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## PAEDERIA FOETIDA LINN: PHYTOCHEMISTRY, PHARMACOLOGICAL AND TRADITIONAL USES

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**ABSTRACT:** *Paederia foetida* (Skunk vine) an indigenous plant belongs to family Rubiaceae. The plant is having a broad spectrum of use as in treatment of ailments like hepatic disorders, rheumatoid arthritis, constipation, diabetes, coughs, asthma, itches, wounds, stomachache, diarrhoea, dysentery, pain, typhoid, pneumonia, toothache, cancer, flatulency, body ache, and bone fractures etc. Literature data reveals the presence of asperuloside, paederosidic acid, phenolic compounds, alkaloid, volatile oil, sitosterols, stigmasterol, campesterol, ellagic acid, lignans, iridoids, methylendioxy compound, tannins, triterpenoids, urosilic acid, epifriedelinol and found to have anti-ulcer, anti-diarrhoeal, anti-hyperglycemic, antioxidant, antitussive, anthelmintic, hepatoprotective activity. This review target at gathering the research work undertaken till date on this plant in order to provide sufficient baseline information for future works and commercial exploitation.

**INTRODUCTION:** Herbal drugs play an important role in the healthcare programs. Ancient literature incorporates a remarkable broad definition of medicinal plants and considers all parts of the plant to be potential source of medicinal substances. The main hindrance in the acceptance of herbal medicines is the lack of documentation and quality control. So it becomes extremely important to make an effort towards standardization of the plant material to be used as medicine<sup>1</sup>. The genus *Paederia* contains 20- 30 species in worldwide generally distributed in Asia, commonly known as skunk vine like shrub, perennial climbing herb, in India it found in Himalayas from Dehradun east wards up to an altitude of 1800 meter and also in Assam, Bihar, Bengal, Orissa and Andhra Pradesh.

*Paederia foetida* Linn, a member of Rubiaceae is an extensive climber: glabrous or puberulous<sup>2,3</sup>. The local name is “*Jyirmi Smaiwtung*”<sup>4</sup>. It is known as Chinese Flower in English, Gandha prasarini in Hindi, Prasarani in Sanskrit<sup>5</sup>.

*Paederia foetida* is native to both temperate and tropical Asia, from India to Japan and South East Asia. It contains bitter taste with having foul smell. *P. foetida* may grow high in to the trees in a variety of habitats from msichammocks to xeric sand hill communities, although it appears to prefer sunny flood plains and bottom lands even grow under water, tree gaps and other disturbed areas<sup>6</sup>.

### Classification, Pharmacognosy and Morphological Characters:

*Paederia foetida* is an extensive, foetid climber. Leaves opposite, ovate or lanceolate, acute or cuspidate, 2.5-3.8 cm long. Surface is glabrous and mostly ovate, green in colour having a characteristic odour indistinct bitter taste. The leaf is distinctly dorsi-ventral with prominent midrib and lamina.

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Epidermal trichomes are sparsely seen both on the upper and lower epidermis. Mesophyll composed of single layered palisade cells and 3-4 layered spongy tissue; in margin of the leaf mesophyll replaced by thick walled cells. Trichomes are present on both surfaces elongate to produce uniseriate trichomes. Midribs composed of single layered epidermis covered with cuticle; ground tissue consisting of 2-5 layered of collenchyma towards upper and lower side and rest parenchyma; a large median crescent-shaped vascular bundle consisting usual elements with xylem towards upper side and phloem towards lower side <sup>7</sup>.

The inflorescence consists of a terminal or axillary cymose panicle that is extremely variable. It grows from widely branched paniculate over 1m long to rather reduced size, normally 10cm long. The bracts are either leaf-like or small and linear, with few to numerous flowers, often in lax coiled cymes with peduncle that is 2-30mm long <sup>8</sup>. The flowers are bisexual, usually 5-merous; in dirty pink or lilac or purplish colour (see **Figure 1**). The corolla lobes are pinkish to whitish on the inside while the throat is dark purple. The sepal is bell-shaped, with 5 normally smooth triangular-lobed with sizes up to 1mm x 0.6mm.



