PHARMACOLOGICAL AND PHYTOCHEMICAL CHARACTERISTICS OF PERGULARIA DAEMIA: A COMPREHENSIVE REVIEW

E. Kowsik[1], V.Vandhana*[1], Anusha T[2] , Dhanushya RD[1], S.G.Raman[3] , Rajesh[4], Marati kavitha[5],Magesh M[1]

1. Saveetha College of Pharmacy, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai – 602 105, Tamil Nadu, India.

2.Sree Sastha Institute of Engineering and Technology, Chembarambakkam, Chennai – 600 123, Tamil Nadu, India.

3.Mohammed Sathak A.J.College of Pharmacy, Sholinganallur, Chennai -600 119, Tamil Nadu, India.

4.Sri Rangapoopathi College of Pharmacy, Alampoondi, Gingee, Villupuram – 604 151

5.Department of pharmacology, RBVRR Women's College of Pharmacy, Barkatpura, Hyderabad-500 027, Telangana, India

***Corresponding author: V. Vandhana**

vandhanav.scop@saveetha.com

Abstract

The utilization of medicinal plants has played a crucial role in the development of effective therapeutic medicines. P. daemia, a plant species rich in diverse phytoconstituents such as flavonoids, glycosides, tannins, and terpenoids, has garnered significant attention in the field of natural medicine. These secondary metabolites have demonstrated potential in the treatment of various chronic disorders, including cancer, arthritis, and diabetes. Moreover, they exhibit noteworthy pharmacological actions such as anti-inflammatory, analgesic, and antibacterial effects. Several studies have highlighted the anti-arthritic and anti-inflammatory effects of alcoholic extracts of P. daemia, while methanolic and aqueous extracts have shown promising results in reducing paw edema and inflammation in animal models. Notably, the ethyl acetate extract has exhibited significant hepatoprotective activity against CCl4-induced hepatic injury in rats. Furthermore, the ethanol extract and its steroidal fraction have demonstrated excellent anti-ulcer properties in a dose-dependent manner. These findings underscore the potential therapeutic applications of P. daemia in managing various health conditions. Overall, this review consolidates the existing knowledge on the pharmacological and phytochemical properties of P. daemia, highlighting its potential as a source of natural medicinal products. The comprehensive understanding of the bioactive compounds present in P. daemia opens avenues for further research and exploration in drug development and treatment strategies for chronic disorders.

Keywords: P. daemia, medicinal plants, phytoconstituents, pharmacological actions, anti-inflammatory, anti-arthritic, hepatoprotective, anti-ulcer.

Introduction

One of the top producers of aromatic and medicinal plant materials worldwide is India. Up to this point, 15 agroclimatic zones in India have been used to purchase almost 20,000 medicinal plants. There are many different plant species, but about 7000–7500 of them are used commercially. Indigenous medical systems with a herbal origin, such as Unani and Ayurveda, have been practiced for ages. Ayurveda, Siddha, Unani, Homeopathy, Modern, and Folk are the Indian medical systems with the highest percentage of plant use [1]. In India, there are about 25,000 herbal pharmaceutical formulations, especially in the past and folk medicines [2]. These pharmaceuticals are others produced directly from the surface of the plant or other elements of the particular plant such as leaves, roots, stems, bark, flowers, and seeds. Some herbs are made from plant-excretory materials, including resin, latex, and gums [3]. A wide variety of bioactive components can be found in plants' secondary metabolites, which are organically produced from primary metabolites. Secondary metabolites represent pharmaceuticals and aromatic plants such as flavonoids, glycosides, tannins, phenols, plant steroids, alkaloids, and terpenoids. The pharmacological characteristics of these secondary metabolites are well known [4, 5]. Because it is not practical to obtain bioactive phytocompounds from all plant kinds, their sources are very limited. Traditional medicine's (Siddha and Ayurveda's) usage of medicinal plants has harmless components that contain physiologically active compounds and contribute to the creation of alternative drugs [6]. In Europe along with other developed nations, the request for herbal extracts and therapeutic herbs is steadily rising. Among the exporters, India is also one of the largest exporters of herbal medicine extracts & herbs with additional value. Various medicinal plants and their extracts are components of herbal medicine, which are complementary forms of medicine. This treatment is the most efficient and secure way to treat patients. Various plant components, including leaves, stembark, roots, barks, flowers, seeds, etc., are used to directly synthesize herbal medications. Herbal preparations were often made using polyherbal formulations in the Ayurvedic system. Additionally, they demonstrated a notable impact against several chronic illnesses. These natural remedies are Churna, Kwatha, Guggul, Taila, Phanta, etc. are only a few examples [7]. In recent decades, scientific research in the field of pharmacology and plant chemistry has led to the development of the next generation of herbs. A vast variety of phytochemical substances that are made by medicinal plants can be employed to carry out crucial biological processes in both humans and animals. Numerous illnesses have been said to be successfully treated by phytochemical components like polyphenolic chemicals, tannins, and terpenoids [8]. Numerous plant chemicals when taken by humans have long-term benefits and they can be successfully used to cure severe prolonged diseases. One or more phytochemical elements in a single medicinal herb work together to produce a pharmacological effect. Therefore, it is acknowledged that plants are a significant source of phytocompounds with significant biological activity [9]. Diabetic pergularia The Asclepiadaceae family is the home of forsk. It is a wild herb that twines perennially and thrives in India by the sides of roads. As an antihelminthic, antiseptic, and antiviral agent, the aerial part of *P. daemia* is used. The treatment of uterine and menstrual symptoms, as well as gastric ulcers, is also done using it. The leaves of this plant, on the other hand, are also employed as a potent remedy for whooping cough, asthma, bronchitis, amenorrhea, dysmenorrhea, infantile diarrhea, leprosy, anemia, hemorrhoids, arthritis, hemorrhoids, amenorrhea, dysmenorrhea, and amenorrhea [10]. To treat boils and wounds, this

plant's latex is employed. The stem, on the other hand, is used to treat pyretic, malaria, and colds [11]. Similar to how it is used as an emetic and an abortifacient, root extract is also used to treat gonorrhea, asthma, and constipation. When combined with ginger or lime, fresh leaf extract demonstrated potent anti-rheumatic swelling effects [12]. Recent findings claim that the pharmacological effect of *P. daemia's* aerial parts can prevent a variety of illnesses.

