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Genus *Baccharis* (Asteraceae): A Review of Chemical and Pharmacological Studies

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Abstract

The genus Baccharis belongs to the family Asteraceae, tribe Astereae and subtribe Baccharidinae, and it is distributed from the United States to Argentine. It contains approximately 400 species, many of them economically important as medicines, ornamentals and sources of essential oil. Some species, popularly called carqueja, show caulinar expansions or wings which constitute cladodes. In folk medicine, these species are considered stomachic and diuretic. Chemical investigations have focused on compounds of the essential oils, diterpenoids, flavonoids and macrocyclic trichothecenes. Pharmacological essays have demonstrated their antiinflammatory, antimicrobial, antioxidant and cytotoxic activities.

Key words : Asteraceae, *Baccharis*, Chemistry, Essential oil, Pharmacology, Trichothecene

Introduction

The Asteraceae Dumort., also known as Compositae Giseke, are one of the major families of Asterales and comprehend approximately 1,500 genera and 23,000 species, found especially in temperate or tropical montane regions and dry habitats (Judd *et al.,* 1999). The family includes herbs, shrubs, lianas and rarely trees. About 98 % of the genera are herbaceous (Barroso, 1991; Joly, 1998). The evolutionary success of the taxon may be attributed to the array of secondary metabolites, such as terpenoid essential oils, caffeic

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acid derivatives, flavonoids, alkaloids and the defense combination of polyacetylenes and sesquiterpene lactones (Emerenciano *et al.,* 1986; Mesquita *et al.,* 1986; Cronquist, 1988). Flavonoids, particularly flavones, are taxonomically relevant at the tribal and subtribal level (Emerenciano *et al.,* 2001). Among the major genera, Baccharis contains about 400 species (Judd *et al.,* 1999).

Systematic aspects

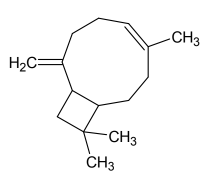
The genus *Baccharis* belongs to the tribe Astereae and subtribe Baccharidinae, and it is distributed from the United States to Argentine, mainly in South America. Many species have been found in Brazil and Andes, and therefore this region is viewed as the probable centre of distribution of the genus. In the Southwest of Brazil, 120 members have been reported. For systematic diagnosis, the leaf morphology and inflorescence type are chiefly important (Barroso & Bueno, 2002).

Morphological characters

Baccharis members are perennial shrubs, dioecious, that attain height of 50 cm to 4 m and in general, have alternate leaves and cymose inflorescences. Female plants bear female flowers and, in male plants, the flowers are morphologically hermaphrodite and functionally male owing to the sterile gynoecium (Ariza-Espinar, 1973; Barroso & Bueno, 2002). Many species show caulinar expansions or wings which constitute cladodes, considered modified stems that play a photosynthetic role. These species are popularly called carqueja in Brazil and Argentine, and exhibit two or three winged cladodes. Some works have dealt with anatomical characters of aerial vegetative organs for pharmacognostic purposes and have pointed out features that many species share, such as anomocytic stomata, glandular and non-glandular trichomes, calcium oxalate crystals, secretory ducts and an evident endodermis or starch sheath (Ariza-Espinar, 1973; Barroso, 1976; Chicourel *et al.,* 1997; Oliveira & Bastos 1998; Cortadi *et al.,* 1999; Gianello *et al.,* 2000; Ortins & Akisue 2000; Budel *et al.,* 2003a; 2003b; 2004a; 2004b). A review on the subject has been recently published (Budel *et al.,* 2005).

Ethnobotanical uses

Baccharis is economically important for providing medicinal plants, ornamentals, hosts of pollinating insects and galls, sources of essential oil and for protecting areas from soil erosion (Barroso, 1976; Matzenbacher, 1985; Carneiro & Fernandes, 1996; Alonso, 1998; Oliveira & Bastos, 1998; Castro & Ferreira, 2001; Midorikawa *et al.,* 2001; Kumazawa *et al.,* 2003; Santos *et al.,* 2003). The winged species, known as carqueja, are used as diuretic and stomachic in folk medicine. Among them, *B. articulata* (Lam.) Pers. (Fig 1), *B. crispa* Spreng., *B. gaudichaudiana* DC. (Fig 2), *B.*



