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Phenolic constituents and biological activity of the genus *pluchea*

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ABSTRACT

The genus Pluchea is belonging to the family Asteraceae and comprises about 90 species distributed mainly in North and South America, Africa, Asia and Australia. The extracts from the species of the genus Pluchea have been used as antioxidant, hepatoprotective, cytotoxic, antiulcer, antipyretic, antibacterial, antifungal, antiviral, Antinociceptive, Anti-amoebic and for venom neutralization. Phytochemical screening of species of the genus Pluchea revealed the presence of flavonoids, tannins, alkaloids, eudesmane-type sesquiterpenoids, monoterpenes, lignan glycosides and triterpenoids. This review summarizes the previously evaluated biological activities of the extracts of species of the genus Pluchea as well as the previously isolated phenolic compounds.

Keywords: Pluchea, Asteraceae, Phenolic constituents, biological activity.

INTRODUCTION

In spite of great advances of modern scientific medicine, traditional medicine is still the primary form of treating diseases of majority of people in developing countries; even among those to whom western medicine is available, the number of people using one form or another of complementary of alternative medicine is rapidly increasing worldwide. Increasing knowledge of metabolic process and the effect of plants on human physiology has enlarged the range of application of medicinal plants. The plants of Pluchea genus have been used traditionally used as astringent, antipyretic, anti-inflammatory, hepatoprotective, diaphoretic in fevers, smooth muscle relaxant, nerve tonics, laxatives and for the treatment of dysentery, lumbago, leucorrhoea, dysuria, haemorrhoids, gangrenous ulcer and disorders causing cachexia [1-7]. The phytochemical fractionation of plant extracts from this genus revealed the presence of phenolic compounds including flavonoids, tannins, phenolic acids, phenyl propanoids and chalcones in addition to eudesmane-type sesquiterpenoids, monoterpenes, lignan glycosides and triterpenoids [8-18].

Previously isolated phenolic compounds from the genus *Pluchea*

The phytochemical studies carried out on the genus *Pluchea* revealed the presence of the phenolic compounds shown in the Table (1).

Table 1: Previously isolated phenolic compounds from the genus *Pluchea*

Phenolic compounds	*Pluchea* Species	References
3,5,7,4'-tetrahydroxy-3'-methyllflavone. Isorhamnetin (3,5,4'-trihydroxy-6,7-dimethylflavone).	*Pluchea carolinensis*	[19]
3-*O*-methylquercetin. transilin (3-*O*-methylquercetin 7-*O*-β-D-glucopyranoside).	*Pluchea dioscoridis*	[20]
Artemetin. Herbacetin-3,7-dimethylether.	*Pluchea Odorata*	[21]
Pluchoic acid (4-hydroxy-2-methoxy benzoic acid). Isorhamnetin (3'-mrthoxy quercetin).	*Pluchea lanceolata*	[22]
Isorhamnetin. Quercetin.	*Pluchea lanceolata*	[23-24]
Casticin.	*Pluchea quitoc*	[25]
1,3,4,5-tetra-*O*-caffeoylquinic acid. 3,4,5-tri-O-caffeoyl quinic acid. Quercetin.	*Pluchea indica*	[26]
Quercetin.	*Pluchea lanceolata*	[27-29]
5,7,3',4'-tetrahydroxy-3,6,8-trimethoxyflavone .	*Pluchea sagittalis*	[30]
3-methyl kaempferol. 3,7,4'-trimethyl kaempferol. 3,6,4'-trimethyl-6-hydroxy kaempferol. 3,6,7,4'-tetramethyl-6-hydroxy kaempferol. 3,3'-dimethyl quercetin. 3,7,3',4'-tetramethyl quercetin. 3,6,3'-trimethyl quercetagetin. 3,6,4'-trimethyl quercetagetin. 3,6,7,4'-tetramethyl quercetagetin. 3,6,7,3',4'-pentamethyl quercetagetin.	*Pluchea odorata*	[31]
Isochlorogenic acids (a mixture of 3,4-; 4,5-;and 3,5-dicaffeoyl quinic acid).	*Pluchea sagittalis*	[32]
1,3,4,5-tetra-*O*-caffeoylquinic acid.	*Pluchea symphytifolia*	[33]
4',7-dihydroxy-3',7-dimethoxyflavone	*Pluchea chingoyo*	[34]
Hesperetin-7-rutinoside. Taxifolin-3-arabinoside.	*Pluchea lanceolata*	[35]
Formononetin-7-*O*-glucoside.	*Pluchea lanceolata*	[36]
Isorhamnetin-3-*O*-sulfate. 3',4',5,6,7-pentahydroxy-3-methoxyflavone.	*Pluchea carolinensis*	[37]

