Active status on phytochemistry and pharmacology of *Pergularia daemia* Forsk. (Trellis-vine): a review

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**Abstract**

**Background:** Medicinal plants play a significant role in the progress of persuasive therapeutic agents. Earlier to the innovation of synthetic drugs, human beings completely relied on the plants for the treatment of various ailments. Natural product extracts, particularly those derived from different plant species, provided the main source of Siddha, Ayurveda and Folk medicines. *P. daemia* is a perennial climber, traditionally reported for the treatment in a variety of diseases. In present review, we focused on the present status of phytochemical and pharmacological activities *P. daemia*.

**Methodology:** With the support of electronic databases such as Science Direct, Google Scholar, Mendeley, Scirus and PubMed central. Traditional knowledge information collected by Indian taxonomical books, survey from local rural and tribal peoples. Pharmacological data’s obtained from scientific journals published from 2000 to 2020.

**Results:** *P. daemia* extract, contains several phytochemicals, especially rich in flavonoids. These secondary metabolites synthesized from *P. daemia* have been reported for the treatment of various chronic diseases. In recent years, *P. daemia* phytoconstituents set as a key role in natural drug development as it harbours many in vitro and in vivo pharmacological activities such as anti-inflammatory, anti-cancer, anti-fertility, anti-arthritic and antimicrobial etc.,

**Conclusion:** *P. daemia* was the less studied plant compared to other medicinal plants. In this context more emphasis has to be laid on studies that discuss on the secondary metabolite activities and molecular mechanisms that work against various chronic diseases.

**Keywords:** Medicinal plants, Antioxidant activity, Phytochemicals, Flavonoids, Pharmacology

**Introduction**

India is one of the world’s leading producers of medicinal and aromatic plant materials. Around 20,000 medicinal plants have been recorded to be procured from 15 agro-climatic zones in India so far. However, only 7000–7500 plant varieties among them are in commercial use. Unani and Ayurveda are the indigenous medicines of herb origin in use since ancient times.

The proportion of plant usage in the different Indian systems of medicine is Ayurveda (2000), Siddha (1300), Unani (1000), Homeopathy (800), Modern (200) and Folk (4500) [1]. Almost 25,000 herbal based drug formulations are used in India particularly in traditional and folk medicine system [2]. These drug formulations are either directly derived from aerial part of the plant or derived from other specific parts like leaf, root, stem, bark, flower and seed. Some of the herbal drugs are derived from plant excretory products such as latex, resins and gum [3]. In general, plants secondary metabolites that are naturally synthesized from primary metabolites comprise an extensive range of bioactive constituents. Medicinal and aromatic plants are rich in bioactive secondary metabolites like phenolic acids, flavonoids,
alkaloids, glycosides, phytosterols, terpenoids, tannins. These secondary metabolites are known for their pharmacological properties [4, 5]. Bioactive phytochemical compounds are very limited source as these are not feasible to obtain from all plant types. Medicinal plants, used in traditional medicine (Siddha and Ayurveda) have less toxicity and withhold biologically active structure that supports in the development of alternative medicines [6]. Herbal extracts and medicinal plants demand are progressively increasing in European and other developed countries. India is the one of the leading exporters of herbs and value added extracts of medicinal herbs (Export of Herbs and Herbal Products, 2019). Herbal medicine is a part of alternative treatment method and it includes the use of different medicinal plants and their extracts. This type of treatment is the most effective and safe mode for treating the patients (Source: Herbal medicine University of Maryland Medical Center). Herbal medicines are directly synthesized from various parts of plants such as leaf, stem bark, roots, barks, flowers, seeds, etc. In Ayurvedic system, herbal compositions were mostly prepared through polyherbal formulations. Also, they proved a significant effect against various chronic ailments. The herbal preparations are named as powers (Churna), decoction (Kwatha), resins (Guggul), oil (Taila) and infusion (Phanta) etc., [7]. In recent decades, the development of scientific research in pharmacology and phytochemistry of medicinal plants lead to the next level of herbal medicines. Medicinal plants have the ability to produce a wide range of phytochemical compounds that are used to execute important biological functions in humans and animals. Phytochemical constituents such as polyphenolic compounds, tannins, terpenoids are reported to be effective against various disorders [8]. Many of these phytochemicals have beneficial effects on long term when consumed by humans and can be used effectively to treat various chronic diseases. A single medicinal herb contains one or more phytochemical components that are synergistically active as a pharmacological agent. Therefore, plants are recognised as major resource for phyto compounds with profound biological activities [9].

