Journal of Applied Pharmaceutical Science Vol. 15(07), pp 037-047, July, 2025
Available online at http://www.japsonline.com
DOI: 10.7324/JAPS.2025.237559
ISSN 2231-3354

Phytochemicals of Beluntas (*Pluchea indica*(L) Less.) and their health benefits

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ARTICLE HISTORY

Received on: 14/01/2025
Accepted on: 10/03/2025
Available Online: 05/06/2025

Key words:
Pluchea indica, natural products, pharmacological, bioactivities, biomedical application.

ABSTRACT

Bioactive compounds derived from plants are acquiring global popularity due to their safety and diverse applications as medicinal agents. Beluntas, also known as *Pluchea indica*, is a shrub abundantly found in coastal regions and is rich in several classes of phytochemicals that are highly significant in the biomedical field, particularly those based on natural products. The purpose of this review is to provide insights by highlighting research related to the bioactive compounds that can be obtained from *P. indica*. This review summarizes research data published in peer-reviewed manuscripts in English. Our search relied on scientific search engines and the following databases: Google Scholar, as well as scientific databases such as Scopus, PubMed, Crossref, and Web of Science, along with various publishers including Taylor and Francis, Elsevier, Wiley, Thieme, Bentham, Sage, SpringerLink, and Wiley–Blackwell. The traditional use of *P. indica* has been documented in several regions of Asia, including Indonesia, Thailand, Malaysia, and India. The phytochemicals of *P. indica* are thought to exhibit pharmacological effects such as antihyperlipidemic, antidiabetic, anticancer, antibacterial, anti-inflammatory, and antioxidant activities. Preclinical studies have demonstrated the pharmacological effects of *P. indica* extracts; however, limited data are available regarding the mechanism of action of this plant in clinical-scale studies. The phytochemicals of *P. indica* hold potential for development as herbal medicines or phytopharmaceuticals, creating possibilities for discovering new therapeutic agents and introducing compounds with previously known pharmacological effects.

INTRODUCTION

Traditional medicine has evolved over centuries across various countries with diverse techniques, such as Traditional Chinese Medicine in China, Kampo therapy in Japan, Traditional Korean Medicine including Sasang in Korea, and Traditional Medicine in Indonesia. Consequently, there are multiple clinical practices, each with its own set of concepts, diagnostic evaluation procedures, structures, rationales for diagnosis, and corresponding treatment approaches [1]. Traditional medicine in Indonesia is a form of cultural heritage, both tangible and intangible, that shapes the identity of a community or society. It is passed down through generations in the form of creativity, practices, and values, which are preserved for the future [2,3].

Indonesia's cultural heritage includes its culinary traditions, featuring both traditional foods and beverages. These foods are prepared exclusively with local ingredients and methods, showcasing rich regional distinctions [4]. Due to Indonesia's abundance of spices, the country offers a wide variety of traditional beverages made from local resources. While many share similar ingredients and preparation techniques, each region brings its own unique qualities and names. This variation is influenced by different socio-cultural backgrounds, local conditions, and available resources. Traditional beverages offer a diverse range of flavors, aromas, and health benefits.

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Bali Province is one of the regions in Indonesia known for its culinary culture and cultural tourism, which attracts many visitors. Traditional medicine, referred to as "Usadha," has emerged as a significant component of Balinese traditional healing practices. Various traditional Balinese beverages, known as "Loloh," are prepared using spices and plants and have been empirically validated as remedies by the Balinese community [5]. These beverages possess functional qualities and can be used experimentally to treat various health disorders. Traditional drinks contain active compounds that promote beauty, health, and body care. The general public is increasingly aware of the benefits associated with a return to nature.

One of the plants processed into traditional beverages is Beluntas leaves (*Pluchea indica* L.), which belongs to the herbaceous family Asteraceae and typically grows wild in dry, rocky areas or is cultivated as medicinal plants. Empirically, Beluntas is often used in traditional medicine to eliminate body and breath odor, enhance appetite, address digestive disorders, relieve pain from rheumatism, bone pain, and lower back pain, reduce fever, and manage irregular menstruation and leukorrhea. Due to its potential to boost the immune system, some literature reports its benefits as an immunostimulant against COVID-19 [6] and for anti-hyperglycemia, dyslipidemia, and obesity [7]. The presence of phytochemicals such as alkaloids, flavonoids, tannins, essential oils, and chlorogenic acid is strongly associated with the mechanisms by which Beluntas leaves may reduce the risk of chronic diseases such as diabetes, cancer, obesity, and cardiovascular diseases.

Despite the potential of *P. indica*, there are still relatively few publications that comprehensively address its phytochemical composition and bioactivity concerning various diseases. Therefore, a review investigating the phytochemicals present in *P. indica* extracts is warranted. This review also emphasizes the numerous health benefits associated with *P. indica*, including cholesterol reduction, blood sugar regulation, anticancer properties, antibacterial effects, antioxidant activity, and anti-inflammatory characteristics. The findings from this review can provide valuable information for researchers interested in exploring *P. indica* extracts further, particularly regarding the development of standardized herbal medicines, phytopharmaceuticals, and its economic potential as a local resource in Indonesia.