**FIGURE 1: PAEDERIA FOETIDA PLANT**

The petal is cylindrical to bell-shaped, and sizes 5-17mm x 2-5mm. The throat and the inside of the long tube are densely hairy with 5 oblong to triangular lobes and sizes between 1-3mm x 1.5-3mm. The margins are wavy and flexed. It has 5 stamens that are inserted in the middle of the tube which includes 2-2.5mm long anthers. The 2-celled and 2 ovuled ovary is inferior with a small disk and 4-15mm long style.

The stigmas joined the style up to 2mm of its length. The 2 stigma branches are thread-like and irregularly twisted.

The sub-spherical fruit is a drupe at 4-6mm in diameter. The fruit walls are thin, dry and brittle. It is crowned by the persistent sepals, shiny pale brown to yellowish-or reddish-brown in color. The 2 semi-orbicular or semi-ellipsoidal kernels are flat on one side and convex or compressed on the other. It is normally slightly smaller than the fruit, without conspicuous wings, black in color and often conspicuously covered with needle-shaped crystals.

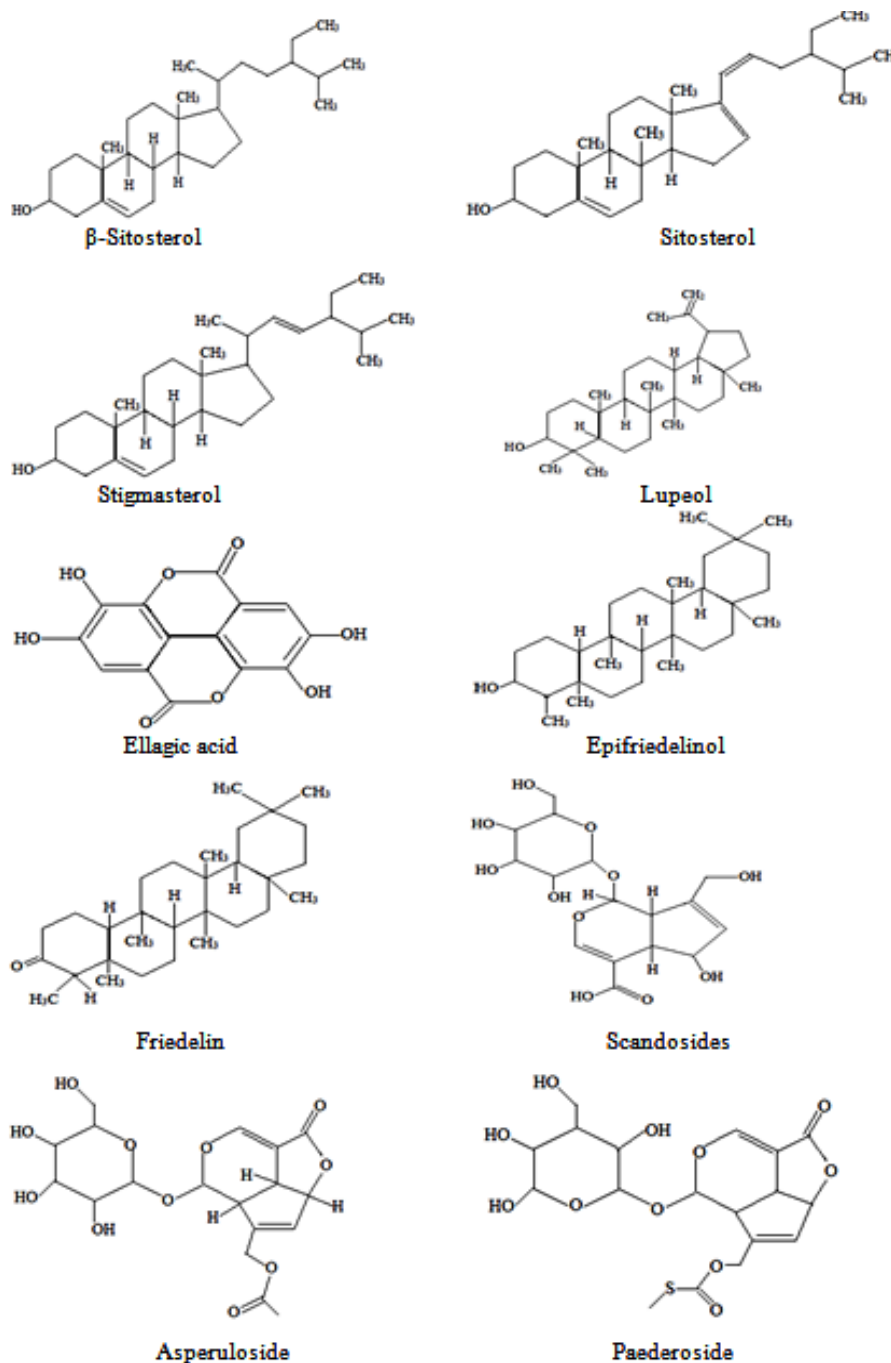
The seedling is germinated above the ground, with cotyledons broadly rounded. The veins are prominent while the first pair of leaves form is elliptical and apex is acuminate. Fruit orbicular, wings pale, 1.1 cm across <sup>8</sup>.