Plant description

P.daemia is widespread in tropical zones and subtropical zones, especially in India, and other parts of Southeast Asia. It is frequently observed in India in hedges that have been cut down to a height of about 900 m in Southern India and 1000 m in the Himalayas. *P.daemia* is a milky sap-producing perennial twining plant. The soft-haired stems can reach a height of 4 meters or more. The thin, heart-shaped, broadly ovate, glabrous, or ciliate-hairy leaves are 5–10 cm long, 3.8–9 cm wide, and have petioles that are 2.0 - 6.3cm long and adolescent. These florets are long peduncled axillary pseudo umbels. Pendulous debuts at night. Corella has long, fringed lobes that are creamy white or greenish in color.

Phytochemicals in *P. daemia*

The therapeutic and pharmaceutical potential of specific plants lies primarily in the isolation of secondary metabolites from extracts of medicinal and aromatic plants. [13]. Occasionally, people treat various disorders with crude extracts of medicinal herbs. On the other hand, it is critical to separate & recognize the bio-active substances and extracts, purify, and understand the mechanism of action of the purified component. Due to this, researchers are now concentrating on confirming historically claimed therapeutic properties as well as identifying bioactive chemicals from medicinal herbs. For the conformation of bioactive phytochemicals, qualitative and quantitative analysis methods are crucial. Various groups of chemicals, including flavonoids, terpenoids, carbohydrates, tannins, flavonoids, glycosides, steroids, and alkaloids are reported to be present in the qualitative phytonutrient examination of *P.daemia* extract in (Tables 1 and 2). The first stage is utilizing phytochemicals in the preparation for the extraction of bioactive components from plant sources. Plant samples that are fresh or dried can be used to extract phytocompounds. The lyophilization procedure frequently retains greater phenolic compounds in plant specimens than dry powdered extraction, Compared to extraction in dry powder [14].

Table 1: Initial qualitative phytochemical evaluation of several solvent-based extracts on the leaves and root of P. daemia shown below

Phytoconstituents	**Leaves**							**Root**				
	AE	**EE**	**ME**	**PEE**	**CE**	**ACE**	**EAE**	**AE**	**EE**	**PEE**	**CE**	**EAE**
Carbohydrates	+	+	+	-	-	-	-	+	+	-	-	-

Glycosides	+	+	NA	+	+	+	-	+	+	-	-	-
Alkaloids	-	-	+	-	+	+	NA	+	-	-	+	-
Steroids	-	-	+	-	+	-	-	+	+	-	+	+
Flavonoids	+	+	+	+	+	-	-	+	+	-	+	-
Tannins	+	-	+	-	+	+	+	+	+	-	+	-
Terpenoids	+	+	+	-	-	+	-	+	+	-	-	-
Phenols	+	+	+	-	+	NA	-	+	+	-	+	-

(+) Presence, (−) Absence, (NA) Not Analyzed

Because of their simplicity, effectiveness, and broad applicability, solvent liquid-liquid extractions are the continuous method most frequently employed to prepare extracts from plant materials. Recent years have seen the development of a wide range of techniques, including supercritical microwave extraction, Among others, reliable-liquid extraction, hypercritical extraction, standard extraction, microwave extraction, and extraction using ultrasound[15]. The identification of bioactive chemicals in plant extracts is frequently done using chromatographic methods. High-performance thin layer chromatography (HPTLC), gas chromatography (GC), and high-performance liquid chromatography are the most widely used analytical methods for the separation of polyphenolic substances (HPLC), Combining detection by DAD detector and mass spectrometry. Right now, this is one of the popular and, widely applied sets of procedures for separating, identifying, and quantifying phenolic chemicals [16]. For determining a biomolecule's mass and revealing its structural details, Mass Spectrometry is a familiar and effective method [17]. The main applications of mass spectrometry (MS) are in the quantitative and measurable examination of biological molecules. This approach is in accordance with gas-phase ions that are divided according to their mass-to-charge ratios (m/z). Mass Spectroscopy is a usual and effective method for determining the mass and illuminating the structure of biological molecules. For the majority of tasks in plant metabolite analysis and drug development, HPLC combined with MS is the analytical method of choice [18–21]. Plant extract from the entire plant, including the leaves, stem, and root, contains a variety of chemical elements like sitosterol, calotropin, lupeol, calactin, oleanolic acid, corotoxigenin, daucosterol, sucrose, and its acetate are all present in the *P.daemia* leaves and root extract [22–25]. Additionally, phytocompounds like pentacosanoic acid polypeptide, hentriacontane, betaine, and the glucoside of P.daemia were discovered in the whole plant preparation. The phytocompounds identified in P. daemia seed extract include dihydrocalotropigenin, corotoxigenin, calactin, protouscharin, calotropigenin, uscharidin, calotropin, and uscharin.

Similar to this, seed extract contained a variety of cardenolides, including uscharidin and calotoxin. They also identified several related substances in the stem extract, including coroglaucigenin, corotoxigenin, uscharidin, and uzarigenin. During a qualitative study, it was discovered that flavonoids were the most significant phytochemicals extracted from *P.daemia* aerial parts. The dried stem of *P.daemia's* vegetative parts was found to contain hyperoside as well as saponins and flavonoids in the fresh flowers and shoots [26, 27]. Numerous studies have