METHODS

An extensive literature study was conducted from 2000 to 2024 and literature was obtained from Google Scholar and scientific databases such as Scopus, PubMed, Crossref, and Web of Science, along with publications from Taylor and Francis, Elsevier, Wiley, Thieme, Bentham, Sage, SpringerLink, and Wiley–Blackwell. The most searched keywords are "Traditional medicine", "Bioactive compounds", "Phytochemistry", "Extraction", *"Pluchea indica"*, "Bioactivity", "Therapeutic use", "Antibacterial activity", "antiviral activity", "antifungal activity", "anticancer activity", "antioxidant activity", "antihyperlipidemic activity", "clinical studies". Current research focuses on the traditional use of *P. indica*, its nutritional composition, phytochemical profile, health benefits, and its applications in both preclinical and clinical studies. The therapeutic uses of *P. indica* and its potential in new drug discovery have been discussed. Articles in languages other than English were ignored. Other literatures that were left out included those in ecology and social dimensions. Chemical structure illustrations of some research results were performed using Chedraw from Pubchem (https://pubchem.ncbi.nlm.nih.gov/).

TRADITIONAL USE OF *P. INDICA* IN SEVERAL COUNTRIES

Pluchea indica, locally known as Beluntas in Indonesia, is an herbaceous plant from the Asteraceae family. It grows wild in dry, rocky areas with relatively hard soil or is intentionally cultivated as a medicinal plant, known as "TOGA" (Tanaman Obat Keluarga) in Indonesia. *P. indica* is commonly found in coastal regions, where it thrives naturally. Beyond Indonesia, Beluntas leaves are also used in traditional medicine in various other countries. For example, in Thailand, Beluntas leaves are processed into herbal tea and marketed as a health drink to treat diabetes, tumors, hypertension, cystitis, and wounds [8]. In Malaysia, herbal practitioners believe that *P. indica* leaves can treat dysentery, rheumatism, leukorrhea, breath, and body odor, as well as boils and ulcers [9]. In India, *P. indica*, also known as Indian Camphorweed, has been noted in Ayurvedic medicine for its anti-diabetic and anti-rheumatic properties. Recent studies further underscore the efficacy and safety of *P. indica* as a dietary supplement or remedy for preventing various diseases [10]. All of the parts of the Beluntas plants are in Figure 1.

The use of *P. indica* as a traditional medicinal preparation varies across different regions of Indonesia and has been empirically validated in each area. *Pluchea indica* is known by various local names in Indonesia, such as Bluntas (Bali), Baruntas (Sunda), Luntas (Java), Baluntas (Madura), Lamutasa (Makassar), and Lenabou (Timor). Internationally, it is referred to as Luan Yi in China, Phatpai in Vietnam, and Marsh Fleabane in English. Traditionally, *P. indica* leaves are prepared as herbal beverages by boiling or steeping fresh or

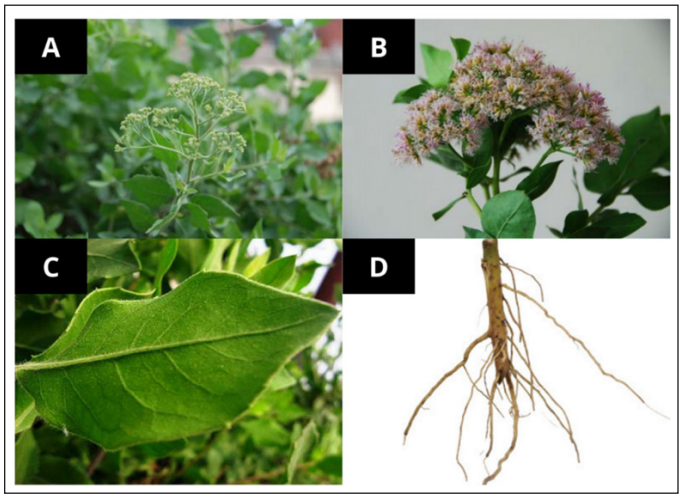

Figure 1. Beluntas parts, (A) overall parts of Beluntas, (B) flower and stem parts, (C) Leaf part, and (D) root part [10].

dried leaves. For wound healing, the fresh leaves are typically crushed and applied directly to the affected area [11].

