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Review Article

# *Pluchea indica*: An updated review of its botany, uses, bioactive compounds and pharmacological properties

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## ABSTRACT

In this article, the botany, uses, bioactive compounds and pharmacological properties of leaves and roots of *Pluchea indica* are reviewed for the first time. The coastal species occurs in open sites at the landward side of mangroves. Main botanical characters for the identification of *P. indica* are bushy shrub life-form, and leaves are short-stalked, obovate, thick papery, tapering base and serrated margin. Crushed leaves are very aromatic. Its traditional uses take the form of medicine and food. The pharmacological properties of *P. indica* are focused on its antioxidant, antibacterial, anti-cancer and anti-inflammatory activities. Caffeoylquinic acids and terpene glycosides are the main bioactive compounds from aerial parts and leaves of *P. indica*, respectively. Antioxidant properties of *P. indica* leaves have been reported to be stronger than those of *Curcuma longa* turmeric rhizomes. Also reported is that *P. indica* tea has stronger antioxidant properties of than green tea of *Camellia sinensis*. Leaves and roots of *P. indica* including tea leaves inhibit the growth of Gram-positive and Gram-negative bacteria, and possess anti-inflammatory properties. Roots are cytotoxic to cancer cells. Leaves and roots of *P. indica* also possess a range of other bioactivities. Some future research and prospects are suggested.

**Keywords:**
Indian camphorweed, Antioxidant, Antibacterial, Anti-cancer, Anti-inflammatory

## 1. INTRODUCTION

Coastal plants are those growing on muddy shores, sandy beaches and rocky promontories. Represented by a wide array of trees, shrubs, vines and epiphytes, they have important ecological and environmental values such as coastal protection and habitats for fauna. Coastal flora are also important food and medicinal plants.

*Pluchea indica* (L.) Less., one of the coastal plants, was chosen for the review since it has been utilized as sources of food and medicine. Its extracts exhibit several pharmacological activities promoting human health benefits. The botany, bioactive compounds and pharmacological properties of *P. indica* are reviewed for the first time. The pharmacological properties including antioxidant, antibacterial, anti-cancer, anti-inflammatory and other activities, are summarized. To date, there is only a review on the nutrition, health benefits and applications of *P. indica* leaves[1]. Three other reviews emphasized on the phytochemistry and biological activities of the genus *Pluchea* Cass[2-4].

Sources of information procured for this review were from Google Scholar, PubMed, PubMed Central, Science Direct, J-Stage, JSTOR, PubChem and Directory of Open Access Journals (DOAJ). The primary keywords for search are *Pluchea indica* and the secondary keywords include constituents, antioxidant, cancer, etc.

## 2. BOTANY AND USES

*Pluchea indica* (L.) Less. (syn. *Baccharis indica*) of the family Asteraceae (previously named as Compositae) is a bushy coastal shrub that grows up to 2 meters in height. Common names of *P. indica* are Indian camphorweed and Indian fleabane. Vernacular names are beluntas in Malaysia and Indonesia, khlu in Thailand,

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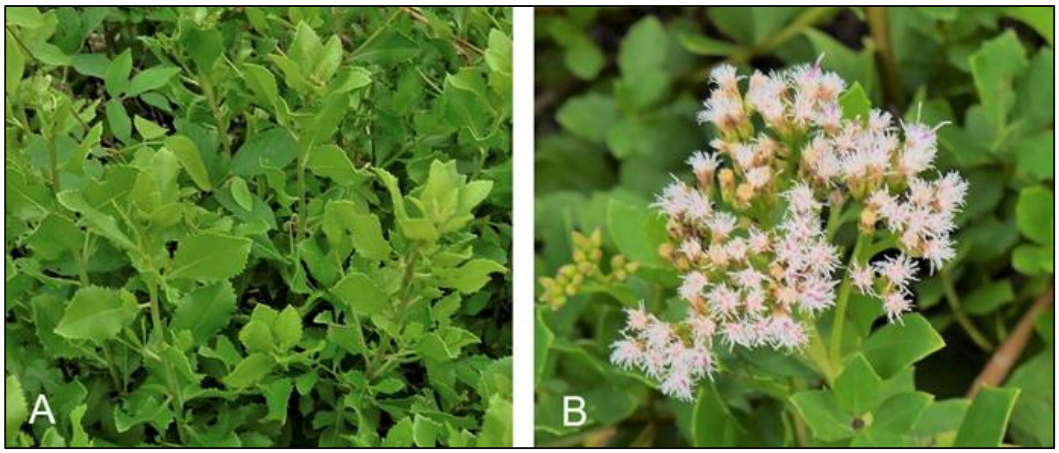



**Figure 1.** Leaves (A) and flowers (B) of *Pluchea indica*.

and kuo bao ju in China[1,5].

