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## BIOACTIVE COMPONENTS OF *PAEDERIA FOETIDA* LINN. AND ITS ROLE IN DISEASE MANAGEMENT

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*Paederia foetida*, Phytochemistry, Ethnobotany, Biological action

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**ABSTRACT:** *Paederia foetida* is one of the lesser-studied plants that has been utilized as food and medicine by several ethnic groups against stomach pain, bowel disease, snake bite, bone fractures burns, or scalding. Scientific research revealed that the plant exhibits extensive pharmacological activity, including antidiarrheal, antibacterial, anti-inflammatory, anti-diabetic, antiemetic, antioxidant and anti-rheumatoid. Based on the online poll results, information was acquired about *P. foetida*'s transition from traditional use to scientific validation. Moreover, qualitative and quantitative phytochemical analysis of the plant indicates the presence of 36 important chemical constituents such as; methyl-mercaptan, phenolic, high percentage of minerals, urosolic acid,  $\beta$ -sitosterol, oleanolic acid, arachidic acid. The different phytoconstituents of the plant justify the ethno-medicinal and pharmacological application of the plant. In conclusion, the results of this analysis will produce a new, safe, and low-cost therapeutic strategy for identify and isolate novel chemical entities in drug discovery. Additionally, it may aid in separating fresh lead compounds for future clinical study research. This plant could be an excellent source of safe and effective medicinal and nutritional herbal remedies for human and animal consumption.

**INTRODUCTION:** Over the past decades, Herbal and Ayurvedic drugs have been considered a subject of World importance with medicinal and economic implications<sup>1</sup>. Researchers are mainly focusing on the traditionally used medicinal plants by various ethnic groups to develop medication against different ailments. *Paederia foetida* is one of the most highly used medicinal plants mainly in the northeastern region of India and is well known for its gastro-protective and anti-diarrheal activity. It is widely available in India, Bangladesh, Japan,

China, Malaysia, Myanmar, Nepal, Thailand, Vietnam, Philippines, Cambodia, and Bhutan. Many ethnic groups have used this plant as a medicine for various health problems since ancient times. The main objective of this review is to accumulate information about different pharmacological activities along with the plant's active constituent, which will give an idea about the previous work on this plant.

*Paederia foetida* belonging to the Rubiaceae family, is a herbaceous climber with a wide range of applicability in society<sup>2</sup>. This distinctive plant can grow up to 1500-1800cm in height producing small pink white color flowers in clusters. Flowers are generally bell shapes, 5-15 mm into 2-6 mm. The flower includes five stamens inserted in the middle of the flower tube, including long anthers<sup>2</sup>. The fresh leaf of the plant is generally 10-15 cm

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long, 5-6 mm wide, and petiole 1.2-6 cm; the surface is glabrous and mostly ovate, green in color, having a characteristic odor. The leaf is distinctly dorsiventral with prominent midrib and lamina. Trichomes are present on both surfaces elongating to produce uniseriate trichomes and mesophyll is composed of single-layered palisade cells and 3-4 layer spongy tissue. The midribs are composed of single-layered epidermis covered with cuticles, ground tissue consists of 2-5 layered collenchyma towards the upper and lower side of parenchyma<sup>3</sup>. Aerial parts contain methyl mercaptan, cysteine, keto alcohol, paederolone, a keto compound, paederone and betasitosterol, protein, carbohydrates, glycosides, essential oils, quinines, alkaloids, iridoid glycosides, sitosterol, stigmasterol, amino acids and volatile oil<sup>4</sup>. The common name of *Paederia foetida* is enlisted in **Table 1**.