NUTRITIONAL COMPOSITION OF *P. INDICA*

Pluchea indica leaves are rich in calcium, vitamin C, dietary fiber, and β-carotene [12]. The calcium content in *P. indica* leaves is seven times higher (251 mg/100 g), and the β-carotene content is twice as high (1,225 g/100 g) compared to basil leaves (32 mg/100 g and 812 g/100 g, respectively) [13]. In detail, the mineral content of *P. indica* leaves in µg/100 ml concentrations are potassium (78.68 ± 0.66), calcium (913.55 ± 9.12), sodium (704.35 ± 2.33), phosphorus (78.68 ± 0.66), magnesium (27.75 ± 0.30), zinc (0.64 ± 0.01), iron (0.01 ± 0.00), manganese (1.23 ± 0.01), selenium (104.95 ± 0.64), copper (0.30 ± 0.00), and chromium (47.39 ± 2.47) [14], respectively. The pounded leaves of *P. indica* emit a distinctive aroma and are characterized by their sweet, astringent, and fragrant flavor. In several Asian countries, fresh or boiled *P. indica* leaves are used as a side dish, often incorporated into chili paste to enhance the spiciness of dishes [15]. The fragrant aroma and spicy flavor of *P. indica* make it a popular ingredient in various traditional dishes, such as Kang Ped (spicy coconut milk soup), yum (spicy and sour salad), and Bothok (steamed meat mixed with *P. indica* leaves).

PHYTOCHEMICALS POTENTIAL IN *P. INDICA*

Pluchea indica is also highly advantageous for development into standardized herbal products and even phytopharmaceuticals due to the diverse phytochemicals present in its various parts. However, it is crucial to note that the quantity of these phytochemicals can vary greatly, influenced by environmental factors, genotypes, or a combination of both. *Pluchea indica* contains a wide range of phytochemicals that can be categorized into several key classes. These classes include flavonoids, alkaloids, tannins, steroids, phenolic acids, and phytosterols. The leaves of *P. indica* are particularly rich in flavonoids, which are organic antioxidants. Traditional medicinal plants often contain varying levels of flavonoids, with the highest concentration typically found in the leaves. Flavonoids, known as potent antioxidants, possess anti-cancer, anti-allergic, anti-inflammatory, and anti-carcinogenic properties, while also supporting the immune system and protecting digestive system function [16,17]. Several notable phytochemical structures in *P. indica* including vanillin, syringaldehyde, esculetin, (+)-isolariciresinol, caryolane-1,9β-diol, stigmasterol, fraxinellone, clovane-2α,9β-diol, and ethyl caffeate (Fig. 2).

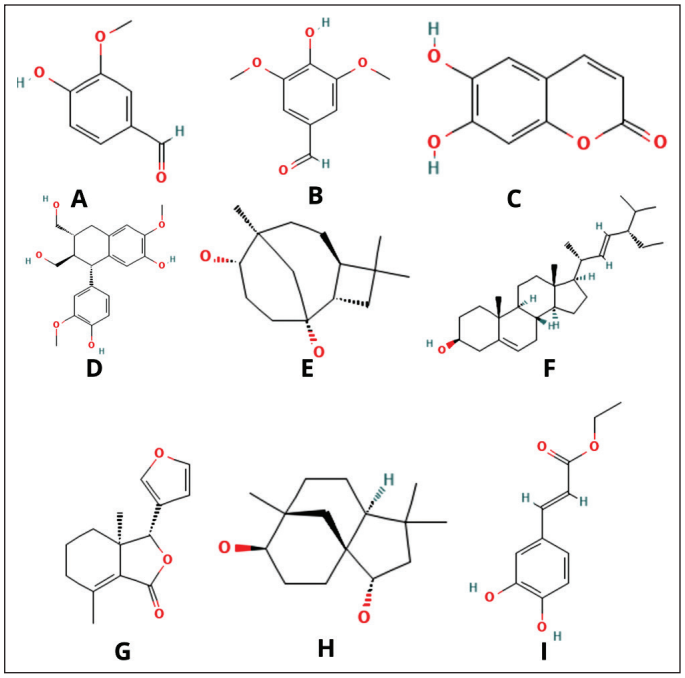

Figure 2. Phytochemical structure of *P. indica*, (A) vanillin, (B) syringaldehyde, (C) esculetin, (D) (+)-isolariciresinol, (E) caryolane-1,9β-diol, (F) stigmasterol, (G) fraxinellone, (H) clovane-2α,9β-diol, and (I) ethyl caffeate [16].

Phenolic content

It is known that the presence of phenolic compounds with antioxidant characteristics can prevent or reduce the progression of diseases related to oxidative stress [18]. Total phenolic content refers to the various phenolic compounds present in an extract, and calculating the levels of these compounds is crucial due to their significant correlation with antioxidant activity [19]. Reactive oxygen species (ROS) can be scavenged by phenolic components exhibiting strong antioxidant activity. These reactive chemical species are commonly associated with cardiovascular diseases, cancer, and neurological disorders [20,21]. Research reports indicate that gamma irradiation applied to *P. indica* leaf extracts can increase antioxidant activity, and total phenolic content, and reduce microbial contamination during storage [22]. Herbal tea made from *P. indica* leaves has been commercially marketed in Indonesia and Thailand and exhibits high phenolic compound content based on phytochemical testing [23]. Comparative studies indicate that the total phenol content in the essential oil of *P. indica* is higher than that of the essential oil from basil leaves, with respective values of 275.21 mg GAE/l of oil and 209.30 mg GAE/l of oil [24]. Phenolic compounds, such as caffeoylquinic acid derivatives, have been successfully validated in *P. indica* leaf extracts using high-performance liquid chromatography (HPLC). Quantitatively, the ultrasonic extraction method employing 50% ethanol achieved the highest concentration of caffeoylquinic acid derivatives from *P. indica* leaf extracts sourced from various regions in Thailand [25]. In addition to Thailand, the phenolic components of *P. indica* leaves have also been analyzed from miscellaneous locations in Malaysia. These phenolic components include 3-O-caffeoylquinic acid, 5-O-caffeoylquinic acid, 3,4-O-dicaffeoylquinic acid, 3,5-O-dicaffeoylquinic acid, and 4,5-O-dicaffeoylquinic acid [26]. Remarkably, the maturity stages of *P. indica* leaves reveal varying total phenol content, with extracts from young leaf buds displaying significantly higher phenolic levels compared to other maturity stages [26].