demonstrated the potential pharmacological effects of phenolic substances such as bioflavonoids and phenolic acids [28, 29]. The presence of bioflavonoids such as anthocyanin, natural compounds coumarin lignans, isoflavones, catechins, flavonoids, and iso catechins is primarily responsible for plants' antioxidant action. Green leafy plants, natural fruit juices, and phenolic compounds like flavonoids and phenolic acids are all quite plentiful. With the use of these anti-inflammatory substances or herbal remedies, artery hardening, clogged arteries, diabetes, Alzheimer's disease, malignant tumors, and other inflammatory disorders can all be prevented. [30]. It's significant to note that phytocompounds have anti-inflammatory properties, and several of them are currently undergoing preclinical testing. These days, a lot of people also prefer these natural remedies because of how affordable and secure they are. The primary phytocompound in the *P. daemia* preparations is flavonoids, with concentrations ranging from 72.549 0.449 to 400.196 0.339 mg/ml. Leaves and stem extracts showed a high amount of flavonoids when compared to other plant components. At a concentration of 10 mg/ml, the equivalent amounts of quercetin in n-hexane, ethyl acetate, and water are 338.725 milligram/gram, 388.627 milligram/gram, and 400.196 milligram/gram, correspondingly. The category of plant phenolics known as flavonoids is the most well-known and widely distributed. It contains flavones, monomeric flavanols, anthocyanidins, flavanones, and flavonols. (Fig 2). These flavonoids could hold back the pro-inflammatory negotiators and further inflammatory agents. (Fig 3). Five flavonoids that have anti-arthritic action against a rat model created by the complete Freund's adjuvant (CFA) have been identified and documented in *P. daemia* extracts like chrysoeriol, formononetin, taxifolin, quercetin, and naringenin. The antioxidant, antibacterial, anti-inflammatory, and immunomodulatory activity of flavonoids is just a small sample of the health-promoting qualities they possess. There are several important subcategories of flavonoids, such as flavanols, anthocyanidins, flavanones, isoflavones, and flavones [31, 32]. Contrarily, numerous therapeutic plants with significant active ingredients remain undiscovered. Among them, P. daemia was identified as a trustworthy source of flavonoids and other bioactive substances. People's trust in newly developed natural medicines has made certain therapeutics like kaempferol, quercetin, myricetin, and morin popular.

Fig.2 Basic skeleton of flavonoids and their subgroups

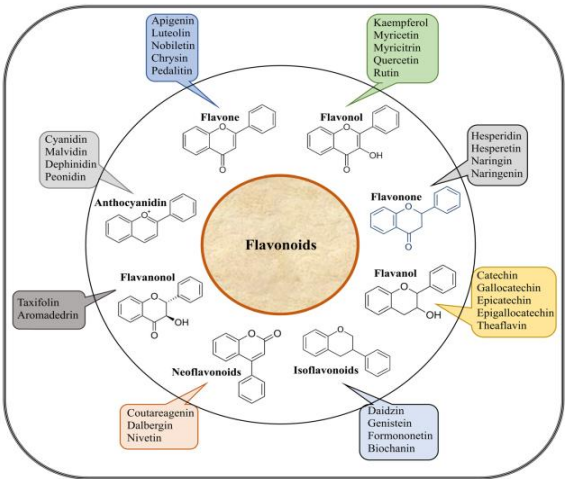
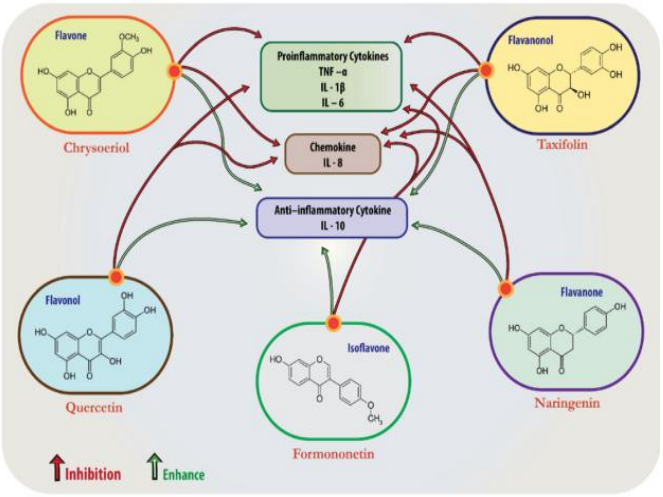


Fig.3 Possible anti-inflammatory inhibition mechanism of flavonoids from P. daemia



Pharmacology studies

Antioxidant activity

According to the latest studies, free radicle damage and its side effects severely harm people's health. The stress state results in the overexpression of reactive oxygen species and reactive nitrogen species. These reactors promote the development of degenerative diseases [33–35]. In normal cell metabolism and electron transport systems, ROS, such as superoxidation anion, nitrogen oxide, hydrogen peroxide, peroxide, and reactive hydrogen is constantly produced. When ROS/RNS is overproduced, the defense system fails and oxidants are released. Antioxidants are substances that hold back the oxidation process, chelate catalytic metals, and neutralize free radicals by oxygen scavengers. According to some studies, these substances can prevent oxidative damage caused by free radicals, reducing the risk of some diseases and degenerative diseases. Our blood plasma naturally contains antioxidants such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), albumin, transferrin, and ceruloplasmin, as well as lipids and water-soluble antioxidants such as tetrachlorophenol, quinine, vitamin C, uric acid, and vitamin E. Anti-oxidants protect biological systems from being harmed by converting ROS and RNS into stable molecules. Synthetic antioxidants are now extensively used in the food and pharmaceutical industries. Examples include butyl hydroxyanisole (BHA), butyl hydroxytoluene (BHT), propyl gallate (PG), and test-butyl hydroxyquinone (TBHQ). These substances have very harmful toxic impacts on the victims. However, several medicinal plant components that have been purified showed strong antioxidant action with the least amount of oxidative damage. By inhibiting two different synthetic free

radicals, namely 2,2′-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) and 1,1-diphenyl-2-picrylhydrazyl, the in vitro antioxidant capacity of *P. daemia* preparations was determined (DPPH).