**TABLE 1: COMMON NAME OF PAEDERIA FOETIDA**

Language	Vernacular Name	Reference
English	King's tonic, Skunk vine	Tanet et al., 2019 <sup>17</sup>
Chinese	Ji shi teng	Tan et al., 2019 <sup>17</sup>
Malaysian	Akar sekenut	Tan et al., 2019 <sup>17</sup>
Assamese	Bhedailota	Das S et al., 2013 <sup>18</sup>
Bengali	Gandhavadulia	Wang et al., 2014 <sup>19</sup>
Odisha	Pasaaruni	Saho et al., 2009 <sup>20</sup>
Hindi	Ghandhali	Saho et al., 2009 <sup>20</sup>
Manipuri	Oinam	Shah et al., 2014 <sup>21</sup>
Sanskrit	Prasarini	De S, Ravishankar B & Bhavsar et al., 1994 <sup>22</sup>

**Geographical Location:** The plant is widely distributed in Bangladesh, India, Japan, Malaysia, Myanmar, Nepal, Thailand, Vietnam, Cambodia, and China<sup>5</sup>. The plant favors a humid, sunny region and is adaptable to different soils. It is found in the Himalayas from Dehradun eastward up to an altitude of 1800 m and also in Bihar, Odisha, Bengal, Assam, Manipur, Nagaland, Tripura, Arunachal Pradesh, Sikkim and Mizoram<sup>11</sup>.

**Traditional Uses:** Mostly tribal people of northeast India use the decoction of the plant for various medicinal purposes. Tribes of Tripura prepare

*Berma baturi* using dry fish and leaves of *Paederia foetida*. Similarly, tribal people of Chittagong hill of Bangladesh and Aka tribes of Arunachal Pradesh consume leaf juice to treat diarrhea, dysentery and gastric irritation<sup>12</sup>. Manipuri people use the plant's curry to treat piles<sup>13</sup>. It has been reported that certain ethnic communities of Orissa cook the leaves with rice to cure different diseases like rheumatism and gout<sup>12</sup>. Assamese people cook this leaves with fish to treat stomach problems. This plant has been used to treat toothaches, dysentery, edema, night blindness, digestive problems ulceration, diabetes and inflammation<sup>5</sup> gout, piles, stomachache, ulcer<sup>8</sup>. Besides that it had been reported for significant antiviral anti-inflammatory, anticancer, anti-tussive, analgesic<sup>11</sup>, anti-helminthic<sup>14</sup> and antioxidant activity. The root of this plant has been utilized in emetic, emollient, carminative, chest pain and regulation of the spleen inflammation<sup>10</sup>.

**Phytochemistry:** The main parts of *Paederia foetida* used for its medicinal activity are leaf, root, bark, and flowers. It contains optically active iridoid glycosides. Cyclopentanoid, Monoterpenes. Paederoside, Asperuloside, and Scandoside are the main Iridoid glycosides. These glycosides are responsible for antioxidant, antibacterial, anti-inflammatory, anti-diabetic, and hepatoprotective activity. The plant also contains alkaloids and volatile oils which can be isolated by using steam distillation from leaves and stems.

On the contrary, many mineral elements like nitrogen, phosphorus, potassium, and magnesium are also found in the plant. The bitter taste and foul-roma are due to the presence of methyl mercaptan<sup>5</sup>. The presence of triterpenoids, saturated fatty acids and  $\beta$ -sitosterol is responsible for its anti-ulcer activity<sup>12</sup>. The leaves also contain a small amount of Vitamin C and phenolic compounds responsible for its antioxidant activity<sup>12</sup>. Different types of phytoconstituents isolated from the plant are listed in **Table 2**.

**TABLE 2: PHYTOCONSTITUENTS ISOLATED FROM THE PAEDERIA FOETIDA**

Active constituents	Plant part	References
	<b>Volatile Oil</b>	
Butanedione	Stems	Wang L et al., 2014 <sup>19</sup>
Pentan-2-on	Leaves	Wang L et al., 2014 <sup>19</sup>
Pant-3-en-2-one	Leaves, stems	Wang L et al., 2014 <sup>19</sup>