Flavonoids

Flavonoids are a class of active polyphenolic compounds found in plants, derived from the core structure

of 2-phenylchromone. These phytochemicals exhibit a C6-C3-C6 structure, characterized by two aromatic rings connected by a three-carbon bridge. In plant physiology, flavonoids are regarded as UV-B absorbers, protecting against UV radiation in response to "excess light" stress [27]. Due to their widespread presence in many plants, they are crucial for meeting human dietary needs [28]. Flavonoids are currently classified into several categories, including flavonols, flavanols, flavones, anthocyanidins, flavanonols, flavanones, and chalcones, based on their structural characteristics [29]. These natural herbal products exhibit anti-inflammatory properties, natural antioxidant activity, and therapeutic effects against cardiovascular diseases, with minimal side effects and safety concerns [30]. Flavonoids have been documented in *P. indica* across various regions, including Asia, the Middle East, and the Americas, demonstrating their capacity to manage inflammation [31]. Compounds such as quercetin, kaempferol, myricetin, luteolin, and apigenin, along with caffeic acid, anthocyanins [32], and essential oils, have also been identified in the extracts of *P. indica* leaves [23]. UV spectrum analysis revealed that flavonoid compounds in *P. indica* leaf extracts absorb at wavelengths of 240–285 nm (band I) and 300–560 nm (band II) [22]. Notably, *P. indica* exhibits a higher flavonoid content compared to *Pluchea sagittalis*, which is linked to its antinociceptive effects [33]. Several vegetable plants in Indonesia, including *P. indica*, contain flavonoids at a level of 6.39 mg/100 g fw, which is lower than that of Cosmos Caudatus (52.19 mg/100 g fw) and Polyscias Pinnata (52.19 mg/100 g fw) [32]. The report indicates that there are no significant differences in flavonoid concentrations concerning the geographical elevation at which *P. indica* is grown. However, the study noted that the choice of solvent in the ethyl acetate fraction yielded a higher flavonoid content compared to methanol, distilled aquades, and n-butanol [34].

Alkaloids

Alkaloids are natural compounds typically characterized by one or more ring structures that possess at least one nitrogen atom in a basic form. These low molecular weight structures are predominantly found in plants and are generally synthesized from amino acids. Over 20,000 distinct alkaloids have been reported, with approximately 20% of all plant species producing alkaloids as secondary metabolites. This class of compounds exhibits greater structural diversity than other secondary metabolites [35]. Despite their potentially harmful effects, plants containing alkaloids have long been utilized in the production of stimulants, sedatives, narcotics, insecticides, aphrodisiacs, and various pharmaceuticals [36]. Plants that contain alkaloids have been integrated into everyday diets. The alkaloid content within the genus *Pluchea*, which is part of the Asteraceae family, varies and has primarily been reported qualitatively in several studies [37,38,23]. However, the mechanisms of action of alkaloid compounds in these plants exhibit parallels with certain diseases. For example, alkaloids demonstrate cytotoxic properties during active mitosis, particularly in the G2 and M phases, and can act as inhibitors of topoisomerase. Traditional plants rich in alkaloids can be isolated, and their efficacy is compared with commonly used medications, such as vincristine and vinblastine, for human treatments [39].

Tannins

Tannins, also known as tannic acid, are water-soluble polyphenols discovered in various plant-based foods. Research suggests that while tannins enhance digestive efficiency, they may decrease the efficiency of converting digested nutrients into new body components. The consumption of tannin-rich foods, such as betel nuts and herbal teas, has been associated with the treatment of degenerative diseases such as cancer, indicating that tannins may possess anticarcinogenic properties. Traditional remedies in Asia often use plant extracts containing tannins to alleviate clinical symptoms of diarrhea and inflammation [40–42]. Tannins have also been found in *P. indica* extracts, as reported in several studies. The bioactive uses of tannins from *P. indica* have been shown to influence glutamic acid levels in the sperm of male white rats, analyzed through HPLC. The decrease in glutamic acid in the *P. indica* extract group of rats was measured at 1,341.40 mg per 100 g, which positively impacted sperm quality [43]. Quantitative analysis revealed that the tannin content in the *Pluchea* species ranges from 8.7 to 20 mg TAE/g, revealing the therapeutic potential of these plants [44].

