A Comprehensive Review: Pharmacognostical and Pharmacological Insights into *Passiflora foetida*

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**ABSTRACT**

*Passiflora foetida*, commonly known as "stinking passionflower," is a medicinal plant with a long history of traditional use in various cultures for its therapeutic properties. This review provides an overview of the pharmacognostical and pharmacological characteristics of *Passiflora foetida*, highlighting its potential as a valuable source of bioactive compounds for pharmaceutical and nutraceutical applications. Pharmacognostical studies of *Passiflora foetida* encompass its morphological, anatomical, and chemical composition. Macroscopic and microscopic examinations reveal distinctive features such as the presence of glandular trichomes, characteristic floral structures, and specific secondary metabolites including flavonoids, alkaloids, and phenolic compounds. These features aid in the identification and quality control of *Passiflora foetida* plant material. Pharmacological investigations have demonstrated a wide range of biological activities associated with *Passiflora foetida* extracts and isolated compounds. These include anti-inflammatory, analgesic, antioxidant, antimicrobial, antidiabetic, and neuropharmacological effects, among others. Mechanistic studies have revealed the involvement of various molecular targets and pathways, supporting its traditional use in managing diverse health conditions. Furthermore, the safety profile of *Passiflora foetida* has been evaluated, with limited reports of adverse effects at recommended doses. However, further toxicological studies are warranted to fully assess its safety profile and potential interactions with other medications. In conclusion, *Passiflora foetida* exhibits promising pharmacognostical and pharmacological properties, validating its traditional use as a medicinal plant. Future research should focus on elucidating its mechanisms of action, exploring potential therapeutic applications, and standardizing extraction methods to harness its full therapeutic potential.

**KEYWORDS:** *Passiflora foetida*, Flavonoids, Alkaloids, Antioxidant, Neuropharmacological effect.
other inflammatory skin conditions [7]. Along with cancer, P. foetida has also been reported to treat anxiety, sleeplessness, convulsions, coughing, and sexual dysfunction [8]. Furthermore, research on P. foetida has shown that plant extracts exhibit a wide range of intriguing bioactivities, including hepatoprotective, anticancer, antibacterial, antinoceptive, analgesic, depressive, anti-inflammatory, and anti-diarrheal properties [7, 9, 10]. In a similar vein, a number of bioactive substances that were separated from P. foetida—particularly flavonoids—have demonstrated significant pharmacological activities. Examples of these include luteolin and chrysoeriol, which have been proven to have strong anti-inflammatory activities [11].

**Chemical Constituents of Passiflora foetida:** In 1980, the first report on chemical ingredient isolation was published. It is discovered that this plant mainly elaborates on flavonoids and their glycosides. The chemical composition of this plant's leaves and stems has been the primary focus of research.

**Constituents of Leaves:** The flavonoid chemicals that have been identified from the leaves include pachypodol [C1], ermanin [C3], and methoxylated derivatives of naringenin and apigenin (7, 4’-dimethoxyapigenin [C2], 4’, 7-O-dimethylapigenin [C4], 4',7-O-dimethylnaringenin [C5]), as well as the 3,5-dihydroxy-4,7-dimethoxy flavonone [C6] [12, 13].

Using a one-step purification process, passifloricidene [C7], an anti-microbial metabolite generated by stress, was isolated from vegetative leaf cuttings of Passiflora foetida [14].

**Constituents of Stem:** Apigenin [C8], luteolin [C9], luteolin-7-O-glucoside [C10], orientin [C11], chrysoeriol [C12], tricin [C13], tamarixetin [C14], and vitexin-2"-O-xylloside [C15] [15] are the ten flavonoids that were extracted from the stem bark of Passiflora foetida. According to reports, the stem has 77.9 weight percent of cellulose material, which is noteworthy for the paper industry [16].

**Constituents of Fruits:** By using hot water extraction, ethanol precipitation, and column chromatography, a new polysaccharide known as PFP1 [C16] was identified and suggested as a possible meal that might strengthen the immune system [17]. From the fruits PFP2 [C17], PFP3 [C18], and PFP4 [C19], three salt-eluted polysaccharides were extracted. Although they had a structural similarity, their molecular weights varied [18].

**Constituents of Resin:** Ten flavonoids, including kumatakenin [C20], 5-hydroxy-7,4’-dimethoxy flavone [C21], quercetin 3,3-dimethyl ether [C22], pachypodol [C1], 5-hydroxyl - 3, 7, 4-trimethoxylavone [C23], persi-cogenin [C24], ermanin [C3], and 5-hydroxy-7,4’-dimethoxy flavanone [C25] [19], were isolated from the ethanolic extract of the resin of Passiflora foetida.