The methanolic preparation of Pergularia daemia particular portion had been immensely efficient in nitric oxide free radicals, similar to gallic acid. *P.daemia* extract's ABTS IC50 concentration was 19.72 milligram/milliliter, which was beyond the concentration of gallic acid. Similar to this, the IC50 value for gallic acid and extract for DPPH scavenging activity was 33.36 and 34.12 mg/ml, respectively. In comparison to the gallic acid standard, the *Pergularia daemia* extract displayed outstanding nitric oxide scavenging activity [36]. On the other hand, a *Pergularia daemia* leaf extract made with ethanol at 70% showed considerable DPPH free radical scavenging action comparable to industry standards like ascorbic acid. Leaves evaporation exhibited a lesser degree of scavenging effect, and their respective EC50 values were 0.149, 0.699, and 2.608 milligram/milliliter. Additionally, these smaller EC50 values displayed higher antioxidant activity. Additionally, the generation of peroxides and hydrogen peroxides was well suppressed by the ethanolic extract. Ascorbic acid, BHT, and extract all had EC50 values of 17.78, 0.5239, and 0.2065 mg/ml, respectively. Iron levels in P. daemia extract may drop from ferric (Fe3+) to ferrous (Fe2+). Ethyl acetate stem extract had IC50 values of 10.19 and 26.99 g/ml for *P.daemia* stem extract, respectively. N-Hexane Extract, 58.20 g/ml, is the next component. The presence of phytosterols, phenols, saponins, alkaloids, tannins, flavonoids, and triterpenes in the leaf extract may be the reason for the antioxidant activity that has been noted. [37, 38].

Anti-inflammatory and analgesic activity

An ordinary biological process known as inflammation defends the tissue from harm by attacking invading agents such as bacteria. Inflammation is typically a quick and self-limiting process, but when there is an aberrant pathological situation, it produces excessive ROS/RNS, which causes persistent inflammation. There is a relationship between this chronic inflammation and major inflammatory disorders such as arthritis, cancer, and neurological, metabolic, and cardiovascular conditions [39,40]. To control this chronic inflammatory condition, researchers have previously created steroidal and non-steroidal anti-inflammatory medications. These medications successfully lessen the intensity of the illness, but they also have a number of negative effects. *P. daemia*, a medicinal herb, has therapeutic properties with the fewest adverse effects. Rats' paw edema is significantly reduced (p 0.001) by *P.daemia* ethanolic extracts when compared to carrageenan- and cotton pellet-induced paw edema. These extracts, at a dosage of 200 mg/kg, demonstrated a reduction in granuloma development of up to 44.18% and 19.87%, respectively. At the same concentration, other preparations, including n-butanol, benzene, and chloroform, display 16.83%, 13.96%, and 15.08%, respectively. [41]. Comparably, whole plant extracts of chloroform and petroleum ether are used to study carrageenan-induced paw edema in rats [42]. The comparison between the treated chloroform extract and the control showed a highly significant (p 0.01) development. By using a technique for stabilizing the membrane of human red blood cells (HRBCs), From the leaf and root of *P.daemia,* the invitro anti-inflammatory efficacy of ethanolic extracts was determined. Their research also showed that the

leaves and root extracts had anti-inflammatory activity when the membrane was stabilized. This method produced the most notable stabilization when compared to the standard medication diclofenac sodium (72.73%) at a concentration of 100 g/ml. Extracts from the *P. daemia* plant also exhibited potent analgesic properties. These extracts are being utilized in place of painkillers. Using Eddy's hot plate technique, the analgesic potency of *Pergularia daemia* aqueous and alcoholic root extracts was assessed. At a dosage of 1000 mg/kg, the effects were considerable (p 0.001) [44]. P. daemia petroleum extract and chloroform both had similar analgesic effects at a dose of 100 mg/kg (p 0.01). P.daemia contains a lot of flavonoids and glycosides, which may have a large analgesic and anti-inflammatory effect.

Anti-arthritic activity

In animal models, flavonoids have demonstrated efficacy in treating anti-rheumatic disease. Formononetin, quercetin, chrysoeriol, taxifolin, and naringenin are among the flavonoids found in *P.daemia* methanolic preparations. Red blood cell (8.38 0.67 million/mm3) and hemoglobin (11.84 0.42 g/dl) levels were dramatically raised in the methanolic extract-treated rat groups, which also successfully reduced paw inflammation. Although the levels of rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), white blood cell count (8.91 0.38thousands/mm3), erythrocyte sedimentation rate (7.91 0.12 mm/h), and C-reactive protein (22.56 0.26 mg / l) were considerably lower compared to the group of rats with arthritis. According to the results of the study, the alcoholic solution t of *the* leaf and root (300 g/ml) could have a strong antiarthritic effect. They verified using a membrane stabilization assay, and they found that leaf activity was higher (54.55%) than root activity (45.55%). Similar to this, *P. daemia* root extracts show 58.89% greater suppression than leaf extracts, which demonstrated 53.33%. In all cases, 100 g/ml of the reference medication diclofenac sodium was used to compare the results of the tests. Extracts of the *Pergularia daemia* leaf in the form of petroleum ether at 300 mg/kg lowered swelling and inflammation in the hind paws, which improved the arthritis state in arthritic rats. Further, it has been suggested that P. daemia's anti-rheumatic effects may be attributed to phytocompounds like flavonoids and sterols.

Anti-cancer activity

The second-most common and dangerous cause of death around the globe is cancer. Secondary metabolites from plant extracts used in herbal treatments lessen the disease's severity while avoiding adverse effects for the treatment of cancer. A whole plant extract of methanol dichloromethane (1:1 v/v) was discovered to inhibit the development of cancerous cells. The molecule alpha-amyrin is in charge of preventing the growth of cancerous cells, however, its effectiveness in preventing this growth was only between 15 and 50 ng/ml[45]. According to a different study, *Pergularia daemia* extract is a significant source for treating oral cancer. Comparing the ethyl acetate extract to the methanolic extract, the ethyl acetate extract (300 mg/kg b.w.) showed superior in live antioxidant research. The effectiveness was assessed in contrast to a DMBA-induced hamster buccal pouch (7, 12-dimethylbenz[a]anthracene). The leaf extract effectively destroyed ovarian cancer cell lines PA-1 and OAW-42, whose respective IC50 values were 30 and 120 mg/ml, respectively. According to scientists, polyphenolic compounds, especially triterpenoids, greatly suppress the growth of cancer cells. The capacity to develop an

oval medicine against cancer was also mentioned, along with a slight structural change of triterpenoids [46].