Saponins

Saponins are amphipathic glycosides featuring a triterpene or steroid structure linked to one or more hydrophilic sugar moieties, such as glucuronic acid, glucose, galactose, rhamnose, and xylose. Most saponins are classified as Monodesmosides or Bidesmosides, indicating the presence of one or two sugar chains at different positions [45,46]. Steroidal saponins describe some of the most significant active compounds, drawing considerable interest due to their pharmacological properties. Researchers are particularly focused on several steroidal saponins as potential therapeutic agents [47]. Qualitative investigations into the presence of saponins in *P. indica* leaf extracts have been conducted in multiple studies. Extraction methods, including maceration, percolation, and Soxhlet extraction, have confirmed the presence of saponins across these techniques [48]. Furthermore, *P. indica* leaf extract, utilized as a natural insecticide against Spodoptera litura, exhibited saponin content when the leaves were macerated for 72 hours [49].

HEALTH BENEFITS OF *P. INDICA*

Anti-hiperlipidemia

Hyperlipidemia is characterized by elevated levels of total cholesterol and/or triglycerides in the blood, along with decreasing levels of high-density lipoprotein (HDL), which predisposes individuals to the development of atherosclerosis [50]. It is also expressed as an imbalance of lipids or lipoproteins in the bloodstream, mainly caused by dietary disorders, obesity, diabetes, and genetic factors [51]. Current studies have reported the effectiveness of *P. indica* extracts as anti-hyperlipidemic agents. The phytochemicals present in *P. indica*, including total phenolics, flavonoids, and several derivatives of caffeoylquinic

acid and gamma-gurjunene, play an essential role in inhibiting hyperlipidemia in high-fat diet (HFD)-induced mice. This study is further supported by histological findings, which demonstrate that the average area and amount of perigonadal fat adiposity in the *P. indica* tea group (400 and 600 mg/kg orally) were significantly lower compared to the control group [7]. The leaf extracts of *P. indica* (administered at doses of 100 and 300 mg/kg/day) for 6 weeks, combined with a high-fat high-fructose diet for 10 weeks, demonstrated a significant increase in fasting blood glucose, oral glucose tolerance, insulin and leptin levels, lipid profiles, and hepatic triglyceride content. The extracts notably downregulated genes involved in lipid synthesis while upregulating genes associated with fatty acid oxidation, thereby effectively preventing dyslipidemia [12]. Furthermore, *P. indica* tea, at concentrations between 250 and 1,000 µg/ml, was shown to enhance pancreatic lipase activity and inhibit adipogenesis in 3T3-L1 cells *in vitro* [52]. Singdam *et al.* [12] discovered that phenolic compound from the extract of *P. indica* leaf alleviates dyslipidemia and hepatic steatosis in high-fat fructose diet rats. The major phenolic compounds found in the leaf of *P. indica* are tannic acid, rutin, quercetin, gallic acid, isoquercetin, and catechin (Fig. 3) [12].

Anti-diabetic

Hyperglycemic crises, such as diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state, are severe complications of diabetes that carry a significant risk of mortality if not efficiently and effectively managed. For example, DKA has become a fatal cause of death among children and adults under 58 years of age with type 1 diabetes, accounting for more than half of the fatalities in pediatric diabetes patients [53]. In contrast, type 2 diabetes mellitus (T2DM) inhibits weight loss in individuals with excess body weight. Various factors underlie these distinct clinical findings, including energy conservation resulting from improved blood glucose management and reduced glucosuria, hyperinsulinemia frequently observed in individuals with T2DM, the potential use of anti-diabetic drugs that may be obesogenic, and contributions from multiple physiological systems [54].

A clinical study involving 45 participants with prediabetes revealed that daily consumption of *P. indica* tea for 12 weeks significantly increased hyperglycemia and reduced serum triglyceride levels by 109.22 ± 5.21 mg/dl and LDL-C levels by 122.20 ± 3.67 mg/dl compared to the placebo group [55]. Furthermore, oral administration of ethanol extract from *P. indica*, starting at a dose of 50 mg/kg and increasing to 100 mg/kg after two weeks, resulted in decreased hyperglycemia and restored the histology of Langerhans islets in streptozotocin-induced diabetic rats. The mechanism of action of *P. indica* extract in hyperglycemic rats involves the reduction of inflammatory response markers such as IFN-γ, TNF-α, and IL-1β, along with the inhibition of caspase-3, caspase-8, and caspase-9. Additionally, it affects the phosphorylation of signal transducer and activator of transcription 1, nuclear factor-κBp65, and inducible nitric oxide synthase. Moreover, the extract was shown to regulate the ability of β-cell proliferation mediated by Bcl-2 and Ki67 [56].