**Phytochemical studies:** Phytochemical investigations reported that *Paederia foetida* contains paderolone, paderone,  $\beta$ -sitosterol, paderoside, asperuloside and their related glucosides <sup>9-11</sup>. The leaves of the plant are also rich in carotene, vitamin C, keto-alcohol and alkaloid <sup>12</sup>. Shreedhara reported to quantify important markers (asperuloside, beta-sitosterol and lupeol) also in leaves <sup>13</sup>. The aerial parts of the plant contain iridoid glucosides (asperuloside, scandoside and paderoside) <sup>14</sup>.

*P. foetida* also contains friedelin, campesterol, ursolic acid, hentriacontane, hentriacontanol, ceryl alcohol, palmitic acid and methyl mercaptan <sup>5</sup>. Ellagic acids <sup>15</sup>, Epifriedelinol, Terpenoids, alkaloids paderine (a-paderine and b-paderine), volatile <sup>16</sup> and an essential oil <sup>15</sup>. The phytochemical structures are illustrated in **figure 2**.

### **Biological activity:**

- 1. Hepatoprotective activity:** Plant extract exhibits ameliorative effects on hepatotoxin-induced liver damage in the Sprague Dawley (SD) rat model. We induced *in vivo* oxidative stress in rats by a single intraperitoneal injection of carbon tetrachloride (CCl<sub>4</sub>) and then administered the plant extract to the rats for three successive weeks.



The anti-hepatotoxic potentials of the plant extract against *in vivo* CCl<sub>4</sub>-induced hepatic lesions were then evaluated. The administration of the extract significantly decreased the levels of hepatic lipid peroxide (LPO) in the CCl<sub>4</sub>-intoxicated rat by about 40%. The CCl<sub>4</sub>-induced increase in the serum enzyme activities such as GPT, GOT, ALP as well as in the bilirubin level were also significantly reduced. The results of the present study suggest that *Paederia foetida* can ameliorate toxin-mediated hepatocellular injuries probably by inhibiting the oxidative stress<sup>17, 18</sup>.

2. **Anthelmintic Activity:** Methanolic extract of the leaves of *Paederia foetida* were screened for its anthelmintic activity against *Pheretima posthuma* and *Tubifex tubifex*. The parameters like the time of paralysis and the time of death were determined by using the extract at the concentrations of 25, 50 and 100 mg/ml. The extract exhibited significant anthelmintic activity at highest concentration of 100 mg/ml as compared with piperazine citrate (10mg/ml) as standard reference and distilled water as control<sup>19</sup>.

