Revista Brasileira de Farmacognosia
BRAZILIAN JOURNAL OF PHARMACOGNOSY
www.journais.elsevier.com/revista-brasileira-de-farmacognosia/

Original article

Survey of plants popularly used for pain relief in Rio Grande do Sul, southern Brazil

Eveline D. Stolz[a,#], *Liz G. Müller*[a,#], *Marilia Trojan-Rodrigues*[b], *Estela Baumhardt*[c], *Mara R. Ritter*[b,c], *Stela M. K. Rates*[a,*]

[a]*Programa de Pós-Graduação em Ciências Farmacêuticas, Faculdade de Farmácia, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil*
[b]*Programa de Pós-Graduação em Botânica, Instituto de Biociências, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil*
[c]*Departamento de Botânica, Instituto de Biociências, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil*

ARTICLE INFO

Article history:
Received: 8 January 2014
Accepted 17 March 2014

Keywords:
Ethnobotany
Folk medicine
Pain
South Brazil

ABSTRACT

Ethnobotanical data can be an important tool in the search for new drugs. The Brazilian Health Surveillance Agency accepts the registration of herbal medicines based on ethnopharmacological and ethnobotanical studies. With the purpose of increasing the knowledge of potentially useful plants for the treatment of painful conditions, we analyzed the ethnobotanical studies carried out in Rio Grande do Sul state (RS-Southern Brazil); we had access to nineteen studies. To our knowledge, this is the first compilation of ethnobotanical studies that focus on pain relief carried out in RS. The species native to RS cited in at least nine (about 50%) of these studies were selected. The search retrieved 28 native species cited as used to alleviate painful conditions, which are distributed in eighteen botanical families, being Asteraceae the most mentioned. The species more frequently cited for pain relief were *Achyrocline satureioides, Baccharis articulata, Baccharis crispa, Lepidium didymum, Eugenia uniflora* and *Maytenus ilicifolia*. The only species not reported in any pre-clinical study associated with pain relief was *B. articulata*. Among the six species cited, no studies on clinical efficacy were found. In conclusion, the folk use of native plants with therapeutic purposes is widespread in RS State (Brazil), being pain relief an important property.

Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage (IASP, 1986). It affects approximately 70% of world population and is associated with deficit in quality of life (WHO, 2007). The Brazilian Society for Pain Study estimates that pain prevalence in the country is of 30% (around 50 million of people) (SBED, 2012).

Despite significant efforts and investments from academia and the pharmaceutical industry, very few new therapies for pain treatment have been introduced to clinical practice (Hruby et al., 2006). As a consequence, pain treatment continues to depend on therapeutic modalities that present limited efficacy and/or

These authors collaborated equally to this study.
* *Corresponding author.*
E-mail: stela.rates@ufrgs.br (S.M.K. Rates).
0102-695X/$ - see front matter
http://dx.doi.org/10.1016/j.bjp.2014.03.007

important adverse effects, such as respiratory depression, constipation, tolerance, dependence, gastritis and ulcers (Brunton et al., 2011).

In this context, medicinal plants may be expected to contribute to the search of new therapeutic strategies, as well as for new molecular patterns with antinociceptive activity, due to chemical diversity (Phillipson, 2007).

The main example of natural compounds relevance in analgesic drug development is the potent opioid alkaloid morphine isolated from *Papaver somniferum* L.; other important plant contributions are salicin and colchicine. Salicin, isolated from *Salix alba* L., is the precursor molecule to acetylsalicylic acid, a nonsteroidal analgesic, antipyretic and anti-inflammatory drug (Brunton et al., 2011). Colchicine is an alkaloid of *Colchicum autumnale* L., largely effective for the treatment of gouty arthritis, a painful inflammatory disease (Brunton et al., 2011). In addition, several other secondary metabolites derived from plants, such as phloroglucinols, alkaloids, terpenoids, methylxanthines and flavonoids have been evaluated in pre-clinical studies on antinociceptive activity (Calixto et al., 2000; Sardella et al., 2008; Galeotti et al., 2010; Haas et al., 2011; Sawynok, 2011; Silva et al., 2011; Radulovic et al., 2012).

The approach for drug development from plant resources depends on defined purposes. Different strategies yield particular active compounds or phytomedicines. The most common strategy is the careful observation of the use of natural resources in the folk medicine of different cultures. The traditional use of plants in primary health care is recognized by WHO (1992) and has increased significantly over the past 20 years (Calixto, 2000; Rates, 2001; Dhanani et al., 2011; Kumar et al., 2011; WHO, 2008). Besides contributing to primary health care, herbal medicine can be used as indicator of pharmacologically relevant activities in drugs development approaches (Rates, 2001).