Leaves of *P. indica* are short-stalked, obovate, thick papery and have a tapering base and serrated margin (Figure 1). Leaves are bright green when young, pale green when mature, and very aromatic when crushed. Flowers are disk-shaped, corolla is 5-lobed, tubular and violet in color, and anthers are also violet and extend beyond the petals. The marginal florets are female while the central florets are bisexual but functionally staminate. Flowering occurs throughout the year. Fruits are top-shaped, ribbed, one-seeded and indehiscent. The species occurs in open sites at the landward side of mangroves especially on bunds surrounding shrimp ponds or salt pans. Geographically, *P. indica* occurs from India to southern China and Taiwan, throughout Southeast Asia and stretches to northern Australia and Polynesia. It is native to tropical and subtropical Asia and has been introduced to the Pacific, including Hawaii[5-7].

Traditional uses of *P. indica* in the form of medicine and food have been reported in countries of Southeast and South Asia. In Indonesia and Malaysia, the leaves are used as a traditional remedy for stomach ache, cough, dysentery and leucorrhoea. In Indonesia, leaves are mixed with other ingredients into poultice for ulcers, sores and rheumatic pains. In Thailand, different plant parts of *P. indica* are used as a diuretic for treatment of kidney stones, ulcers, lumbago and leucorrhoea. A plant paste is applied externally to treat skin diseases and hemorrhoid. In Vietnam, a decoction of the roots or leaves is used for treating fever, headache, rheumatism, sprains, dysentery and dyspepsia. A decoction of fresh leaves is used as inhalant to cure colds. In Vietnam and Cambodia, leaves of *P. indica* are crushed in alcohol for treating lumbago. In India roots astringent and antipyretic[1,7].

In Malaysia, Indonesia and Thailand, leaf shoots of aromatic herbs including *P. indica* are consumed as ulam, a Malay word for traditional salad[8-9]. They form an important component of the traditional diet. Ulam herbs are consumed raw or blanched as a side-dish and condiment for flavoring. Besides whetting the appetite during meals, the regular intake of ulam herbs is believed to have health-promoting properties[8-9]. In Vietnam and Cambodia, an infusion of *P. indica* leaves is consumed as tea[7]. Khlu tea is has been commercially available in Thailand as a health-promoting drink[1,8-9].

## 3. BIOACTIVE COMPOUNDS

The main constituents of aerial parts and leaves of *P. indica* are caffeoylquinic acids, phenolic acids, flavonoids and thiophenes (Table 1). Recently, from the aerial parts, 20 caffeoylquinic acids, 19 phenolic acids, 14 flavonoids and 12 thiophenes have been reported[10-12]. Other scientists have also reported the presence of flavonoids from the leaves[13-14] and thiophenes from aerial parts[15-16] of *P. indica*.

Caffeoylquinic acids are esters of caffeic and quinic acids[17]. Phenolic acids are derivatives of benzoic acid ($C_6$-$C_1$) and cinnamic acid ($C_6$-$C_3$) while flavonoids are ubiquitous phenolic compounds having a $C_6$-$C_3$-$C_6$ skeleton in which two benzene rings are linked by a $C_3$ ring[18]. Thiophenes are five-membered heterocyclic $C_4H_4S$ compounds containing a sulphur atom[19].