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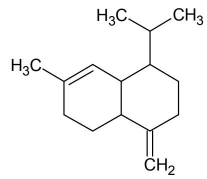

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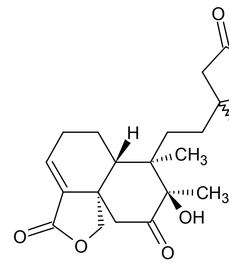

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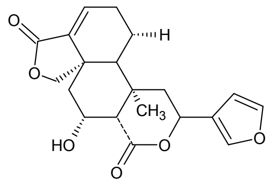

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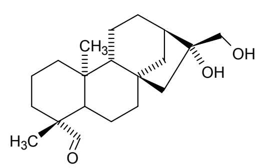

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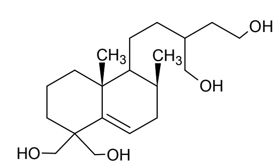

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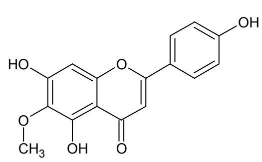

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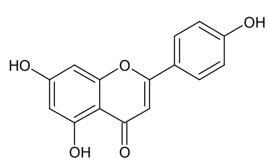

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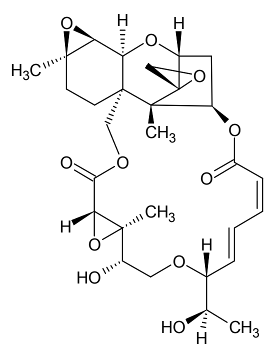

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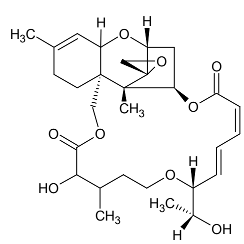

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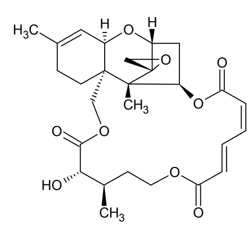

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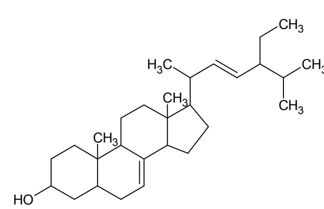

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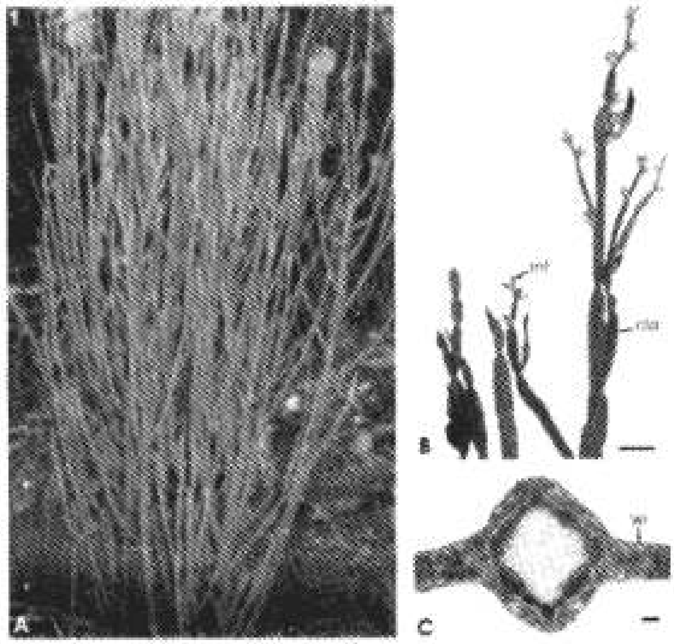

Fig 1. *Baccharis articulata* (Lam.) Pers.: **A.** Aspect of cladodes; **B.** Detail of inflorescences (inf) and cladodes (cla); **C.** Cross-section of a cladode with two wings (wi).

microcephala Baker, *B. myriocephala* DC., *B. pseudovillosa* I.L. Teodoro and J.E. Vidal, *B. sagittalis* (Less.) DC., *B. stenocephala* Baker, *B. trimera* (Less.) DC., *B. usterii* Heering and *B. vincaefolia* Baker are found (Ariza-Espinar, 1973; Corrêa, 1984; Barroso & Bueno, 2002; Budel *et al.*, 2005). Apart from carquejas, *B. dracunculifolia* DC. (Fig 3) is also a medicinal plant whose leaves are used to treat gastric disorders (Mors *et al.*, 2000) and yield a prized essential oil in perfumery (Craveiro *et al.*, 1981).

