



## Review Article

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### TRADITIONAL USES, PHYTOCHEMICAL AND PHARMACOLOGICAL ASPECTS OF *EMILIA SONCHIFOLIA* (L.) DC

Dash Gouri Kumar\*, Abdullah Mohd. Syafiq and Yahaya Ruhaiyem  
Faculty of Pharmacy and Health Sciences, Universiti Kuala Lumpur Royal College of Medicine Perak, Ipoh,  
Perak, Malaysia

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#### \*Corresponding author

Dr. Gouri Kumar Dash, Professor and Head (Research and Post Graduate Studies), Faculty of Pharmacy and Health Sciences, Universiti Kuala Lumpur Royal College of Medicine Perak, 30450 Ipoh, Perak, Malaysia. Email: gkdash2@gmail.com

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#### ABSTRACT

*Emilia sonchifolia* (L.) DC (Family: Asteraceae), commonly known as 'lilac tassel flower' is an important edible medicinal plant found to be used as one of the popular ingredients of traditional vegetable salads in Malaysia, Bangladesh and India. In addition to its use as a vegetable, the plant is documented in ethnomedicine to possess several medicinal benefits in treating night blindness, epilepsy, fever and inflammatory diseases, malaria, asthma, liver diseases, eye inflammation, influenza, burns and breast abscesses. The pharmacological studies have shown that the plant possesses numerous notable biological activities such as antimicrobial, analgesic, anti-inflammatory, antioxidant, anticancer, antidiabetic, hepatoprotective, antianxiety, anticataract and anticonvulsant activities. A few phytoconstituents have been isolated from the plant. The plant is rich with flavonoids. Presence of pyrrolizidine alkaloids have been reported in the plant. Pyrrolizidine alkaloids are considered to be hepatotoxic and therefore, the use of the plant either as a food or in ethnomedicine need to be restricted. With the availability of primary investigations, further investigations are recommended to study the toxicity of the plant in detail before rationalizing its use as a health food.

**Keywords:** *Emilia sonchifolia* (L.) DC, traditional use, pharmacological activities, pyrrolizidine alkaloids

#### INTRODUCTION

Plants have always remained associated in our life either as a source of medicine or vegetables. Several studies have been shown that vegetables provide a good source of remedy against several diseases and ailments. Dietary antioxidants such as flavonoids and polyphenols have attracted the attention of the researchers since they can protect the body from oxidative stress, which is regarded as prime cause of several deadly diseases including ageing, cardiovascular diseases and cancer<sup>1</sup>.

*Emilia sonchifolia* (L.) DC (Family: Asteraceae), commonly known as 'lilac tassel flower' is an annual herb with erect or prostrate at base and up to 10-150 cm tall. It often branches from the very base, usually purplish-green and deep rooting. The leaves (4-16 cm x 1-8 cm) are sessile, with alternate arrangement, dark green above and lighter green or tinged with purple beneath, and more or less irregularly coarsely dentate. The inflorescence is a terminal head and few together in slender corymbs or rarely solitary. The flowers are orange, pink, purple and white in colour. The fruit is one seeded (2.5-3.0 mm), linear oblongoid, soft and brown in colour. The plant occurs frequently as a weed in grassy fields, roadsides or in croppy fields and teak forests, ascending up to 1,350 m in the hills<sup>2,3</sup>.

#### TRADITIONAL USES

In Malaysia, the plant is commonly known as 'Setumbak merah' and contributes to one of the popular ingredients

of traditional vegetable salads 'Ulam'. The plant is sold in local markets as an edible wild vegetable. The flowers are fried with batter and the leaves eaten raw<sup>4,5</sup>. The leaves are edible and used as a traditional salad in Bangladesh<sup>6</sup>. In India, the fresh stems and leaves are eaten as a salad or cooked as vegetable<sup>7</sup>. It is considered to be one among the "Ten Sacred Flowers" of Kerala state in India, collectively known as 'Dasapushpam' ('Dasa' means ten and 'pushpam' means flowers) which are predominately used by the traditional healers in treating cancer and other malignant conditions<sup>8</sup>.