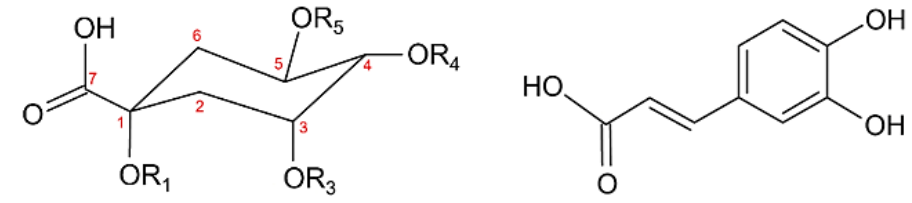
Caffeoylquinic acids (CQAs) of *P. indica* included CQAs[20-22], diCQAs[20-24], triCQAs[23,25] and tetraCQAs[23,25]. CQAs included 3-CQA (chlorogenic acid), 4-CQA (cryptochlorogenic acid), and 5-CQA (neochlorogenic acid) (Table 1). DiCQAs included 1,3-diCQA, 1,4-diCQA, 1,5-diCQA, 3,4-diCQA, 3,5-diCQA and 4,5-diCQA. TriCQA were represented by 1,3,4-triCQA, 1,3,5-triCQA and 3,4,5-tri-*O*-CQA, while tetraCQA included 1,3,4,5-tetra-*O*-CQA. Methyl esters of triCQA and tetraCQA have also been reported[23]. Chemical structures of CQAs, diCQAs, triCQA and tetraCQA are shown in Figure 2. Among the phenolic acids in the leaves of *P. indica*, the content of 3-CQA (20.0 mg/100 g) was the highest followed by caffeic acid (8.65 mg/100 g)[14]. The contents of CQAs were highest in the juvenile leaf shoots of *P. indica*

**Table 1.** Main chemical constituents of aerial parts and leaves of *P. indica*.

| No. | Compound type | Compound name | Plant part | Reference |
|---|---|---|---|---|
| 1 | Caffeoylquinic acids | 3-Caffeoylquinic acid (3-CQA) | Aerial | 12, 20-22 |
| 2 | | 4-Caffeoylquinic acid (4-CQA) | Aerial | 12, 20-22 |
| 3 | | 5-Caffeoylquinic acid (5-CQA) | Aerial | 12, 20-22 |
| 4 | | 1,3-di-*O*-Caffeoylquinic acid (1,3-diCQA) | Aerial | 12 |
| 5 | | 1,4-di-*O*-Caffeoylquinic acid (1,4-diCQA) | Aerial | 12 |
| 6 | | 1,5-di-*O*-Caffeoylquinic acid (1,5-diCQA) | Aerial | 12 |
| 7 | | 3,4-di-*O*-Caffeoylquinic acid (3,4-diCQA) | Aerial | 12 |
| | | | Leaves | 20-24 |
| 8 | | 3,5-di-*O*-Caffeoylquinic acid (3,5-diCQA) | Aerial | 12 |
| | | | Leaves | 20-24 |
| 9 | | 4,5-di-*O*-Caffeoylquinic acid (4,5-diCQA) | Aerial | 12 |
| | | | Leaves | 20-24 |
| 10 | | Ethyl 3,4-di-*O*-caffeoyl quinate | Aerial | 12 |
| 11 | | Ethyl 3,5-di-*O*-caffeoyl quinate | Aerial | 12 |
| 12 | | Methyl 3-*O*-caffeoyl quinate | Aerial | 12 |
| 13 | | Methyl 3,4-di-*O*-caffeoyl quinate | Aerial | 12 |
| 14 | | Methyl 3,5-di-*O*-caffeoyl quinate | Aerial | 12 |
| 15 | | Methyl 4,5-di-*O*-caffeoyl quinate | Aerial | 12 |
| | | | Leaves | 23 |
| 16 | | Methyl 3,4,5-tri-*O*-caffeoyl quinate | Aerial | 12 |
| | | | Leaves | 23 |
| 17 | | 1,3,4,5-tetra-*O*-Caffeoylquinic acid (1,3,4,5-tetraCQA ) | Aerial | 12 |
| | | | Leaves | 23,25 |
| 18 | | 1,3,4-tri-*O*-Caffeoylquinic acid (1,3,4-triCQA) | Aerial | 12 |
| 19 | | 1,3,5-tri-*O*-Caffeoylquinic acid (1,3,5-triCQA) | Aerial | 12 |
| 20 | | 3,4,5-tri-*O*-Caffeoylquinic acid (3,4,5-triCQA) | Aerial | 12 |
| | | | Leaves | 23,25 |
| 1 | Phenolic acids | *trans*-Caffeic acid | Aerial | 10 |
| 2 | | *trans*-Coniferyl aldehyde | Aerial | 10 |
| 3 | | Dibutylphthalate | Aerial | 10 |
| 4 | | 3,4-Dihydroxybenzaldehyde | Aerial | 10 |
| 5 | | 3,4-Dihydroxybenzoic acid | Aerial | 10 |
| 6 | | 2,3-Dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-propan-1-one | Aerial | 10 |
| 7 | | 3,4-Dihydroxy-5-methoxybenzaldehyde | Aerial | 10 |
| 8 | | (–)-(7*S*,7'*S*,8*R*,8'*R*)-4,4'-Dihydroxy-3,3',5,5'-pentamethoxy-7,9': 7', 9-diepoxy-lignane | Aerial | 10 |
| 9 | | Esculetin | Aerial | 10 |
| 10 | | Ethyl caffeate | Aerial | 10 |
| 11 | | *trans*-Ferulic acid | Aerial | 10 |
| 12 | | *p*-Hydroxybenzoic acid | Aerial | 10 |
| 13 | | (+)-Isolariciresinol | Aerial | 10 |
| 14 | | (+)-9'-Isovaleryllariciresinol | Aerial | 10 |
| 15 | | *erythro*-2,3-bis-(4-Hydroxy-3-methoxyphenyl)-3-ethoxypropan-1-ol | Aerial | 10 |
| 16 | | *threo*-2,3-bis(4-Hydroxy-3-methoxyphenyl)-3-ethoxypropan-1-ol | Aerial | 10 |
| 17 | | 3-Methoxy-4-hydroxybenzoic acid | Aerial | 10 |
| 18 | | Syringicaldehyde | Aerial | 10 |
| 19 | | Vanillin | Aerial | 10 |
| 1 | Flavonoids | Casticin | Aerial | 11 |
| 2 | | Centaureidin | Aerial | 11 |
| 3 | | Chrysosplenol C | Aerial | 11 |
| 4 | | Cynaroside | Aerial | 11 |
| 5 | | Isorhamnetin | Aerial | 11 |
| 6 | | Kaempferol | Aerial | 11 |
| | | | Leaves | 13,14 |
| 7 | | Kaempferol 3-*O*-*β*-D-glucopyranoside (astragalin) | Aerial | 11 |
| 8 | | Luteolin | Aerial | 11 |
| 9 | | Myricetin | Leaves | 13,14 |
| 10 | | Quercetin | Aerial | 11 |

