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A COMPREHENSIVE REVIEW OF THE MEDICINAL PLANT *PASSIFLORA FOETIDA* LINN

Shubashini K. Sripathi* and R. Dhanya Sruthi

Department of Chemistry, Avinashilingam Institute for Home Science and Higher Education for Women, Coimbatore - 641043, Tamil Nadu, India.

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Correspondence to Author:

Shubashini K. Sripathi

Professor,
Department of Chemistry,
Avinashilingam Institute for Home
Science and Higher Education for
Women, Coimbatore - 641043, Tamil
Nadu, India.

E-mail: adusks2@gmail.com

ABSTRACT: *Passiflora foetida*, commonly known as stinking passion flower has been used as traditional medicine in treating diseases such as throat infection, giddiness, liver disorder, diarrhea, tumor, nervous disorder, anxiety; sleep disorders, skin infections, hysteria and asthma. In addition, *P. foetida* has been reported to have potential antioxidant, anti-inflammatory, antiepileptic, anti hyperglycemic, cardio protective, anti-diarrheal, and anti-cancer properties. Metabolites isolated from this plant are mainly flavonoids, polysaccharides, α -pyrones and cyanohydrins. The compounds have been isolated from the leaves, stems, seeds, resins and fruits. The stems of *P. foetida* have high cellulose content. The leaves and fruits of *Passiflora foetida* have high nutritional value that they find use as herbal tea, tablets and nutritional powders. Vitexin was quantified by a high-performance thin-layer chromatographic technique. These compounds tend to have diverse biological properties. This review article highlights the secondary metabolites, quantification of phytochemicals, proximate parameters, chemical constituents their activities and applications.

INTRODUCTION: The *Passiflora* is a genus of about five hundred and fifty species of flowering plants belonging to the Passifloraceae family. *Passiflora foetida* is a valuable medicinal plant native to tropical northern South America and West Indies. This species which is naturalized in many areas due to its properties, is polymorphic and is available in thirty-seven varieties. It is an important fruit crop used for medicinal and ornamental purposes¹. It grows at the edge of forests, plantations, river and creek banks, abandoned fields, roadsides, and moist lands, up to 1000m above sea level on all soil types and wet areas. The medicinal properties of this species is utilized in

folkloric medications for ailments like skin infections, diarrhea, throat infections, wound dressing, liver disorder, itching, tumor, headache, anxiety, nausea, and sleep disorders, as an insecticide, in treating neurological disorders, giddiness, asthma and hysteria². In India, the unripe fruit is used as an emetic, while the decoction of the dried herb is said to contain a diuretic effect. In Brazil, this plant is used as a poultice for erysipelas and for treating skin diseases with inflammation. It is reported to aid in treating the digestive problem like dyspepsia and as an astringent and expectorant for spasms¹.

The plant possesses anti-inflammatory, anti-tumor, anti-microbial, anti-oxidant, gastroprotective, and hepatoprotective activity. The taxonomic description of this plant is found at <https://www.itis.gov> (Taxonomic serial 22225). There are a few earlier reviews on *Passiflora foetida*. A review of the morphological characteristics of the whole plant, its

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phytopharmacology, and medicinal uses and propagation methods is also reviewed³. Another study elaborates on the status of the plant nationally and internationally, its geographical distribution, and habitat. The phytochemicals present and the pathway by which components are biosynthesized are summarized⁴. A thorough review of *Passiflora foetida* through search of available literature from 1989 to 2021 about the following aspects is presented in this paper.

- Proximate analysis of *Passiflora foetida*
- Quantification of constituents of *Passiflora foetida*
- Chemical constituents of *Passiflora foetida*
- Compounds quantified from HPTLC
- Constituents identified by gas chromatographic analysis
- Nano studies on *Passiflora foetida*
- Medicinal potential of *Passiflora foetida*
- Patents on *Passiflora foetida*

Qualitative Phytochemical Analysis of *Passiflora foetida*: The vast majority of the *Passiflora* plants grow wild in Southern and Central America and Mexico. However many species are also seen in the tropics too. Phytochemical screening of various parts of *Passiflora foetida* revealed the presence of essential oils and the common classes of secondary metabolites. It is host to cardiac glycosides also.

The fresh leaves are found to be cyanogenic in nature. However the mature leaves, fruits and seeds are of good medicinal potential. Phytochemical screening of the leaves indicated presence of alkaloids, saponins, tannins, glycosides, anthraquinones, carbohydrates, sugars and phenolic compounds in addition to vitamins and volatile oils^{5, 6}. Fresh fruits contain carbohydrates, flavonoids, alkaloids, phenols, terpenoids, tannins and saponins^{6, 7}. The seeds were found to contain alkaloids, flavonoids, tannins, phenol, and saponins⁷.

