

# The active compounds of *Passiflora* spp and their potential medicinal uses from both in vitro and in vivo evidences

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## Abstract

Plants belonging to the Genus *Passiflora* have been commonly used in traditional medicine for a variety of health conditions. The major bioactive components present in these plants are identified as flavonoids, alkaloids, glycosides and phenolic compounds. Six species belonging to the Genus *Passiflora* which have been well documented are *P. alata*, *P. caerulea*, *P. edulis*, *P. foetida*, *P. incarnata*, *P. ligularis*. Also, the subspecies *P. edulis* Sims f. *Flavicarpa* has been well documented for its phytochemical composition and human healthcare applications. There are well documented evidence-based scientific studies which are continuing to be reported on the medicinal value of these plants. These studies include both in vitro and in vivo studies using cell lines and animal models, respectively. The studies highlight the importance of these plant species for their therapeutic values in gastrointestinal conditions, neurological complications, cardiovascular conditions, inflammation and as anti-anxiolytic agents. We present in this review a systematic account on the phyto-constituents present in various plant parts of the six different species of this Genus along with the in vitro and in vivo experiments that highlighted their pharmacological importance.

## Key words

*Passiflora*; extracts; phytochemicals; in vitro evidences; in vivo evidences

## 1. Introduction

The Genus *Passiflora* comprises of more than 550 species which are commonly referred to as the passion vines or passion flowers. The diversity among the species belonging to this Genus includes herbs, woody trees and vines with tendrils. The Genus *Passiflora* belongs to the Order *Malpighiales* and the Family *Passifloraceae*. The plants belonging to this Genus have been used in traditional medicine for a variety of conditions such as gastrointestinal conditions, neurological complications, cardiovascular conditions, inflammation and anxiety. These uses were attributed to the presence of several active compounds such as phenolics compounds, alkalides, glycosides, flavanoids and saponins [1]. Of the several species belonging to this Genus, six species and one sub-species have been well documented for their human medicinal value. We present in this review, the medicinal importance of these six species namely *P. alata*, *P. caerulea*, *P. edulis*, *P. foetida*, *P. incarnata* and *P. ligularis*. We have systematically presented the major medicinally important phytoconstituents of the various parts of these plants namely the fruits, the flowers, the leaves, the seed and the stem. Also, the medicinal applications of these parts and their constituent phytochemicals are presented, the overview of which is illustrated in Figure 1.

The sub-species *P. edulis* Sims f. *Flavicarpa*, commonly known as the yellow passion fruit is known to have significant medicinal values in traditional medicine. Hence, we present comprehensively the phytochemicals present in the various parts of this plant, the manner in which they are used, along with the

conditions for which they have been commonly used for human health care in Table 1.

We present here comprehensively the in vitro and in vivo experiments reported using the extracts of these species on cell lines and animal models, respectively as Tables 2 and 3. Most of the references we have cited in this review are recent ones and were published in the past decade. Also, several recognized sources of literature were referred to for obtaining the information. This current review demonstrates the-usefulness of the plants, their significant role in traditional medicine and the continuing increase in experimental evidence-based studies that are being reported for better understanding and utilizing these plants for human medicinal applications. Apart from these reasons, the previous comprehensive review in similar terms was published in 2011 [1] and there is a need for an update owing to the potential promises for drug discovery that these plant species offer.

## 2. Uses in Traditional medicine

### 2.1 *Passiflora alata*

*Passiflora alata*, the winged-stem passion flower is an evergreen vine which grows up to 6 metres or more. It is native to the Amazon and found from Peru to Eastern Brazil. The fruits, leaves and seeds of this plant are known to have several medicinal properties.

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**Table 1.** The major parts of the plant *P. edulis* Sims f. *Flavicarpum* that are used medicinally include the bark, fruit, flower, leaves and seeds. The major phytochemicals of these parts include flavanoids, sterols, phenolics compounds, polyphenols and carotenoids. The extracts from the various parts have specific constituents with well documented uses in traditional human health care. The plant parts of *P. edulis* Sims f. *Flavicarpum*, the extracts obtained from these parts, the active compounds present in the extracts and their traditional uses in human health care are presented.