**Table 1.** Main chemical constituents of aerial parts and leaves of *P. indica*.(cont.)

| No. | Compound type | Compound name | Plant part | Reference |
|---|---|---|---|---|
| | Flavonoids | Quercetin | Leaves | 13,14 |
| 11 | | Quercetin-3-*O*-*β*-D-galactopyranoside | Aerial | 11 |
| 12 | | Quercetin-3-*O*-*β*-D-glucopyranoside | Aerial | 11 |
| 13 | | 5,7,3',4'-Tetrahydroxy-3-methoxyflavonol-3'-*O*-*β*-D-glucopyranoside | Aerial | 11 |
| 14 | | 5,6,4'-Trihydroxy-3,7-dimethoxyflavone | Aerial | 11 |
| 1 | Thiophenes | 2-(3-Acetoxy-4-hydroxybut-1-yn-1-yl)-5-(penta-1,3-diyn-1-y1) thiophene | Aerial | 15 |
| 2 | | 2-(3,4-Dihydroxybut-1-yn-1-yl)-5-(penta-1,3-diyn1-yl) thiophene | Aerial | 15 |
| 3 | | 3"-Ethoxyl-(3"*S*)-pluthiophenol | Aerial | 11 |
| 4 | | 3"-Ethoxyl-(3"*S*)-pluthiophenol-4"-acetate | Aerial | 11 |
| 5 | | 2-(4-*O*-*β*-Glucopyranosyl-3-hydroxybut-1-yn-1-yl)-5-(penta-1,3-diyn-1-yl) thiophene | Aerial | 15 |
| 6 | | 2-(4-Hydroxy-3-methoxybut1-yn-1-yl)-5-(penta-1,3-diyn-1-yl) thiophene | Aerial | 15 |
| 7 | | 2-(Penta-1,3-diyn-1-yl)-5-(4-acetoxy-3-hydroxybuta-1-yn-1-yl) thiophene | Aerial | 16 |
| 8 | | (3"*R*)-Pluthiophenol | Aerial | 11 |
| 9 | | (3"*R*)-Pluthiophenol-4"-acetate | Aerial | 11 |
| 10 | | 2-(Prop-1-inyl)-5-(6-acetoxy-5-hydroxyhexa-1,3-diinyl) thiophene | Aerial | 16 |
| 11 | | 2-(Prop-1-inyl)-5-(5,6-dihydroxyhexa-1,3-diinyl) thiophene | Aerial | 16 |
| 12 | | 2-(Prop-1-yn-1-yl)-5-(6-acetoxy-5-hydroxyhexa-1,3-diyn-1-yl) thiophene | Aerial | 15 |