Anti-cancer agents

Cancer is a fatal degenerative disease that poses a significant public health challenge due to its high prevalence and the growing number of affected patients [57,58]. Natural compounds, such as those derived from *P. indica*, have been shown to exhibit bioactive properties in various studies. Notably, substantial reductions in cell viability and proliferation have been reported in breast and cervical cancer cells treated with ethanol and aqueous extracts of *P. indica*. The proposed mechanism of action involves an increase in intracellular ROS levels, which negatively correlates with cancer cell viability. It implies that intracellular oxidative stress may contribute to the anti-cancer effects of *P. indica* [59]. Further research reports indicate that the aqueous extract from *P. indica* leaves and roots inhibits the proliferation, viability, and migration of GBM8401 and HeLa cells over 48 hours. In GBM8401 and HeLa cells treated with *P. indica* extract, the phosphorylation of p53 and p21 proteins was observed, while phosphorylated AKT expression decreased in HeLa cells treated with the aqueous extract [60].

The molecular mechanisms behind the anti-cancer properties of *P. indica* extract have also been reported to inhibit human nasopharyngeal carcinoma cells (NPC-TW01 and NPC-TW04) in a dose-dependent manner. The apoptosis mechanism induced by *P. indica* extract involves the regulation of pro-apoptotic Bax proteins and Bcl-2, increasing the Bax/Bcl-2 protein ratio, with similar effects seen on the p53 protein [61]. The ethyl acetate fraction of *P. indica* exhibits strong anti-inflammatory effects by inhibiting NO production and iNOS expression through the NF-κB pathway suppression [62]. iNOS production can lead to oxidative stress, resulting in DNA damage and promoting cancer cell growth [63]. Computational investigation of *P. indica*

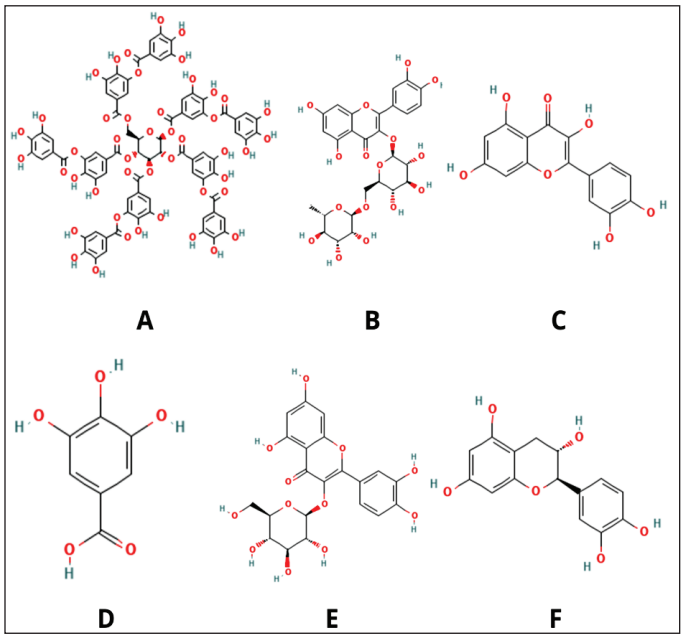

Figure 3. Notable phytochemical compounds related to anti-hiperlipidemia, (A) tannic acid, (B) rutin, (C) quercetin, (D) gallic aicd, (E) isoquercetin, and (F) catechin. Sources: https://pubchem.ncbi.nlm.nih.gov/[12].

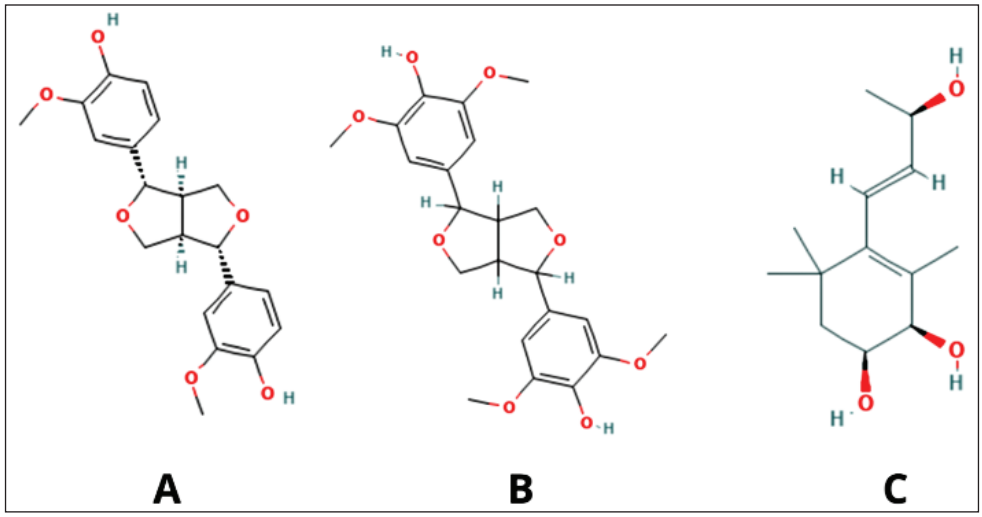

Figure 4. Notable phytochemical compounds related to anti-cancer activity, (A) pinoresinol, (B) syringaresinol, and (C) plucheoside. Sources: https://pubchem.ncbi.nlm.nih.gov/ [64].

with pinoresinol, syringaresinol, and plucheoside showed the inhibition mechanism targeting peroxisome proliferator-activated receptor gamma in the cancer cell. The notable phytochemical compounds for its anti-cancer activity from Beluntas showed on Figure 4. Molecular dynamics analysis also showed that the complex of phytochemical compounds with receptor stable in the cell with RMSF <2 Å [64]. It means that those compounds can be useful as anti-cancer drug candidates.