Anti-proliferative activity

The oral keratin-forming tumor cell line HeLa (KB) cells were resistant to the proliferative effects of *P.daemia* methanolic extract, by using a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide test, the activity was measured (MTT). Measurements of ROS production, membrane potential, antioxidant status, and cell cycle arrest were made to corroborate the antiproliferative effect. They demonstrated the strongest cytotoxic activity against oral KB cells at the maximum dose (160 g/ml) of *P.daemia* methanolic extract. The MTT assay was used to calculate the IC50 value of methanolic extract against cancer cell lines, which was 90%. The apoptotic morphology of KB cells pre-treated with *P.daemia* extract was dramatically altered, and this apoptotic morphological change was caused by elevated ROS levels and a decrease in matrix metallopeptidases (MMPs). The apoptosis that occurs in KB cells as a result of the demise of the cancer cell causes DNA damage and the formation of ROS and lipid peroxidation (LPO) in the intracellular region. By encouraging apoptosis and stopping proliferation in malignant cells, *P. daemia's* polyphenolics (phenolic acid and flavonoids) may be a key factor in reversing this process.

Anti-diabetic activity

Next to cancer and cardiovascular diseases, diabetes mellitus is emerging as the third "killer" disease in human history. It is a chronic metabolic condition that has an impact on both our body's physical and psychological processes. The potential for anti-hyperglycemic activity was discovered in the first study on *Pergularia daemia* extract at a concentration of 300 mg/kg effectively reduced blood glucose levels in diabetic rats after streptozotocin (STZ) induction[47]. The diabetic mice were treated for 21 days with chloroform leaf extract, which resulted in blood glucose levels of 160.68 mg/dl, 132.61 ml/dl in ethanol, 152.80 mg/dl in aqueous extract, 123.26 mg/dl in ethanol extract of callus, and 194.6 mg/dl in glibenclamide (600 g/kg).

When alloxan was utilised as the test medication, the administration of alcoholic and aqueous extracts from the whole plant of D. extensa led to a loss in vitality [48]. The blood glucose level (BGL) was significantly (P 0.01) decreased by alcohol extract in a single dose after 1 hour. The anti-diabetic activity was comparable to that of chlorpropamide, a common medication. *P. daemia* extract has recently been shown to have anti-hyperglycemic efficacy against STZ-induced rat models. On a dose-dependent basis, the blood glucose level considerably dropped. Flavonoids and their phenols, glycosides, triterpenes, saponins, phytosterols tannins, alkaloids, and alkaloids are among the bioactive substances in plants that have hypoglycemic effects [49].

Hepatoprotective activity

The liver is a remarkable organ that serves as the body's primary chemical laboratory. It is essential to the body's metabolism and detoxification of the many toxins and chemicals that enter it. The biochemical control of biomolecules like lipids, carbohydrates, amino acids, and proteins

is greatly influenced by the elimination of exogenous poisons and medications. ROS are crucial in liver injury. A common ailment known as liver damage or injury can be brought on by an excessive amount of ROS being produced, which damages the hepatic cells and surrounding tissue. The liver-damaging compounds are produced by a variety of substances, including the toxin itself, carbon tetrachloride, acetaminophen, amanitin, pyrrolizidine alkaloids, ethanol, bromobenzene, and polycyclic aromatics [50]. Because antioxidants are so powerful at scavenging free radicals, they can protect liver cells from CCl4-induced damage. Recent studies suggested that natural antioxidants can guard against liver issues brought on by oxidative stress [51–53]. The CCl4-induced hepatic rat model is significantly (P 0.05) protected against the ethanolic and aqueous preparation of P. daemia. Additionally, they found that rats given ethanolic extracts at a dose of 200 mg/kg had lower levels of the enzymes total protein (TPTN), total albumin (ALB), total bilirubin, and total cholesterol, and higher levels of the enzymes aspartate aminotransferase, glutamic pyruvic transaminase, and alkaline phosphatase [54]. It targets fatty acids that are polyunsaturated. because experimental animals' altered liver microsomal membrane hepatotoxicity was discovered. Aqueous and ethanolic extracts of *P. daemia* roots are also significantly protective against the rat hepatotoxic effects of paracetamol and CCl4 [55]. Similar to CCl4, paracetamol also led to an increase in blood liver enzymes like bilirubin and cholesterol. The biochemical indicators of SGOT and SGPT were significantly inhibited by both aqueous and ethanolic extracts at doses of 100 and 200 mg/kg. LPO and malonaldehyde (MDA) levels were lower in treated rats compared to control rats, while serum protein antioxidant enzymes glutathione (GSH) levels were higher. Since these extracts contain bioactive compounds like flavonoids, terpenoids, glycosides, and saponins, they may have a hepatoprotective impact. The flavonoids and triterpenoids found in the ethanolic extract of *P.daemia* leaf are what are most likely to be responsible for the hepatoprotective effect[56]. Using quercetin-3-glucoside as a reference in HPTLC, the flavonoids from the ethanol extract and ethanol fraction in P. daemia were verified. These findings show that flavonoids have hepatoprotective properties [57].

Diuretic activity

Rats were used in a dose-dependent study of the diuretic efficacy of *P. daemia* preparations[58]. Furosemide was utilized as a reference medication in this study along with the Lipschitz test. According to the findings, the diuretic activity of the *P. daemia* alcoholic extract peaked at 0.93 at a concentration of 400 ml/kg. Except for the petroleum ether, all examined extracts that were tested for urine production produced significant findings (P 0.001) when compared to the control. Importantly, plant extracts also have an impact on electrolyte excretion through the urine. Alcoholic, ethyl acetate and n-butanol extracts further increased the excretion of sodium and potassium ions (Na+ and K+) in urine. The alcoholic extract had a diuretic activity of 2.04 units, which was almost identical to the normal dose of furosemide (2.19 units). The urinary Na+ and K+ ions level was raised and the urine's pH level was somewhat raised by extracts like alcohol, ethyl acetate, n butanol, and the common medication furosemide. These results overwhelmingly point to the fact that *Pergularia daemia* extracts have a diuretic effect. Possible candidates for the diuretic effect of *P.daemia's* secondary metabolites include alkaloids, flavonoids, and steroids.