Parts of the plant	Active Compound present	Role of the active compounds	Uses in Traditional medicine	Processing of the plant parts	Ref.
Bark	Pectin (soluble fibers) Carotenoids Phenols	The treatment with bark of <i>Passiflora edulis</i> (BPe) was effective in reducing cholesterol and triglyceride levels  Increases antioxidant protection and decreases lipid peroxidation which may avoid manifestation of oxidative stress associated with diseases such as hepatic and renal failure	Antihypertensive effect reduces the risk of diabetes, obesity and cardiovascular disease	The fruit bark (exocarp) was washed, cut into pieces and oven dried at 60°C. The dried barks were crushed in a mill. The commercial chow was ground, moisture removed and pelleted for consumption	[45]
Fruit (Peel)	Dietary fibers (soluble and insoluble) Hemicellulosic polysaccharides Pectin	Soluble dietary fiber composed of 92% of alpha-galactosidase (GalA) units and presented high methyl esterified homo galacturonan  Oral administration of soluble dietary fibre (SDF) significantly reduced gastric ulcerations induced by ethanol and prevented depletion of growth stimulating hormone (GSH) levels and gastric wall mucous	Reduction in fasting blood glucose and glycated hemoglobin in type 2 diabetes individuals  Reduces triglycerides level in hyper cholesteramic women	The peels were cut and dried at 50°C to reach 10% of moisture. After drying it was ground in a hammer mill to obtain flour and stored. Passion fruit peel (PFP) flour was defatted, air dried to obtain soluble and insoluble dietary fibers	[46]
Fruit (peel)	Pectin	Pectin contributes gelification, emulsion stabilization and nutritional fiber delivery  High methoxy pectins are mostly used for jams and serves as a stabilizer	Anti- diarrhoeal, gastro-esophageal reflux diseases	The pulp and the seeds of the passion fruit peel were washed with distilled water. Batch culture was performed for the production of the enzyme from <i>Geotrichum klebahnii</i> called proto pectinase. The crude enzyme was separated by centrifugation and stored. The fresh peel was added with 60 ml of sodium citrate	[47]
Fruit (pulp peel seed)	Quercetin	Quercetin is known for its anti-inflammatory, vasodilator effect, anti-obesity and anti-atherosclerotic activity	The nutraceutical compounds present in different parts have biological activities in the health, protective effect against degenerative and chronic diseases as well as acts as mutagenesis and carcinogenesis inhibitor.	The yellow passion fruits were collected, separation of pulp, peel and seeds were made. They were packed in plastic bags and stored in freezer. Further physiochemical analysis, yield and proximate composition were determined by triplicate analysis.	[48]
Fruit (pulp)	Beta -cryptoxanthin (carotenoid) Tocopherol	Vitamin E (alpha-tocopherol) is the most biologically active form which prevents body from harmful free radicals  Beta- cryptoxanthin is a precursor of Vitamin A which is an essential element for eyesight and immune response	Antioxidant activity	The passion fruits were obtained and allowed to ripen. The samples were immediately evaluated in triplicate. The seeds were separated and pulp was homogenized in a mixture and the biocompounds were separated using different chromatographic techniques	[49]

Fruit (pulp)	Beta-carotene	The beta-carotene plays a crucial role against free radical scavenging  Improves cognitive functions and prevents erythropoietic protoporphyria	Antioxidant property	The mesocarp of passion fruit was centrifuged at 1027 g for 10 min at 15 °C. The precipitate was blended with corn starch in different concentrations. The blend was homogenized for 20 minutes using blender at minimum speed and passed through a 0.60 mm mesh.	[50]
Fruit (pulp)	Carotenoid	A sufficient intake of carotenoid to support the body's own antioxidative network could therefore combat the development of diseases such as hypertension, cardiovascular diseases	Antihypertensive effect	The bioactive compounds in the pulp were separated using high performance liquid chromatography (HPTLC). This was connected in series with photodiode array and mass spectrometry detectors with ion trap analyzer.	[51]
Fruit (pulp)	Flavonoids	Flavonoids present in the plant play a role in anti-coagulation by inhibiting intrinsic and extrinsic coagulation factor  Also, a mild trypsin inhibitory activity was observed	Anxiolytic, anti-fungal and anti-coagulant activity	The pulp was mechanically separated from seeds and centrifuged for 20 min. The supernatant was precipitated with acetone. The heat stability of trypsin inhibitor was done by heating <i>P. edulis</i> acetone fractionation (Pe-AF) at 100°C. The anti-coagulant activity was performed by Partial thromboplastin time (PTT) assay (coagulant assay)	[52]
Fruit (seed)	Linoleic acid (n-6) Alpha linolenic (n-3) acid	High amount of linoleic acids were obtained from the non-polar solvent such as propane and hexane  The seed oil containing alpha-linolenic acid exhibited antimicrobial property indicating the potential for their use as natural preservative	High antioxidant capacity  Regulates a variety of physiological and biological functions and provides protective effect	The pulp containing seeds was removed, washed and dried in a circulating oven. The dried seeds were grounded in a blender and separated using a series of sieves with the help of a mechanical stirrer	[53]
Fruit (seed)	Piceatannol	Piceatannol, a polyphenol exhibits a higher antioxidant activity  Polyphenols have ability to donate electrons or hydroxyl radicals to the DPPH (1,1-diphenyl- 2-picryl hydrazyl) radicals to become a stable diamagnetic molecule	The bio-active compounds exert health benefits such as protection against the development of chronic non-communicable diseases	Seeds were sanitized, freeze-dried and milled for storage in polyethylene containers at 20 °C. The chemical characterization of the sample was done by inductively coupled plasma optical emission spectrometry. The total phenol content and total flavonoid content were determined	[54]
Leaf	Flavonoids	Due to the presence of flavonoids in the aqueous extract, it has been evaluated to have anti-cancer activity  They prevent the action of matrix-metalloprotease-2 (MMP-2) and MMP-9 enzymes, therefore they inhibit tumor invasion and metastasis	Antioxidant , inhibition of tumor invasion and metastasis	Fresh leaves were desiccated in a circulating air oven, converted into powder and extract was obtained using 500 mL of 96% ethanol. The chlorophyll was separated by liquid-liquid extraction. The ethanol was evaporated and the solid was resuspended in DMSO and filtered. The compounds in the extract were identified by HPLC-DAD. Different assays were performed to detect its biological activity	[55]
Leaf	Polyphenol	The polyphenolic content was higher in leaf extract, the cell viability increased with concentration of extract  The leaf extract has pro-apoptotic activity in liver cancer cells (in vitro)	Anti cell-proliferative effect	The ethanolic extract of leaves was obtained by using 96% of ethanol, a process lasting 8 days	[56]