Quinic acid Caffeic acid

| Compound | $R_1$ | $R_3$ | $R_4$ | $R_5$ |
|---|---|---|---|---|
| 3-CQA | H | caffeoyl | H | H |
| 4-CQA | H | H | caffeoyl | H |
| 5-CQA | H | H | H | caffeoyl |
| 3,4-diCQA | H | caffeoyl | caffeoyl | H |
| 3,5-diCQA | H | caffeoyl | H | caffeoyl |
| 4,5-diCQA | H | H | caffeoyl | caffeoyl |
| 3,4,5-triCQA | H | caffeoyl | caffeoyl | caffeoyl |
| 1,3,4,5-tetraCQA | caffeoyl | caffeoyl | caffeoyl | caffeoyl |

**Figure 2.** Chemical structures of caffeoylquinic acids (CQAs) and derivatives.

compared to mature leaves before flowering and mature leaves during flowering[22]. In the juvenile leaf shoots, 4,5-diCQA (19-28%) was the dominant CQA, followed by 3,5-diCQA (6.2-12%) and 3-CQA (3.4-7.3%). The contents of CQAs depend on the extraction methods used[21]. Highest yield was obtained using ultrasound with 50% ethanol and the results were 4,5-diCQA (31%) followed by 3-CQA (19%) and 3,5-diCQA (13%). From the leaves of *P. indica*, flavonoids included quercetin, myricetin and kaempferol[13-14]. Their contents were 5.21, 0.90 and 0.28 mg/100 g, respectively. From the twigs of *P. indica* in Vietnam, stigmasterol, 1-eicosanoyl glycerol, 2-(prop-1-ynyl)-5-(5,6-dihydroxyhexa-1,3-diynyl)-thiophene, stigmasterol 3-*O*-*β*-D-glucopyranoside and *β*-sitosterol 3-*O*-*β*-D-glucopyranoside have been isolated[26]. The essential oil of *P. indica* leaves yielded 66 components[27]. Dominant components were (10*S*,11*S*)-himachala-3-(12)-4-diene (17%) and caryophyllene (12%).

With regard to the chemical constituents of roots of *P. indica*, meagre work has been done. Pioneering investigation afforded the isolation of a new monoterpene glycoside (plucheoside C), three new eudesmane-type sesquiterpenes (plucheols A & B, and plucheoside E) and three new lignan glycosides (plu-

cheosides $D_1$, $D_2$ & $D_3$)[28]. Later, two new thiophene derivatives and two new pentacyclic triterpenes[29], R/J/3, a pure compound[30], and PITC-2, a new thiophene derivative[31] have been identified.

## 4. PHARMACOLOGICAL PROPERTIES

### 4.1. Antioxidant activities

Out of 11 types of herbs studied, *P. indica* ranked second to *Cosmos caudatus* Kunth in terms of antioxidant activities as measured by 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging, ferric reducing power (FRAP), and 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radical scavenging, and inhibition of linoleic acid oxidation[13]. FRAP and DPPH radical scavenging of *P. indica* leaves were 4 and 2 times those of rhizomes of *Curcuma longa* L. (turmeric)[32]. When the antioxidant properties of different parts of *P. indica* extracted with different solvents, the strongest DPPH radical scavenging were from the methanol leaf extract[33]. Ranking in DPPH radical scavenging were methanol leaf extract > methanol stem extract > hexane leaf extract > hexane stem extract. Another study reported that polar solvents such as methanol yielded the strongest DPPH radical scavenging and FRAP[34]. As follow-up, lemon juice was added to *P. indica* tea aimed at improving the sensory properties of the tea[35]. Results showed that citric acid and ascorbic acid from the lemon juice could hydrolyze the glycoside bonds or ester bonds of phytochemical compounds in *P. indica* tea. The product from hydrolyzation caused enhancement of antioxidant and antidiabetic activities.