3. **Antibacterial activity:** The test microorganisms included two Gram-positive (*Staphylococcus aureus*, *Enterococcus faecalis*) and three Gram-negative (*Escherichia coli*, *Salmonella typhimurium*, *Shigella flexneri*) bacteria. The extract showed significant antibacterial activities against *S. flexneri*, *S. aureus*, *E. coli* and *E. faecalis*. The preliminary screening experiment revealed that the most susceptible bacterium was *S. Flexneri* while the most resistant was *S. typhimurium*. The results of experiment clearly indicate that *Paederia foetida* plant could be used for its antibacterial activity<sup>20</sup>.
4. **Antihyperglycemic activity:** Antihyperglycemic activity studies were conducted by oral glucose tolerance tests in glucose-loaded Swiss albino mice with crude methanol extract of stems of *Paederia foetida*. Methanol extracts of stems of *Paederia foetida* also exhibited significant and dose-dependent reductions in serum glucose levels when administered to glucose-loaded mice. The extract at the four different doses of 50, 100, 250 and 500 mg/kg body weight, reduced serum glucose levels by 7.7, 25.3, 31.0, and 31.2%, respectively. Overall, the results demonstrate significant antihyperglycemic activities of stems of *Paederia foetida*<sup>21</sup>.
5. **Anti-inflammatory activity:** The anti-inflammatory activity of the butanol fraction of a methanol extract (BMEL) of the defatted leaves of *Paederia foetida* was undertaken to find the pharmacological basis for the ethnomedical use of the plant. This fraction produced a significant inhibition of granulation tissue formation in cotton-pellet implanted rats. It decreased liver aspartate transaminase activity without affecting serum aspartate transaminase activity.  
  
It did not, however, affect adrenal weight and ascorbic acid content significantly, thus ruling out a stimulation of the adrenal-pituitary axis. BMEL antagonised hyposaline-induced haemolysis of human red blood cells and an elevation of rat serum acid phosphatase activity, indicating the presence of a membrane stabilising activity. It also inhibited the elevation of serum orosomucoid levels in rats, suggesting the possibility of the presence of disease-modifying antirheumatic activity<sup>22, 23</sup>.
6. **Anti-ulcer activity:** The anti-ulcer screening was performed using two methods that is pyloric ligation method and aspirin induced ulcerations in rats. Volume of gastric acid, total acidity and free acidity were also measured to assess the anti-ulcer potential. Therefore expressed that the roots of *P. foetida* exerts anti-ulcer activity which may be due to anticipated inhibition of H<sub>2</sub> receptors resulting in inhibition of gastric acid secretion elicited by histamine and gastrin. The work justifies its use in the traditional system of medicine<sup>24</sup>.
7. **Antinociceptive Activity:** The significant antinociceptive activity of hexane and methanol extract of the whole plant of *P. foetida* might be due to the presence of analgesic principles acting with the prostaglandin pathways. Swiss albino mice were using for study. Although the extracts of *P. foetida* exhibited significant analgesic activity, further study is required to isolate active constituents of this plant. The antinociceptive activity of different extracts of *P. foetida* was determined by the acetic acid induced writhing inhibition method<sup>25</sup>. The antinociceptive activity of the ethyl acetate extract was not significant in both doses<sup>26</sup>.
8. **Antioxidant activity:** The antioxidant activity of fresh and dried plant extracts of *Paederia foetida* was studied using  $\beta$ -carotene bleaching and the 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical cation assay. The percentage of antioxidant activity for all extract samples using both assays was between 58 and 80%. The fresh samples of both plants had higher antioxidant activity than the dried samples. The results of the  $\beta$ -carotene bleaching assay were correlated (R<sup>2</sup> = 0.9849) with those of the ABTS assay<sup>27</sup>.
9. **Antitussive activity:** The ethanolic extract of *Paederia foetida* (*P. foetida*) in conscious cats by mechanical stimulation of laryngopharyngeal (LP) and tracheobronchial (TB) mucous areas of airways. The oral dose of 200 mg·kg<sup>-1</sup> b.w. had a cough-suppressive effect.