Proximate Analysis of *Passiflora foetida*: The proximate parameters of fruits of *Passiflora foetida* reported earlier are tabulated in **Table 1**. Other parts of the plant are not yet screened for these parameters⁸.

TABLE 1: PROXIMATE ANALYSIS FOR FRUITS OF *PASSIFLORA FOETIDA*

Part	Composition (g/100g fresh fruit)	Weight (g)
Fruit	Edible portion	62.73-8.85
	Inedible portion	10.15-37.27
	Water content	76±1
	Fat content	13±2
	Protein	0.15±0.01
	Ash	1.7±0.3

Nutritional Composition: The nutrient content of the fruits as reported⁸ is presented in **Table 2**. The data indicates that the fruits are rich in sugars, organic acids, amino acids and minerals

TABLE 2: NUTRIENT CONTENT OF THE FRUITS

Sugars	
Sugars	Total sugars (%)
Glucose	47.90
Fructose	47.90
Sucrose	4.20
Organic Acids	
Organic acids	Total organic acids (%)
Oxalic acid	29.17
Tartaric acid	4.17
Malic acid	4.17
Ascorbic acid	12.50
Citric acid	50.00
Amino Acids	
Amino acids	Total amino acids (%)
Aspartic acid	10.02
Serine	5.20
Glutamic	18.51
Glycine	5.74
Alanine	5.31
Cystine	1.64
Tyrosine	1.55
Phenylalanine	7.02
Arginine	12.76
Proline	4.20
Methionine	0.91
Threonine	3.71
Isoleucine	3.68
Leucine	6.75
Lysine	5.34
Histidine	2.61

Mineral Composition: *Passiflora foetida* fruits contain minerals such as phosphorus and potassium in higher levels⁸.

TABLE 3: MINERAL CONTENT OF THE FRUITS OF *PASSIFLORA FOETIDA*

Minerals	Total minerals (%)
Manganese	0.05
Copper	0.04
Iron	0.15
Zinc	0.17
Phosphorus	14.44
Sodium	1.68
Magnesium	6.71
Potassium	75.70
Calcium	1.06

Quantification of Phytochemical Content: Phytochemicals like alkaloids, phenols, flavonoids, saponins, and carbohydrates were quantified from the leaves and fruits of the plant.

Leaves are rich in alkaloids, phenol, flavonoids, and carbohydrates, whereas fruits contain more flavonoids and saponins.

TABLE 4: PHYTOCHEMICALS QUANTIFIED FROM DIFFERENT PARTS OF *PASSIFLORA FOETIDA*

Phytochemical	Method	Standard used	Concentration mg/g		Reference
			Leaves	Fruits	
Alkaloids	Bromocresol Green reagent	Atropine	5.162	0.260	[6]
Phenols	Folin Ciocalteu reagent	Gallic acid	2.464	1.66	[6]
Flavonoid	Aluminium chloride colorimetric method	Quercetin	0.238	4.56 1	[6]
		Rutin	17.10	-	[9]
Saponin	Separation procedure	Diosgene	0.953	1.442	[6]
Carbohydrate	Phenol sulphuric acid method	D-Glucose	3.897	-	[9]

Chemical Constituents of *Passiflora foetida*: The first report on the isolation of chemical constituents was made in 1980. This plant is found to elaborate largely on flavonoids and their glycosides.

Three salt-eluted polysaccharides were isolated from the fruits PFP2 [C17], PFP3 [C18], PFP4 [C19] they were structurally similar but had different molecular weights¹⁶.

The leaves and stems of this plant have been mainly investigated for their chemical constituents. The chart below gives the structure of the compounds isolated from *Passiflora foetida*.

Constituents of Resin: Ten flavonoids were isolated from the ethanolic extract of the resin of *Passiflora foetida*, namely kumatakenin [C20], 5-hydroxy-7,4'-dimethoxy flavone [C21], quercetin 3,3-dimethyl ether [C22], pachypodol [C1], 5-hydroxyl - 3, 7, 4-trimethoxyflavone [C23], persicogenin [C24], ermanin [C3] and 5-hydroxy-7,4'-dimethoxy flavanone [C25]¹⁷.