Amongst *P. indica* ethanol leaf extracts of different development stages, the juvenile leaf shoots had the strongest antioxidant activities (based on DPPH, ABTS and FRAP assays) compared to mature leaves before flowering and mature leaves during flowering[22]. The stronger antioxidant activities of juvenile leaf shoots may be attributed to their significantly higher concentrations of the bioactive and phenolic compounds. Out of three CQAs and three diCQAs, strongest DPPH and ABTS radical scavenging was 5-CQA and 4,5-diCQA, respectively. 3,4-diCQA and 4,5-diCQA had the strongest FRAP activity[22].

Results of a comparison of antioxidant activities based on DPPH radical scavenging of ethanol extracts of different parts of *P. indica* showed highest values were the roots. Ranking of DPPH radical scavenging was roots > stems > twigs > flowers ~ leaves[36]. Values in DPPH radical scavenging of dried samples were lower than those of fresh samples, possibly due to degradation of phenolic compounds during the extended drying process (oven drying at 60ºC for 2 days). Antioxidant properties of *P. indica* tea leaves (young leaves pan fried at 50ºC for 2 h) were stronger than oven-dried leaves. Recently, the antioxidant activities of *P. indica* tea were compared to those of green tea of *Camellia sinensis* (L.) Kuntze[37]. The *P. indica* leaf tea exhibited stronger DPPH and nitric oxide (NO) radical scavenging but weaker ABTS radical scavenging than green tea. Surprisingly, the tea infusions were brewed using hot phosphate buffer saline (PBS) instead of using hot water.

In another comparative study, methanol and hexane extracts of leaves and stems of *P. indica* were analyzed for total phenolic content and DPPH radical scavenging activity[33]. Results showed that the methanol leaf extract possessed the highest content (574 mg GAE/100 g) and strongest activity ($IC_{50}$=24.5 µg/ml). The hexane stem extract possessed the lowest content (63 mg GAE/100 g) and weakest activity ($IC_{50}$=402 µg/ml).

### 4.2. Antibacterial activities

Ethanol extracts of different parts of *P. indica* were tested for their antibacterial properties using Gram-positive *Bacillus cereus*, *Pseudomonas fluorescens* and *Staphylococcus aureus*, and Gram-negative *Escherichia coli* and *Salmonella typhimurium*[36]. Antibacterial properties were based on diameter inhibition zone and minimum inhibitory concentration. Fresh roots, stems and twigs inhibited the growth of all five species of bacteria tested. Inhibition of dried samples was weaker than that of fresh samples. Tea leaves of *P. indica* (prepared by pan frying young leaves at 50ºC for 2 h) also inhibited the growth of all species of bacteria tested. Another *in vitro* study suggested the potential of aqueous extract of ground dried aerial parts of *P. indica* for urinary tract infection treatment by its inhibitory effect towards *Klebsiella pneumoniae* and *E. coli*[38]. An *in vivo* study reported that the methanol root extract of *P. indica* administered to mice at doses of 0.5 and 1.0 mg/kg body weight significantly protected the animals with typhoid fever caused by *S. typhimurium*[39]. The antibacterial properties of *P. indica* have attracted scientists to develop topical antibiotics such as roll-on deodorant[40] and foot-spray[41].

### 4.3. Anti-cancer properties

The crude aqueous extracts of *P. indica* roots and leaves are cytotoxic to GBM8401 brain glioblastoma and HeLa cervical cancer cells *via* suppression of cell proliferation, viability and migration[42]. Treatment with the extracts at various concentrations for 48 hours resulted in 75% and 70% inhibition on proliferation and viability of GBM8401 and HeLa cells, respectively. It was found that phosphorylated-p53 and -p21 were induced in GBM8401 and HeLa cells. In HeLa cells, apoptosis was promoted and the expression of phos-

phorylated-AKT decreased. In anti-cancer activities, phosphorylated-p53 and -p21 are critical tumor suppressor molecules that decrease the expression of phosphorylated-AKT, an important survival signaling molecule[42].

The hexane fraction of *P. indica* root extract inhibited proliferation and induced autophagy in U87 glioblastoma cells[43]. Cell proliferation was suppressed by induction of cell cycle arrest and autophagy. There was significant up-regulation of acidic vesicular organelle (AVO). The expression levels of microtubule-associated light chain 3-II (LC3-II) protein, phosphorylated c-Jun N-terminal kinase (JNK) and phosphorylated p38 were significantly increased, confirming the occurrence of autophagy during the process[43]. The root extract combined with LY294002 (pan-PI3K inhibitor) further decreased cell viability, suggesting an additive anti-cancer effect. The ethanol root extract of *P. indica* induced apoptosis, anti-proliferation and migration in NPC-TW 01 and NPC-TW 04 nasopharyngeal carcinoma cells[44]. The strong anti-cancer activity of the root extract was attributed to the up-regulation of p53 and Bcl-2-associated X (Bax), and to the down-regulation of B-cell lymphoma 2 (Bcl-2) proteins.