Leaf	Polyphenol	Polyphenols have antioxidant property  Plays a significant role in pathophysiological process associated with oxidative stress	Leaf extract plays a major role in neutralizing the free radicals and effective for Diabetes mellitus therapy/management Anxiolytic, sedative, anti-hypertensive, anti-inflammatory, cytotoxic and anti-fungal properties	Pre- and post-interventional design or Quasi design by the collection of fresh leaves	[57]
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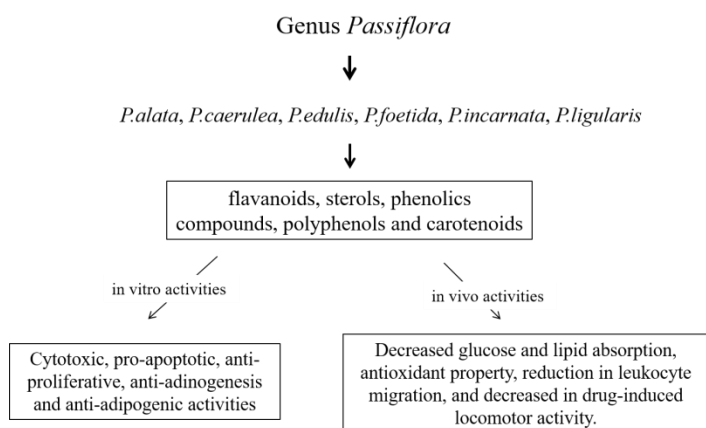
**Table 2.** The in vitro studies in *Passiflora edulis* Sims f. *Flavicarpa* were chiefly performed using extracts from leaves and seeds. Typically, the extracts were aqueous, ethanol and hydro-alcoholic ones. The major cell lines used were SW-480, HepG2, 3T3- L1 and MCF-7. The results indicated useful cytotoxic, pro-apoptotic, anti-proliferative, anti-adenogenesis and anti-adipogenic activities.

Parts of the plant	Bioactive component	Cell lines used	Cell line culture conditions	Concentration of the extracts	Observations	Result	Ref.
Leaf	Flavonoids Rutin Quercetin	SW-480 (human colon adenocarcinoma cell line and Caco-2 (human colonic adenocarcinoma cells))	Dulbecco's Modified Eagle Medium (DMEM) supplemented with 25mM of glucose, 2mM L-glutamine, 100UI/ml penicillin and 100µg/ml streptomycin and 1% of non-essential amino acids	The cell lines were inoculated in 2 ml volume of ITS medium and maintained at 48 hrs. After incubation, the cells were resuspended in 1 ml of DMEM medium. The extracts concentration studied were added 5%, 5.5% 7%. An aliquot of 200 ml was taken from each concentration and mixed with 2ml of ITS solution and cells were cultured for 7 days	Cell viability was significant after 24 hrs of treatment for concentrations higher than 5%. The cell cycle distribution of the exposed cells showed an increased cell proportion in the S phase and decreased in the G <sub>2</sub> /M phases. The ethanolic extract induced a stronger response in Caco-2 cells compared to SW-480 cells	The ethanolic extract induced both cytotoxic and anti-proliferative effects. The extracts induced cell death in both cell lines	[55]
Leaf	Polyphenol	HepG2 (human liver cancer cell line)	Cells were cultured in DMEM medium supplemented with 10% fetal bovine serum, 100U/mL streptomycin and maintained at 37°C in a humidified atmosphere with 5% CO <sub>2</sub>	The evaluation of the cytotoxicity of the extracts was performed using MTT ((4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) assay. After 24 hrs of culture, the cells were exposed to 25µg/ml, 50 µg/ml, 100 µg/ml, 200 µg/ml, 400 µg/ml concentrations of the extract for 24, 48 and 72 hrs	The yield of leaf extract was 2% and that of the leaf was 39%. The leaf extract has more polyphenolic content than the juice extract	In comparison with other cell lines, HepG2 cells showed greater resistance to the biological activity of both polyphenols and polysaccharides. The potent cytotoxic effect was attributed to β-carbonyl alkaloid present in the extract	[56]