Constituents of Leaves: The flavonoid compounds pachypodol [C1], ermanin [C3] and methoxylated derivatives of apigenin and naringenin (7, 4'-dimethoxyapigenin [C2], 4', 7-O-dimethylapigenin [C4], 4',7-O-dimethylnaringenin [C5]) and the 3,5-dihydroxy-4,7-dimethoxy flavanone [C6] have been isolated from the leaves^{10,11}.

Further, the resin was extracted with ethanol to give three polyketide α -pyrones named passifloricins [C26], [C27], [C28]¹⁸.

Passifloricidine [C7], a stress-induced antimicrobial metabolite, was extracted by a one-step purification method from the vegetative leaf cuttings of *Passiflora foetida*¹².

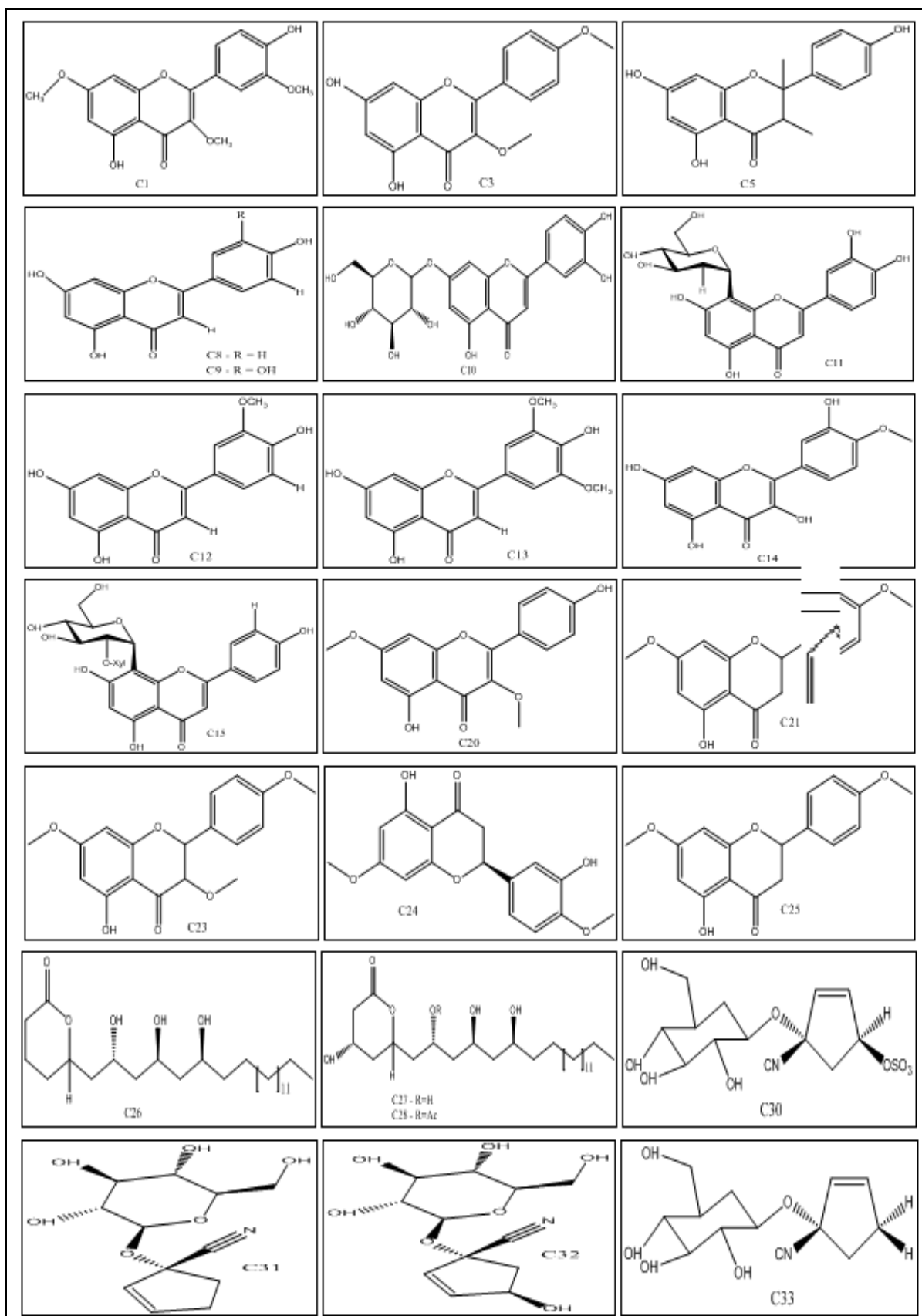
Constituents of Seeds: Seeds of *Passiflora foetida* collected on the Galapagos Islands were found to contain five cyanohydrins glycosides with a cyclopentene ring and characterized as tetraphyllin A [C29], tetraphyllin B sulphate [C30], deidaclin [C31] and volkenin [C32].

