Eupatorium buniifolium Hook. ex Hook. & Arn.

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Eupatorium buniifolium. Plant (Zuloaga 9497, SI). Branches (Zuloaga 14,568, SI). Capitula (Zuloaga 14,568, SI). Photos: Fernando O. Zuloaga, courtesy Instituto de Botánica Darwinion (CONICET - ANCEFN)

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Abstract *Eupatorium buniifolium* Hook. ex Hook. & Arn. (Asteraceae) is an aromatic and medicinal plant. Its area is spreading from the Southern parts of Bolivia, Brazil, Paraguay and Uruguay to the northern and central parts of Argentina. It is known as "chilca negra", "romerillo", "chilca", "chirca", "romero colorado". The infusion of leaves and stems is used as a digestive for stomachache, against diarrhea and for liver inflammation. Some studies have confirmed the digestive, hepatoprotective, anti-inflammatory and antioxidant potential of this plant. The main chemical components responsible for its known biological activities have been identified as flavonoids. From *E. buiniifolium* leaves also an essential oil has been obtained that is useful due to its potential insecticidal, antifungal and varroacide activities, both by direct contact and their vapors against the tested organisms. The essential oil has been demonstrated to be bioactive against the Chagas' disease vector *Triatoma infestans*.

Keywords "Chilca" · Asteraceae · Aromatic · Flavonoids

1 Introduction

The genus *Eupatorium* (tribe Eupatorieae, Asteraceae) is represented by almost 1200 species growing in the tropical regions of Americas, Europe, Africa, and Asia. Some species exert a pleasant and have been considered as aromatics. Several species in this genus have also been used in folk medicine as antimalarial, antibacterial, antifungal and anti-inflammatory (Nogueira Sobrinho et al. 2017). *Eupatorium* species is a source of an important number of bioactive metabolites, mainly terpenes, phytosterols and sesquiterpene lactones (being the latest chemotaxonomic markers of the group) which could be a promising bioresource for the development of potential drugs and value-added products (Liu et al. 2015; Zhanga et al. 2008). In the current review, we summarize the progress in the phytochemical isolation of compounds from *Eupatorium buniifolium,* over the last decades. The biological activities of compounds isolated from this species are also included.

2 Taxonomic Characteristics

The genus *Eupatorium* belongs to the Eupatorieae, which is one of the 13 tribes of the Asteraceae (Frohne and Jensen 1979; Woerdenbag 1992). The Index Kewensis listed over 1000 species of *Eupatorium,* but the genus has been taxonomically revised to contain 44 species (Hooker and Jackson 1960; Robinson and King 1985). Species of *Eupatorium* show luxuriant growth, exert allelopathic action and have become major intractable weeds in many parts of the world. The fast growth of members of this genus is disturbing the overall ecology by encroaching upon pastures and replacing forest biomass (Sharma and Dawra 1994; Sharma et al. 1998).

The overt impact is in terms of loss of pastures. In addition, the huge biomass of *Eupatorium* is not used in agriculture and animal husbandry operations, since several species are known to exhibit adverse interactions with livestock and humans.

E. bunififolium has several common names: "chilca negra", "romerillo", "chilca", "chirca", "romero colorado". However, "chilca" seems to be the most common.

Synonyms *Acanthostyles buniifolius* (Hook. & Arn.) R.M. King & H. Rob., *Acanthostyles saucechicoënse* (Hieron.) R.M. King & H. Rob., *Eupatorium buniifolium* Hook. & Arn. var. *buniifolium*, *Eupatorium buniifolium* Hook. & Arn. var. *saucechicoënse*, *Eupatorium buniifolium* Hook. & Arn. var. *bakerii*, *Eupatorium buniifolium* Hook. & Arn. var. *hieronymi*, *Eupatorium crithmifolium* Griseb., *Eupatorium pinnatifidum* DC. *nom. Illeg*., *Eupatorium pinnatifidum* DC. var. *virgata*, *Eupatorium saucechicoënse* Hieron., *Eupatorium virgatum* D. Don ex Hook. & Arn., *Acanthostyles buniifolius* (L.) R.M. King & H. Rob. var. *saucechicoënse*, *Eupatorium pinnatifissum* H. Buek (Zuloaga et al. 2008).

3 Crude Drug Used

Its crude drug consists of the dried leaves harvested independently of their maturation stage. Aqueous and hydroalcoholic extracts of *E. buniifolium* have an aromatic and pleasant odor and a slightly bitter flavor, being the main application as digestive (Lombardo 1959; Alonso Paz et al. 1992).