By the year 2007, herbal medicine revenue in Brazil earned US$160 million (WHO, 2008). Ethnobotanical studies demonstrate the popular use of plants for pain relief, as it was the case in Rio Grande do Sul state (Garlet, 2000; Marodin, 2000; Di Stasi, 2002; Agra et al., 2007; Matos, 2007). The Brazilian National Health Surveillance Agency (Anvisa) accepts the traditional uses reported by ethnopharmacological and/or ethnically oriented studies as evidence of efficacy of phytopharmaceuticals or herbal drugs used with therapeutic purpose (Anvisa, 2010; 2014). Furthermore, the Brazilian government has expressed interest in including phytotherapy in the public health system, and published a list of species considered relevant for research aiming at future therapeutic use (MS, 2009).

In the light of the above, a compilation of ethnobotanical studies carried out in the state of Rio Grande do Sul, Brazil, was performed with special focus on the knowledge of the plants potentially useful for the treatment of painful conditions, with special focus on native species.

Materials and methods

The present study comprises nineteen ethnobotanical studies (including original articles, theses and dissertations), which present data from communities living in Rio Grande do Sul (RS) state. The studies were found by performing searches within virtual databases (PubMed, SciELO and Portal de Periódicos CAPES), using the following keywords: folk medicine, *medicina popular*, ethnobotany, *etnobotânica*; combined with Rio Grande do Sul, southern Brazil and *sul do Brasil*. Regional university libraries were also assessed. The criteria for selection were: accessibility, presence of a botanist in the team of researchers, publication time interval from 1997 to 2009.

These studies were grouped according to the eleven physiographic regions of RS territory defined by Fortes (1959) (Fig. 1): Depressão Central - Possamai (2000), Soares et al. (2004), Vendruscolo (2004) and Casagrande (2009); Encosta do Sudeste - Martha (2003), Veiga (2003), Zanandrea (2003) and Ceolin (2009); Litoral - Marodin (2000) and Haas (2003); Encosta Inferior do Nordeste - Sebold (2003) and Barbosa (2005); Alto Uruguai - Kubo (1997) and Löwe (2004); Serra do Sudeste - Fernandes (2001) and Leitzke (2003); Missões - Barros et al. (2007); Campos de Cima da Serra - Ritter et al. (2002); Planalto Médio - Garlet (2000); Campanha and Encosta Superior do Noroeste - no studies were found.

The species (native and exotics) cited in at least nine (about 50%) of the nineteen studies were listed; furthermore, those cited as useful for alleviating painful conditions were selected. The search terms considered as related to painful conditions were: pain (*dor*), headache/migraine (*dor de cabeça/enxaqueca*), sore throat (*dor de garganta*), stomachache (*dor de estômago*) and backache (*dor nas costas*), abdominal pain (*dor abdominal*), kidney pain/inflammation (*dor/inflamação nos rins*), leg pain (*dor nas pernas*), bellyache (*dor de barriga*), sprain pain (*dor de entorse*); or related ones, like colics (*cólica*), baby's colics (*cólica de bebê*), and rheumatism and pain of the joints (*reumatismo/dor nas articulações*). From the cited species, we selected the native ones cited in at least five (about 50%) of the eleven RS physiographic regions, in order to analyze published scientific data related to their antinociceptive activity and toxicity.

Pre-clinical and clinical studies were searched in PubMed, SciELO, Scopus and Portal de Periódicos CAPES. The scientific name of the plant combined with the terms "pain", "antinociceptive", "analgesic", "toxicity", "*dor*", "*analgesia*" and "*toxicidade*" were used as keywords. Additionally, the total number of publications for each species in Pubmed and SciELO Brazil was registered. In the Banco de Teses CAPES only the number of theses was considered. All these searches covered studies published until January 2013.

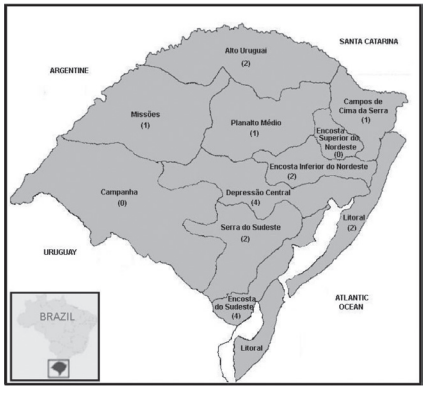

Figure 1 - Physiographic regions of the Rio Grande do Sul state (southern Brazil) defined by Fortes (1959). The number of studies found in each region is in parentheses.

The valid names of the species and the authors were confirmed using The Plant List (2014) and Lista da Flora do Brasil (2014) databases. The botanical families were updated based on the APG III classification system (Stevens, 2012).