S-methyle thioacetate	Leaves	Wang L et al., 2014 <sup>19</sup>
Dimethyle-disulfide	Leaves, stems, flowers	Wang L et al., 2014 <sup>19</sup>
Hexanal	Leaves, stems, flowers	Wang L et al., 2014 <sup>19</sup>
Limonere	Leaves, stems	Wang L et al., 2014 <sup>19</sup>
3-methylbutane-1-ol	Leaves, stems	Wang L et al., 2014 <sup>19</sup>
Pantane -1 ol	Leaves, flowers	Wang L et al., 2014 <sup>19</sup>
3-methylbut-2-en-1-ol	Leaves, stems	Wang L et al., 2014 <sup>19</sup>
Hexanol	Leaves, stems, flowers	Wang L et al., 2014 <sup>19</sup>
Hex-3-en-1-ol	Leaves	Wang L et al., 2014 <sup>19</sup>
Dimethyl trisulfide	Leaves, stems	Wang L et al., 2014 <sup>19</sup>
S, s-dimethyl dithiocarbonate	Leaves	Wang L et al., 2014 <sup>19</sup>
Phenylacetaldehyde	Leaves and stems	Wang L et al., 2014 <sup>19</sup>
2-furanmethanol	Leaves stems flowers	Wang L et al., 2014 <sup>19</sup>
Benzofuran	Leaves stems flowers	Wang L et al., 2014 <sup>19</sup>
$\alpha$ -terpinrol	Leaves stems flowers	Wang L et al., 2014 <sup>19</sup>
Methyl salicylate	Leaves stems flowers	Wang L et al., 2014 <sup>19</sup>
Nerol	Leaves stems flowers	Wang L et al., 2014 <sup>19</sup>
Geraniol	Leaves stems flowers	Wang L et al., 2014 <sup>19</sup>
Eugenol	Leaves stems	Wang L et al., 2014 <sup>19</sup>
2,3-dihydrobnezofuran	Leaves stems flowers	Wang L et al., 2014 <sup>19</sup>
<b>Glycosides</b>		
Asperuloside	Leaves stems flowers	Chanda S et al., 2013 <sup>24</sup>
Scandoside	Leaves stems flowers	Chanda S et al., 2013 <sup>24</sup>
Paederoside	Leaves stems flowers	Chanda S et al., 2013 <sup>24</sup>
Paederosidic acid	Leaves and Stems	Wang L et al., 2014 <sup>19</sup>
Deacetylasperuloside	Leaves and Stems	Wang L et al., 2014 <sup>19</sup>
<b>Alkaloids</b>		
Paederine a	Leaves and stems	Chanda S et al., 2013 <sup>24</sup>
Paederine b	Leaves and stems	Chanda S et al., 2013 <sup>24</sup>
<b>Essential Oils</b>		
Linalool	Leaves, stems and flowers	Chanda S et al., 2013 <sup>24</sup>
Methyl mercaptan	Leaves, stems and flowers	Chanda S et al., 2013 <sup>24</sup>
Tepineol	Leaves, stems and flowers	Chanda S et al., 2013 <sup>24</sup>
Geraniol	Leaves, stems and flowers	Chanda S et al., 2013 <sup>24</sup>
2-methyl-3-ethylmaleic anhydride	Leaves, stems and flowers	Chanda S et al., 2013 <sup>24</sup>