Anti-tuberculosis activity

Plant extracts appear to have potential benefits for treating TB in the Ayurvedic medical system. Recently found that the hydro-alcoholic leaf extract of *P. daemia* had a protective effect against the liver damage caused by anti-tuberculosis medications (ATDs)[59]. ATD administration dramatically reduced albumin and glucose levels. Furthermore, elevated amounts of cholesterol, bilirubin, triglycerides, aspartate aminotransferase, alkaline phosphatase, and alanine aminotransferase were found. Glutathione reductase, glutathione, peroxidase, catalase, glutathione, superoxide dismutase, and glucose-6-phosphate dehydrogenase levels decreased and lipid peroxidation levels increased after exposure to ATDs. As a result, compared to the control, P. daemia extracts notably continued these serum biochemical parameters and antioxidant components.

Anti-fertility activity

P. daemia's ethanolic extract and its steroidal fraction demonstrated a possible anti-fertility effect. A significant effect against female mice during the pre-implantation stage was seen with a steroidal fraction of 200 mg/kg. The late-term abortifacient effect of ethanolic extracts, however, was 600 mg/kg. Within 48 hours of medication therapy, the extract exhibited 100% activity with no mortality. These findings suggest that the steroidal and ethanolic extracts of *P. daemia* may inhibit reproduction in female mice.[60]

Anti-ulcer activity

Dehydration, ethanol's direct imposition of cytotoxic effects during the pathophysiology of ulcer formation, and interference with mucosal cellular membranes all contributed to the progression of the inflammatory response [61]. Leukocytes, which cause inflammatory reactions, oxidative stress, and apoptosis, also indirectly contributed to the harmful effects of alcohol. NF-kappa B (NF-B) is critical in mediating the development of illness conditions during this process [62]. Numerous studies have documented the anti-ulcerogenic properties of secondary metabolites like flavonoids, tannins, and triterpenes [63]. These phytochemicals are present in *P. daemia* and may be the cause of the anti-ulcer action. P. daemia showed a healing effect on the ethanol-induced ulcer in rats. The inhibition percentage for the group treated with the standard treatment was 78.73%, whereas the percentage for the extracts (400 mg/kg) was 63.01. Excellent anti-ulcer action is provided by ethanolic extracts of *P. daemia* leaf in a dose-dependent way.

Conclusion

One of the less investigated and reported medicinal plants is *P. daemia*. We contend that *P.daemia* had excellent pharmacological action based on historical accounts and literature surveys. Qualitative analyses of compounds from various P. daemia parts, including flavonoids, terpenoids, proteins, amino acids, and saponins. Phytochemicals and bioactive substances can be found naturally in medicinal plants. The key bioactive substances found in P. daemia preparations are claimed to be natural flavonoids and cardenolides. Due to their anti-inflammatory, antioxidant, and other pharmacologically useful properties in humans, bioactive substances like *P. daemia* solvent extracts are administered to prevent cancer, arthritis, and other

disorders like inflammation. In general, it should be understood that *P. daemia's* phytochemistry and pharmacological state do not offer sufficient resources for herbal compositions. However, the clinical studies' mechanisms of action are unknown. Additional research is needed to determine the other beneficial chemicals in *P. daemia* as well as their precise mechanisms of action in treating the disease. These investigations will aid in popularising herbal compositions based on *P. daemia*.

References

1. Pandey M, Rastogi S, Rawat A. Indian traditional ayurvedic system of medicine and nutritional supplementation. Evid-Based Complement Altern Med. 2013;2013:376327.

2. Subhose V, Srinivas P, Narayana A. Basic principles of pharmaceutical science in Ayurvĕda. Bull Indian Inst Hist Med Hyderabad. 2005;35(2):83–92.

3. Pandey MM, Rastogi S, Rawat A. Indian herbal drug for general healthcare: an overview. J Evid Based Integr Med. 2008;6(1):1–12.

4. Santosh MK, Sharanabasappa GK, Shaila D, Seetharam YN, Sanjeevarao I. Phytochemical studies on Bauhinia racemosa lam., Bauhinia purpurea Linn. And Hardwickia binate Roxb. E-J Chem. 2007;4:21–31.

5. Jain C, Khatana S, Vijayvergia R. Bioactivity of secondary metabolites of various plants: a review. IJPSR. 2019;10(2):494–504.

6. Patwardhan B, Warude D, Pushpangadan P, Bhatt N. Ayurveda and traditional Chinese medicine: a comparative overview. Evid-Based Complement Altern Med. 2005;2(4):465–73. https://doi.org/10.1093/ecam/ neh140.

7. Frawley D, Ranade S. Ayurveda, nature’s medicine. Wisconsin: Lotus Press; 2000. p. 1–7.

8. Shad AA, Ahmad S, Ullah R, AbdEl-Salam NM, Fouad H, Ur Rehman N, et al. Phytochemical and biological activities of four wild medicinal plants. Sci World J. 2014;2014:857363.

9. Meena AK, Bansal P, Kumar S. Plants-herbal wealth as a potential source of ayurvedic drugs. Asian J Tradit Med. 2009;4:152–70.

10. Yoganarasimhan SN. Medicinal plants of India (Vol. 1). Bangalore: Interline Publishing Pvt. Ltd.; 2000.

11. Dokosi OB. Herbs of Ghana. Accra: Ghana Universities Press; 1998.

12. Karthishwaran K, Mirunalini S. Therapeutic potential of Pergularia daemia (Forsk.): the Ayurvedic wonder. Int J Pharmacol. 2010;6(6):836–43. https:// doi.org/10.3923/ijp.2010.836.843.