_Pergularia daemia_ Forsk belongs to the Asclepiadaceae family. It is a perennial twining herb, which grows wild along the road sides of India. The aerial parts of _P. daemia_ are used as an anti-helminthic, antiseptic and anti-venom agent. It is also used in treating gastric ulcers, uterine and menstrual complaints. On the other hand, the leaves of this plant are also used as an effective medicine for anemia, leprosy, arthritis, hemorrhoids, amenorrhea, dysmenorrhea, infantile diarrhea, body pain, asthma, bronchitis and whooping cough [10]. Latex of this plant is used to treat boils and sores. While, the stem is used to treat cold, malarial fever and pyretic [11]. Similarly, root extract is used as an abortifacient, emetic and also used to treat against asthma, constipation and gonorrhoea. Fresh leaf extract when mixed with lime or ginger exhibited strong activity against rheumatic swelling [12]. The pharmacological action of aerial parts of _P. daemia_ has been reported to prevent various ailments in recent reports. Based on this background study of _P. daemia_, we confer the existing status of phytochemistry and pharmacological activities of _P. daemia_ in the present review.

Methodology

Scientific information and resources related to _P. daemia_ was obtained from scientific databases such as Science Direct, Google Scholar, Mendeley, Science Open, Springer Link, African Journals Online, Wikipedia, Scirus and PubMed central. Other information is obtained from local Indian taxonomical books, Ph.D. thesis and local survey.

Scientific classification

| Kingdom                 | Plantae – Plants |
|-------------------------|------------------|
| Subkingdom              | Tracheobionta – Vascular plants |
| Superdivision           | Spermatophyta – Seed plants |
| Division                | Magnoliophyta – Flowering plants |
| Class                   | Magnoliopsida – Dicotyledons |
| Subclass                | Asteridae |
| Order                   | Gentianales |
| Family                  | Asclepiadaceae – Milkweed family |
| Genus                   | Pergularia |
| Species                 | _daemia_ (Forsk.) Chiov. |

Common and local names

| Tamil          | Uttamani, Seendhalkodi and Veliparuthi |
|----------------|---------------------------------------|
| English        | Trellis-vine, Hariknot plant and Pergularia |
| Kannada        | Juttuve and Talavaranaballi |
| Hindi          | Utaran and Akasan |
| Malayalam      | Veliparatti |
| Sanskrit       | Kurutakah and Visanika |
| Telugu         | Jittupaku and Dustapuchettu |

Botanical description

_P. daemia_ is widely distributed in the tropical and subtropical regions particularly India, Africa, Arabia, Malaya, Pakistan, Afghanistan and some parts of south east Asia (Fig. 1). In India, it is commonly found in hedges through cut most of cenfry to an altitude about 1000 m in Himalaya and 900 m in Southern India. _P.
*Pergularia daemia* is a perennial twining herb with milky sap. The stems grow up to 4 m or more, covered in soft hairs. Leaves are thin 5–10 by 3.8–9 cm in length and heart or broadly ovate or glabrous shaped and margins margin ciliate hairy and cordate at the base petioles 2–6.3 cm in length, pubescent. The flowers are in axillary pseudo umbels on long peduncles. Pendulous opens in the evening. Corella is creamy white or greenish, sometimes tinged with purple and long lobes fringed (Fig. 2).

**Phytochemicals in *P. daemia***

Secondary metabolites extracted from the medicinal and aromatic plant extract are mostly responsible for the therapeutic and pharmacological potential of the particular plants [13]. In some cases, the crude extracts of medicinal plants are used as an agent for the treatment of various diseases. On the other hand, isolation and identification of the bioactive compounds, extraction, purification and the mechanism of action of the purified compound is very important. Hence, recently researchers are focused to validate traditionally reported medicinal property and as well as to identify bioactive compounds from medicinal plants. Both qualitative and quantitative method of analysis is very important for the validation of bioactive phytochemicals. The qualitative phytochemical analysis *P. daemia* extract are reported to exhibit various group of compounds including alkaloids, flavonoids, terpenoids, tannins, steroids, glucoside, carbohydrates, proteins, amino acids, saponins, glycosides, fixed oils, gums and mucilage (Tables 1 and 2). The extraction of bioactive compounds from plant materials is the first step in the utilization of phytochemicals in the preparation of
dietary supplements, pharmaceutical and products. Phytocompounds can be extracted from fresh or dried plant samples. Freeze drying extraction method, generally retains higher levels of phenolic content in plant samples when compared to dried powdered extraction [24].

Solvent extractions are the most commonly used procedure to prepare extracts from plant materials due to their ease in use, efficiency, and wide applicability. Various number of methods have been developed recently, like supercritical extraction (SCE), solid-liquid extraction (SLE), Microwave extraction (ME), Conventional Extraction (CE) and Ultrasound Extraction (USE) etc. [25]. Chromatographic techniques are widely used for identification of bioactive compounds from plant extracts. The most frequently used analytical technique for the separation of polyphenolic compounds is high performance thin layer chromatography (HPTLC), gas chromatography (GC) high performance liquid chromatography (HPLC),