Biological activity of the Genus *pluchea*

The genus *Pluchea* contains many species having important medicinal properties Pharmacological studies demonstrated anti-inflammatory activities of different Pluchea species. The anti-inflammatory activity of aqueous and dichloromethane extracts of *Pluchea sagittalis* were evaluated by carrageenan-foot oedema test. The aqueous extract and dichloromethane extract of *Pluchea sagittalis* produced a total inhibition of 50.85% and 41.16% respectively [38]. The effect of the methanol fraction of *Pluchea indica* and certain standard drugs were evaluated on platelet activation factor (PAF)-induced inflammation, gastric necrosis, ulceration and haematological picture. Pre-treatment with *Pluchea indica* and certain standard drugs significantly inhibited inflammation and incidences of lowered gastric damage [39]. The influence of the methanol fraction of *Pluchea indica* Less root extract was evaluated *in vivo* for anti-inflammatory activity. PIRE produced significant anti-inflammatory activity against glucose oxidase induced paw oedema [40]. The anti-inflammatory and antinociceptive activities of the ethanolic extract from aerial parts of *Pluchea quitoc* DC. (Asteraceae) were evaluated in mice and rats. The results support the folkloric use of the plant in inflammatory processes [41]. The ethanolic extract of *Pluchea lanceolata* exhibited significant anti-inflammatory activity, which was further investigation after fractionation. The result showed that activity was localized in the hexane fraction [42]. Neolupenol, a pentacyclic triterpene isolated from *Pluchea lanceolata* flowers, was found to exhibit anti-inflammatory activity against carrageenin-induced rat-paw edema [27]. Ethanolic extract of *Pluchea indica* leaf (PIL) was used to investigate its anti-inflammatory and antinociceptive activities by using carrageenan- induced oedema model and acetic acid induced writhing test. The results indicate that PIL exhibits significant anti-inflammatory and antinociceptive effects [43]. The effect of the methanolic fraction of *Pluchea indica* Less root extract was evaluated on various models of inflammation and ulcer. The findings reveal the anti-inflammatory and antiulcer activity of this fraction [44]. A methanolic fraction of a chloroform extract of defatted *Pluchea indica* roots was investigated for its anti-inflammatory potential against several models of inflammation. The extract showed significant inhibitory activity against several models of inflammation [45]. The ethanolic extract of *Pluchea indica* root exhibited significant anti-inflammatory activity, which was further localized

in the hexane fraction, from which Ψ-taraxasterol acetate was isolated which proved to be one of the active constituents [46]. *Pluchea sagittalis* was studied for anti-inflammatory and antioxidant activities. The results correlate the reduction of free radical production with the anti-inflammatory effect of this plant [38]. A dichloromethane extract of *Pluchea sagittalis* was tested for bioactivity using carrageenan-induced paw edema in rats and TPA-induced ear edema in mice. This extract showed good anti-inflammatory activity in both tests. Flavonoid present in this extract may be responsible for this activity [47]. The methanolic fraction of the root extract of *pluchea indica* possesses significant anti-inflammatory and antioxidant activity. This study was designed to assess the degree of inhibitory effect of *pluchea indica* on croton oil-induced mouse ear oedema, lipid hydroperoxide formation, peroxidizability of the epidermal layer and also in-*vitro* lipid peroxidation (using $FeCl_3$/ADP/NADPH and CCl_4 systems) [48]. The petroleum ether extract of the roots of *Pluchea lanceolata* exhibiting 45.4% anti-inflammatory activity yields sorghumol and sorghumol acetate. The chloroform soluble portion of the methanolic extract showing 54.5% anti-inflammatory activity affords boehmerol acetate [49].