## Pharmacological Activity:

**TABLE 3: ACTIVITIES OF PAEDERIA FOETIDA**

Activity	Pharmacological effects	References
Antioxidant effect	Decreases free radicals <i>in-vitro</i> (DPPH, ABTS, EDA assay). Inhibition of lipid peroxidation and increase. SOD, GPx, and CAT.	Tan et al., 2019 <sup>17</sup> , Kumar V et al., 2014 <sup>28</sup>
Anticancer effect	Inhibit cellular viability and induced apoptosis. Inhibition of DNMT1, HDACs and proinflammatory IL-6, IL1- $\beta$ , TNF- $\alpha$ , and anti-inflammatory IL-10 genes in cancer and THP1 cell lines. Expression of E-caderin (CDH1) and proapoptotic gene Bax increases significantly. Increase cytotoxicity in brine shrimp lethality bioassay.	Pradhan et al., 2019 <sup>29</sup> Sayeed MA et al., 2013 <sup>31</sup>
Anti-arthritic effect	Protection against CFA induced arthritis	Kumar V et al., 2015 <sup>32</sup>
Anti-hyperlipidemic	Lowering the level of lipid profile and decreasing the intercalated disc space in the heart.	Kumar V et al., 2014 <sup>28</sup>
Gastroprotective	Anticipated inhibition of H2 receptors resulting in decrease gastric acid secretion.	Reddy KS et al., 2011 <sup>33</sup>
Antidiarrhoeal	Decrease purging index value (PI). Decrease intestinal motility	Afroz S et al., 2006 <sup>34</sup>
Hepatoprotective	Decrease blood urea nitrogen (BUN), bilirubin, AST, ALT, triglycerides, and total cholesterol.	Borgohain MP et al., 2017 <sup>30</sup>
Renoprotective	Decrease concentration of thiobarbituric reactive substances in renal tissue. It showed dose-dependent inhibition of NF-Kb activation in the kidney	Borgohain MP et al., 2017 <sup>30</sup>
Anti-bacterial	Most effective in the growth of 8 multi-drug resistant enteropathogenic bacteria	Rath S et al., 2015 <sup>35</sup>

Analgesic activity	Involvement of endogenous opioids peptides in the mediation of analgesic activity	Das S <i>et al.</i> , 2012 <sup>36</sup>
Thrombolytic activity	It produces positive control to streptokinase	Ahmed A <i>et al.</i> , 2014 <sup>37</sup>
Anti-diabetic activity	Inhibit $\alpha$ -amylase and $\alpha$ -glucosidase	Tan <i>et al.</i> , 2019 <sup>17</sup>

**Anti-diabetic Activity:** Diabetes is a common endocrine disorder that occurs due to disturbances in carbohydrate metabolism. Inadequate secretion of insulin may be a significant cause of diabetes. Researchers are always trying to develop an alternative therapy using medicinal plants as additional therapy besides insulin therapy. Most of the studies on *Paederia foetida* have shown that it can help in reducing blood glucose levels. Vikash Kumar *et al.* has performed *in-vivo* anti-diabetic activity of *Paederia foetida* leaf extract on streptozocin induced diabetic albino Wistar rats. Three doses of PF leaves extract (100, 250, 500mg/kg) and standard glibenclamide were administered for 28 days to decrease the blood glucose level. It was reported that the maximum lowering of blood glucose level observed was 69.12% at the dose of 500mg/kg. The remaining two-dose 100 and 250mg/kg also showed a remarkable lowering of blood glucose level 55.74% and 61.76%<sup>26</sup>.

D.C Tan *et al.* reported the pronounced reduction of blood glucose level based on  $\alpha$ -amylase and  $\alpha$ -glucosidase inhibitory assay. The chloroform extract showed remarkable  $\alpha$ -amylase and  $\alpha$ -glucosidase inhibitory activity with an IC<sub>50</sub> value of 9.60±0.01 mg/mL and 245.6±0.01 mg/mL respectively<sup>5</sup>.

PF chloroform extract showed the highest anti-diabetic activity based on the two enzymatic inhibition assay models. PF chloroform extract inhibited  $\alpha$ -amylase activity with an IC<sub>50</sub> value of 9.60 ± 0.01 mg/mL comparable to standard acarbose (16.37 ± 0.01 mM). The inhibitory potential of the PF chloroform extract was significantly different (p<0.05) from that of other extracts. The PF chloroform extract also showed the strongest inhibition on the  $\alpha$ -glucosidase enzyme among all the extracts with IC<sub>50</sub> of 245.6 ± 0.01 mg/mL and p<0.05. Similarly, it shows a significant effect on the oral glucose tolerance test. Oral administration of different doses of PF extract and glibenclamide significantly decline (P <0.001) the rise in blood glucose levels, after glucose administration.

