acute toxicity studies revealed the non-toxic nature of the methanol extract of *L. nodiflora* exerts significant antidiabetic and hypolipidaemic effect in STZ-induced diabetic rats.

#### Neuropharmacological activity

The neuropharmacological profile of petroleum, chloroform and ethanolic extracts of aerial part of *Lippia nodiflora* Linn was reported. With experimental models using test such as potentiation of diazepam-induced sleeping time, locomotor activity, motor coordination, exploratory behavior pattern, elevated plus maze and maximal electroshock convulsions, It showed that the ethanolic extract of *L. nodiflora* at both doses (250 and

500 mg/kg p.o.) and its chloroform extract at a higher dose of 500 mg/kg produced central inhibitory (sedative) effect, anticonvulsant effect and anxiolytic effect in mice. Values were statistically significant ( $P < 0.05$  and  $P < 0.01$ ) when compared to the control group. The petroleum ether extract of plant at both dose levels (250 and 500 mg/kg p.o.) did not produce any central effects. The ethanolic and chloroform extracts showed the central inhibitory activity due to the presence of flavonoids. The pet ether extract did not showed any central effect as flavonoids were not present in it.<sup>46</sup>

#### Miscellaneous activity

Zheng suggested that since *L.nodiflora* contains nodifloretin,  $\beta$ -sitosterol glucoside, stigmasterol glucoside, nodifloridin A, and nodifloridin B, it could be used in proper doses for the treatment of hepatitis.<sup>47</sup> Narayanan *et al* suggested that the plant extracts of any of the two plants *Datura metel*, *Murraya koenigii*, *L. nodiflora*, and *Wrightia tinctoria* possess antidandruff application.<sup>48</sup>

The Anti inflammatory analgesic and anti pyretic activity in rodents of plant extracts was used in African medicine.<sup>49</sup>

A pilot study was done on the simple Siddha remedy for hizhuvettu (alopecia area).<sup>50</sup>

#### CONCLUSION

*Phyla nodiflora* is widespread all over the world. It has been used by the different tribes as traditional medicines. Certain compound has been isolated. However more investigations are to be done on the biological activity and for the action of more biologically active compounds. Presence of large number of phytochemicals indicates towards its future perspective to use it as an indigenous medicine in the pharmaceutical industry.

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