Chemical and pharmacological studies

This review collates data about investigations which focus on chemical and pharmacological essays of *Baccharis*. A summary of the different studies is presented in Tables 1 and 2.

This genus is a source of essential oil and various works have dealt with the identification of compounds, such as α-cadinene, camphene, carquejil acetate, carquejol, β-caryophyllene[1], limonene, γ-muurolene [2], α-pinene, β-pinene and spathulenol (Siqueira *et al.*, 1985; Weyerstahl *et al.*, 1990; 1996; Ferracini *et al.*, 1995; Loayza *et al.*, 1995; Zunino *et al.*, 1997; 1998; 2000; Frizzo *et al.*, 2001; Agostini *et al.*, 2005). Diterpenoids and flavonoids are the major chemical groups found in *Baccharis*. The former

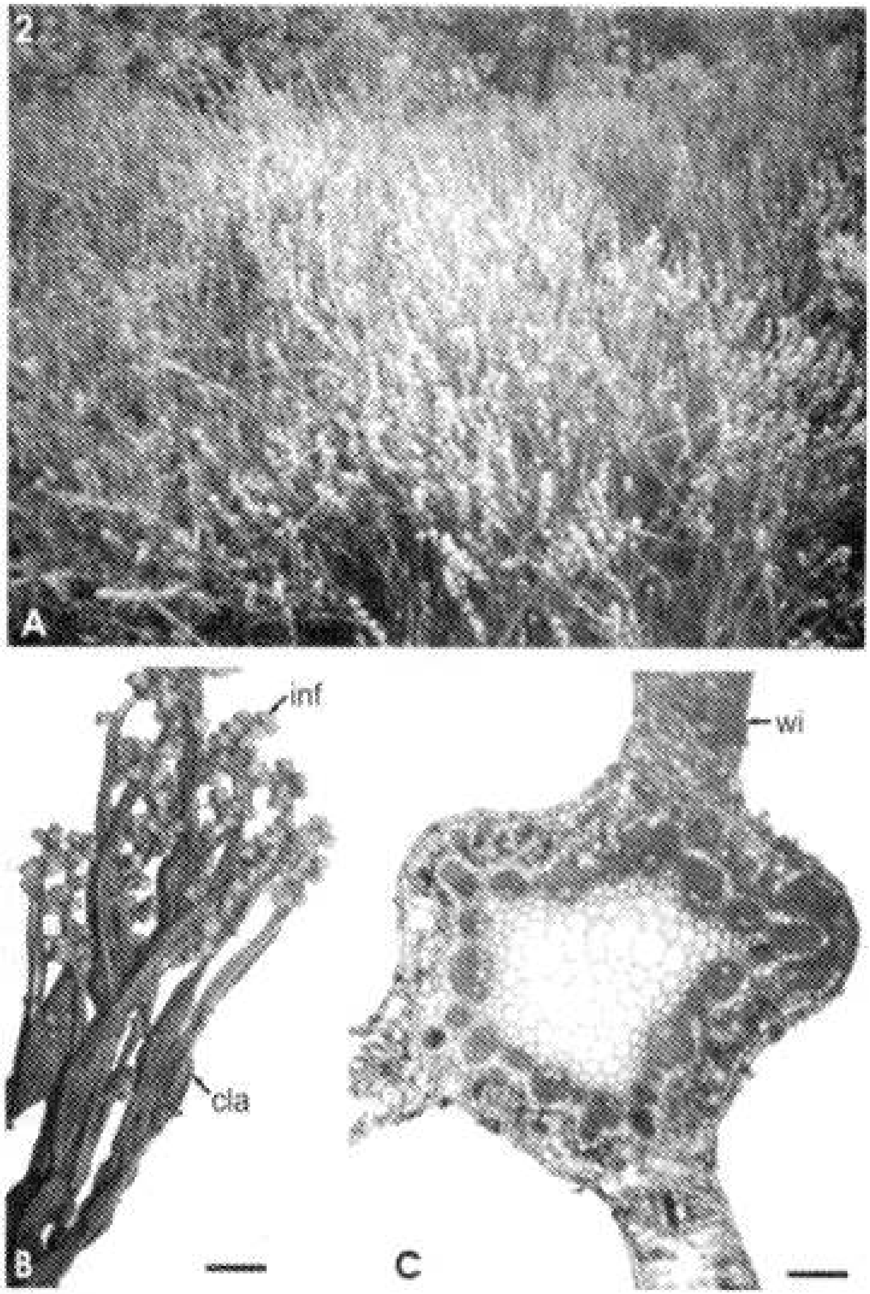

Fig 2. *Baccharis gaudichaudiana* DC.: **A.** Aerial vegetative and reproductive organs; **B.** Inflorescences (inf) & cladodes (cla); **C.** Cross-section of a cladode with three wings (wi).

Fig 3. *Baccharis dracunculifolia* DC.: **A.** Aspect of the plant; **B.** Apical stems bearing inflorescences (inf) & leaves (le).

includes clerodanes, *e.g.* 8β-hydroxy-7-oxo-*ent*-cleroda-3-en-15,18-diacid-16,19-dilactone [3] and 7α-hydroxybacchotricuneatin A [4], kauranes, *e.g.* 14α-17-dihydroxy-*ent*-kauran-19-al [5], and labdanes, *e.g.* gaudichaudol A [6] (Zdero *et al.*, 1991; Dai *et al.*, 1993; Wachter *et al.*, 1999; Cifuente *et al.*, 2001a; Hikawczuk *et al.*, 2002; Akaike *et al.*, 2003). Of the different types of flavonoids found in the genus, the flavones are the most diverse group (Bandoni *et al.*, 1978; Sharp *et al.*, 2001; Moreira *et al.*, 2003a). Some of the biologically active flavones isolated are hispidulin [7] and apigenin [8] (Soicke & Leng-Peschlow 1987; Moreira *et al.*, 2003b).

Moreover, macrocyclic trichothecenes have been recorded in *Baccharis*, *e.g. B. coridifolia* DC., *B. megapotamica* Spreng. and *B. artemisioides* Hook. and Arn. in Hook. (Jarvis *et al.*, 1988; 1991; Bergmann *et al.*, 1992; Rizzo *et al.*, 1997; Varaschin & Alessi, 2003). This group of chemicals has antiviral properties and has been tested for cancer treatment. Baccharin [9], a trichothecene obtained from *B. megapotamica*, and roridins, *e.g.* roridin A [10], and verrucarins, *e.g.* verrucarin A [11], isolated from *B. coridifolia* are considered bioactive molecules against various tumour cell lines.