| Phytochemicals | Leaf | Root |
|----------------|------|------|
|                | AE   | EE   | ME  | PEE | CE  | ACE | EAE | AE | EE | PEE | CE | EAE |
| Carbohydrates  | +    | +    | +   | –   | –   | –   | –   | +  | +  | –   | –  | –   |
| Proteins & Amino acids | –   | –    | –   | +   | –   | NA  | –   | –  | –  | –   | –  | –   |
| Glycosides     | +    | +    | NA  | +   | +   | +   | –   | +  | +  | –   | –  | –   |
| Alkaloids      | –    | –    | +   | –   | +   | NA  | –   | +  | –  | –   | +  | –   |
| Steroids       | –    | –    | +   | –   | +   | –   | –   | +  | –  | –   | –  | +   |
| Favonoids      | +    | +    | +   | +   | –   | –   | –   | +  | +  | –   | –  | +   |
| Saponins       | +    | +    | NA  | +   | +   | NA  | –   | +  | +  | –   | –  | –   |
| Tannins        | +    | –    | –   | +   | +   | +   | –   | +  | +  | –   | –  | +   |
| Fixed oils & Fats | –   | –    | +   | +   | NA  | –   | –   | –  | –  | +   | –  | –   |
| Gums & Muclage’s| –   | –    | –   | NA  | –   | –   | NA  | –  | –  | –   | –  | –   |
| Terpenoids     | +    | +    | +   | –   | –   | –   | +   | –  | –  | +   | –  | –   |
| Coumarins      | NA   | +    | NA  | +   | +   | NA  | –   | NA | NA | NA   | NA | NA  |
| Phytosterols   | NA   | +    | +   | +   | +   | NA  | +   | NA | NA | NA   | NA | NA  |
| Phenols        | +    | +    | +   | –   | +   | NA  | –   | +  | +  | –   | –  | +   |

Table 1 Preliminary qualitative phytochemical screening of different solvent extracts on *P. daemia* leaf and root

| Phytochemicals | Solvent extracts whole plant |
|----------------|-----------------------------|
|                | AE* | EE* | PEE | CE  | BE  | EAE | NBE |
| Carbohydrates  | +   | +   | –   | +   | –   | +   | +   |
| Proteins & Amino acids | –   | –    | –   | –   | –   | –   | –   |
| Glycosides     | +   | –    | +   | –   | +   | –   | –   |
| Alkaloids      | +   | –    | –   | –   | –   | –   | –   |
| Steroids       | NA  | NA  | NA  | NA  | NA  | NA  | NA  |
| Favonoids      | +   | +    | +   | –   | –   | –   | –   |
| Saponins       | +   | –    | –   | –   | –   | –   | –   |
| Tannins        | +   | –    | –   | NA  | –   | –   | –   |
| Fixed oils & Fats | –   | –    | +   | NA  | NA  | NA  | NA  |
| Gums & Muclage’s| NA  | NA  | NA  | NA  | NA  | NA  | NA  |
| Terpenoids     | +   | +    | –   | –   | –   | –   | +   |
| Coumarins      | NA  | NA  | NA  | NA  | NA  | NA  | NA  |
| Phytosterols   | NA  | NA  | NA  | NA  | NA  | NA  | NA  |
| Phenols        | +   | +    | –   | –   | –   | –   | +   |

Table 2 Preliminary qualitative phytochemical screening of different solvent extracts on *P. daemia* whole plant

+ presence, – absence, NA not analyzed (AE Aqueous extract; EE Ethanol extract; ME Methanol extract; PEE Petroleum ether extract; CE Chloroform extract; ACE Acetone extract; EAE Ethyl acetate extract)
with diode array detection (DAD) and mass spectrometry (MS) detection. Currently, this is one of the most widely and commonly used combination of techniques for separation, identification and quantification of polyphenolic compounds [26]. MS is a well known and successful technique for mass determination and structural elucidation of biomolecules [27]. Mass spectrometry (MS) is mainly used for both quantitative and qualitative analysis of biomolecules. This method is based on the gas phase ions that are separated to their mass-to-charge ratios (m/z). MS is a well known and successful technique for mass determination and structural elucidation of biomolecules. The HPLC coupled with MS is the analytical technique of choice for most tasks both in plant metabolite analysis and discovery of new drugs [28–31].