The anti-cancer properties of the root extract of tissue-cultured *P. indica* against Ehrlich ascites carcinoma cells in mice have also been reported[45]. PITC-2 (a thiophene) isolated from the root extract of tissue-cultured *P. indica* inhibited the growth of sarcoma-180 cancer cells in mice[46].

### 4.4. Anti-inflammatory properties

Early studies have reported on the anti-inflammatory properties of the root extract of *P. indica* in rats and mice[47]. The anti-inflammatory properties involve the 5-lipooxygenase pathway[48] and have a protective effect against gastric damage[49]. Besides having anti-inflammatory effects, the ethanolic leaf extract of *P. indica* also possesses antinociceptive properties[50].

Hot water extract of *P. indica* tea had potent inhibitory effects against lipopolysaccharide-induced NO and prostaglandin E2 production in RAW 264.7 macrophages with $IC_{50}$ values of 315 and 49 μg/ml, respectively[51]. Recently, the ethanol extract of *P. indica* tea leaves was reported to exhibit anti-inflammatory effects on tumour necrosis factor (TNF) $\alpha$-induced endothelial cells by reduction of reactive oxygen species (ROS) production and decreasing the expression of ICAM-1 and VCAM-1 proteins that is mediated partly through the up-regulation of heme oxygenase-1 (HO-1)[52]. A follow-up study on the molecular mechanisms underlying the anti-inflammatory activities of *P. indica* leaves in RAW 264.7 macrophages involved the inhibition of NO production and suppression of inducible nitric oxide synthase (iNOS), mediated *via* the suppression of NF-kB activation but not the phosphorylation of mitogen-activated protein kinase (MAPK)[53].

### 4.5. Other properties

Other pharmacological properties of *P. indica* are listed in Table 2. They include $\alpha$-glucosidase inhibitory, collagenase inhibitory, matrix metalloproteinase inhibitory, acetylcholinesterase inhibitory, anti-nociceptive, analgesic, anti-diabetic, anti-obesity, anti-ulcer, hepatoprotective, lipid-lowering, adipogenesis inhibitory, hypoglycemic, neuropharmacological, CNS depressant, venom neutralizing, wound healing and diuretic activities.

## 5. CONCLUSIONS

Caffeoylquinic acids and terpene glycosides are the main bioactive compounds from leaves and roots of *P. indica*, respectively. Antioxidant properties of *P. indica* leaves have been reported to be stronger than those of *C. longa* rhizomes. Also reported is that *P. indica* tea has stronger antioxidant properties of than green tea of *C. sinensis*. Leaves and roots of *P. indica* including tea leaves inhibit the growth of Gram-positive and Gram-negative bacteria, and possess anti-inflammatory properties. Roots are cytotoxic to cancer cells. Leaves and roots of *P. indica* also possess a range of other bioactivities. There are prospects to develop useful products such as *P. indica* tea, including antibiotic deodorant, foot-spray, cream, gel, etc. Among others, further research is needed for the following aspects: 1. To isolate and identify bioactive compounds from roots of *P. indica* as information is meagre. Furthermore, there is no information on bioactive compounds from flowers and fruits of *P. indica*. Therefore, there are prospects for encountering novel compounds. 2. To develop innovative drying protocols of *P. indica* leaves to produce the tea without affecting the antioxidant and sensory properties since extended oven-drying reduces antioxidant activities by degrading phenolic compounds. 3. To evaluate appropriate additives to *P. indica* tea aimed at improving its sensory properties and other bioactivities, 4. To conduct more clinical trials on *P. indica* as there is only one trial to date, and 5. To develop derivatives of compounds with enhanced bioactivities e.g., anti-cancer properties *via* structure-activity relationship (SAR) studies.

## 6. ACKNOWLEDGEMENT

The authors are grateful to Prof. Shigeyuki Baba for taking the photos of leaves and flowers of *P. indica* in Chanthaburi, Thailand.

**Conflict of interest**

The authors have no conflict of interest to declare .