Anti-bacterial activity

Pathogenic bacteria exist in various forms. When pathogenic microorganisms transfer from their source to humans through different products and food channels, they provoke several human diseases known as foodborne illnesses, and these microorganisms are referred to as foodborne pathogens [65–67]. Zoonotic transmission is mainly attributed to the presence of foodborne pathogens in animal products such as eggs, dairy products, meat, poultry, and others [68]. Common foodborne pathogens include *Listeria monocytogenes, Escherichia coli, Campylobacter jejuni, Clostridium botulinum, Bacillus subtilis, Salmonella typhi*, and *Staphylococcus aureus*, which provoke infections such as campylobacteriosis, listeriosis, salmonellosis, and *E. coli* infections in humans [69]. Natural compounds have long been reported to possess antibacterial properties, offering various mechanisms of action in their bioactivity.

The antibacterial potential of *P. indica* extract against *E. coli* and *B. subtilis* has been reported using different extraction methods. The highest inhibition against *E. coli* and *B. subtilis* was achieved using *P. indica* extract prepared through Soxhlet extraction, compared to two other methods—maceration and percolation [48]. Fermented *P. indica* leaf extract supplemented with the cell-free supernatant of S. *cerevisiae* revealed enriched antibacterial activity against *E. coli* and *S. aureus*, with inhibition zone diameters ranging from 3.85 to 4.81 mm and 4.63 to 5.12 mm, respectively [70]. A deodorant roll-on containing *P. indica* extract was tested for its antibacterial activity against *S. epidermidis*, revealing that the extract successfully inhibited the growth of S. *epidermidis*. Moreover, the deodorant roll-on stored at 28°C for 8 weeks maintained stable color, odor, and homogeneity, and did not irritate [71]. The antibacterial mechanism of *P. indica* extract is often attributed to the influence of its phytochemical compounds. Herbal compounds like those found in *P. indica*, and their formulations with other herbs, have been shown to damage cell membranes and walls, inhibit nucleic acid and protein synthesis, and increase intracellular osmotic pressure [72].

Anti-inflammatory activity

Herbal plants have consistently played a crucial role in human healthcare through their various biologically active compounds, which often display anti-inflammatory properties [73]. Inflammation is recognized as a protective process that helps maintain physiological balance within the body [74]. This response involves a complex series of changes in tissues aimed at eliminating the initial cause of cell injury, which may result from contagious agents or their metabolites (microorganisms and toxins), as well as physical agents (radiation, burns, and trauma), or chemical substances (caustic agents) [75]. For instance, the methanol fraction of the chloroform extract of *P. indica* root has demonstrated anti-inflammatory activity in several inflammation models. The extract inhibits inflammatory processes by blocking carrageenan, histamine, serotonin, hyaluronidase, and sodium urate. It also suppresses protein exudation and leukocyte migration, as well as granuloma formation and joint edema [76]. Inflammation provoked by hyperglycemia can be alleviated utilizing the ethanol extract of *P. indica* in streptozotocin-induced rats. Markers associated with liver inflammation, including interleukin-6, tumor necrosis factor-α, NF-κB p65, transforming growth factor-β1, and protein kinase C, were reduced following treatment with *P. indica* extract at a dose of 100 mg/kg for 8 weeks [77]. The ethyl acetate fraction of *P. indica* ethanol leaf extract exhibited anti-inflammatory activity in acute inflammatory phases, as observed in ethyl phenylpropionate-induced ear edema and carrageenan-induced paw edema in rat models [62].

ROLE OF *P. INDICA* IN CLINICAL STUDIES

The clinical evidence for the efficacy of *P. indica* remains relatively limited compared to *in vitro* and *in vivo* studies. A clinical study involving 45 participants with pre-diabetes treated with *P. indica* tea, consumed once daily for 12 weeks, demonstrated antihyperglycemic and antidyslipidemic effects in the participants. The results also showed that *P. indica* tea significantly reduced triglyceride and LDL-c levels compared to the placebo. Notably, the administration of *P. indica* tea significantly increased HDL-c levels to 57.56 ± 3.05 mg/dl, compared to only 46.44 ± 2.47 mg/dl in the placebo group [55]. Based on these findings, clinical trials involving *P. indica* leaf extracts are urgently needed to develop standardized herbal medicinal products and phytopharmaceuticals supported by scientific validation.