The plant is documented in ethnomedicine to possess medicinal benefits in treating diarrhoea, night blindness and sore throat<sup>9,10</sup>, rashes, measles, inflammatory diseases, eye and ear ailments<sup>11</sup>, fever<sup>12,13</sup>, stomach tumor<sup>14</sup>, malaria<sup>15</sup>, asthma<sup>12,16,17</sup>, liver diseases<sup>18</sup>, eye inflammation<sup>19</sup>, earache<sup>20</sup> and chest pain<sup>21</sup>. In China, the leaves are used for the treatment of dysentery and roundworm infestations, wounds and abscesses, influenza, burns and snake bites<sup>22,23</sup>. In India, the leaf paste in doses of one spoonful once a day at bed time for about 2-3 months is recommended to treat night blindness<sup>24</sup>. The crushed leaves are used externally to treat breast abscesses among tribal women. The leaves are rubbed on the forehead to relieve headache<sup>25</sup>. The Africans consume the leaves as vegetable for its laxative property. The plant has been documented in the Nigerian folk medicine for the treatment of epilepsy in infants<sup>26,27</sup>.

In addition to its several traditional uses, *E. sonchifolia* is also listed in Ayurveda and Siddha system of medicine.

Ayurveda recommends the plant for treatment of gastropathy, diarrhoea, ophthalmia, nyctalopia, cuts and wounds, intermittent fevers, pharyngodyma and asthma<sup>28</sup>. In Siddha system of medicine, the plant is recommended for treating intestinal worms and bleeding piles<sup>2</sup>.

### PHYTOCHEMICAL STUDIES

A few chemical constituents have been reported from this plant. The aerial parts afforded two pyrrolizidine alkaloids, identified as senkirkine and doronine<sup>29</sup>. Srinivasan and Subramanian<sup>30</sup> reported presence of quercetin quercitrin, rutin, kaempferol 3- $\beta$ -D-galactoside, ursolic acid, n-hexacosanol and triacontane in the aerial parts. The ethyl acetate fraction of 90% ethanolic extract of aerial parts yielded rhamnetin, isorhamnetin, luteolin, triclin-7-O-beta-D-glucopyranoside, 8-(2"-pyrrolidinone-5"-yl) -quercetin, 5, -2', 6'-trihydroxy-7, 8-dimethoxyflavone-2'-O-beta-D-glucopyranoside, succinic acid, fumaric acid, p-hydroxybenzoic acid, 4-hydroxy isophthalic acid, 3, 4-dihydroxycinnamic acid, esculetin, isowedelolactone and uracil respectively<sup>11</sup>. A new cyclohexylacetic acid derivative, named 2-{4-hydroxy-7-oxabicyclo [2.2.1] heptanyl}-acetic acid together with a known analogue, 2-(1,4-dihydroxy cyclohexanyl)-acetic acid was reported from the aerial parts<sup>31</sup>.

Presence of a flavone glycoside, characterized as 5, 7, 8-trihydroxy-6, 4'-dimethoxy flavone-7-O- $\alpha$ -L-rhamnopyranosyl-1 $\rightarrow$ 4-O- $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 4)-galactopyranoside was reported from the stems along with three known compounds Kaempferol 3-O- $\alpha$ -L-rhamnopyranosyl-(1 $\rightarrow$ 2)- $\beta$ -D-glucopyranoside, Mearnssetin-3-O- $\alpha$ -L-rhamnopyranoside and Gehuain (isoflavone) respectively<sup>32</sup>. Gao *et al.*<sup>33</sup> isolated simiril, beta-sitosterol, stigmasterol, and palmitic acid from the whole plant. Yadava and Raj<sup>34</sup> reported presence of flavone glycoside 3,7,3',4'-tetrahydroxy-flavone-3-O- $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 3)-O- $\beta$ -D-galactopyranosyl-(1 $\rightarrow$ 4)-O- $\alpha$ -L-rhamnopyranoside along with two other known compounds Luteolin-7-O-  $\beta$ -D-glucoside and Isoetin 5'-methyl ether in the seeds.

### PHARMACOLOGICAL ACTIVITIES

Due to its several ethnomedicinal uses, *E. sonchifolia* has been investigated for a good number of pharmacological activities.