**Table 2.** Other pharmacological activities of *Pluchea indica*.

| Activity | Plant part/ product | Description | Reference |
|---|---|---|---|
| $\alpha$-Glucosidase inhibition | Leaf | Activity was in the following order: juvenile leaf shoots > mature leaves before flowering > mature leaves during flowering. | 22 |
| $\alpha$-Glucosidase inhibition | Leaf | A SAR study showed that inhibition by CQAs depends on both methyl esterification of quinic acid and the number of caffeate groups in the molecule. | 23 |
| Collagenase and MMP inhibition | Leaf | 3,4,5-TriCQA and 1,3,4,5-tetraCQA inhibited collagenase, and 1,3,4,5-tetraCQA inhibited MMP-2 and -9. | 25 |
| AChE inhibition | Leaf and stem | Methanol and hexane extracts were detected to have inhibitory properties. | 33 |
| Anti-ulcer activity | Root | Activity of extract involved decrease of gastric volume and acidity, and protection of the gastric mucosa in rats, possibly due to inhibition of the 5-LOX pathway. | 48 |
| Antinociceptive effect | Leaf | Extract exerted peripheral effect in acetic acid-induced writhing test on mice. | 50 |
| Anti-ulcer activity | Root | Extract possessed significant activity in rats and guinea pigs by affording protection against gastric lesions. | 54 |
| Analgesic activity | Root | Infusion had 77.5% of pain reduction at 29 mg/20 g body weight of mice. | 55 |
| Hypoglycemic and antihyperglycemic effects | Leaf | Extract exerted effects on streptozotocin-induced diabetic rats. | 56 |
| Attenuated β-cell apoptosis | Leaf | Extract attenuated activity in streptozotocin-induced diabetic mice. | 57 |
| Alleviated liver injury | Leaf | Extract alleviated injury in streptozotocin-induced diabetic mice. | 58 |
| Ameliorated hyperglycemia and dyslipidemia | Tea | In a clinical trial, tea lowered serum TG and LDL-C, and increased serum HDL-C. | 59 |
| Ameliorated obesity | Tea | Tea reduced weight gain in high fat diet (HFD) mice, and is non- toxic to the kidney, liver and blood. | 60 |
| Hepatoprotective activity | Root | Extract exhibited significant activity against $CCl_4$-induced hepatotoxicity in rats and mice. | 61 |
| Lipid lowering | Tea | Tea decreased lipid accumulation, inhibited adipogenesis in 3T3-L1 adipocytes and inhibited lipase activity. | 62 |
| CNS depressant activity | Root | Extract exerted potent activity in rats and mice *via* inhibition of spontaneous motility and prolongation of sleeping time. | 63 |
| CNS depressant activity | Root | Extract exerted potent activity in rats and mice that included muscle relaxant, inhibition of aggressive behavior and increase brain GABA concentration. | 64 |
| Neuropharmacological effects | Root | Extract had neuropharmacological effects on mice *via* decreased locomotor activity and increased pentobarbital sleep. | 65 |
| Neutralized viper venom-induced lethality | Root | Methanol extract significantly neutralized viper venom-induced lethality and haemorrhagic activity in mice. | 66 |
| Neutralized viper and cobra venom | Root | *β*-Sitosterol and stigmasterol from extract neutralized viper and cobra venom. | 67 |
| Wound healing | Root | Tissue-cultured extract had potent activity in rats based on wound contraction, epithelialization period, skin breaking strength and dry granulation tissue weight. | 68 |
| Wound healing | Leaf | Extract containing nanoparticles displayed wound healing activity in oral mucosal cells *via* oral spraying. | 69 |
| Wound healing | Leaf | Extract at 80 mol/L prevented hyperproliferation of fibroblasts. | 70 |
| Wound healing | Leaf | Extract accelerated activity in the oral mucosa by decreasing inflammatory cells and increasing collagen density. | 71 |
| Diuretic effects | Leaf | Infusion exerted diuretic effects on both rats and human subjects. | 72 |
| Diuretic effects | Leaf | Tissue-cultured extract had significant diuretic activity in rats. | 73 |

AChE=acetylcholinesterase, $CCl_4$=carbon tetrachloride, CNS=central nervous system, CQA=caffeoylquinic acid, GABA=gamma aminobutyric acid, HDL=high-density lipoprotein, HFD=high fat diet, LDL=low-density lipoprotein, LOX=lipoxygenase, MMP=matrix metalloproteinase, SAR=structure-activity relationship, and TG=triglyceride.

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