4 Major Chemical Constituents and Bioactive Compounds

The aerial parts *Eupatorium buniifolium* contains a great number of biologically active compounds, principally flavonoids, in their different hydroxylated and glycosylated options, the most studied components: 5,7,5′-trihydroxy-3,6,2′,4′-tetramethoxyflavone (Muschietti et al. 1994; Zhang et al. 2008), 6-methoxy flavonoids (Caula et al. 1991), hydroxycinnamic acids and their derivatives (Muschietti et al. 1990; Caula et al. 1991), flavonoid glycosides (Muschietti et al. 1990) and two 2′-oxygenated flavonoids (5,7,5′-trihydroxy-3,6,2′,4′- tetramethoxyflavone and 5,2′-dihydroxy-3,6,7,4′,5′-pentamethoxyflavone (Muschietti et al. 1993,1994). *Eupatorium buniifolium* was also investigated for diterpenoid (Caula et al. 1991) and triterpenoid contents. Methyl *ent*-labd-8(17)-en-18-oic acid-15-oate, 15-hydroxy-*ent*-labd-8(17)-en-18-oic acid, 15,16-epoxy-15-methoxy-*ent*--labd-8(17)-en-18-oic acid and 15-methoxy- ent-labd-8(17)-13-dien-18-oic acid methyl ester-16,15-olide were isolated and spectroscopically characterized (Carreras et al. 1998). Visintini et al. (2013) also isolated and characterized from this species the compound euparin, a benzofuranic structure: 1-[6-hydroxy-2-(1-methylethenyl)-5-benzofuranyl] ethenone, possessing antipoliovirus activity. From *E. buniifolium*

leaves has also been obtained an essential oil by steam distillation. By GC-MS, 44 components were identified. Monoterpene and sesquiterpene hydrocarbons, especially α-pinene (14.7%), β-elemene (12.2%), germacrene D (11.5%), *trans*-β-guaiene (6.5%) and (*E*)-caryophyllene (4.3%), were the major constituents found in the oils. The metabolomic characterization of *E. buniifolium* was performed by enantioselective GC by evaluation of the enantiomeric ratios of α-pinene, sabinene, β-pinene, limonene, terpinen-4-ol and germacrene D (Lorenzo et al. 2005).

E. buniiflium oil was used as substrate of endophytic microorganisms in order to diversify its chemical composition, mainly by increasing the oxygenation degree of monoterpene hydrocarbons. The essential oil was modified, containing most valuable oxygenated monoterpenes (Cecati et al. 2018).

5 Morphological Description

Native to Bolivia, Brazil, Uruguay and Argentina (Malme 1931; Cabrera 1963, 1974, 1978; King and Robinson 1971; Sayagués et al. 2000; Grossi et al. 2011), this plant is a perennial shrub resinous that can reach 50–100 cm in high. Stems striate, glabrous. Leaves resinous, mainly opposite, rarely alternate in some terminal branches, usually petiolate, blades entire, narrowly lobed to pinnatifid or bipinnatifid, surface glandular, punctate. Inflorescences are pendent or suberect, long, paniculate cyms. Capitula discoid, homogamous. Involucres cylindrical, rarely campanulate; phyllaries subimbricata, 3–5 seriate, the outer surface usually glandular; receptacles convex, epaleate, glabrous, with irregular surface. Florets usually 5 per capitulum; corolla tubular funnelform, purplish or whitish; lobes ovate–triangular, outer surface glandular; anther collar elongate, cylindrical; anther appendages ovate to triangular; anther bases rounded; style bases not enlarged, glabrous, nectary lacking; style branches longlinear, with stigmatic papillae, elongated in two lines, flagelliform apical sterile appendages with large non-septate sweeping hairs scattered along the entire surface. Cypselae prismatic, 4- or 5-costate, with short twin hairs, carpopodium inconspicuous or minutely annuliform; pappus of ~30–40 bristles, persistent, uniseriate, basally fused in a ring, barbellate, not enlarged at the apex, yellowish or whitish. Pollen grains with noticeably short spines (King and Robinson 1971). Stems rich in leaves; *E. buniifolium* differs from other *Eupatorium* spp. by polymorph leaves, sometimes simple and linear, others with pinnate leaves with linear sections.

6 Geographical Distribution

Eupatorium buniifolium is a South American species that is spreading from the southern parts of Bolivia, Brazil, Paraguay and Uruguay to the northern and central parts of Argentina, growing as a weed in overgrazed fields.

The "chircales" in Uruguay, whose predominant species is *E. buniifolium*, occupy areas of several hundred hectares, with little or no pastoral utility, being mechanical and chemical control methods expensive and difficult to apply (Bayce and Del Puerto 1989).

7 Ecological Requirements

Typically, *E. buniifolium* prefers sandy, rocky soils, on stream embankments, hillsides and roadsides. It occurs in shrubby vegetation, forests and grasslands (Alonso Paz and Bassagida 1999; Marchesi 2005; Brussa and Grela 2007; Marchesi et al. 2013).