The antinociceptive effects of ethanolic extract of *Pluchea sagittalis* was evaluated in mice. And was found to be a potent antinociceptive agent [50]. The methanol root extracts of *Pluchea indica* (Less) were explored for the first time for neutralization of snake venom *(Viperu russellii)* activity. The *Pluchea indica* root extracts significantly neutralized the viper venom-induced lethality and haemorrhagic activity in albino rat and mouse. These observations confirmed that certain Indian medicinal plants like *Pluchea indica* possess significant snake venom neutralizing capacity and need further examination for their active constituents [51]. The neutralization of viper and cobra venom by β-sitosterol and stigmasterol isolated from the root extract of *Pluchea indica* Less. (Asteraceae) was evaluated in experimental animals. This study suggests that β-sitosterol and stigmasterol may play an important role, along with antiserum, in neutralizing snake venom induced actions [52].

Neuropharmacological studies were conducted in rodents with *Pluchea indica* Less root extract. The observations suggest that the root extract of *Pluchea indica* possesses a potent central nervous system depressant action [53]. The effect of *Pluchea indica* Less root extract (PI-E) on locomotor activity and Pentobarbital-induced sleep, social isolation-induced aggressive behavior, motor coordination on the rotarod test, pentylenetetrazaole-induced convulsion and nociceptive response in the tail-pinch test were examined in mice. The results suggest that PI-E attenuates Pathophysiological changes caused by social isolation stress in mice, and that the GABAergic system in partly involved in the action of PI-E on a social isolation-induced decrease in pentobarbital [54]. The methanol fraction of *Pluchea indica* Less root extract (PIRE) was evaluated *in vitro* for free radical-scavenging activities, CCl_4-induced lipid peroxidation and the metabolism of arachidonic acid by lipoxygenase. PIRE showed inhibition of hydroxyl radical and superoxide generation, lysis of erythrocytes induced by hydrogen peroxide, CCl_4-induced lipid peroxidation and also dioxygenase activity of lipoxygenase (both in the presence and absence of hydrogen peroxide) [40]. Extracts from *Pluchea indica* were screened for flavonoid content, total phenolics, and antioxidant activity. *Pluchea indica* Less. extracts inhibited linoleic acid oxidation and had the DPPH, ABTS, and ferric cyanide antioxidant capacities. Therefore, the plant may contribute to dietary antioxidant intake [55]. The antioxidant activity of *Pluchea arabica* was investigated in *vitro* using DPPH and phosphomolybdenum assay methods. The aqueous ethanol extracts of *Pluchea arabica* showed the inhibition of DPPH radical [56]. The antioxidant activities of the methanolic root extract of tissue cultured *Pluchea indica* (L.) Less was evaluated in various *in vitro* models. The methanolic extract of *Pluchea indica* (MEPI) has a significant antioxidant activity [57]. A study was undertaken to evaluate the antioxidant and acetylcholinesterase inhibition properties of stems and leaves of hexane and methanolic extracts of *Pluchea indica*. Methanolic extract of leaves showed the highest antioxidant activity while hexane extract of both leaves and stems exhibited lower or negligible level of antioxidant activity [58].

The methanolic fraction of *Pluchea indica* root extract was found to possess significant antiulcer activity in different experimental animal models. Significant enhancement of healing process in acetic acid-induced chronic gastric lesions was also observed in the extract-treated animals [59]. The methanol fraction of the extract of *Pluchea indica* roots exhibited significant hepatoprotective activity against experimentally induced hepatotoxicity by carbon tetrachloride in rats and mice. The extract caused significant reduction of the increased bromosulphalein retention by CCl_4 treatment. These findings suggested a potent hepatoprotective effect of the extract of *Pluchea indica* roots [60]. The volatile fractions obtained by hydrodistillation of the fresh leaves of *Pluchea dioscoridis* were analysed by GC-MS technique. *Pluchea dioscoridis* showed a marked mosquito larvicidal activity against *Culex pipiens* [61].