Table 1. Chemical studies of *Baccharis* species.

***Baccharis* species**	**Results**	**References**
B. sarothroides A. Gray	Isolation of two flavonols: 3',4'-dimethoxy-3,5,7-trihydroxyflavone and centaureidine	Kupchan & Bauerschmidt (1971)
B. crispa Spreng.	Identification of 5-hydroxy-7,4'-dimethoxyflavone and 5,3'-dihydroxy-7,4'-dimethoxyflavone	Bandoni *et al.* (1978)
B. articulata (Lam.) Pers., *B. crispa* Spreng., *B. gilliesii* A. Gray, *B. myrtilloides* Griseb., *B. pingraea* DC., *B. ulicina* Hook. and Arn.	Characterization of jaceidin and oleanolic acid in *B. gilliesii*, jaceosidin and lupeol in *B. myrtilloides*, chondrillasterol [12] in *B. ulicina* and *B. pingraea*, acacetin and cirsimaritin in *B. articulata*, salvigenin and 7,4'-dimethylapigenin in *B. articulata* and *B. crispa*	Gianello & Giordano (1984)
B. chilco Kunth, *B. eggersii* Hieron., *B. hutchisonii* Cuatrec., *B. microcephala* Baker, *B. nitida* (Ruiz and Pav.) Pers., *B. phylicoides* Kunth, *B. scoparia* (L.) Sw.	Isolation of five clerodanes, three labdane derivatives and a *nor*-diterpene, α hydroperoxide derived from 4α-hidroxygermacra-1(10),5-deine	Bohlmann *et al.* (1985)
B. articulata (Lam.) Pers., *B. trimera* (Less.) DC.	Principal constituents identified, respectively: carquejil acetate (45.0% and 67.0%), camphene (23.0% and 3.7%), carquejol (9.0% and 18.5%), β-pinene (5.0% and 3.0%) and α-pinene (3.0% and 0.5%)	Siqueira *et al.* (1985)
B. incarum (Wedd.) Cuatrec.	Isolation of five neo-clerodane diterpenes: a kolavane derivative, two clerodane lactones, 7α-hidroxybacchotricuneatin A [4] and 1α-acetylbacchotricuneatin A	Givovich *et al.* (1986)
B. trimera (Less.) DC.	Identification of quercetin, luteolin, nepetin, hispidulin [7] and apigenin [8]	Soicke & Leng-Peschlow (1987)
B. coridifolia DC.	Isolation of macrocyclic trichothecenes similar to *Myrothecium* fungus	Jarvis *et al.* (1988)