In *P. daemia* plant extract (whole plant, leaves, stem and root) consist of different chemical compounds. *P. daemia* leaves and root extract contains β-sitosterol, lupeol, oleanolic acid, calactin, calotropin, corotoxigenin, daucosterol, sucrose, α-amyrin, β-amyrin and its acetate [12, 14, 32–35] (Fig. 3a). Also phytocompounds such as betaine, hentriacontane and pentacosanoic acid polypeptide and glucoside of Daemia extensa (synonymous *P. daemia*), were identified from the entire plant extract [14, 35]. *P. daemia* seed extract has phytocompounds such as calactin, calotropin, calotropigenin, corotoxigenin, dihydrocalotropigenin, protouscharin, uscharadin, uscharin [14]. Similarly, Mittal et al. [36] identified a variety of cardenolide including uscharadin and calotoxin in seed extract. In addition, they recorded other similar compounds such as coroglaucigenin, corotoxigenin, uscharadin and uzarigenin in stem extract (Fig. 3b). Flavonoids were found to be the major and important phytochemicals obtained from extract of *P. daemia* aerial part during qualitative analysis. Vegetative parts of *P. daemia* reported for hyperoside (flavonol) in the dried stem and flavonoids and saponins in fresh shoots and flowers [37, 38]. Similarly, Sinha and Dogra [37] also reported for the presence of hyperoside (flavonol) in dried stem extracts. Recently our group identified five pharmacology important flavonoids from the methanoic leaf extract of *P. daemia* [13] (Fig. 3c). Many research reports revealed the potential role of polyphenolic compounds such as flavonoids and phenolic acids for its pharmacological property. Well known examples of phytocompounds include phenols, flavonoids, phenolic glycosides, saponins and cyanogenic glycosides [39, 40]. Particularly the antioxidant activity of the plants is due to the presence of flavonoids such as flavones, isoflavones, flavonoids, anthocyanin, coumarin lignans, catechins and iso catechins [15]. Green leafy vegetables and fresh fruit juices are rich source of polyphenolic compounds like flavonoids and phenolic acids. These herbal based antioxidant compounds or drugs prevents diseases like atherosclerosis, stroke, diabetes, alzheimer’s disease, cancer, and other anti-inflammatory disorders [41]. Importantly, anti-inflammatory activities of phytocompounds have been described in earlier reports and some of them are in preclinical trials at present [16]. Nowadays many people prefer these natural medicines additional for their advantage of being cost-effective and safe.

Flavonoids are the major phytocompound present in the *P. daemia* extracts and the concentration ranged from 72.549 ± 0.449 to 400.196 ± 0.339 mg/ml. On
comparison with other parts in plant, leaf and stem extract exhibited the vast flavonoids content. At the concentration of 10 mg/ml n-hexane 338.725 mg/g, ethyl acetate 388.627 mg/g and 400.196 mg/g respectively with an equivalence to quercitin content [17]. Flavonoids are the most familiar and extensively distributed group of plant phenolics. It includes monomeric flavanols, flavones, anthocyanidins, flavones and flavanols (Fig. 4). These flavonoids have the potential inhibit the pro-inflammatory mediators and other inflammatory agents (Fig. 5). Ananth et al. [13] identified and reported that *P. daemia* extracts consist of five flavonoids (formononetin, quercetin, chrysoeriol, taxifolin and naringenin) which has anti-arthritic activity against complete freund’s adjuvant (CFA) induced rat model [13]. Flavonoids have wide range of heath promoting properties such as antioxidant, antimicrobial, anti-inflammatory and immunomodulatory activity. The important sub classes of flavonoids are flavanols, flavanones, iso flavones, flavones, and anthocyanidins [18, 42, 43]. On the other hand, there are plenty of medicinal plants with enormous active components which are yet to be revealed. *P. daemia* was among those and found to be a reliable source of flavonoids and other bioactive compounds. Quercetin, kaempferol, myricetin and morin are popular among the category of therapeutics due to people’s reliability on emerging natural therapeutics.

**Pharmacology**

**Antioxidant activity**

Recent reports suggests that oxidative stress and its related factors cause an important problem to human health. The flavonoids have been shown to possess strong antioxidant activity through their ability to scavenge free radicals, inhibit lipid peroxidation, reduce the formation of reactive oxygen species and modulate the expression of pro-inflammatory mediators. Flavonoids are also known to possess anti-inflammatory activity by inhibiting the production of pro-inflammatory cytokines and enzymes. The antioxidant and anti-inflammatory properties of flavonoids make them potential candidates for the treatment and management of various diseases and disorders.
health. Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) were over expressed during the stress condition. These reactive species promote degenerative diseases [44–46] ROS such as superoxide anion (O$^-$), nitric oxide (NO$^-$) radicals, hydrogen peroxide (H$_2$O$_2$), peroxyl radicals (ROO$^-$) and reactive hydroxyl radicals (OH$^-$) are continuously generated as a by product during electron transport system and normal cell metabolism [47]. Overproduction of ROS/RNS lead to failure in the defence mechanism by release of oxidant substances. Antioxidants are the compounds that are capable of neutralizing free radicals by interfering with oxidation process, chelating catalytic metals and acts as oxygen scavengers [48]. These compounds are reported to prevent free radical mediated oxidative damage and thereby reducing the risk of causing various degenerative diseases and disorders [44]. In nature our blood plasma consists of antioxidants like superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), albumin, transferrin, ceruloplasmin, lipid and water-soluble antioxidants like tocopherol, quinines, ascorbic acid and uric acid and vitamin-E. Antioxidants act by transforming ROS/RNS to form a stable molecule and prevents damage to the biological system. Nowadays synthetic antioxidants such as butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), propyl gallate (PG) and tert-butylhydroquinone (TBHQ) are widely used in food and therapeutic industry, which cause severe toxic effects to the victims. On the other hand, number of purified compounds from medicinal plants exhibited high antioxidant activity with least or no side effects. In vitro antioxidant potential of *P. daemia* extracts were determined by inhibition of two different synthetic free radicals such as 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS), 1,1-diphenyl-2-picrylhydrazyl (DPPH). Methanolic extract of *P. daemia* areal part was highly potent in neutralizing ABTS, DPPH and nitric oxide free radicals and was comparable with that of gallic acid. The ABTS IC$_{50}$ concentration of *P. daemia* extract was 19.72 mg/ml and was nearly higher than of gallic acid (14.55 mg/ml). Similarly, DPPH scavenging activity IC$_{50}$ value was at 33.36 and 34.12 mg/ml for extract and gallic acid respectively. *P. daemia* extract exhibited excellent nitric oxide scavenging activity (IC$_{50}$ – 32.37 mg/ml) compared with gallic acid standard (IC$_{50}$ – 34.19 mg/ml) [49]. While, 70% ethanolic extract of *P. daemia* leaf revealed significant DPPH free radical scavenging activity on par with commercial standards of ascorbic acid and BHT. Leaf extract had less scavenging effect and the EC$_{50}$ values were 0.149, 0.699 and 2.608, mg/ml respectively, and interestingly