After extracting the resin with ethanol, three polyketide α-pyrones known as passiflorisins [C26], [C27], and [C28] were obtained [20].

**Constituents of Seeds:** Five cyanohydrin glycosides with a cyclopentene ring were discovered in Passiflora foetida seeds that were gathered in the Galapagos Islands. These glycosides were identified as volkenin [C32], deidaclin [C31], tetraphyllin A [C29], and tetraphyllin B sulphate [C30]. Tetraphyllin B sulfate [C30], volkenin [C32], and cyclopentanone tetraphyllin B [C33] were found in seeds of the same plant that were gathered on Reunion Island. The species refined the Reunion Island-derived glycoside linamarin [C34], which is produced from valine [21].

**Medicinal Potential of Passiflora foetida:** The therapeutic qualities of Passiflora foetida are widely recognized. The antimicrobial, anti-inflammatory, hepatoprotective, antiepileptic, analgesic, anti-ulcer, antioxidant, hyperglycemic, cytotoxic, anti-diarrheal, cardioprotective, anti-dyslipidemia, osteoporotic, apoptic, and hypersensitivity activities of the extracts have all been examined. With an IC50 of 25.18 µg/mL in the ABTS experiment, its ethyl acetate extract notably demonstrates a strong potential for antioxidant activity [22].

**PHARMACOLOGICAL ACTIVITIES**

**Cytotoxic, Antiapoptotic effects:**

The purpose of this work was to analyze Passiflora foetida's cytotoxic and apoptotic effects and then identify the functional groups in charge of these effects. The methanol extract of P. foetida was used in this study to examine the cytotoxic and apoptotic effects on HeLa cell line cultures. The extract was added at different concentrations (25, 50, 75, 100, and 125 µg/ml) and the activity was confirmed using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay and propidium iodide staining. Using Fourier transform infrared spectroscopy analysis (FTIR), the functional groups of the bioactive substances were identified in order to determine the efficacy of the therapy. A dose-dependent rise in cytotoxic activity was observed, with an inhibitory concentration value of 21.55 µg/mL, indicating a successful apoptosis. Moreover, functional groups of alkaloids, flavonoids, saponins, steroids, terpenoids, phenols, and cardiac glycosides were validated by FTIR analysis, and these groups may be in charge of the previously mentioned action. P. foetida was shown to have highly potent cytotoxic and apoptotic properties, and its tenable functional groups were discovered [23].

**Anti-inflammatory activity:**

In traditional medicine, Passiflora foetida L. (Passifloraceae), a perennial climber in general, is used to cure a variety of illnesses. This study examined the role of nuclear factor-κB (NF-κB) signaling in the control of inflammation as well as the anti-inflammatory properties of methanolic extracts of P.
foetida L. (PFME). In lipopolysaccharide (LPS)-induced macrophage cells, PFME inhibited the expression of inducible cyclooxygenase-2 (COX-2) and the synthesis of prostaglandin E2 (PGE2). Furthermore, PFME inhibited the release of cytokines that promote inflammation. Furthermore, PFME inhibited the phosphorylation of MAPKs (ERK1/2, p38, and JNK) in LPS-induced RAW264.7 cells. Moreover, PFME prevented LPS-induced NF-κB activation, which was linked to nuclear p65 levels and the prevention of IκBα degradation and ensuing declines. These findings showed that the PFME suppressed the oxidative and inflammatory reactions brought on by LPS. Consequently, we suggest that the PFME could be useful in the treatment of inflammatory illnesses [24].

Antioxidant and antimicrobial activity:
The objective of this investigation was to ascertain the leaf extract of wild passion fruit (Passiflora foetida L.) and its chemical composition (IR), mineral characteristics (ICP-OES), antioxidant activity, total phenols, inhibition of acetylcholinesterase (AChE), and antibacterial activity. There was 16.78 mg of gallic acid equivalent 100 g-1 extract in the total phenolic content. The hexane extract showed 17.97% inhibition of free radicals in antioxidant activity. 96.46% suppression of AChE activity was observed. Regarding microorganisms, the extract shown inhibition of Salmonella (82.74%), Gram-negative Citrobacter freundii (82.74%), Gram-positive Bacillus cereus (77.93%), and Staphylococcus aureus (88.25%) yeast C. albicans (53.29%) and typhimurium (83.21%) [25].