Leaf	Phenols Flavonoids	3T3- (murine adipose tissues)	L1	The stock cultures of the cell lines were propagated in DMEM medium supplemented with 10% in activated foetal bovine serum, penicillin, streptomycin and amphotericin B in a CO <sub>2</sub> at 37°C until confluent  Harvest of cells was performed using 0.2% trypsin, 0.02% ethylene diamine tetra acetic acid (EDTA) in PBS solution  All experiments were carried out in 96-well plates	The concentration of the test drugs tested ranged from 50µg to 450µg  100 ml of different test concentration of test drugs were added on to the partial monolayer confluent  The effect of plant extracts was analysed using MTT assay MTT reagent to the final concentration of 0.5 mg/ml of total volume was added to the wells  Simvastatin was used as a positive control and the absorbance was read using an ELISA reader at 570 nm and 630 nm	The percentage yield obtained from ethanolic extracts were found out to be 24.73%  The cell viabilities were 69.53% and 42.06% at 50 µg and 150 µg respectively  Ethanolic extract of <i>P.edulis</i> (EEPE) exhibited anti-adipocytic activity  EEPE extract prevented lipid accumulation  EEPE and simvastatin were significantly found to reduce lipid accumulation, suggesting their anti-obesity activity	Anti- adinogenesis activity in vitro  The ethanolic extract has potential applications in the treatment of hyperlipidemia and obesity	[58]
Seed	Linoleic acid Stearic acid Palmitic acid Oleic acid Lauric acid	MCF-7 (human breast adenocarcin oma cells)		The cells were cultured at 37°C, 5% CO <sub>2</sub> atmosphere and 95% of air humidity  DMEM was supplemented with 10% fetal bovine serum, penicillin (100U/mL), streptomycin (100µg/mL)	After the MCF-7 reached 80% confluency, the medium was removed and replaced with medium containing extracts (10-500µg/mL) for 24, 48 and 72 hrs	Super critical fluid extract (SFE) prepared with ethanol were cytotoxic after 72 hr treatment at EC <sub>50</sub> (effective concentration) of 264.6µg/mL	Induction of oxidative stress in tumor cells through the assessment of lipid peroxidation and protein carbonylation Increase in cytotoxicity and the probable mechanism responsible for such effect is the intracellular reactive oxygen species (ROS) over generation through mitochondrial damage Cell cycle arrest and apoptosis	[59]
Aqueous extract (Different plant parts)	Flavonoids Quinones Sterols	SW480 cell line and SW620 (lymph node metastasis) cell line		Cells were cultured in DMEM medium with 25mM glucose and 2mM L- Glutamine supplemented with 10% horse serum 100 U/ml penicillin, 100 µg/ml Streptomycin and 1% non-essential amino acids  The serum was reduced to 3% and the medium was supplemented with insulin (10µg/ml), transferrin (5 µg/ml) and selenium (5ng/ml)	The different concentrations of the extracts used were 1%,2%,5%,7% and 10% After 24 hrs, they were treated with MTT, incubated at 37° C for 4 hrs and treated with 100µl isopropanol for the cytotoxic assessment  For apoptosis induction effect, the cells were seeded in a culture medium and incubated for 48 hrs with the extracts Cell analysis was performed using FACS cento II flow cytometer	Among the two cell lines, SW480 cells were more susceptible with highest reduction of cell viability (above 264µg/ml)  Apoptosis induction was observed as 45% in SW480 cells and 49% in SW620 cells	The study demonstrated that the aqueous extract has proapoptotic and cytotoxic potential in the cell lines used  The extract exerted an increase in sub G0/G1 stage cells Exposed cells stained positive for annexin-V	[60]

**Table 3.** The in vivo studies on *Passiflora edulis* Sims f. *Flavicarpa* mainly used extracts from leaves, fruits and the stem. The animals on which these extracts were tested included Sprague Dawley rats, Swiss mice, C57BL/6J mice and male Wistar albino rats. The results indicated decreased glucose and lipid absorption, antioxidant properties, reduction in leukocyte migration, and decrease in drug-induced locomotor activity.