![Fig. 5 Possible anti-inflammatory inhibition mechanism of flavonoids from P. daemia](Image)
these lower EC$_{50}$ also showed better antioxidant activity. Also ethanolic extract effectively inhibited the formation of peroxides and hydrogen peroxides. Importantly $P$. daemia extract have the ability to reduce iron from ferric (Fe$^{3+}$) to ferrous (Fe$^{2+}$) and the EC$_{50}$ value was recorded for extract, ascorbic acid and BHT were 17.78, 0.5239 and 0.2065 mg/ml respectively. Very recently, Dosumu et al. [17] reported inhibitory percentage from 34.65% to 84.90% in $P$. daemia leaf extract over DPPH radical scavenging activity. The IC$_{50}$ values was found to be 6.27 µg/ml (ethanol), 17.78 µg/ml (ethyl acetate) and 22.49 µg/ml (n-hexane) and the standard ascorbic acid (5.67 µg/ml) extracts, respectively. Similarly, the IC$_{50}$ values of $P$. daemia stem extract was 10.19 and 26.99 µg/ml for ethyl acetate stem extract, followed by 58.20 µg/ml for n-hexane extract. Phytochemicals such as phenols, alkaloids, flavonoids, phytosterols, saponins, tannins and triterpenes found in the leaf extract might be responsible for the observed antioxidant activities [17, 50, 51].

**Anti-inflammatory and analgesic activity**

Inflammation is a usual biological process act against the foreign substances including microbes to protect the tissue from injury. Usually inflammation is a rapid and self limited process, but during abnormal pathological condition it generates excessive ROS/RNS leading to chronic inflammation condition. This chronic inflammation linked with serious inflammatory diseases including arthritis, cancer, neurological, metabolic and cardiovascular diseases [52, 53]. Researchers already developed steroidal and non steroidal anti-inflammatory drugs to reduce this chronic inflammatory state. These drugs effectively reduce the disease severity, but on the other hand, they also cause has many side effects. However, medicinal plants like $P$. daemia have curative effects with least side effects [13]. The ethanolic extracts of $P$. daemia has significant ($p < 0.001$) reduction in paw edema against carrageenan induced paw edema and cotton pellet granuloma methods in rats. These extracts at the concentration of 200 mg/kg showed upto 44.18% and 19.87% reduction in the granuloma formation. Other extracts such as n-butanol, benzene and chloroform showed 16.83%, 13.96% and 15.08% respectively at the same concentration [54]. Similarly Venkataraman et al. [55] investigated carrageenan induced paw edema in rats using chloroform and petroleum ether extract of whole plant. Results demonstrated that the chloroform extract treated were found to be highly significant ($p < 0.01$) improvement in comparison to the control. Very recently Hina and Rose [56] determined in vitro anti-inflammatory activity of $P$. daemia ethanolic extracts in leaf and root by human red blood cell (HRBC) membrane stabilization method. Their findings also illustrated anti-inflammatory activity by membrane stabilization method in the ethanolic leaf (54.55%) and root (45.55%) extract at a concentration of 300 µg/ml and produced most significant stabilization compared to that of standard drug diclofenac sodium (72.73%) at 100 µg/ml concentration. $P$. daemia plant extracts also showed an effective analgesic activity. Currently, these extracts are used an alternative to pain killer drugs. One of the studies conducted to evaluate the analgesic activity of $P$. daemia aqueous and alcoholic root extracts on eddy’s hot plate method showed significant ($p < 0.001$) effects at the concentration of 1000 mg/kg [57]. Similar analgesic results were recorded at the concentration of 100 mg/kg ($p < 0.01$) with chloroform and petroleum extract of $P$. daemia [55]. The presence of rich flavonoids and glycosides in $P$. daemia might be a major reason for exhibiting anti-inflammatory and analgesic activity.