Antihypertensive activity:
According to Ichimura et al. (2006), in spontaneously hypertensive rats (SHRs), oral administration of the plant's methanol extract (10 or 50 mg/kg) or luteolin (50 mg/kg), one of the extract's consistent polyphenols, dramatically reduced the SHRs' systolic and diastolic blood pressure. Liquid chromatography tandem mass spectrometry (LC-MS/MS) quantitative analysis revealed that the extract contained 41 g/g of luteolin-6-Cglucoside and 20 g/g of luteolin dry weight. Gamma amino butyric acid (GABA, 2.4 mg/g dry weight by LC-MS/MS), which has been described as an antihypertensive substance, was also present. The antihypertensive impact of the extract in SHRs may be mostly attributed to the GABA-induced antihypertensive effect and somewhat to the vasodilatory action of polyphenols, especially luteolin. The extract contained a comparatively high concentration of GABA [26].

Antiepileptic and analgesic activity:
The antiepileptic activity of Passiflora foetida was assessed in mice through two methods: maximum electroshock (MES) induced convulsions and pentylentetrazole induced convulsions. The analgesic activity was screened using Eddy’s hot plate method with aspirin as the standard drug. Results showed that doses of 100mg/kg and 300mg/kg of Passiflora foetida significantly reduced the severity of seizures compared to the standard drugs phenytoin and diazepam in MES and pentylentetrazole induced convulsions, respectively. Particularly, at these doses, Passiflora foetida completely abolished convulsions induced by pentylentetrazole. In terms of analgesic activity, the methanol extract of Passiflora foetida exhibited maximum effect at 120 minutes post-administration. Additionally, the study indicated that the methanol extract demonstrated good analgesic activity at a dose of 100mg/kg compared to 50mg/kg. In summary, Passiflora foetida showed promising antiepileptic and analgesic properties in the evaluated experimental models, warranting further investigation for potential therapeutic applications [27].

Anxiolytic activity:
Throughout history, plant-based remedies have held a crucial role in healthcare due to their accessibility, affordability, and acceptance by communities. Passiflora, a genus known for its medicinal properties, particularly in treating nervous disorders, was the focus of our study. We aimed to analyze the presence of secondary metabolites in the methanolic extract of Passiflora foetida and assess its potential anti-anxiety effects using the Elevated Plus Maze (EPM) animal model. Our investigation revealed the presence of various secondary metabolites in the crude extract, including alkaloids, coumarins, flavonoids, glycosides, oils, fats, phenols, resin, sterols, steroids, saponins, tannins, and quinones. We then tested the extract's anxiolytic activity at doses of 200 and 400 mg/kg administered orally to mice, comparing its efficacy with the standard anxiolytic drug, diazepam (3 mg/kg, i.p). The results demonstrated a dose-dependent increase in the number of entries into and time spent in the open arms of the maze, indicating anxiolytic effects. These findings provide scientific support for the traditional medicinal use of Passiflora foetida for its anxiolytic properties [28].

Hepatoprotective activity:
The potential protective effects of Passiflora foetida's aqueous extract (AEPF) on liver damage induced by paracetamol was explored in albino rats. Rats were divided into groups and treated for seven days: one group received distilled water (normal control), another received distilled water without AEPF (negative control), a third group received silymarin as a positive control, and the remaining groups were given different doses of AEPF. On the seventh day, all groups except the normal control were given paracetamol. After 24 hours, blood samples and liver tissues were collected for analysis. The results revealed that paracetamol caused significant increases in liver enzymes (ALT, AST and PAL) and bilirubin levels, as well as significant decreases in cholesterol, triglyceride, and protein levels in the rats. Additionally, the liver tissue showed severe damage. However, pretreatment with silymarin and AEPF mitigated these adverse effects in a dose-dependent manner. These findings suggest that Passiflora foetida may offer...
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hepatoprotective effects similar to silymarin, possibly due to its content of saponins, phenols, and flavonoids [29].