13. Ananth DA, Rameshkumar A, Jeyadevi R, Aseervatham GSB, Sripriya J, Bose PC, et al. Amelioratory effect of flavonoids rich Pergularia daemia extract against CFA induced arthritic rats. Biomed Pharmacother. 2016;80:244–52. https://doi.org/10.1016/j.biopha.2016.03.019.

14. Abascal K, Ganora L, Yarnell E. The effect of freeze-drying and its implications for botanical medicine: a review. Phytother Res. 2005;19(8):655– 60. https://doi.org/10.1002/ptr.1651.

15. Naczk M, Shahidi F. Extraction and analysis of phenolics in food. J Chromatogr A. 2004;1054(1–2):95–111. https://doi.org/10.1016/S0021-9673(04)01409-8

16. Downey MO, Rochfort S. Simultaneous separation by reversed-phase highperformance liquid chromatography and mass spectral identification of anthocyanins and flavonols in shiraz grape skin. J Chromatogr A. 2008; 1201(1):43–7. https://doi.org/10.1016/j.chroma.2008.06.002.

17. Dai J, Mumper RJ. Plant phenolics: extraction, analysis and their antioxidant and anticancer properties. Molecules. 2010;15(10):7313–52. https://doi.org/1 0.3390/molecules15107313.

18. Hamburger M, Wolfender JL, Hostettmann K. Search for chlorinated sesquiterpene lactones in the neurotoxic thistle Centaurea solstitialis by liquid chromatography-mass spectrometry, and model studies on their possible artifactual formation. Nat Toxins. 1993;1(6):315–27. https://doi.org/1 0.1002/nt.2620010602.

19. Fang N, Yu S, Prior RL. LC/MS/MS characterization of phenolic constituents in dried plums. J Agric Food Chem. 2002;50(12):3579–85. https://doi.org/10.1 021/jf0201327.

20. Ye M, Yan Y, Da G. Characterization of phenolic compounds in the Chinese herbal drug Tu-Si-Zi by liquid chromatography coupled to electrospray ionization mass spectrometry. Rapid Commun Mass Spectrom. 2005;19(11): 1469–84. https://doi.org/10.1002/rcm.1944.

21. Seeram NP, Lee R, Scheuller HS, Heber D. Identification of phenolic compounds in strawberries by liquid chromatography electrospray ionization mass spectroscopy. Food Chem. 2006;97(1):1–11. https://doi.org/1 0.1016/j.foodchem.2005.02.047.

22. Anjaneyulu A, Raju D, Rao S. Chemical examination of Pergularia extensa. Indian J Chem B. 1998;37:318–20.

23. Seshadri T, Vydeeswaran S. Chemical examination of Luffa echinata. Phytochem. 1971;10(3):667–9. https://doi.org/10.1016/S0031-9422(00)94 717-4.

24. Rakhit S, Dhar MM, Anand N, Dhar ML. Chemical investigation of Daemia extensa. J Sci Ind Res (India). 1954;18B:422–6.

25. Raman SP, Barua A. Chemical investigation of Daemia extensa R. Br J Am Pharm Assoc (Scientific ed). 1958;47(8):559–60.

26. Sinha S, Dogra J. A survey of the plants of Bhagalpur and Santhal pargana for saponin, flavonoids, and alkaloids. Int J Crude Drug Res. 1985;23(2):77–86. https://doi.org/10.3109/13880208509069006.

27. Subramanian SS, Nair A. Flavonoids of some asclepiadaceous plants. Phytochemistry. 1968;7(9):1703–4. https://doi.org/10.1016/S0031-9422 (00)88630-6.

28. Shahidi F. Antioxidant factors in plant foods and selected oilseeds. Biofactors. 2000;13(1–4):179–85. https://doi.org/10.1002/biof.5520130129.

29. Shahidi F, McDonald J, Chandrasekara A, Zhong Y. Phytochemicals of foods, beverages, and fruit vinegars: chemistry and health effects. Asia Pac J Clin Nutr. 2008;17(S1):380–2

30. Devasagayam T, Tilak J, Boloor K, Sane KS, Ghaskadbi SS, Lele R. Free radicals and antioxidants in human health: current status and prospects. J Assoc Physicians India. 2004;52:794–804.

31. Lin J-K, Weng M-S. Flavonoids as nutraceuticals. In: The science of flavonoids: Springer; 2006. p. 213–38.

32. López-Lázaro M. Distribution and biological activities of the flavonoid luteolin. Mini-Rev Med Chem. 2009;9(1):31–59. https://doi.org/10.2174/13 8955709787001712.

33. Ambriz-Pérez DL, Leyva-López N, Gutierrez-Grijalva EP, Heredia JB. Phenolic compounds: a natural alternative in inflammation treatment. A review. Cogent Food Agric. 2016;2:1131412.

34. Emerit J, Edeas M, Bricaire F. Neurodegenerative diseases and oxidative stress. Biomed Pharmacother. 2004;58(1):39–46. https://doi.org/10.1016/j. biopha.2003.11.004.

35. Kumar KR, Lohmann K, Klein C. Genetics of Parkinson's disease and other movement disorders. Curr Opin Neurol. 2012;25(4):466–74. https://doi.org/1 0.1097/WCO.0b013e3283547627.

36. Cook NC, Samman S. Flavonoids—chemistry, metabolism, cardioprotective effects, and dietary sources. J Nutr Biochem. 1996;7(2):66–76. https://doi. org/10.1016/0955-2863(95)00168-9.

37. Karthishwaran K, Mirunalini S. Assessment of the antioxidant potential of Pergularia daemia (Forsk.) extract in vitro and in vivo experiments on hamster buccal pouch carcinogenesis. Asian Pac J Trop Dis. 2012;2:S509– S16. https://doi.org/10.1016/S2222-1808(12)60212-6.

38. Sarkodie J, Squire S, Kretchy I, Domozoro C, Ahiagbe K, Twumasi M, et al. The antihyperglycemic, antioxidant, and antimicrobial activities of Ehretia cymosa. J Pharmacogn Phytochem. 2015;4(3):105–11.