After loading the glucose, it was observed that glucose control group rats showed higher AUC glucose values. Oral administration of the different doses of the PF (100, 250 and 500 mg/kg) showed significantly (P < 0.001) lowers AUC glucose values as compared to the glucose control group rats<sup>26</sup>.

**Gastroprotective Activity:** Peptic ulcer disease is the inability of gastric or duodenal mucosa to resist the corrosive hydrochloric acid powder. Other than these *Helicobacter pylori* infection and oxidative stress are the major cause of the development of a gastric ulcer. Silpi Chandra *et al.*, 2015 has investigated the anti-ulcer activity of *Paederia foetida* on an animal model and observed inhibited gastric acid secretion and acid output in a dose-dependent manner by the administration of methanolic extract of two different doses (100 and 200mg/kg) of *Paederia foetida* on indomethacin-pylorus ligation model.

The gastric ulcer index was significantly decreased, showing 72 and 78% ulcer protection at 100 and 200mg/kg doses, respectively. After statistical analysis, the effect was found highly significant (p<0.001) for both doses. Similarly, it showed significant ulcer protection *i.e.* 59% and 72% to oral administration of ethanol-induced ulceration, whereas standard drug sucralfate showed 81% ulcer protection.

These doses also showed highly significant dose-dependent ulcer protection (62% and 67%) to the stomach mucosa of rats against the water immersion stress-induced ulcer (WISIU) model. In contrast, standard drug lansoprazole showed 70% protection. Similarly, the root extract of PF shows a significant result in pylori ligated ulceration and aspirin-induced model<sup>21</sup>. It significantly reduces the gastric acid volume to a significant extent P<0.01 whereas ranitidine reduced the volume of P<0.001. The ulcer index was significantly reduced with all the test samples. The order of reduction of ulcer score observed was ranitidine < ethanol extract < aqueous extract. Similarly, in the case of the aspirin-induced ulceration model, the PF extract



reduces the ulcer index significantly. It accelerates the ulcer healing by forming an ulcer adherent complex.

**Cardiovascular Disease:** Cardiovascular disease is a complex and multifactorial disease that includes elevation of lipids, increased plasma fibrinogen and coagulation factors, and increased platelet activation. The reactive oxygen species leads to the oxidative modification of LDL, which is considered as the major causative factors for the development of atherosclerosis<sup>16</sup>. The STZ-treated diabetic rats are found to have increased levels of cholesterol, triglyceride, LDL (low-density lipoproteins) VLDL (very low-density lipoproteins) and decreased HDL (high-density lipoproteins) compared to the normal control rats. Oral administration of different doses (100mg/kg, 250mg/kg and 500mg/kg p.o.) of extract showed percentage reduction in cholesterol (14.80%, 22.90%, 32.82%), triglyceride (11.48%, 21.07%, 33.72%), LDL (26.82%, 44.18%, 65.08%) and VLDL (11.48%, 21.07%, 33.72%), compared to the diabetic control rat group and the level of HDL (29.93%, 49.64%, 69.34%), was increased when compared to the diabetic control rat. Oral administration of 500mg/kg showed maximum benefits compared with other doses and standard drug glibenclamide in reducing the level of cholesterol, triglyceride, LDL and VLDL and increasing the level of HDL compared to the STZ induced diabetic control rat<sup>16</sup>.

**Cytotoxic Activity:** Cancer is a complex multifactorial disease arising through genetic and epigenetic factors. Proinflammatory stages are associated with multiple tumor development factors. The cytotoxic activity of Methanolic extract *Paederia foetida* (MEPF) is because of lupeol and  $\beta$ -sitosterol, which was examined by colorimetric MTT assay in both prostate cancer cell lines, PC-3 and DU-145 as well as in normal keratinocyte cells (HaCaT). A remarkable decrease in cellular viability was observed with an increase in the concentration of drugs in prostate cancer cell lines. But in the case of normal HaCaT cells, no significant lethal effect was observed as compared to the other two drugs and almost all cells remain viable even at a higher concentration of all drugs. The IC<sub>30</sub> values of MEPF, lupeol and  $\beta$ -sitosterol for PC-3 cells were found to be 20mg/ml, 50 $\mu$ M