Constituents of Stem: Ten flavonoids were isolated from the stem bark of *Passiflora foetida*, namely apigenin [C8], luteolin [C9], luteolin-7-O-glucoside [C10], orientin [C11], chrysoeriol [C12], triclin [C13], tamarixetin [C14] and vitexin-2''-O-xyloside [C15]¹³. The stem is reported to contain 77.9 wt% of cellulosic content, which is significant in paper industry¹⁴.

Seeds of the same plant collected on Reunion Island contained cyclopentanone tetraphyllin B [C33], volkenin [C32], and tetraphyllin B sulphate [C30]. The species elaborated the valine-derived glycoside linamarin [C34] from Reunion Island.

Constituents of Fruits: A novel polysaccharide PFP1 [C16] was isolated by hot water extraction, ethanol precipitation, and column chromatography and proposed as a potential immune-enhancing food¹⁵.

This study revealed the significance of the plant's geographical location in synthesizing its constituents and its morphological characteristics¹⁹.



Compounds Quantified from HPTLC: The flavonoid vitexin was quantified in the leaves of *Passiflora foetida*²⁰ and in herbal formulations

containing leaves of *Passiflora foetida* by High-Performance Thin-Layer chromatographic method. The protocols adopted are given below in **Table 5**.

TABLE 5: QUANTIFICATION OF VITEXIN FROM LEAVES OF PASSIFLORA FOETIDA

Parameter	Protocol – I ²⁰	Protocol – II ²¹
Standard phase	Silica gel 60 F254 HPTLC plate	20 × 10 cm glass-coated silica gel 60 F254 plates
Mobile phase	Ethyl acetate: methanol: distilled water: formic acid (50:2:3:6, v/v)	Ethyl acetate: methanol: water: formic acid 30:4: 2: 1(% , v/v/v/v)
Detector	TLC Densitometric detector	TLC Densitometric detector
Wavelength	340nm	340nm
Injection Volume	10µL	10µL
Rf	0.70	0.49
Range of Linearity (µg/mL)	2.5–17.5	0.1-0.7
Correlation coefficient	0.996	0.9966
LOQ (mg/mL)	0.879	0.0065
LOD(mg/mL)	0.290	0.01512

Protocol II is a simple and efficient method for the estimation of vitexin since it revealed better Rf value and linearity range than protocol I²¹.

Constituents Identified by Gas Chromatographic Analysis: Gas chromatographic analysis has analyzed extracts of the various parts of

Passiflora foetida. The protocols adopted and the compounds predicted are listed in the tables below.

Protocol I was adopted for seeds and fruits⁷ and protocol II for the essential oil from fruits and stems²².

TABLE 6: PROTOCOLS ADOPTED IN GC-MS ANALYSIS

Parameters	Protocol I ⁷	Protocol II ²²
Instrument	Gc Clarius 500 Perkin Elmer) Analyzer	Agilent 7809a Gas Chromatograph
Ion Source Temperature	-	200°C
Spectral Range M/Z	-	50-700
Scan Rate Amu/Sec	-	1428
Column	Elite-1	Hp-5ms
Length (M)	30	30
Diameter (Mm)	0.25	0.25
THICKNESS (µm)	1	0.25
Flow Rate MI/Min	1	1