#### Antimicrobial activity

The methanol extract and its fractions with chloroform, diethyl ether, ethyl acetate and butanol from the aerial parts were studied against 20 bacterial species, 3 yeast species, and 12 filamentous fungi at 10 mg/ml concentrations<sup>35</sup>. The results of the study revealed antibacterial activity of *E. sonchifolia* extract and its fractions against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Citrobacter freundii*, *Escherichia coli*, *Acinetobacter calcoaceticus*, *Acinetobacter anitratus*, *Bacillus licheniformis*, *Micrococcus* spp, *Staphylococcus epidermidis*, *Erwinia* spp, *Bacillus cereus*, *Serratia*

*marcescens*, *Staphylococcus saprophyticus*, *Yersinia enterocolitica*, *Shigella sonnei*, *Morganella morganii* and *Enterobacter aerogenes*. The test samples were also active against yeast species *Candida albicans* and *Cryptococcus neoformans*. However, they were ineffective against the bacteria *Salmonella typhi*, *Klebsiella pneumonia* and *Bacillus subtilis*, yeasts *Rhodotorula rubra* and fungi *Rhizophus* spp., *Fusarium* spp., *Penicillium* spp, *Mucor* spp, *Trichoderma viride*, *Trichophyton rubrum*, *Microsporium canis*, *Trichophyton mentagrophytes*, *Fusarium oxysporium*, *Aspergillus flavus*, *Aspergillus niger* and *Microsporium gypseum* respectively.

In another study, the flavonoid fraction showed stronger antibacterial activity against *Staphylococcus aureus* in the concentration of 0.8 g/ml and weaker antibacterial activity against *Escherichia coli* and *Bacillus subtilis*<sup>36</sup>. The alkaloidal fraction also revealed antibacterial activity to *Escherichia coli*, *Bacillus subtilis* and *Staphylococcus aureus* when the concentrations of the alkaloids were in the range of 600-800 mg/ml<sup>37</sup>.

#### Antiviral activity

Yadava and Raj<sup>34</sup> reported the antiviral activity of the isolated flavones glycoside 3,7,3',4'-tetrahydroxy-flavone-3-O- $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 3)-O- $\beta$ -D-galactopyranosyl-(1 $\rightarrow$ 4)-O- $\alpha$ -L-rhamnopyranoside against Japanese Encephalitis Virus in vitro (Vero cells). The compound showed 50% antiviral activity at 62.5 $\mu$ g/ml.

#### Analgesic and anti-inflammatory activities

The aqueous extract of *E. sonchifolia* is reported to possess more promising anti-inflammatory activity than the methanol extract<sup>38</sup>. In a study, Essien *et al.*<sup>39</sup> reported the anti-inflammatory and analgesic activities of the methanol extract of the leaves. The LD<sub>50</sub>, preliminary phytochemical screening, anti-inflammatory and analgesic activities were investigated using carrageenan, egg albumin, capsaicin-induced paw oedema, formalin-induced paw licking, acetic acid induced writhing and hot plate nociception in mice. The LD<sub>50</sub> (i. p.) was found to be 2874.02mg/kg. The preliminary phytochemical screening revealed presence of terpenes, tannins, flavonoids, saponins and alkaloids. The extract demonstrated dose dependent inhibition of the inflammation and nociception in mice.

The antinociceptive activity of hydroethanolic extract from aerial parts was evaluated in mice by Couto *et al.*<sup>40</sup> using chemical and thermal models of nociception. The results revealed significant antinociceptive activity at 100 and 300 mg/kg, p.o. in all tests with an observation of more promising effect than morphine. Further, the antinociceptive effect was completely inhibited by the extract at 100 mg/kg, after administration naloxone, indicating the extract possess opioid mediated antinociceptive activity. The extract was further subjected

to HPLC analysis which revealed the presence of phenolic compounds.

In another study, Rahman *et al.*<sup>41</sup> investigated the analgesic and anti-inflammatory effects of *Ageratum conyzoides* and *E. sonchifolia* alcoholic extracts in animal models. Analgesic effects were investigated in mice using acetic acid induced writhing model and formalin induced licking model. The anti-inflammatory effect was studied in rats using carrageenan induced paw edema model. The study demonstrated significant analgesic and inflammatory activities of *E. sonchifolia* extract.