and 80 $\mu$ M respectively and for DU-145 values were 1 mg/ml, 40 $\mu$ M and 70 $\mu$ M respectively. Similarly, in the THP1 cell line, cell viability assay was performed with varying concentrations of MEPF, lupeol and  $\beta$ -sitosterol for 24 h. A reduction in cell viability in a dose dependent manner was observed. IC<sub>50</sub> values of MEPF, lupeol and  $\beta$ -sitosterol in THP1 cells lines were found to be 25 mg/ml, 40  $\mu$ M, and 120  $\mu$ M respectively. Similarly, Methanolic extract of PF showed remarkable cytotoxic Activity with LC<sub>50</sub> value 51.59 $\mu$ g/ml, compared to vincristine sulfate, a reference drug, LC<sub>50</sub> 0.52  $\mu$ g/ml.

**Antioxidant Activity:** The crude extracts of *Paederia foetida* are well known for their antioxidant activity. Many researchers have investigated the activity using different solvent systems and assay techniques like DPPH, ABTS, SO and FRAP. The chloroform extract showed the strongest scavenging activity followed by ethyl acetate with IC<sub>50</sub> values of 27.27 $\pm$ 0.01 and 35.85 $\pm$ 0.05<sup>12</sup>. Moreover, Ojha *et al.* studied the change in antioxidant activity according to storing conditions. The fresh and shade dried leaf shows different maximum activity to methanol extract for 48-hour duration<sup>27</sup>.

**Antimicrobial Study:** Morshed *et al.*, have performed the antimicrobial assay by using the disc diffusion method. All the fractions of the plant, like methanol, n-hexane, ethyl acetate, and chloroform, were tested against gram-positive, gram-negative bacteria and fungal strains. The investigation showed that methanol extract of the whole plant neither possesses anti-microbial nor having antifungal activity at a concentration of 300 $\mu$ g where standard Kanamycin (30 $\mu$ g/disc) showed a zone of inhibition of 32-39 mm. The study was done for two times for the confirmation of no inhibitory effect.

But, in case of n-hexane fraction of the whole plant, it shows a moderate antibacterial activity for two gram-positive bacteria like *Bacillus cereus* (12mm) & *Staphylococcus aureus* (14mm) & two gram-negative strains *Escherichia coli* (18mm) and *Vibrio mimicus* (16mm) where *Pseudomonas aeruginosa* (10mm) possess less effect in-contrast to standard Kanamycin. The experiments also revealed that n-hexane extract possesses a very less

antifungal activity for *Candida albicans* (8mm) & *Sacharomyces cerevaca* (7mm)<sup>28</sup>.

**Anti-inflammatory Activity:** Subrata de *et al.*, reported that PF extract possesses significant anti-inflammatory activity in the cotton pellet granuloma model of inflammation. It remarkably decreases the inflammation 52% and 59% at 100mg/kg b.w. and 200mg/kg b.w. respectively<sup>10</sup>. Das *et al.*, showed that the ethanolic extract of PF of dose 500mg/kg b.w. produce a significant reduction of carrageenan induced paw edema<sup>24</sup>.

**Anti-diarrheal Activity:** *Paederia foetida* produced a remarkable anti-diarrheal effect in mice at 200 and 300mg/kg in castor oil-induced diarrhea. The aqueous and ethyl acetate extract showed significant ( $p < 0.001$ ) decreased number of excreted feces after oral administration of castor oil. For aqueous extract the values are  $7.20 \pm 0.37$  (200mg/kg) and  $6.40 \pm 0.51$  (300mg/kg), whereas, for ethyl acetate extract the values are  $7.20 \pm 0.37$  (200mg/kg) and  $6.40 \pm 0.51$  (300mg/kg). On the other hand, standard drug loperamide decreased the number of feces to  $4.80 \pm 0.37$  at the dose of 5mg/kg compared to the control group<sup>4</sup>. On the other hand, the ethanolic extract of PF leaves is found effective on acetic acid-induced colitis. It results in significant improvement in colon architecture macroscopically and microscopically. It reduces the ulcer size and improves the tissue level of CAT, SOD ( $P < 0.05$ ) and decrease in the levels of MPO, MDA ( $P < 0.05$ ). However, the standard drug 5-ASA showed improvement in all parameters<sup>24</sup>.