TABLE 7: CHEMICAL CONSTITUENTS PREDICTED BY GC-MS ANALYSIS OF PASSIFLORA FOETIDA

Plant Part analyzed and Compounds Predicted			
Protocol I ⁷		Protocol II ²²	
Seeds	Fruits	Essential oil of Stems	Essential oil of Fruits
Cyclopropane	1,3,5-Cycloheptatriene	(R)-(-)-14-Methyl-8-	5-butyldocosane
dodecanoic acid, 2-octyl, methyl ester	11,14-Eicosadienoic acid, methyl ester	hexadecyn-1-ol	7a-isopropenyl-4,5-dimethyloctahydronide
Oxalic acid, isobutyl nonyl ester	11,14-Eicosadienoic acid, methyl ester	Bromoacetic acid, tetradecylester	n-4-ylmethanol
Nonanoic acid, 9-oxo-, methyl ester	2',3'-Dideoxyribonolactone	Cyclotetradecane	9-Tricosane
Hexadecanoic acid, methyl ester	2-Furancarboxaldehyde, 5-methyl	Diethylphthalate	Carbonic acid
11-Octadecenoic acid, methyl ester	4H-Pyran-4-one, 2,3-dihydro-	E,E-6,11-Tridecadien-1-ol acetate	octadecylvinylester
Hexadecanoic acid, 15-methyl-methyl ester	3,5- dihydroxy-6-methyl	Hexahydrofarnesyl acetone	Caryophyllene
11-Octadecenoic acid, methyl ester	5-Hydroxymethylfurfural	Methylpalmitate	Cyclotetradecane
Hexadecanoic acid, 15-methyl-methyl ester	7-Hexadecenoic acid, methyl ester, (Z)	Oleamide	Ethyllinoleate
11-Octadecenoic acid, methyl ester	Furan	Pentadecanal	Galaxolide
Octane, 2,4,6-trimethyl	Furfura	Phthalic acid, 8 chlorooctylisobutyl ester	Heneicosane
Octane, 2,4,6-trimethyl	Hexadecanoic acid, 15-methyl-, methyl ester	Phytol	Linoleic acid
Heptadecane, 2,6-dimethyl	Hexadecanoic acid, 15-methyl-, methyl ester	Tetradecanal	Octadecane
9,12-Octadecadienoic acid, methyl ester	Levogluosenone	Z,Z-7,10-	Oleamide
Phthalic acid, isobutyl octyl ester	N-Aminopyrrolidine	Hexadecadienal	Palmitic acid
	Propargyl alcohol		Tetradecanal
			Trans 3-eicosane
			Tricosane
			Trogodermal

Nanoparticle Synthesis: Bio-mediated nanoparticle synthesis is the decade's trend. Silver, iron oxide, and copper nanoparticles were synthesized from leaf extracts of *Passiflora foetida*. Iron oxide nanoparticles prepared using leaf aqueous extract of *Passiflora foetida* were found to be spherical with size ranging from 10 to 16nm²³. Copper and silver nanoparticles synthesized by conventional methods from leaf extract of *Passiflora foetida* showed absorption maximum at 350 and 435.13nm, respectively²⁴, Reddy *et al.*, (2018). Zinc oxide nanoparticles synthesized by cavitation technique from fruit peels of *Passiflora foetida*. The nanoparticles were confirmed to have hexagonal wurzite structure with 58nm size²⁶. A low-cost silver nanoparticle fabrication was attempted by immersing a circular disk of

Passiflora foetida leaf (2 cm) in silver nitrate solution. This method is proposed as a cost-effective process of synthesis of stable nanoparticles²⁷.

Medicinal Potential of *Passiflora foetida*: *Passiflora foetida* is well known for its medicinal properties. The extracts have been analyzed for their anti-microbial, anti-inflammatory, hepatoprotective, antiepileptic, analgesic, anti-ulcer, antioxidant, hyperglycemic, cytotoxic, anti-diarrheal, cardioprotective, anti-dyslipidemia, osteoporotic, apoptic and hypersensitivity activity. Notably, its ethyl acetate extract exhibits a high anti-oxidant potential with an IC₅₀ of 25.18 µg/mL in ABTS assay.