**Anti-arthritic activity**

Flavonoids are known to be effective phytocompounds in treating the anti-rheumatic condition in animal models [13]. $P$. daemia methanolic extracts contains flavonoids such as formononetin, quercetin, chrysoeriol, taxifolin and naringenin. Study on the methenolic extract treated rat groups effectively reduce the paw inflammation and also serum biochemical markers such as hemoglobin (11.84 ± 0.42 g/dl) and red blood cells (RBC) (8.38 ± 0.67 million/mm$^3$) levels were significantly increased. Whereas, other arthritis indicator biomarkers including white blood cells (WBC) count (8.91 ± 0.38 thousands/mm$^3$), rheumatoid factor (RF) (17.94 ± 0.45 IU/ml), erythrocyte sedimentation rate (ESR) (7.91 ± 0.12 mm/h) and C-reactive protein (CRP) (22.56 ± 0.26 mg/l) levels were significantly decreased when compared arthritic induced rat group [56]. Ethanolic extract of $P$. daemia leaf and root (300 µg/ml) have the potential to have significant anti arthritic activity as per the study reports. They confirmed by membrane stabilization assay, and the highest % activity was observed in leaf (54.55%) than root (45.55%). In similar way, the root extracts of $P$. daemia showed 58.89% of inhibition than the leaf extracts which showed 53.33%. In both the cases, assays were compared with standard drug diclofenac sodium at the concentration of 100 µg/ml. Petroleum ether extract of $P$. daemia leaf at 300 mg/kg showed improvement in arthritis condition in arthritic rats by reducing the hind paw edema and inflammation [58]. It is also suggested that phytocompounds such as flavonoids and sterols might be responsible in this anti-rheumatic activity of $P$. daemia [13].

**Anti-cancer activity**

Worldwide cancer is the dangerous and second most important reason for mortality. Herbal based therapies by secondary metabolites from plant extracts known to
reduce the disease severity without side effects for cancer treatment. Khorombi et al. [59] reported that methanol dichloromethane (1:1 v/v) extract of the whole plant extract inhibited the growth of the cancerous cells. Alpha-amyrin is a compound responsible for the cancerous cell growth inhibition, but rate of growth inhibition was having low potency, between 15 and 50 μg/ml. Another study revealed that *P. daemia* extract has an important source to cure oral cancer disease. Particularly ethyl acetate extract (300 mg/kg b.w.) exhibited excellent in vivo antioxidant activity in comparison to the methanolic extract. The activity was compared against on 7, 12-dimethylbenz[a]anthracene (DMBA) induced hamster buccal pouch [19]. Leaf extract showed an effective cytotoxic activity against ovarian cancer cell lines (PA-1 and OAW-42) and IC$_{50}$ value of cell lines recorded 30 and 120 mg/ml, respectively. Authors suggested that polyphenolic compounds principally triterpenoids play a vital role against growth of cancer cells. In addition, they mentioned small structural modification of triterpenoids as the ability to establish an oval drug against cancer [60].

**Anti-proliferative activity**

Mirunalini et al. [20] study revealed that *P. daemia* methanolic extract exhibited an anti-proliferative effect against oral keratin-forming tumor cell line HeLa (KB) cells. The activity was determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyllumizolium bromide assay (MTT). ROS generation and antioxidant status, membrane (potential) potential and cell cycle arrest were determined for the confirmation of anti-proliferative activity. At the highest concentration (160 μg/ml) of *P. daemia* methanolic extract, they confirmed maximum cytotoxic effect against oral KB cells. The IC$_{50}$ value of methanolic extract calculated 90% on MTT assay against cancer cell lines. Pre-treated KB cells with *P. daemia* extract significantly changed the apoptotic morphology of the cells, this apoptotic morphological change occurred by the increased levels of ROS and reduction in the matrix metallopeptidases (MMPs). The death of the cancer cell initiates ROS generation and lipid peroxidation (LPO) in intra cellular region and damages DNA by initiating apoptosis in KB cell [20]. Polyphenolics (phenolic acid and flavonoids) of *P. daemia* might play a crucial role in reversing this process by promoting apoptosis and arresting proliferation in cancerous cells.