#### Anticancer activity

Search for anticancer factor from plants always remained a potential area of investigation. In an *in vitro* study, it was observed that the methanol extract of *E. sonchifolia* is cytotoxic to Dalton's lymphoma (DL), Ehrlich ascites carcinoma (EAC) and mouse lung fibroblast (L-929) cells, but non toxic to normal human lymphocytes. Further, the extract at 100 mg/kg, p.o., in mice decreased the development of both solid and ascites tumors with an increase in the life span. The extract also inhibited DNA synthesis<sup>42</sup>. As a continuation to the research, Shylesh *et al.*<sup>43</sup> reported the anticancer activity of an active terpene fraction, isolated by TLC from the n-hexane extract of *E. sonchifolia* in mice using Dalton's lymphoma ascitic (DLA) cells. Cytotoxicity of the extract and the isolate to macrophages, thymocytes and DLA cells was measured using MTT assay, DNA ladder assay and DNA synthesis in culture. Short term toxicity evaluation of the active fraction was also carried out in mice. Results of the study revealed that the hexane extract was most active and it showed *in vitro* cytotoxicity to DLA and thymocytes, but not to the macrophages. The extract induced membrane blebbing, nuclear condensation, DNA ladder formation and formation of apoptotic bodies which are characteristic to apoptotic cell death. On the other hand, the n-hexane fraction protected 50% of mice challenged intraperitoneally with 106 DLA cells. The active terpene fraction induced cell-specific apoptosis.

Cibin *et al.*<sup>44</sup> reported the antioxidant and antitumor properties of the flavonoid fraction isolated from the whole plant of *E. sonchifolia*. The ability of the flavonoid fraction to inhibit Cu<sup>2+</sup> induced lipoprotein oxidation in human serum and superoxide production was measured to assess the antioxidant property in comparison to quercetin. The results revealed potent antioxidant and anticancer effects of the flavonoids present in the plant.

A study was conducted to investigate the apoptosis induction and molecular mechanisms in human colorectal cancer cells treated with the methanol extract *in vitro*<sup>45</sup>. The extract induced cell growth inhibition in a concentration and time dependent manner suggesting that both extrinsic and intrinsic apoptotic pathways may be involved in extract provoked apoptotic death in the cancer cells.

Sophia *et al.*<sup>46</sup> reported the effect of n-hexane extract of *E. sonchifolia* on azaserine (O-diazoacetyl-L-serine)-induced pancreatic dysplasia in rats. Results of the study revealed a significant decrease of pancreatic and hepatic enzymatic antioxidants like catalase (CAT), superoxide dismutase (SOD), glutathione-S-transferase (GST), glutathione peroxidase (GPx) and non-enzymatic antioxidants like vitamin C, glutathione (GSH) content, and a significant increase in pancreatic serum amylase and lipase, and levels of hepatic marker enzymes viz. alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP). Treatment with the extract for 16 weeks resulted in a concomitant reduction in pancreatic and hepatic damage.

#### Antioxidant activities

A number of antioxidant studies on *E. sonchifolia* have been carried out by different researchers. In a study, the fresh juice and methanol extract of the leaves were reported to be potent inhibitors of superoxide radical generation and hydroxyl radical formation *in vitro*. The extract also showed significant anti-inflammatory activity<sup>47</sup>.

Gayathri Devi *et al.*<sup>25</sup> studied the protective effects of the flavonoid fraction isolated from the whole plant of *E. sonchifolia* on perchlorate-induced oxidative damage in female albino rats. The level of TBARS, catalase, SOD, glutathione reductase (GR), glutathione peroxidase (GPx), glutathione-S-transferase (GST) and concentration of reduced glutathione (GSH) were estimated. The results revealed that the flavonoid fraction is a potent inhibitor of peroxidase damage.

An *in vitro* study was conducted to evaluate the free radical scavenging activities of n-hexane extract of the whole plant<sup>48</sup>. The extract was evaluated for DPPH radical, superoxide radical and hydrogen peroxide scavenging activity. The results of the study indicated potential antioxidant effect of the extract. Further, the HPTLC analysis of the extract revealed presence of terpenoids. The same group of researchers, in another study investigated the protective effect of *E. sonchifolia* against oxidative stress in rats induced by high protein diet<sup>49</sup>. The test animals were fed with high protein diet (100% raw soya flour) for one month along with n-hexane extract at 250 mg/kg, p.o. The extract significantly prevented the increase in lipid peroxidation with increase in the levels of CAT, SOD, GPx, GSH, GST and vitamin C. Again in another study, the efficacy of the n-hexane extract was examined against ethanol induced pancreatic dysfunction in rats. The extract successfully reduced the pancreatic enzymatic antioxidants SOD, catalase, lipid peroxidation, glutathione peroxidase, glutathione and vitamin C. Histopathological examination showed normal architecture of the pancreas against the damage induced by ethanol<sup>50</sup>.

Sophia *et al.*<sup>51</sup> examined the enzymatic and non-enzymatic antioxidant levels in the whole plant of *E. sonchifolia* and found that the plant possesses

predominant amount of enzymatic antioxidants like SOD, catalase, GPx, ascorbate oxidase, GST, peroxidase and non-enzymatic antioxidants such as total reduced vitamin C and glutathione. The study inferred that the plant may be considered as a promising source of natural antioxidants.