8 Traditional Use (Part(s) Used) and Common Knowledge

E. buniifolium has been employed in folk medicine as a tincture for its hepatoprotective and disinfectant properties (Saggese 1959; Zardini 1984; Muschietti et al. 1994). The ethanolic extracts of the plant also show good antiherpetic activity against herpes simplex virus (García et al. 1990; Zanon et al. 1999). The decoction of the aerial parts has been used as a disinfectant (Rojas Acosta 1905), for the treatment of liver and nervous diseases (Saggese 1959) and as digestive and antirheumatic (Ríos et al. 1993; Marchesi and Davies 2004). Occasionally, it has been mentioned as "a very interesting plant for honey production" (Marchesi and Davies 2004).

9 Modern Medicine Based on Its Traditional Medicine Uses

The essential oil (EO) was demonstrated to be active against Varroa in laboratory assays. Although activity was less than that for oxalic acid (the positive control), this EO was less toxic to bees than the control, encouraging further studies (Umpiérrez et al. 2013).

Some of the main popular uses of *E. buniifolium* recorded in the scientific literature are as digestive, hepatoprotective (Saggese 1959; Zardini 1984; Muschietti et al. 1994) and antioxidant (Paya et al. 1996; Gorzalczany et al. 2008).

Many laboratory studies on *E. buniifolium* have proved its pharmacological potential as antiviral, using a Herpes simplex virus-VERO cells system (García et al. 1990; Visintini et al. 2013); being also active on murine normal splenocytes proliferation (Fernández et al. 2002). Methanol extract from *Eupatorium buniifolium* was assayed *in vitro* for antifungal activity against yeasts, hialohyphomycetes as well as dermatophytes with the microbroth dilution method showing strong effect

(Muschietti et al. 2001, 2005). Anti-inflammatory activity was detected in the CH_2Cl_2 extract of the aerial parts of *Eupatorium buniifolium* using the TPA-mouse ear model. Three compounds isolated from this extract, by bioassay-guided fractionation, significantly inhibited the inflammatory response (5,7,5′-trihydroxy-3,6,2′,4′-tetramethoxyflavone, scopoletin and centaureidin) (Muschietti et al. 2001).

Preliminary studies indicate that some active principles of *E. buniifolium* act provoking antinociceptive effect was not reversed by pretreatment with naloxone. Inhibition of only the second phase of the formalin test and no significant effects observed in the hot plate test suggest that the antinociceptive activity is unrelated to the activation of the opioid system (Miño et al. 2005). Pharmacological investigations of aqueous extract of this plant evaluated the neuropharmacological profile in mice. The results found suggest that the activity of *E. buniifolium* may be a CNS-depressant (Miño et al. 2007).

In search for new strategies in pest and disease control, essential oils, as botanical pesticides, can provide a potential resource to develop more environmentally friendly and less toxic products. In this sense, the essential oil from *E. buniifolium* was also evaluated in view of its possible insecticidal potential, as well as antifungal and varroacide activities both in direct contact and with their vapors against the tested organisms (Umpiérrez et al. 2012, 2013, 2017).

Guerreiro et al. (2018) also studied bioactivities toward the Chagas' disease vector *Triatoma infestans* (Klug) (Hemiptera: Reduviidae) by the essential oil of *E buniifolium*. The results provided an interesting scope in relation to the potential use of this oil for the control of this insect at the nymph stage as repellent as well as for decreasing the population by the ovicidal effect. Considering the abundance of the wild plant under study and the fact that its essential oil is easy to obtain, it is suggested that it could be an adequate natural resource to control this vector in a sustainable way as a complementary approach to conventional methods.

In another study, Tasso de Souza (2007) evaluated the antioxidant and anticholinesterasic activities on the essential oil finding positive results as antioxidant in a bioautographic assay against DDPH. When the oil was evaluated in a bioautographic assay against acetylcholinesterase enzyme, the activity found was also positive and correlated to the high percentage of monoterpenes present in the oil.

Lancelle et al. (2009) investigated toxic and repellent properties of the essential oils from four *Eupatorium* species toward *Tribolium castaneum* Herbst adults. Contact toxicity assays showed that all the evaluated essential oils were toxic, and mortality was dose dependent. The main repellency was observed for *E. buniifolium* essential oil.

10 Conclusions

E. buniifolium is a species with a wide range of reported ethnomedicinal uses, as well as many biological activities. These activities can be attributed to its both volatile and non-volatile components. The invasion of this species impacts in terms of

loss of pastures. Remarkably, the huge biomass of *E. buniifolium* is not yet used in agriculture and animal husbandry. Several *Eupatorium* species are known to exhibit adverse interactions with livestock and humans. The ecological behavior of this species represents a paradigmatic situation, as there are no difficulties in the availability and reproduction of plant material. *E. buniifolium* remains to be underexploited, as aromatic or medicinal species.

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