Baccharis species	Results	References
B. bigelovii A. Gray, *B. halimifolia* L., *B. heterophylla* Kunth, *B. neglecta* Britton, *B. potosina* A. Gray, *B. pteronioides* DC., *B. salicifolia* (Ruiz and Pav.) Pers., *B. salicina* Torr. and A. Gray, *B. sarothroides* A. Gray, *B. thesioides* Kunth	Isolation of seven *ent*-clerodanes andseven labdanes, three of them glycosides, a kaurane and a lactone derived from geranyllinalol	Jakupovic *et al.* (1990)
B. paniculata DC.	Isolation of two *ent*-labdanes	Faini & Castillo (1990)
B. dracunculifolia DC.	Identification of iso-humbertiol and dracunculifoliol	Weyerstahl *et al.* (1990)
B. gaudichaudiana DC.	Characterization of gaudichaudiosides A-E	Fullas *et al.* (1991)
B. coridifolia DC., *B. megapotamica* Spreng.	Isolation of macrocyclic trichothecenes	Jarvis *et al.* (1991)
B. petiolata DC., *B. santelicis* Phil.	Isolation of dimeric sesquiterpenes and five labdane derivatives in *B. petiolata* and furoclerodanes and phenolics in *B. santelicis*	Zdero *et al.* (1991)
B. gaudichaudiana DC.	Identification of gaudichaudioside F	Fullas *et al.* (1992)
B. articulata (Lam.) Pers., *B. cylindrica* (Lam.) Pers., *B. microcephala* Baker, *B. trimera* (Less.) DC., *B. usterii* Heering	Characterization of triterpenes in all species, as well as flavonoids, polyphenols and cardiac glycosides in *B. articulata*, saponins in *B. cylindrica*, alkaloids, flavonoids and saponins in *B. microcephala*, polyphenols, flavonoids and saponins in *B. trimera*, flavonoids andsaponins in *B. usterii*	Bianchi *et al.* (1993)
B. articulata (Lam.) Pers.	Isolation of two clerodane diterpenes: 8β-hydroxy-7-oxo-*ent*-cleroda-3-en-15,18-diacid-16,19-dilactone [3] and 15,16-epoxy-7α,18-dihydroxy-15-methoxy-*ent*-cleroda-3-ene	Dai *et al.* (1993)
B. gaudichaudiana DC.	Isolation of the labdane diterpenes gaudichaudol A	Fullas *et al.* (1994)

Table 1. (Contd.)