As a continuation to earlier work, Sophia *et al.*<sup>52</sup> investigated the effect of oral administration of the n-hexane extract for 30 days on the extent of oxidative damage and changes in the histopathological and biochemical parameters in the pancreas of the rats fed high protein diet. The results demonstrated significant increase in serum levels of amylase, lipase, AST, ALT, urea, uric acid, creatinine, tissue DNA and RNA content and showed a significant decrease in the pancreatic antioxidants, indicating *E. sonchifolia* as a pancreato-protective herb.

Raj<sup>32</sup> reported the antioxidant activity of the isolated flavones glycoside5, 7, 8-trihydroxy-6, 4'-dimethoxy flavone-7-O- $\alpha$ -L-rhamnopyranosyl-1 $\rightarrow$ 4)-O- $\beta$ -D-xylopyranosyl-(1 $\rightarrow$ 4)-galactopyranoside. The compound showed potent antioxidant activity.

#### Anti-diabetic activity

The effects of the aqueous extract of *E. sonchifolia* on glucose concentration and liver function enzymes were assessed by Comfort *et al.*<sup>53</sup>. The results demonstrated that the aqueous extract could decrease the blood glucose level and demonstrated hepatoprotective effects in experimental diabetes.

In another study, the antidiabetic and antilipidemic effects of the alkaloidal fraction in dithizone induced diabetic rats were assessed. The results of the study also revealed significant reduction in the blood glucose, cholesterol and triacylglycerol levels<sup>54</sup>.

#### Hepatoprotective effects

The effect of ethanol extract of the leaves on the haematological parameters and histomorphology of the liver of mice infected with *Plasmodium berghei berghei* was reported by Edagha *et al.*<sup>55</sup>. The results indicated that the extract promotes erythropoiesis at 325 mg/kg, and haemolytic at 650 mg/kg, mild toxic effect on histopathology at 325 mg/kg but also appeared to offer hepatoprotective effect in infected mice.

#### Neurobehavioural effects

Edagha *et al.*<sup>56</sup> reported the effects of ethanol extracts from the leaves of *Nauclea latifolia* and *E. sonchifolia* on anxiety, fear and locomotion in mice infected with *Plasmodium berghei berghei*. The mice were first infected with the parasite intraperitoneally followed by oral administration of the extracts for five days. Behavioural tests were performed on pre-treatment and post-treatment of the parasites. The results indicated that the extracts are

effective in reducing anxiety and fear and enhance locomotion in the infected mice.

#### Anti-cataract activities

An in vivo study was performed to investigate the modulatory effects of the flavonoids against selenite cataract by Lija *et al.*<sup>57</sup>. The study was carried out based on the earlier reports that the flavonoid fraction contributed a significant antioxidant activity. The results revealed that the flavonoid fraction increased the activities of SOD, catalase and reduced glutathione, suggesting that the flavonoids can modulate lens opacification and oxidative stress in selenite induced cataract.

#### Anticonvulsant activity

Asijea *et al.*<sup>58</sup> reported the anticonvulsant activity of the ethanol, chloroform and aqueous extracts from the leaves of *E. sonchifolia* in chicks and mice through maximal electroshock and strychnine induced seizures. The aqueous extract revealed promising anticonvulsant effect compared to other extracts under the study. The research findings agreed upon the ethnomedicinal use of the aqueous leaf extract in treating infantile convulsion by the traditional healers in Nigeria.

#### CONCLUSION

The phytochemical examination of *E. sonchifolia* revealed presence of a wide range of chemical constituents that are responsible for its promising multidimensional pharmacological activities, such as antimicrobial, analgesic, anti-inflammatory, antioxidant, anticancer, antidiabetic, hepatoprotective, antianxiety, anticonvulsant activities. However, the main concern is the presence of pyrrolizidine alkaloids, since the plant is considered edible and used primarily as an ingredient in salads in many countries including Malaysia. Pyrrolizidine alkaloids are believed to be hepatotoxic. They cause irreversible hepatic damage and toxicity signs are a consequence of impaired liver function. Thus, its use either as a food or in ethnomedicine need to be restricted. With the availability of primary investigations, further investigations are recommended to study the toxicity of the plant in detail before rationalizing its use as a health food.

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