TOXICOLOGICAL STUDY OF *P. INDICA*

Toxicity studies are vital for the drug development process involving natural products. Our review has revealed several reports on the toxicological properties of *P. indica*. Notably, methanol extracts from micropropagated *P. indica* leaves demonstrated diuretic activity in Wistar albino rats. The acute oral toxicity study established a Lethal Dose of 2.825 mg/kg body weight [78]. Furthermore, the oral glucose tolerance test investigating the efficacy of *P. indica* tea in mitigating hyperglycemia was conducted *in vivo*. The toxicity evaluation of *P. indica* leaf tea administered at a dosage of 600 mg/kg/day, alongside a high-fat diet, indicated that serum creatinine, alanine transaminase, alkaline phosphatase, and complete blood count levels in the treatment group with a HFD and *P. indica* tea did not exhibit significant differences compared to the normal control diet, which similarly showed no significant disparities when compared to the normal control group (without a high-fat diet) [7].

FUTURE DIRECTIONS

People in tropical locations, notably Indonesia, have commonly employed *P. indica*-based medicines to treat a variety of ailments. Although various research indicates that this plant has economic and health promise, there is currently little information available on this commercially packaged product. The preceding portion of this research described the phytochemical composition of *P. indica* extract, including flavonoids, alkaloids, tannins, and steroids. This has great industrial application potential. Traditional medicine is highly helpful in building a green economy because of numerous variables such as time, energy usage, high extraction yields, little solvent use, low economic expenses, and environmental friendliness [79,80].

Pluchea indica's pharmacological qualities, as detailed in the parts of this review, make it potentially useful in herbal therapy. According to the available data, *P. indica* can be packed as an extra supplement to be eaten daily in the form of herbal tea or capsules. This *P. indica*-based health supplement may be used as an antihyperglycemic and antidyslipidemic treatment with a low toxicity level up to a dose of 600 mg/kg/day [55]. The development of *P. indica* as a health supplement can be permitted by the US Food and Drug Administration or national authorities since requirements are less severe than those for manufactured pharmaceuticals. Further study into *P. indica* as a standardized herbal medication should concentrate on certain of its bioactivities to ensure its efficacy in treating specific ailments.

In general, this plant is abundant and often regarded as a weed, thus in order to raise its selling value, it must be developed as a raw material for medication. Using this plant as a base component in medication can provide both health and economic advantages. This plant grows quite easily and does not require special care, making it suitable for cultivation as part of local communities' herbal medicine development efforts. A technological technique based on tissue culture can also be used to improve the extract's biological activity [81], particularly its phenolic content. This plant still requires post-harvest management, particularly in terms of harvesting procedure, storage period, and basic handling. Interestingly, a clinical trial study on 45 people was done to determine the antihyperlipidemic and antiglycemic efficacy of this plant extract. Following the efficacy and effectiveness of this plant in clinical testing, it is now commercially accessible and ready for general use as a complimentary medication to synthetic pharmaceuticals. The findings of this study support the use of *P. indica* as a therapeutic agent in the treatment of antihyperlipidemic and antihyperglycemic conditions, as well as the possibility of testing it on other illnesses in the clinical phase.

CONCLUSION

Pluchea indica is an herbal plant widely utilized by communities for ethnomedicinal purposes across various regions, including Indonesia. As previously discussed, the biochemical uniqueness of *P. indica* lies in its distinctive bioactive compounds, which have the potential to lead to the discovery of herbal remedies and semi-synthetic drugs. However, the full potential of this plant has not yet been thoroughly explored, particularly through clinical testing. This review highlights that *P. indica* leaf extracts exhibit anticancer, antimicrobial, antidiabetic, anti-inflammatory, and antioxidant activities, contributing to biomedical applications. Therefore, substantial efforts and scientific validation are still required to unlock new opportunities in the development of the phytochemical potential of *P. indica*. Research findings in this area could significantly support the pharmaceutical industry by introducing new therapeutic agents. The use of *P. indica* as a natural remedy not only enhances medical sovereignty, but it can also assist farmers by encouraging the cultivation of plants for medicinal purposes. Clinical studies, both stages 1–3, are highly recommended in attempts to advance *P. indica* extracts in the biomedical sector.

ACKNOWLEDGMENTS

The author would like to thank the Doctoral Program in Medical Sciences, Faculty of Medicine, Udayana University, and the Nursing Profession Program, Stikes Bina Usada Bali for supporting the implementation of this research.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and

interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

FINANCIAL SUPPORT

This research was funded by the Ministry of Education, Culture, Research, and Technology (KEMDIKBUDRISTEK) of the Republic of Indonesia in 2022 through the Indonesian Education Scholarship Programme (BPI) with Contract Number: 02523/J5.2.3./BPI.06/9/2022.

CONFLICT OF INTEREST

The author reports no financial or any other conflicts of interest in this work.

ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

DATA AVAILABILITY

All data generated and analyzed are included in this research article.

PUBLISHER'S NOTE

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USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declares that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

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How to cite this article:
Putra PWK, Jawi IM, Subawa AAN, Astawa NM, Indrayani AW, Widhiantara IG, Wiradana PA, Herdiansyah MA. Phytochemicals of Beluntas (*Pluchea indica*(L) Less.) and their health benefits. J Appl Pharm Sci. 2025;15(07):037–047. DOI: 10.7324/JAPS.2025.237559