Baccharis species	Results	References
B. gaudichaudiana DC.	[6], B andC, the clerodane diterpenoid gaudichaudone, the clerodane articulin acetate, hispidulin [7], apigenin [8], spathulenol andursolic acid	
B. dracunculifolia DC., *B. latifolia* (Ruiz and Pav.) Pers., *B. salicifolia* (Ruiz and Pav.) Pers.	Identification of δ-cadinene, β-caryophyllene [1], γ-elemene, germacrene-D, limonene, α-phellandrene, β-pinene, α-thujene and verboccidentafuran among others	Loayza *et al.* (1995)
B. dracunculifolia DC.	Constituents isolated: limonene (8.4%), β-caryophyllene [1] (6.2%), β-pinene (5.9%), δ-cadinene (5.6%), germacrene-D (3.6%), aromadendrene (3.3%), α-pinene (2.9%) and γ-muurolene [2] (2.1%)	Weyerstahl *et al.* (1996)
B. crispa Spreng., *B. salicifolia* (Ruiz and Pav.) Pers.	Main constituents identified: *trans*-nerolidol (27.0%) in *B. crispa*, α-cadinol (9.4%) andgermacrene-D (8.8%) in *B. salicifolia*	Zunino *et al.* (1997)
B. pingraea DC.	Isolation of the furolabdane angeloyl-gutierrezianolic acid, two novel diterpenoids furolabda-6,8-dien-17-oic acid andfurolabda-7-en-17-oic acid andthe linear diterpenoid (10*E*)-centipedic acid	Wachter *et al.* (1999)
B. cordobensis Heering	Major constituents: *trans*-nerolidol (15.8%), T-cadinol (14.7%) andcubenol (8.8%)	Zunino *et al.* (2000)
B. dracunculifolia DC.	Characterization of β-D-glucopyranose, β-D-apiofuranosyl-(1→6)-β-D-glucopyranose anddracunculifosides A-J	Nagatani *et al.* (2001 & 2002)
B. trinervis Pers.	Isolation of three flavones: pectolinarigenin, salvigenin andpenduletin	Sharp *et al.* (2001)

Table 1. (Contd.)

***Baccharis* species**	**Results**	**References**
B. uncinella DC.	Quantitative determination of α-pinene (16.0%), β-pinene (15.0%), limonene (13.0%), spathulenol (10.0%), globulol (5.0%), (*E*)-nerolidol (4.0%), bicyclogermacrene (3.0%) and terpinen-4-ol (2.0.%)	Frizzo *et al*. (2001)
B. medullosa DC.	Isolation of two labdane diterpene glycosides	Cifuente *et al*. (2001a)
B. flabellata Hook. and Arn.	Characterization of three diterpenoid derivatives: 2,19;15,16-diepoxy-neo-clerodan-3,13(16),14-trien-18-oic acid, 15,16-epoxy-5,10-seco-clerodan-1(10),2,4,13(16),14-pentaen-18,19-olide and15,16-epoxy-neo-clerodan-1,3,13(16),14-tetraen-18,19-olide	Hikawczuk *et al*. (2002)
B. pseudotenuifolia Malag.	Isolation of oleanolic acid, α-spinasterol, hispidulin [7], naringenin, 3'-methoxy-luteolin, apigenin [8], kaempferol, eriodyctiol, aromadendrin, quercetin, 3'-methoxy-quercetin, quercetin-3-*O*-rhamnoside and quercetin-3-*O*-glucoside	Moreira *et al*. (2003b)
B. grisebachii Hieron.	Isolation of two diterpenes, eight *p*-coumaric acid derivatives and two flavones	Feresin *et al*. (2003)
B. gaudichaudiana DC.	Isolation of the *ent*-clerodane diterpene bacchariol	Akaike *et al*. (2003)
B. ligustrina DC.	Characterization of acid triterpenes and flavonoids	Moreira *et al*. (2003a)
B. dracunculifolia DC.	Isolation of the compounds isosakuranetin, aromadendrin-4'-methylether, baccharis oxide, ferulic acid, dihydrocinnamic acid, 3-prenyl-4-(dihydrocinnamoyloxy)-cinnamic acid andfriedelanol	Silva-Filho *et al*. (2004)
B. illinita DC.	Isolation of kaurene diterpenes and flavonoids	Verdi *et al*. (2004)

Table 2. Pharmacological studies of *Baccharis* species.