Part of the plant	Animal model used	Experimental design	Concentration of the extract used	Inference	Ref.
Fruit (peel)	Sprague Dawley rats	24 male Sprague Dawley rats of 3-week-old were maintained in individual cages under controlled conditions of temperature (22°C±2) and a light-dark cycle (22/22h) for one week and fed with a standard diet Animals were divided into 3 groups C (control) group fed with normal diet, HF group fed with High Fat diet and HFPF (High Fat <i>Passiflora</i> peel Flour) group fed with high fat diet where 50% of cellulose was replaced by PEPF ( <i>Passiflora edulis</i> peel flour) The three groups received their respective diets for a period of 10 weeks	The peels were obtained, cut, dried and ground in a mill to obtain the flour. The HFPF group were fed with 25 g/kg of PEPF	The soluble and insoluble dietary fibres in PEPF contributed to decrease in glucose and lipid absorption Reduction in weight gain and fatness in HFPF group were observed Antioxidant activity was observed which was attributed to the presence of ferulic (phenolic) acid in the fruit peel flour	[61]
Leaves	Swiss mice	Different group of animals received air injection on 3 alternate days to induce air pouch On the 6 <sup>th</sup> day the animals received phlogistic agents and 24 hrs later they were sacrificed by an overdose of ether for evaluation of cell migration One set of animals received different doses of aqueous lyophilized extract (AE) (25-100mg/kg), butanolic fraction (BuOH) or aqueous residual fraction (AR) Another set was treated with a single dose of AE (100mg/kg), BuOH (50mg/kg) or AR (100mg/kg) at different time points (0.5-4h) The inflammatory parameters were evaluated 24h after the induction of inflammation	AE (100mg/kg), BuOH (50mg/kg), AR (100mg/kg)	AE reduced leukocyte migration at the dose of 100mg/kg BuOH was effective in reducing the leukocyte migration at 50 and 100 mg/kg concentrations	[62]
Leaves and fruits	C57BL/6J mice (6 - 12 weeks age)	The mice were maintained in individual cages under controlled conditions of temperature (25°C±2) and 12h light-dark cycle On the day of experiment, the mice were weighed and orally dosed (N=8-12 mice per group) The animals were tested every week under same experimental conditions All surgeries were done under aseptic conditions, anaesthesia was maintained by 1-3% isoflurane delivered by nose cone Meloxicam (1mg/kg) was administered by injection for analgesia	Extract was prepared in three different concentrations (300 mg/kg, 600 mg/kg, 1200 mg/kg) with de-ionized water containing 0.5% poly ethylene glycol (PEG) 200 (solubilizer) The mice were administered extract orally with 0.15 ml/30g body weight Control animals received H <sub>2</sub> O+ PEG 200 (0.5%)	For validation of telemetry system, caffeine was used as negative control and Midazolam as positive control After oral administration of caffeine, locomotor activity significantly increased while midazolam decreased the locomotor activity when compared to that of control group 300 mg/kg of extract from PE showed decrease in locomotor activity 600 mg/kg of PE induced a more pronounced decrease in the activity The highest dose of PE leaf extract (1200 mg/kg) showed rapid onset of action compared to lower doses	[63]
Leaves and stem	Male Wistar albino rats (5 to 8 weeks old)	Oral injection of streptozotocin (STZ) dissolved in citrate buffer was used to induce diabetes in the experimental animals Animals were divided into 4 groups of 10 rats each Control rats were orally injected with same volume of citrate buffer Second group was treated with <i>P. edulis</i> Flavicarpa ethanolic extract (PefEt) Third group comprised of streptozotocin-induced diabetic rats Fourth group comprised of diabetic rats administered with PefEt alcoholic extract	The fresh leaves and stems were collected, dried and powdered 50g of the powder was mixed with 300 ml of ethanol for 24 hrs 250 mg/kg of this extract was orally administered daily for 4 weeks	Untreated rats showed elevated levels of low density lipoprotein (LDL) and very low density lipoprotein (VLDL) cholesterol compared with control rats The diabetic rats treated with PefEt showed normal lipid profile The serum high density lipoprotein (HDL) cholesterol level was significantly increased in PefEt administered diabetic rats when compared to STZ induced rats	[64]



**Figure 1.** Six species and one sub species of the Genus *Passiflora* have been traditionally used for human healthcare applications. The major active compounds found in the various parts of these plants from different types of extracts such as aqueous, ethanolic and methanolic extracts were identified and studied by both in vitro and in vivo experiments.

### 2.1.1 Fruits

Fruit extracts are known to contain polyphenols and flavonoids having anti-oxidant properties. They have been used traditionally to treat conditions such as Alzheimer's disease, cancer, Parkinson's disorder and liver diseases [2].

### 2.1.2 Leaves

*P. alata* Curtis leaf extract has been identified to have gastro-protective and neuroprotective activities. The leaf extracts have been tested for their protective activity on the Central Nervous System and the digestive system owing to their neuroprotective and anti-ulcer properties. Nanoencapsulation of the active compounds found in the leaf extract was found to be an effective technology to improve the beneficial effects of *P. alata* as presented in Renisus, a Brazilian database that provides a list of medicinal plants [3]. Aqueous leaf extracts of *P. alata* proved to have excellent anti-inflammatory property. It has been reported that the leaf extract also has anti-diabetic property which is attributed to the presence of phenolic compounds such as catechin, epicatechin and rutin. These bioactive compounds are known to decrease oxidative stress, apoptosis and the number of inflammatory cells in pancreas [4-5].

*P. alata* has been used as a sedative and for anxiolytic purposes. These effects are attributed to the presence of certain secondary metabolites such as saponins and C-glycosidic flavonoids. The main saponin constituent, triterpene quadranguloside is considered chiefly responsible for the anxiolytic activity. Consumption of high amounts of aqueous leaf extract of *P. alata* altered the feeding behaviour in mice resulting in reduced weight gain and also reduced the relative liver weight [6]. *P. alata* is used as a folklore medicine against hysteria, neurasthenia and insomnia. Also, the other neuroprotective effects include its anxiolytic and diuretic functions apart from being a sedative and analgesic. The leaves of this plant are rich in polyphenols; especially flavones C-glycosides such as vitexin, isovitexin, orientin and isoorientin. The leaf extract of *P. alata* Dryander, when administered orally showed positive effect against oxidative damage in rats. It is believed that daily consumption of the tea leaf extract provides protection to liver and heart against oxidative damages [7]. The leaf extract tea contains high amounts of polyphenols and flavonoids which have been tested for their anti-oxidant potentials [8].