TABLE 8: ACTIVITY STUDIES REPORTED IN THE EXTRACTS OF PASSIFLORA FOETIDA

S. no.	Plant Part	Extracts	Activity Studied and method adopted	Activity Potential	Reference
1.	Fruits	Ethanol extract	Hepatoprotective (in albino mice)	-	[28]
2.	Leaf	Methanol	Antiepileptic (in swiss albino mice by maximum electroshock-induced convulsions and pentylenetetrazol-induced convulsions)	Maximum activity was found at 100mg/kg and 300mg/kg.	[29]
3.	Leaf	Methanol	Analgesic	Maximum activity at 100mg/kg.	[29]
4.	Leaf	Ethanol extract	Analgesic (Hot plate test and Writhing test in mice)	Writhing test (37.50±0.65) and hot plate test (13.50±0.43)	[30]
5.		Ethanol extract	Anti-Ulcer (aspirin-induced model and absolute ethanol-induced model)	100 and 200mg/kg reduced ulcer index to 67.83 and 79.45% and 64.30 and 71.66% in aspirin and ethanol models, respectively	[31]
6.	Fruits	-	Anti-oxidant activity (DPPH method)	SC ₅₀ = 2.75-6.38mg/mL	[8]
7.	Leaf	Ethyl acetate	Anti-oxidant activity (DPPH and ABTS method)	IC ₅₀ for DPPH= 614.405 µg/mL and IC ₅₀ for ABTS = 25.18 µg/mL	[32]
8.	Leaf	Ethanol	Anti-inflammatory activity (Carrageenan-induced acute paw edema and Histamine induced acute paw edema)	significant acute anti-inflammatory effect carrageenan [(1.302±0.079) mL] Histamine [1.523±0.052) mL]	[30]
9.	Leaf	Methanol	Anti-inflammatory		[33]
10.	Leaf	Aqueous	Anti-hyperglycemic	Highest activity was observed at 90mins at a dose of 433mg/kg.	[34]
11.		Ethanol	Anti-hyperglycemic	Lowers blood sugar at 400mg/kgbw	[35]
12.		Ethanol	Anti-diarrhoeal activity	Decreased the number of stools at the dosage of 500 and 250 mg/kg.	[36]
13.		Ethanol	Cytotoxic activity (Brine shrimp assay)	LC ₅₀ of the extract at 320µg/mL was 80µg/mL	[36]
14.		Methanol	Cytotoxicity (HeLa cell line culture)	IC 50 – 21.55µG/ml	[37]
15.	Seeds	Ethanol	Cardioprotective activity	100mg/kg body weight	[38]
16.	Leaves	E thanol	Anti-dyslipidemia	At the dose of 500 mg/kg, body weight showed a significant lowering effect on dextrose-induced diabetic rats	[39]
17.		Butanol and Ethanol	Osteoporotic activity	Ethanolic extract – 500 and 750mg/kg/day and butanolic	[40]

				fraction -50 and 100mg/kg/day were effective	
18.	Leaves	Methanol	Apoptic activity	-	[41]
19.		Ethanol	Hypersensitivity		[42]
20.		Ethyl acetate	Anti-bacterial activity	MIC values are 0.4%, 0.8% and 1.6%. MBC 0.8% and 1.6%.	[43]

Toxicity Studies: Administration of *Passiflora foetida* leaf extract did not affect rats' food intake, body weight and organ weight as reported in a toxicity assay⁴⁴. It was proposed that the presence of C-glycosyl flavonoids such as vitexin and isovitexin may play a major role in decreasing corticosteroid synthesis in the adrenal cortex, indicating the safety of the use of the leaf extract. However, yet another study reported the leaves to be toxic to goats, which, when administered two days after collection at a dose of 40g per kg body weight, was found non-toxic. Still, the plant, when administered immediately after collection at a rate of 4-8g was found to have toxic effects. The goat, administered with 8g of the extract, showed clinical signs but recovered after treatment with thiosulfate. In a subsequent study, the leaves were fed to goats in different seasons, and the results showed that this plant was more toxic in the summer than in the rainy season⁴⁵.

Patents on *Passiflora foetida*: Patents on herbal teas, nutritional powders, and tablets prepared with leaves and fruits of *P. foetida* have been reported. Leaves of *Passiflora foetida* made into herbal tea, and other herbs are reported to arrest cough and moisten the lungs. This tea which has a sweet taste and low sugar content, is proposed to have no adverse effects even on long-term administration⁴⁶. Health tablets were made with *Passiflora foetida* and *Gynura bicolor* as base materials to help detoxify and clean the lungs to relieve cough, stop bleeding and remove swelling⁴⁷.

The fruit of *Passiflora foetida* is made into a nutritional powder and used as a beverage for detoxification. It helps remove the heat from the lungs, warming the stomach, getting rid of swelling, and detoxifying⁴⁸. A healthy tea was made using the fruits of *Passiflora foetida* and the flowers of vitex. It was found to produce health benefits like elevating qi (energy) to alleviate pain, helping in curing malaria, and detoxifying the lungs. The product is said to have a rich aroma and high nutritional value⁴⁹.

CONCLUSION: Medicinal plants pave the way for the discovery of novel drugs used to cure many diseases. These drugs come with improved efficacy and efficiency. This review contains complete information about the plant *Passiflora foetida*. The quantitative and qualitative aspects of phytochemicals, bioactive components, biomarkers, folkloric use, isolated compounds, and activities are reviewed in this paper. *Passiflora foetida* predominantly elaborates flavonoids. The stems are found to be a good source of cellulose (77.9 wt %) and hence proposed as an alternate source of the paper making of cellulosic content

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