It caused a significant ( $p < 0.05$ ) decrease of the number of cough efforts (NE) and frequency of cough (NE.min-1) from both LP and TB areas. The intensity of a cough attack was significantly decreased only during inspiration (IA-). Also a significant ( $p < 0.05$ ) decrease was observed of the intensity of maximal effort in expiration (IME+) from TB area and inspiration (IME-) from both LP and TB areas. The antitussive activity of the ethanolic extract of *P. foetida* was lower than that of the classical narcotic antitussive drug - codeine, but similar to that of the non-narcotic antitussive agent dropropizine. The antitussive activity of the ethanolic extract of *P. foetida* may be connected with its previously demonstrated anti-inflammatory activity<sup>28</sup>.

**10. DPPH radical scavenging activity:** DPPH radical scavenging of leafy vegetables of wild *Paederia foetida* in two villages of Pandaan City, East Java, Indonesia, has been done. A focus group discussion (FGD) and in-depth interview showed that the wild plants are well recognized and commonly consumed by local people. The samples, collected from local forest of the two villages, were analyzed for the proximate composition, dietary fibers, minerals, vitamin C and total phenol contents; and DPPH radical scavenging activity. Both leafy vegetables are potential dietary fiber, Ca, Na, K and Fe sources.

Vitamin C content of the leafy vegetable of *Paederia foetida* ( $271.40 \pm 42.65$  mg/100g) was much higher than that of *Erechtites hieracifolia* ( $20.62 \pm 1.63$  mg/100 g). Both leafy vegetables are potential antioxidant sources with IC50 values of 4.53 mg/mL and 8.46 mg/mL, respectively for methanolic extract of leafy vegetable of wild *Paederia foetida*<sup>29</sup>.

**11. Anti-diarrhoeal activity:** Antidiarrhoeal activity of 90% ethanol extract of *Paederia foetida* was investigated in this study using castor oil and magnesium sulphate-induced diarrhoea models in mice. The extract significantly increased the latent period of diarrhoea in both the models. In the castor oil study, the purging index (PI) value lowered in 1 h of the study at (100, 250 and 500 mg/kg) doses.

The effect continued up to 6-h period only at 500 mg/kg dose. The plant notably reduced the purging index value in a dose-dependent manner in magnesium sulphate-induced diarrhoea. *P. foetida*, in general, reduced the gastrointestinal motility with barium sulphate milk both in 15- and 30-min time intervals. The extract significantly decreased the cisplatin-induced gastrointestinal motility at all doses at both time intervals. The extract also enhanced the morphine-induced reduction of motility at 500 mg/kg dose level at both time intervals<sup>30, 31</sup>.

**CONCLUSION:** The available scientific research on *Paederia foetida* has shown that it is an important medicinal plant used in a wide range of ethnomedical treatments, especially for constipation, stomachache, dysentery, blood disorders, broken or fractured bones and sprains. Although it has not been reported that *Paederia foetida* might be slightly toxic the plant has been in use for a long period of time without any documented serious adverse effects.

The detailed information presented in this review provides evidence for its various traditional uses. The pharmacological studies that have tested the validity of traditional uses confirmed its anti-inflammatory, antimicrobial and hepatoprotective activities etc. support the use of *Paederia foetida* to increase renal functions. Reports of the use of this plant for the same ailments in different areas and countries indicate that the plant is of huge biological importance.

*Paederia foetida* contains different types of secondary compounds that have different structural characteristics with different pharmacological effects. Different compounds such as Phenolic compounds have successfully proven themselves as antioxidants.

The traditional use of the plant for the treatment of dysentery has been supported by the observation that the crude extract inhibited the growth of *Shigella dysenteriae*, the causative agent of dysentery in humans. The extract of *P. foetida* could be further explored in the future as a source of useful phytochemicals for the pharmaceutical industry.

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