**Anti-diabetic activity**

Diabetes mellitus is becoming the third “killer” disease next to cancer and cardiovascular diseases in mankind. It is a long term metabolic disorder that affects our body in terms of both physical and psychological functions. The first study on *P. daemia* extract has reported the potential of anti-hyperglycaemic activity. Kumar and Ramesh [61] revealed that *P. daemia* extracts at a concentration of 300 mg/kg, decreased the blood glucose level significantly against streptozotocin (STZ) induced in diabetic rats. After 21 days of the treatment the diabetic animals with chloroform leaf extract 160.68 mg/dl, ethanol extract 132.61 ml/dl, aqueous extract 152.80 mg/dl, ethanol extract of callus showed 123.26 mg/dl and glibenclamide (600 μg /kg) 194.6 mg/dl of blood glucose. Wahi et al. [62] reported that administration of alcoholic and aqueous extracts from the whole plant of *D. extensa* produced a vital reduction and evaluated using alloxan (120 mg/kg; i.p.). Importantly, alcoholic extract twisted a significant (*P* < 0.01) decrease in blood glucose level (BGL) in a single dose after 1 h. Anti-diabetic activity was equivalent with standard drug chlorpropamide. Recently, Sarkodie et al. [63] revealed that that *P. daemia* extract has anti-hyperglycaemic activity against STZ-induced rat models. The blood glucose level significantly reduced on dose dependent manner. Flavonoids and its glycosides, phytosterols, saponins, phenols, alkaloids, triterpenes, tannins and alkaloids are bioactive ingredient in hypoglycaemic activity in plants [63].

**Hepatoprotective activity**

Liver is an incredible organ and is fundamental chemical laboratory of our body which plays a crucial role in the metabolism and detoxification of various chemicals and toxins enter into the body. The disposition of exogenous toxins and therapeutic agents are acting as a major part in the biochemical regulation of biomolecules such as fats, carbohydrates, amino acids and protein. The ROS plays a vital role in liver damage. Liver injury or damage is a well known disease which can be caused by excessive production of ROS that lead to the hepatic cells and tissue damage. Several compounds, such as carbon tetrachloride (CCl$_4$), α-amanitin, acetonaphen, pyrrolizidine alkaloids, bromobenzene, ethanol and polycyclic aromatics and the toxin produced metabolites which cause liver injury [64]. Antioxidants play an important role to prevent the liver cells from CCl$_4$ induced damage because they effectively neutralize the free radicals [56]. Recent research indicated that natural antioxidants capable of preventing oxidative stress related liver problems [65–67]. Sureshkumar and Mishra [68] reported that the ethanolic and aqueous extract of *P. daemia* possesses a significant (*P* < 0.05) hepatoprotective effect against CCl$_4$ induced hepatic rat model. They also found that ethanolic extracts treated rats decreased the serum aspartate aminotransferase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALKP), total bilirubin (TBL) and total cholesterol (CHL) levels and increased level in total protein (TPTN) and total albumin (ALB) at dose of 200 mg/kg. Highly reactive trichloro free radical was generated by CCl$_4$. 
which attacks polyunsaturated fatty acids. Due to the alteration in liver microsomal membrane hepatotoxicity found in experimental animals [21]. *P. daemia* roots aqueous and ethanolic extracts also have significant protective effects against paracetamol and CCl4 induced hepatotoxicity in rats [69]. Paracetamol also caused increase of serum liver enzymes such as bilirubin and cholesterol similar like CCl4. Both aqueous and ethanolic extracts at the dose of 100 and 200 mg/kg caused significant inhibition in the biochemical markers of SGOT and SGPT. Compared with control rats there was decrease in LPO, malonaldehyde (MDA), and increase in serum protein antioxidant enzymes glutathione (GSH) in *P. daemia* extract treatment. Hence, the presence of bioactive compounds such as flavonoids, terpenoids, glycosides and saponins in these extracts might be responsible for hepatoprotective activity. Sureshkumar and Mishra [70] suggested that *P. daemia* leaf ethanolic extract containing flavonoids and triterpenoids are the most responsible for the hepatoprotective activity. The flavonoids from ethanol extract and ethanol fraction in *P. daemia* confirmed by HPTLC using quercetin-3-glucoside as a standard. These results indicated that flavonoids are the principal bioactive compound for hepatoprotective activity [13, 71].

**Diuretic activity**

Bhavina et al. [72] studied the diuretic activity of the *P. daemia* extracts at a dose dependant manner by orally in rats. Lipschitz test used for this study and furosemide used as a standard drug. Based on the results diuretic activity of *P. daemia* alcoholic extract showed a highest activity of 0.93 at 400 ml/kg concentration. Urine output of all tested extracts except the petroleum ether showed significant results (*P* < 0.001) in comparison to control. Importantly plant extracts also affect the urinary electrolyte excretion. Further alcoholic, ethyl acetate and *n*-butanol extracts increased the urinary excretion of sodium and potassium ions (Na+ and K+). Diuretic action of alcoholic extract was found to be 2.04 units, which was almost similar to standard furosemide (2.19 units). Extracts such as alcoholic, ethyl acetate, *n*-butanol and standard drug furosemide increased the urinary Na+ and K+ ions level and slightly acidified the urine. These findings strongly suggest that the *P. daemia* extracts act as a diuretic agent. Secondary metabolites such as alkaloids, flavonoid and steroids might be the possible candidates responsible for the diuretic activity of *P. daemia*.