Results and discussion

From the nineteen ethnobotanical studies consulted, 625 species were collected. All species were mentioned in at least one study and some of them were cited in more than one study, which resulted in a total of 2,208 plant cited. Seventy-four species (natives, exotics, and subspontaneous) were mentioned as having some traditional use in at least nine (about 50%) of the ethnobotanical studies, which constitutes 42.3% (934) of the total citations. Out of these 74 species, 70 species were mentioned for relieving some kind of symptom related to pain, confirming that painful conditions represent an important health complaint in the state. Sixty percent (60%) of the species used for pain relief are exotic (Chart 1) and 40% native (Chart 2). We speculate that the process of population formation in Southern Brazil, which results from the miscegenation between original inhabitants (amerindians), Europeans and Africans, could be one factor that contributes to the widespread use of exotic plants. The African slaves and European immigrants brought several species considered to have a medicinal or ritualistic value in their original countries, which were acclimated and incorporated to the Brazilian folk medicine (Brandão et al., 2008).

In Chart 2, the native species are listed by popular name, botanical family, part of plant used, form of preparation and symptom/claim reported in each studied region (with respective authors) are shown. Native species were identified as members of 18 botanical families, and Asteraceae (n = 7) the family more frequently cited. These results are in accordance to those previously published by Giulietti et al. (2005) who demonstrated that Asteraceae is the second largest family in Brazil, comprising 1900 species. Some studies reported the antinociceptive activity of species belonging to Asteraceae family, including RS native plants (Conde et al., 2011; Figueredo et al., 2011).

Leaves are the most frequently utilized part of the plant (45%), followed by aerial parts (11%), flowers (11%), roots (8%), stems (8%), whole plant (4%), inflorescences (5%), fruits (4%), buds (2%), barks (1%) and rhizomes (1%). The preference for leaves has been previously reported by others (Garlet, 2000; Borba and Macedo, 2006).

The predominant preparation form cited was tea (including decoction and infusion) (63%) followed by ethanolic extract (8%) and syrup (6%). The use of plants combined with *chimarrão* (6%) was also cited. *Chimarrão* (also known as "mate") is an aqueous beverage of *Ilex paraguariensis* St. Hill. leaves prepared with water at 70ºC, which is largely consumed in southern Brazil. In general, this beverage is taken daily and represents an important social habit inherited from South American Indians (Lessa, 1986; MTG, 2014).

The native species more frequently mentioned (cited in at least five of nine RS physiographic regions) for treating pain were *Achyrocline stureioides* (Lam.) DC., *Baccharis articulata* (Lam.) Pers, *Baccharis crispa Spreng, Lepidium didymum* L., *Eugenia uniflora* L. and *Maytenus ilicifolia* Mart. ex. Reissek. *Eugenia uniflora*,

Chart 1
Exotic and subspontaneous species used for pain relief mentioned in ethnobotanical studies in Rio Grande do Sul, Brazil.

Family	Species
Adiantaceae	*Adiantum raddianum* C. Presl
Amaranthaceae	*Allium cepa* L.
	Allium sativum L.
Apiaceae	*Dysphania ambrosioides* (L.) Mosyakin and Clemants
	Foeniculum vulgare Mill.
	Petroselinum crispum (Mill.) Nyman ex A.W. Hill
Asparagaceae	*Aloe arborescens* Mill.
Asteraceae	*Achillea millefolium* L.
	Artemisia absinthium L.
	Bidens pilosa L.
	Calendula officinalis L.
	Cynara cardunculus subsp. *flavescens* Wiklund
	Matricaria chamomilla L.
	Tanacetum vulgare L.
	Taraxacum officinale Weber
Boraginaceae	*Symphytum officinale* L.
Brassicaceae	*Nasturtium officinale* R.Br
Lamiaceae	*Melissa officinalis* L.
	Mentha x piperita L.
	Ocimum carnosum (Spreng.) Link and Otto ex Benth..
	Plectranthus barbatus Andrews
	Rosmarinus officinalis L.
	Salvia microphylla Kunth
	Salvia officinalis L.
Lauraceae	*Cinnamomum verum* J.Presl
	Persea americana Mill.
Lythraceae	*Punica granatum* L.
Malvaceae	*Malva parviflora* L.
	Malva sylvestris L.
Moraceae	*Ficus carica* L.
Myrtaceae	*Psidium guajava* L.
Phytolaccaceae	*Petiveria alliacea* L.
Plantaginaceae	*Plantago major* L.
Poaceae	*Cymbopogon citratus* Stapf
	Zea mays L.
Rosaceae	*Eriobotrya japonica* (Thum.) Lindl
Rutaceae	*Citrus limon* (L.) Burm
	Citrus reticulata Blanco
	Citrus sinensis (L.) Osbeck
	Ruta graveolens L.
Verbenaceae	*Aloysia citriodora* Palau
Violaceae	*Viola odorata* L.