Immunomodulatory activity:
The study aimed to assess the immunomodulatory potential of ethanol, petroleum ether, and ethyl acetate extracts of Passiflora foetida Linn, an Indian medicinal plant belonging to the Passifloraceae family, known to contain alkaloids and flavonoids. The research followed OECD Guideline No. 425 for acute toxicity testing. Immunomodulatory activity was evaluated through in vitro phagocytosis assessment using PMNs phagocytic activity and in vivo macrophage phagocytosis using the carbon clearance assay method. The ethanol extract, at concentrations of 300 μg/ml in vitro and 300 mg/kg body weight in vivo, exhibited significant dose-dependent immunostimulatory effects compared to the control group. This activity is likely attributed to the presence of flavonoids, glycosides, and phytosterols in the ethanol extract. The findings suggest that Passiflora foetida Linn holds promise as a potential treatment for immune disorders, supporting its traditional use in folk medicine [30].

Antidiabetic activity:
This research explored the potential of Passiflora foetida (PF) methanolic extract to lower blood sugar levels in diabetic albino mice induced with alloxan. Diabetes, characterized by prolonged high blood sugar levels, poses significant health risks, and discovering effective treatments is crucial for reducing associated mortality and morbidity. The study induced diabetes in mice using alloxan and then administered varying concentrations of PF methanolic extract orally. Blood glucose levels were monitored at intervals over a 4-hour period. The extract demonstrated a significant reduction in blood glucose levels in diabetic mice (P<0.001). Additionally, key kinetic parameters such as area under the glucose concentration-time curve (AUC0-4hG), glucose mean residence time (MRTG), and glucose clearance rate (CLG) were notably improved in PF-treated groups compared to control groups. These findings suggest the presence of hypoglycemic components in the plant extract [31].

Antiulcer activity:
The current study aimed to assess the impact of an ethanolic extract derived from the entire Passiflora foetida plant on gastric ulcers. Researchers administered doses of 100 and 200 mg/kg of the extract and examined its effects on gastric ulcers induced by ethanol and aspirin. They also evaluated antioxidant levels and examined histological changes in the gastric tissue of ulcer-afflicted rats in both models. The results indicated that Passiflora foetida treatment significantly decreased ulcer severity and raised gastric pH levels in rats with ethanol and aspirin-induced ulcers. Additionally, the extract demonstrated notable reductions in lipid peroxidation and increases in reduced glutathione levels, affirming its antiulcer and antioxidant properties [32].

Antiosteoporotic activity:
The effect of butanolic fraction (BF) from Passiflora foetida was assessed on skeletal health in mice with estrogen deficiency-induced bone loss. The study was conducted on female Balb/c mice that underwent ovariectomy (OVx). The mice were given BF orally at doses of 50 and 100mg/kg/day for 8 weeks. We examined the microarchitecture of their long bones, assessed biomechanical strength, observed the formation of mineralized nodules by bone marrow osteoprogenitor cells, evaluated osteoid formation, and measured bone turnover markers. Statistical analysis using one-way ANOVA was employed to determine the significance of Passiflora foetida’s effects. Our results showed that OVx mice treated with BF exhibited improved microarchitectural parameters at different anatomical sites, enhanced bone biomechanical strength, and increased osteoprogenitor cells in the bone marrow compared to the OVx group. Importantly, BF did not demonstrate estrogenic effects on the uterus. Overall, oral administration of BF at both doses (50 and 100mg/kg/day) derived from Passiflora foetida demonstrated anti-osteoporotic effects under conditions of estrogen deficiency, likely by stimulating osteoblast function and inhibiting osteoclast function [33].

CONCLUSION
Passiflora foetida, widely distributed globally, hold promise for bio-prospecting and pharmaceutical development, particularly in addressing ailments like anxiety, insomnia, convulsions, sexual dysfunction, cough, cancer, and postmenopausal syndrome. Despite ongoing research, numerous avenues for exploring its medicinal properties remain unexplored. A detailed examination of its chemical components is presented in this review, revealing a wide array of pharmacological effects on various organs and physiological processes, including brain function, blood circulation, cardiovascular health, and nervous system regulation. The diverse range of preparations, extracts, and individual compounds derived from Passiflora foetida demonstrate a broad spectrum of therapeutic potential, impacting processes such as proteosynthesis, reproductice health, and sexual function. Harnessing the phytochemicals and minerals present in these plants holds promise for furthering their therapeutic applications.

ACKNOWLEDGEMENTS
Authors would like to express their sincere gratitude to Principal and Management of Gokaraju Rangaraju College of Pharmacy, for their invaluable guidance and support throughout this review project. Their expertise and insights have been instrumental in shaping the direction of our work.

CONFLICT OF INTEREST
Authors doesn’t have conflict of interest with the publication of manuscript.
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