**Anti-tuberculosis activity**

According to world health organization (WHO) report (2017), approximately 10.4 million cases of tuberculosis (TB) were reported in 2016 and one major possible cause of deaths. In Ayurvedic medicinal system, plants extract shows a potential positive effect against treating TB. Recently, Mishra et al. [73] reported that ameliorative effect of *P. daemia* hydro alcoholic leaf extracts against *anti-tuberculosis drugs* (ATDs) induced liver injury. Administration of ATDs significantly decreased the level of glucose and albumin. Besides, high levels of aspartate aminotransferase, alkaline phosphatase, alanine aminotransferase, bilirubin, triglycerides, cholesterol were also recorded. After ATDs exposure, they found reduction in glutathione, peroxidase, glutathione reductase catalase, superoxide dismutase, glutathione and glucose-6-phosphate dehydrogenase, and also increase in the level of lipid peroxidation. Hence, *P. daemia* extract significantly maintained these serum biochemical parameters and antioxidant components when compared to control [73].

**Anti-fertility activity**

Ethanolic extract and their steroidal fraction of *P. daemia* showed a potential anti-fertility activity. Steroidal fraction of 200 mg/kg showed significant activity against female mice at the stage of pre-implantation. Whereas, ethanolic extracts exhibited late abortifacient activity with 600 mg/kg. The extract showed 100% activity without any mortality within 48 h of drug treatment. These results reveal that *P. daemia* steroidal and ethanolic extract have potential to display anti-fertility activity on female mice [22].

**Anthelmintic activity**

Kumar et al. [74] reported the ethanolic extract of *P. daemia* are better than the aqueous extract in exhibiting anthelmintic potential. They evaluated the leaf extracts against round worm (*Ascaris lumbricoides*), earthworm (*Eudrillus eugeniae*), and tapeworm (*Taenia solium*) taking 100 mg/ml concentration, with albendazole as a reference drug. The paralysis and time of death was recorded in ethanolic extract for round worm (20.86 ± 0.54 and 61.84 ± 0.54 min) earthworm (16.86 ± 0.74 and 27.12 ± 0.52 min) and tape worm (54.12 ± 0.49 and 110.17 ± 0.59 min) respectively. Similarly, aqueous extract showed paralysis and time of death was (32.33 ± 0.67 and 76.19 ± 0.56 min) for roundworm, (20.91 ± 0.31 and 30.89 ± 0.45 min) for earthworm and (64.44 ± 0.54 and 172.14 ± 0.81 min) for tapeworm respectively. *P. daemia* extracts induced paralysis followed by the death in the warms with a concentration of 100 mg/ml exhibiting (*P* < 0.01) anthelmintic activity compared to that of standard drug.

**Anti-ulcer activity**

During pathogenesis of ulcer formation dehydration, interference of mucosal cellular membranes and
cytotoxic effects was directly imposed by ethanol and finally its lead to proliferation of the inflammatory reaction [75]. In the meantime, indirectly alcohol led to destructive effects via leukocytes which generate inflammatory responses, oxidative stress and apoptosis. In this process NF-kappa B (NF-κB) plays a vital role in mediating to developing disease condition [76]. Secondary metabolites such as flavonoids, tannins and triterpenes has been extensively reported for anti-ulcerogenic activity [77]. *P. daemia* contains these phytochemicals which might be the responsible for anti-ulcer activity. *P. daemia* revealed curative effect against ethanol induced ulcer in rats. Extracts (400 mg/kg) exhibited an inhibition percentage of 63.01 and the standard drug treated group showed 78.73%. Dhananjayan et al. [23] suggested that ethanolic extracts of *P. daemia* leaf possessed excellent anti-ulcer activity in dose dependent manner.

**Conclusion**

*P. daemia* is the one of the less studied and scientifically reported medicinal plant. Based on the traditional reports and literature reviews, we propose that *P. daemia* exhibited excellent pharmacological activity. Qualitative analysis of phytochemicals including flavonoids, terpenoids, phytosterols, proteins, amino acids and saponins have been isolated and identified from different parts of *P. daemia*. Medicinal plants are known to be a natural source of phytochemicals and bioactive compounds. Natural flavonoids and cardenolides are the important bioactive components reported in *P. daemia* extracts. Bioactive compounds involved in pharmacological activities due to its antioxidant, anti-inflammatory and other related properties in human. Administration of solvent extracts of *P. daemia* prevents inflammation and various diseases including arthritis and cancer. Generally, it is notable that the existing phytochemistry and pharmaceutical status of the *P. daemia* are insufficient resources for herbal formulations. Whereas, the clinical studies and its mechanisms of action are not clear. Further studies are required to identify other bioactive compounds of *P. daemia* along with their specific mechanism in disease management. These studies will fetch in bringing the practise of *P. daemia* based herbal formulations.

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**Authors’ contributions**

D.A.A, G.D and V.M: Conceptualization, Methodology, Data collection, Writing- Original draft preparation. D.A.A, G.D and V.R.B: Writing- Reviewing and Editing. The author(s) read and approved the final manuscript.

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The authors declare that they have no competing interests.

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