The saponin present in *P. alata* was found to exhibit insecticidal activity and hence for its usefulness as a bio-pesticide. This activity was pronounced against *Spodoptera frugiperda* which is a polyphagous insect parasitic on rice grains and maize. The saponins are known to affect the development stages of the insect thus functioning as potential bio-pesticides [9].

### 2.1.3 Seed

The seeds of *P. alata* are rich in oil which constitute about 30-40% of their entire contents. Most work on the seed extracts were performed on the oil constituent and it was observed that 80-84% extraction efficiency could be achieved by using compressed propane technology for the seed oil extraction. Such extracted oil was observed to have anti-oxidant property [10].

### 2.2 *P. caerulea*

*P. caerulea*, the blue passion flower is a tendril vine which grows up to 10 metres or more. It is native to South America and the fruits and leaves of this plant have been used extensively due to their medicinal properties.

#### 2.2.1 Fruit

The fruit of *P. caerulea* contains significant amounts of polyphenols such as catechin, resveratrol, epigallocatechin gallate, rutin and quercetin. The polyphenols are known for their protective effect for chronic neurodegenerative diseases. The pulp and seeds are typically collected, homogenized, dehydrated and grounded to obtain a powder. The powder is mixed well with water, blended, filtered and stored. In one study, the total phenolic and flavonoid contents of this extract (PCAE) was determined by RP-HPLC. The extract was tested on pilocarpine-induced epileptic Male Swiss albino mice and results indicated a neuroprotective activity as evidenced by reduction in seizures in the mice supplemented with the fruit extract [11].

#### 2.2.2 Leaf

The phytochemical investigations carried out on the petroleum ether extract of the leaves of *P. caerulea* showed the presence of fatty acids, esters, sterols and hydrocarbons. Also, three esters were fractionated by chromatographic fractionation [12]. Aqueous, ethanolic and methanolic leaf extract of these plants have been studied for their medicinal properties. Aqueous leaf extract is typically prepared by soaking the leaves in double distilled water, boiling and filtering. In a recent report, silver nanoparticles (AgNPs) were prepared using such aqueous leaf extracts. The anti-dermatophytic activity of synthesized AgNPs was determined for different species of fungal pathogens. The results showed that the zone of inhibition decreased as the concentration of AgNPs increases thus indicating the usefulness of such nanoparticles as anti-fungal agents [13].

The ethanolic leaf extract was used for treating different pathologies associated with the gastrointestinal tract. The ethanolic leaf extract contains phytochemicals such as isoorientin, vitexin, isovitexin and vicenin-2. When tested in female Swiss mice, the phytochemicals showed antinociceptive, anti-diarrhoeal, antioxidant and anti-inflammatory properties. Thus, the ethanolic leaf extract showed promise as a potential therapeutic alternative for inflammatory bowel disease (IBD) [14]. The methanolic leaf extracts were obtained and the FTIR analysis proved the presence of alkenes, alkyl halides, amide, acid and alkane compounds. The antimicrobial potential of these extracts were studied by measuring the zone of inhibition against bacteria, fungi and yeast [15] which showed promising results.

### 2.3 *P. edulis*

The *P. edulis* is commonly known as passion fruit and is of two major varieties, the purple fruited *P. edulis* Sims and the yellow fruited *P. edulis* f. *Flavicarpa*. It is native to Southern Brazil and the fruit, leaves, seed and stem of this plant are used widely for their medicinal values.

#### 2.3.1 Fruit

*P. edulis* Sims is one of the popular species in the *Passifloraceae* family. In traditional medicine, it has been used for treatment of anxiety and insomnia. The fruit epicarp of this purple passion fruit showed anti-fatigue activity when studied in mice. This was attributed to the presence of three major anthocyanins, the cyanidin 3-O-glucoside, cyanidin 3-O-rutinoside and peonidin 3-O glucoside [16]. The effect of passion fruit on melanogenesis and collagen synthesis in dermal cells and the components responsible for these effects were studied. The ethanolic seed extract contained piceatannol which exhibited antioxidative properties and melanin inhibitory activity [17]. The crude extract of passion fruit peel contains flavonoids, cyanogenic, phenolics and polysaccharides. These components are found to be effective against hyperglycemia, neurodegenerative and cardiovascular diseases [18].