The anti-neoplastic potential of *Pluchea odorata* was investigated against severe inflammatory conditions such as neuritis, rheumatism, arthritis, coughs, bruises and tumors. The freeze dried extracts from five solvents of increasing

polarity was tested against HL-60 and MCF-7 cells. The inhibition of proliferation and the induction of cell death were investigated as hallmark endpoints to measure the efficiency of anti-cancer drugs. The dichloromethane extract of *Pluchea odorata* exhibited pronounced anticancer activity [62]. Aqueous and organic extracts of *Pluchea sagittalis* was tested *in vitro* for cytotoxic activity against human solid tumor cell lines. The extracts were screened against HT29 human colon adenocarcinoma cells and NCI-H460 human non-small cell lung cancer cells. The *Pluchea sagittalis* extracts produced differential sensitivity across the cell lines [63]. *Pluchea lanceolata* was found to be a potent chemopreventive agent and suppresses Fe-NTA-induced renal carcinogenesis and oxidative damage response in Wistar rat [64]. The effect of *Pluchea quitoc* on the growth and differentiation of bone marrow granulocyte macrophages progenitors (CFU-GM) in Ehrlish ascites tumor-bearing mice was investigated. *Pluchea quitoc* enhanced survival of tumor-bearing mice. This suggests an immunoregulatory role in counteracting the tumor-induced myelopoiesis suppression as well as usefulness as adjuvant treatment of cancer [65]. The immunosuppressive potential of 50% ethanolic extract of *Pluchea lanceolata* and its bioactive chloroform fraction was investigated with basic models of immunomodulation. The findings revealed that *Pluchea lanceolata* causes immunosuppression by inhibiting Th1 cytokines [66]. The *in vitro* antifungal activity of the aqueous, ethanol, chloroform, petroleum ether, and residue extracts from *Pluchea ovalis* was evaluated using the agar well diffusion assay against four filamentous fungi and two yeasts monitored by standard antifungal disks. The results showed that all the extracts from *Pluchea ovalis* revealed elevated inhibitory effect against all microbes evaluated [67].

The *Pluchea indica* aqueous extract was tested against both gram positive and gram negative bacteria using agar diffusion susceptibility test. The positive result showed the possibility of using *Pluchea Indica* as an alternative therapy in the treatment of urinary tract infections [68]. The methanolic root extract of tissue cultured *Pluchea indica* (L.) Less was tested for its antibacterial potentiality against 18 strains of *Shigella* species which is well known gram negative *Bacillus* functioning as common pathogen in humans.

The results obtained suggest marked antibacterial activity of the root extract of tissue cultured *Pluchea indica* [69]. The antibacterial and antifungal activity of five crude extracts obtained by fractionating the leaves of *Pluchea carolinensis* (Jacq.) G. Don were evaluated and two flavonoids isolated from AcOEt crude extracts. The crude extracts $CHCl_3$, AcOEt y n-BuOH showed positive antibacterial results, while the flavonols isolated and identified as eupalitin and isorhamnetin are not the responsible for the biological effect found in the AcOEt crude extract [19]. The essential oil of *Pluchea arabica* was found to be active against *Staphylococcus aureus* (ATCC 29213), *Candida albicans* (ATCC 10231) and *Bacillus subtilis* when tested against seven organisms. The oil was found to be less fragrant than *Ocimum forskaoli* oil in an odour test [70]. The aqueous extract of *Pluchea symphytifolia was* found to have weak antibacterial and antisecretory activity; the lipophilic extract showed a modest anthelmintic activity. The higher caffeoylated quinic acids participated in the antimicrobial and anti athelmintic activity [33] Aqueous, methanol and dichloromethane extracts from Pluchea sagittalis used in the Traditional Medicine of South America, are studied for activity on the respiratory burst and the inducible heat shock protein of 72 kD (hsp72) synthesis. The best inhibitory activity was shown by the dichloromethane extracts of *Pluchea sagittalis* that were active in all the assays. The aqueous extract of *Pluchea sagittalis* was also active in most assays [71]. The antimalarial properties of crude extract and a compound isolated from tissue cultured plant *Pluchea indica* traditionally used medicine in various regions of India was evaluated for antimalarial property. Ethyl acetate insoluble fraction and isolated compound prove significant antimalarial effects [72].

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