***Baccharis* species**	**Results**	**References**
B. sarothroides A. Gray	Cytotoxic activity against human carcinoma cell lines	Kupchan & Bauerschmidt (1971)
B. glutinosa Pers.	Antimicrobial action of pinocembrine against *Alternaria* fungus	Miyakado *et al.* (1976)
B. trimera (Less.) DC.	Molluscicidal effect of a diterpene lactone	Santos-Filho *et al.* (1980)
B. trimera (Less.) DC.	Antihepatotoxic effect	Soicke & Leng-Peschlow (1987)
B. anomala DC.	Mutagenic activity	Vargas *et al.* (1991)
B. articulata (Lam.) Pers., *B. crispa* Spreng., *B. trimera* (Less.) DC.	Anti-inflammatory effect	Gene *et al.* (1992)
B. articulata (Lam.) Pers., *B. cylindrica* (Lam.) Pers., *B. microcephala* Baker, *B. trimera* (Less.) DC., *B. usterii* Heering	Toxic effects of aqueous extract of *B. articulata* and *B. usterii*	Bianchi *et al.* (1993)
B. gaudichaudiana DC.	Cytotoxic activities	Fullas *et al.* (1994)
B. pedunculata (Mill.) Cabrera	Antifungal activity against human pathogenic and phytopathogenic fungi	Rahalison *et al.* (1995)
B. trimera (Less.) DC.	Anti-inflammatory and analgesic activities	Gene *et al.* (1996)
B. glutinosa Pers.	Antimicrobial action	Verastegui *et al.* (1996)
B. coridifolia DC.	*In vitro* anti-oxidant and cytotoxic activities	Mongelli *et al.* (1997)
B. trinervis Pers.	Anti-oxidant activity	Heras *et al.* (1998)
B. tucumanensis Hook. & Arn.	Anti-inflammatory effect	Muschietti *et al.* (1998)
B. heterophylla Kunth	Antispasmodic effect	Rojas *et al.* (1999)
B. teindalensis Kunth, *B. trinervis* Pers.	Antiviral activity	Abad *et al.* (1999)
B. articulata (Lam.) Pers.	Antiviral activity	Zanon *et al.* (1999)
B. grisebachii Hieron.	Cytotoxic and DNA interaction activities	Mongelli *et al.* (2000)
B. trimera (Less.) DC.	Bacteriostatic and bactericidal activities	Avancini *et al.* (2000)

Table 2. (Contd.)

Baccharis species	Results	References
B. medullosa DC., *B. rufescens* Spreng.	Anti-inflammatory effect	Cifuente *et al.* (2001b)
B. notosergila Griseb.	Antimicrobial action	Cobos *et al.* (2001)
B. grisebachii Hieron.	Antimicrobial action	Feresin *et al.* (2001)
B. coridifolia DC., *B. ochracea* Spreng.	*In vitro* cytotoxic activity against human solid tumour cell lines	Monks *et al.* (2002)
B. trinervis Pers.	Potent anti-HIV activity in a MTT cell proliferation assay	Sanchez-Palomino *et al.* (2002)
B. conferta Kunth	Antispasmodic effect	Weimann *et al.* (2002)
B. articulata (Lam.) Pers.	Anti-oxidant activity	Oliveira *et al.* (2003)
B. heterophylla Kunth	Activation of the Ca^{2+} dependent chloride channels in *Xenopus laevis* oocytes.	Rojas *et al.* (2003)
B. illinita DC.	Gastroprotective effects	Baggio *et al.* (2003)
B. trimera (Less.) DC.	Relaxant effect on the smooth muscle of the *corpus cavernosum* of guinea pig	Hnatyszyn *et al.* (2003)
B. grisebachii Hieron.	Antimicrobial action	Feresin *et al.* (2003)
B. dracunculifolia DC.	Trypanocidal effect	Silva-Filho *et al.* (2004)
B. trimera (Less.) DC.	Anti-proteolytic and anti-hemorrhagic properties against snake venoms	Januário *et al.* (2004)
B. grisebachii Hieron.	Free radical scavenging action and inhibition of lipoperoxidation in erythrocytes	Tapia *et al.* (2004)
B. trimera (Less.) DC.	Antidiabetic activity	Oliveira *et al.* (2005)
B. crispa Spreng., *B. trimera* (Less.) DC., *B. usterii* Heering	Radical scavenging activity	Simões-Pires *et al.* (2005)
B. latifolia (Ruiz & Pav.) Pers., *B. obtusifolia* Kunth, *B. pentlandii* DC., *B. subulata* D. Don	Anti-inflammatory effect	Abad *et al.* (2006)

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