#### 2.3.2 Leaf

The alcohol extract of the leaves contains cycloartane triterpenoid saponins that include cyclopassifloside XII and XIII and six other cycloartane triterpenoids. The extract also contains cyclopassifloside IX and XI which exhibited antidepressant-like effect when orally administered in mice [19]. The hydroethanolic leaf extract of *P. edulis* showed the presence of flavonoids which exhibited antioxidant and wound-healing activities [20]. Different types of leaf extracts were obtained using hexane, water, ethyl acetate, methanol and these extracts showed antibacterial activity which was attributed to the presence of compounds such as glycosides, flavonoids, alkaloids, phenols, resins and balsam [21]. The phytochemicals such as saponins, steroids, tannins, alkaloids, flavones obtained from different types of leaf extracts (ethanol, methanol, chloroform, petroleum ether, isopropanol, benzene) have been found to possess antimicrobial activity against different bacteria. Of these, the ethanolic extracts were found to have the maximum antimicrobial potential against *E. coli* [22].

#### 2.3.3 Seed

Passifilin is one of the proteins present in the seeds of *P. edulis* Sims which has anti-fungal activity. Also, this protein functions as a potent inhibitor of proliferation in MCF-7 breast cancer cells [23].

#### 2.3.4 Stem

Ethanolic extracts was obtained from air-dried stems which was filtered and stored. These extracts exhibited antidepressant-like activity in mice which was attributed to the presence of cycloartane triterpenoids [19].

### 2.4 *P. foetida*

*P. foetida*, also known as stinking passion flower is a creeping vine and native to South-western United States. The fruits and leaves are the major parts of this plant which are used for their medicinal value.

#### 2.4.1 Fruit

The main constituents present in the fruit extract of *P. foetida* are flavonoids, glycosides, phenols, alkaloids and cyanogenic compounds. They are mainly used for their anti-inflammatory and immunomodulatory effects [24]. The pulp of *P. foetida* Linn was used as a folklore medicine for the treatment of stress, insomnia, anxiety and hysteria. Also, the pulp was used in the treatment of fever, cough, and skin inflammation. These beneficial effects were attributed to the presence of hydrocyanic acid, flavonoids and harmon alkaloids in the fruit pulp. A recent report focused on the usefulness of the fruit pulp for the treatment of women infertility [25].

#### 2.4.2 Leaves

The phytochemical analysis of *P. foetida* L. leaf extract showed the presence of alkaloids, flavonoids, proteins, tannins and steroids. *P. foetida* L. leaf extract proved an efficient product for alternative medicine in the management of rheumatism, abdominal pain, diarrhoea, adenosine receptor antagonists, remedy of gout and for its aphrodisiac activity. Also, the in vitro chromosomal aberration assay using human blood lymphocytes indicated that the plant extract is non-mutagenic [26]. One major bioactive compound in the leaf extracts was found to be vitexin by High Performance Liquid Chromatography (HPLC) analysis. Vitexin showed anti-oxidant, anti-inflammatory and anti-hepatotoxic properties [27]. The leaves of *P. foetida* contain bioactive components such as tannins, coumarin alkaloids, flavonoids, tyrosine and glycine. Apigenin-8-C- $\beta$ -D-glucopyranoside present in the leaf decoction exhibited anticancer, anti-oxidant, antiviral, anti-inflammatory, anti-thyroid, anti-arteriosclerotic, anti-hypertensive and anti-hepatotoxic properties [28].

The ethanolic leaf extract of *P. foetida* was investigated for its analgesic action in mice. The anti-inflammatory activity was evaluated by the carrageenan-induced acute paw edema and histamine-induced acute paw edema procedures in mice. The results indicated the analgesic activity in the leaf extracts which was attributed to the presence of sterols and flavonoids [29]. The ethanolic leaf extracts of *P. foetida* showed remarkable antibacterial activity against *Pseudomonas putida*, *Vibrio cholera*, *Shigella flexneri* and *Streptococcus pyogenes*.

*P. foetida* is also known for its anti-oxidant, immunomodulatory and hypoglycemic activity. The activity of the leaf ethyl acetate extract showed immunomodulatory activity at higher dose. The leaf extract showed the ability to enhance antibody production and hypersensitivity responses [30]. The methanolic extract of *P. foetida* L. (PFME) has anti-inflammatory activity which was through the nuclear factor- $\kappa$ B signalling in the regulation of inflammation. PFME is traditionally used in herbal medicine to decrease the release of inflammatory mediators and hence used as a therapeutic medicine for treating inflammatory diseases [31]. The leaf of *P. foetida* was studied for determining its anxiolytic and antidepressant activity, for management of stress, insomnia, cough, fever and hysteria. It was established in murine experiments that the harmon alkaloids present in the methanolic extracts act as a reversible monoamine oxidase inhibitors and thus regulate the metabolic degradation resulting in inducing antidepressant activity [32].

The leaf extract of *P. foetida* has been used extensively as the herbal cream owing to its excellent wound healing property. The herbal creams were prepared with chloroform and ethanol extract. It was shown that the activity of ethanol extract ointment has a better wound-healing property [33].



### 2.5 *P. incarnata*

*P. incarnata*, commonly known as wild passion vine is a fast growing perennial vine with climbing or trailing stems. It is native to South-eastern United States. The flowers, leaves and seeds are the widely used parts of this plant for medicinal applications.