39. Calder PC, Albers R, Antoine J-M, Blum S, Bourdet-Sicard R, Ferns G, et al. Inflammatory disease processes and interactions with nutrition. Br J Nutr. 2009;101(Suppl):S1–45.

40. Libby P. Inflammatory mechanisms: The molecular basis of inflammation and disease. Nutr Rev. 2007;65(suppl-3):S140–S46.

41. Usman MRM, Salgar SD, Pati SA. Anti-inflammatory activity of the whole plant of Pergularia daemia Linn. Int J Pharma Sci Res. 2012;3:258–67.

42. Venkataraman S, Sini B, Meera R, Devi P. Anti-inflammatory, the analgesic and antipyretic activity of Pergularia daemia Forsk. Int J Pharm Biol Sci Arch. 2010;1(4):371–5.

43. Hina I, Rose JC. In vitro anti-inflammatory and anti-arthritic activity of Pergularia daemia leaves and roots. J Int J Drug Dev Res. 2018;10:10–3.

44. Nikajoo LT. Analgesic activity of aqueous and alcohol root extracts of Pergularia daemia (Forsk.) Chiov. Int J Pharm Pharm Sci. 2009;1(Suppl1):33–7.

45. Khorombi TE. A chemical and pharmacological investigation of three south African plants. Pietermaritzburg: University of KwaZulu-Natal; 2006.

46. Martin S, Kavitha PD, Rathi MA, Kumar DG, Gopalakrishnan VK. Cytotoxic activity of Pergularia daemia against ovarian cancer cell lines OAW-42 and PA-1. J Nat Pharm. 2011;2(4):203–9.

47. Kumar PV, Ramesh N. Anti-hyperglycaemic activity of Pergularia daemia (Forssk.) Chiov. J Phytopharmacol. 2014;3(1):29–34.

48. Wahi A, Ravi J, Hemalatha S, Singh P. Anti-diabetic activity of Daemia extensa R. Br J Natl Remedi. 2002;2(1):80–3.

49. Sarkodie JA, Squire SA, Bekoe EO, Domozoro CYF, Kretchy IA, Ahiagbe MKJ, et al. Antioxidant and antimicrobial capacities of ethanolic extract of Pergularia daemia leave a possible substitute in diabetic management. J Comp Integr Med. 2016;13(3):239–45.

50. Adesanoye OA, Farombi EO. Hepatoprotective effects of Vernonia amygdalina (Astereaceae) in rats treated with carbon tetrachloride. Exp Toxicol Pathol. 2010;62(2):197–206. https://doi.org/10.1016/j.etp.2009.05.008.

51. Tan BL, Norhaizan ME, Liew WP, Sulaiman RH. Antioxidant and oxidative stress: a mutual interplay in age-related diseases. Front Pharmacol. 2018;16(9):1162.

52. Dhanasekaran D, Sivamani P, Panneerselvam A, Thajuddin A. Rajakumar, Selvamani S. biological control of tomato seedling damping off with Streptomyces sp. Plant Pathol J. 2005;4(2):91 –5. https://doi.org/10.3923/ppj.2 005.91.95 .

53. Wang BJ, Liu CT, Tseng CY, Wu CP, Yu ZR. Hepatoprotective and antioxidant effects of Bupleurum kaoi Liu (Chao et Chuang) extract and its fractions fractionated using supercritical CO 2 on CCl 4 induced liver damage. Food Chem Toxicol. 2004;42(4):609 –17. https://doi.org/10.1016/j.fct.2003.11.011

54. Sureshkumar S, Mishra S. Hepatoprotective effect of extracts from Pergularia daemia Forsk. J Ethnopharmacol. 2006;107(2):164 –8. https://doi.org/10.1016/ j.jep.2006.02.019 .

55. Bhaskar V, Balakrishnan N. Protective effects of Pergularia daemia roots against paracetamol and carbon tetrachloride-induced hepatotoxicity in rats. Pharm Biol. 2010;48(11):1265 –72. https://doi.org/10.3109/13880201003 730667.

56. Sureshkumar S, Mishra S. Hepatoprotective activity of extracts from Pergularia daemia Forsk. Against carbon tetrachloride-induced toxicity in rats. Pharmacogn Mag. 2007;3(11):187 –91.

57. Sureshkumar S, Mishra S. Hepatoprotective effect of Pergularia daemia (Forsk.) ethanol extract and its fraction. Indian J Exp Biol. 2008;46(6):447 –52.

58. Bhavin V, Ruchi V. Diuretic potential of whole plant extracts of Pergularia daemia (Forsk.). Iran J Pharm Res. 2011;10(4):795 –8.

59. Mishra G, Chandra HK, Sahu N, Nirala SK, Bhadauria M. Ameliorative effect of Pergularia daemia (Forssk.) Chiov. Leaves extract against anti-tuberculosis drugs induced liver injury in rats. Asian Pac J Trop Med. 2018;11(9):518 –25.

60. Kumar VK, Kumar P, Venkatachalam T. Investigation of anthelmintic activity of Pergularia daemia leaves. Pharmacophore. 2014;5(1):44 –8.

61. Park SW, Oh TY, Kim YS, Sim H, Park SJ, Jang EJ, et al. Artemisia asiatica extracts protect against ethanol-induced injury in the gastric mucosa of rats. J Gastroenterol Hepatol. 2008;23(6):976 –84. https://doi.org/10.1111/j.1440-174 6.2008.05333.x .

62. Sangiovanni E, Vrhovsek U, Rossoni G, Colombo E, Brunelli C, Brembati L, et al. Ellagitannins from Rubus berries for the control of gastric inflammation: In vitro and in vivo studies. PLoS One. 2013;8(8):e71762. https://doi.org/10.13 71/journal.pone.0071762.

63. Borrelli F, Izzo AA. The plant kingdom is a source of anti-ulcer remedies. Phytother Res. 2000;14(8):581 –91. https://doi.org/10.1002/1099-1573(200012)14:83.0.CO;2-S.