**Anti-arthritic Activity:** Arthritis is a chronic, systematic, and typical inflammatory disease that influences more than 1% of the total population globally. The pathological process involves swellings in joints, destruction of gristle and progressive ruination of subchondral bone and cartilage. Complete Freund's adjuvant (CFA) contains 1 mg/ml of dry heat killing tubercle bacillus (*Mycobacterium tuberculosis*) per sterile paraffin oil. CFA produced the inflammation through the liberation of blood cells, mastocyte activation, cytokines and the formation of free radicals. Subcutaneous injection of CFA caused serve arthritis throughout the rat hind paw. CFA induced rats treated with PF significantly ( $P < 0.001$ ) inhibited the paw edema a dose-

dependently. While the oral administration of PF (25 mg/kg b.w.), restrained the paw edema 1.158 with 28.61% inhibition, the paw edema followed by 50 mg/kg b.w. was 0.982 with 39.46 % inhibition and that at 100 mg/kg b.w. was only 0.65 with 59.93% inhibition. The paw edema inhibition with the indomethacin (10 mg/kg b.w.) was 0.71 with 56.23% inhibition<sup>20</sup>.

**Analgesic Activity:** The ethanolic extracts of the leaves of *Paederia foetida* produced significant analgesia, both centrally and peripherally. The combination of ethanolic extract (500 mg/kg s.c) of the plant and pethidine (5mg/kg i.p) along with the combination of the ethanolic extract (500mg/kg orally) and aspirin (100mg/kg orally) showed a significant reduction of the paw edema and increasing retention time induced by carrageenan thereby suggesting a good analgesic activity<sup>24</sup>.

**Anti-pyretic Activity:** Mir Muhammad Nasiruddin *et al.*, revealed that methanol and chloroform extracts of the plant showed significant antipyretic activity similar to that of paracetamol. The lower dose of methanol (200 mg/kg b.w) and chloroform (200 mg/kg b.w) showed a maximum reduction of temperature. Moreover the extracts (200 mg/kg b.w) showed significant ( $*p < 0.05$ ;  $**P < 0.01$ ) antipyretic activities in mice<sup>29</sup>.

**Nephroprotective Activity:** Borgohain *et al.*, 2017 reported that the methanolic extract of *Paederia foetida* leaf has a predominant nephroprotective action in the early stage of diabetes mellitus. This action is due to attenuation of renal oxidative stress and inhibition of NF-kB which is responsible for renoinflammation. They also reported that the creatinine clearance, an index of GFR, was significantly reduced in the diabetic untreated rats. A significant improvement was observed while treated with MEPF; especially at the 500 mg/kg b.w dose. Diabetic control rats exhibited marked elevated serum bilirubin, BUN, AST, and ALT; whereas serum albumin content significantly decreased. Although MEPF oral administration reversed these changes, the effects were more pronounced at 500 mg/kg b.w.

On the other hand, concerning plasma lipid contents (TRIGs & TCHOL), MEPF in both 250 and 500 mg/kg b.w. doses; significantly normalized

its level. The standard drug GLB showed overall significant results<sup>18</sup>.

**CONCLUSION:** This review article provides the maximum information of *Paederia foetida* about its traditional, phytochemicals, nutritional, Pharmacological benefits in society. The plant is widely distributed in South Asian countries like Bangladesh, India, Japan, Malaysia, Myanmar, Nepal, Thailand, etc. Thus the therapeutic value can reach a vast population in the world. It can be considered as a part of the diet to influence the degree of protection.

**CONFLICTS OF INTEREST:** The authors don't have any conflicts of interest.

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