#### 2.5.1 Flower

The extracts of *P. incarnata* flowers have been found to have beneficial effects on various sleep parameters such as sleep duration, sleep onset latency and duration of rapid eye movement, as evidenced by electroencephalography. When administered to insomnia patients, the flower extracts resulted in significant improvement in sleep patterns and in reducing anxiety [34]. *P. incarnata* L has been widely used as a medicinal plant for treating chronic insomnia and also has anti-oxidant, sedative and anti-convulsant activity. The administration of the passion flower extract has proven to minimize physiological and behavioural changes and improve cognitive and memory functions. A study indicated that the compound vitexin present in the flower extract had exhibited enhanced neuroprotective and neurogenesis effect in rodents. The study also provided enhanced learning and memory in rodents apart from improved sleep and memory [35]. The study also indicated that there are no adverse effects on the other biological activities in the experimental animals.

#### 2.5.2 Leaves

The *P. incarnata* leaves contain several active compounds such as alkaloids, phenols, glycosyl flavonoids and cyanogenic compounds. Among these, the most important active compounds are the glycosyl flavonoids (vitexin, isovitexin, orientin and chrysin). Chrysin has tremendous biological activities and it actively inhibits inflammatory enzymes such as iNOS and COX-2 by inducing PPAR [36]. In a study, the dry leaf extracts of *P. incarnata* is used to treat dyslipidemia, hypertrophy and hepatic oxidative stress. They were also proven to reduce the effects of high-fat diet by decreasing total cholesterol and triglycerides levels while increasing the levels of high-density lipoprotein. The results suggested that the extract had an anti-oxidant effect thereby preventing cardiac and hepatic diseases related to oxidative stress [37]. The leaf of *P. incarnata* mainly constitutes flavonoids and indole alkaloids having the  $\beta$ -carboline ring system such as harman, harmine, harmalol and harmaline. Harmine and harmaline alkaloids are known to be effective for treating Parkinson's disorder. The butanol leaf extract (BEPI) of *P. incarnata* contains both antioxidant and antiparkinsonian activity and also for preventing progressive neurodegeneration [38]. The leaves of *P. incarnata* are known to induce several CNS-depressing effects and in inducing sleep [35].

#### 2.5.3 Seeds

Recent studies on the seeds of *P. incarnata* focused on their usefulness for hypercholesteremic and cholecystectomy. The major active compound present in the seeds is the steroid  $\beta$ -Sitosterol and the usefulness of this compound for the treatment of hypercholesteremia was demonstrated [39]. The study also proved that  $\beta$ -Sitosterol had greater effect on plasma lipid content compared to chitosan which is known for its hypocholesteremic and anti-inflammatory activity.

### 2.6 *P. ligularis*

*P. ligularis* is commonly known as sweet granadilla and is native to Peru, Bolivia, Ecuador, Colombia and Venezuela. It is an evergreen climbing shrub whose stems can grow up to 5 metres long. The fruits and leaves of this plant were extensively used for traditional medicinal applications.

#### 2.6.1 Fruit

The aqueous extract obtained from the fruits of *P. ligularis* was analysed for its anti-diabetic activity. A study performed in streptozotocin-induced diabetic male albino rats showed that the extract controlled elevated glucose levels in the experimental animals, an activity attributed to the presence of alkaloids and flavonoids in the extract [40]. The fruit extracts *P. ligularis* were obtained using different solvents such as petroleum ether, chloroform, acetone and methanol. The antimicrobial activities of these extracts were ascertained by testing them against bacteria and fungi. The results indicated that the acetone extract exhibited potent inhibitory effect which was attributed to the polyphenolic compounds such as gallic acid, rutin, kaempferol and caffeic acid in the extracts [41]. The lipophilic fractions of *P. ligularis* were shown to have high antioxidant activity compared to the hydrophilic fractions [42]. Also, the polysaccharide xyloglucan biopolymer that was isolated from the peels of *P. ligularis* was shown to have biotechnological applications.

#### 2.6.2 Leaf

The methanolic extract was obtained from the leaves and tested against three Gram-positive and three Gram-negative bacteria. The isolated pure compound showed significant activity against *Staphylococcus aureus* and *Proteus vulgaris* compared to the methanolic extract. Also, the activity was higher compared to the standard drug ciprofloxacin. [43]. Two different extracts were prepared from the leaves of *P. ligularis* using water and methanol. Preliminary analysis showed the presence of phytoconstituents such as alkaloids, glycosides, tannins, steroids, terpenoids and flavonoids in these extracts. Of the two extracts, the methanolic extracts showed higher inhibitory activity against *E. coli* [44].

### Conclusion

The various species and sub-species of the Genus *Passiflora* have been well documented traditionally for their human medicinal value. The importance of the plant and its use had warranted extensive scientific analysis of the various constituents in the different parts of the plant. Also, apart from simple analysis of such phytochemicals and active compounds, scientific interest was evidenced by a growing number of systematic, experimental-based studies. It is also interesting to note that the scientific analysis or studies have extended into in vivo studies, a trend which has been exponential in the recent past years. These evidences will pave way for understanding the mechanisms of actions of the active compounds found in the Genus *Passiflora* and for new drug discovery and development.

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