Chart 2
Native species used for pain-relief mentioned in ethnobotanical studies in Rio Grande do Sul (RS) - Brazil were distributed by family, part of plant used and preparation form reported by each studied region with references. The physiographic regions of RS territory: *DC-Depressão Central*; *ES-Encosta do Sudeste*; *LT-Litoral; EN-Encosta Inferior do Nordeste; AU-Alto Uruguai; SS-Serra do Sudeste; MS-Missões; CS- Campos de Cima da Serra; PM-Planalto Médio*.

Family Species	Popular name	Used part	Prepare form	Symptom or claim	References (Regions/ Authors)
Adoxaceae					
Sambucus australis Cham. and Schltdl.	Sabugueiro	Barks, inflorescences		Rheumatism	*DC*/ Vendruscolo (2004)
		Flowers, leaves		Rheumatism	*LT*/ Haas (2003)
				Rheumatism, antiinflammatory	*AU*/ Löwe (2004
		Flowers, fruits, leaves		Antiinflammatory, rheumatism, pain	*SS*/ Leitzke (2003)
Alismataceae					
Echinodorus grandiflorus (Cham. and Schltr.) Micheli	Chapéu-de-couro	Leaves	Decoction, infusion	Rheumatism	*DC*/ Possamai (2000)
				Rheumatism	
		Leaves	Tea, ethanolic extract	Rheumatism	Soares (2004)
		Rhizome, leaves	Cataplasm, tea, syrup, gargle	Rheumatism, sore throat	*EN*/ Sebold (2003)
		Leaves	Tea	Rheumatism, antiinflammatory	*SS*/ Leitzke (2003)
					PM/ Garlet (2000)
Aristolochiaceae					
Aristolochia triangularis Cham. and Schltdl.	Cassaú, cipó-mil-homens	Leaves, stem	Decoction, infusion, tincture, syrup	Pain, headache, rheunatism, backache, toothache, sore throat	*DC*/ Casagrande (2009)
		Stem	Tea, ethanolic extract		*EN*/ Sebold (2003)
Asteraceae					
Achyrocline satureioides (Lam.) DC.	Marcela	Inflorescences, aerial parts	-	Headache, bellyache, toothache, stomachache	*DC*/ Vendruscolo (2004)
		Inflorescences	*Chimarrão*, infusion, decoction, syrup	Sore throat, stomachache, Bellyache	Possamai (2000)
		Flowers, leaves, branches	*Chimarrão,* plaster, infusion or decoction in water or milk, with burnt sugar or eggnog	Bellyache	Casagrande (2009)
			Infusion	Stomachache, headache, sore throat	*ES*/ Veiga (2003)
		Flowers		Bellyache	Ceolin (2009)
			Tea	Headache	
		Inflorescences		Headache	*EN*/ Barbosa (2005)
				Colics, rheumatism	*AU*/ Kubo (1997) Löwe (2004)
		Flowers, leaves, branches		Headache, stomachache	
		Inflorescences	Tea, infusion, eggnog with milk	*Dor na bexiga*	*SS*/ Leitzke (2003)
					CS/ Ritter et al. (2002)
					PM/ Garlet (2000)
Baccharis articulata (Lam.) Pers.	Carquejinha	Stem	Decoction, infusion	Stomachache	*DC*/ Possamai (2000)
		Flowers, leaves	Infusion, decoction, *chimarrão*, syrup, fresh (chewing)	Backache, headache, bellyache	Casagrande (2009)
			Infusion, decoction	Stomachache	*ES*/ Ceolin (2009)
		Aerial parts	Tea	Bellyache	*EN*/ Sebold (2003)
			Tea	Bellyache	*AU*/ Kubo (1997)
				Rheumatism	*SS*/ Leitzke (2003)
			Decoction, infusion	Stomachache, headache	*MS*/ Barros et al. (2007)
Baccharis crispa Spreng.	Carqueja	Flowers, leaves	Decoction (3 min), infusion, syrup, fresh (chewing)	Headache, backache, Bellyache	*DC*/ Casagrande (2009)
				Bellyache	*ES*/ Veiga (2003)
		Flowers, leaves	Tea	Bellyache	*EN*/ Sebold (2003)
				Stomachache	*SS*/ Leitzke (2003)
				Bellyache	*CS*/ Ritter et al. (2002)

(Cont.)

Chart 2 *cont.*

Family Species	Popular name	Used part	Prepare form	Symptom or claim	References (Regions/ Authors)
Chaptalia nutans (L.) Polak	Arnica-do-mato	Whole plant	Decoction	Rheumatism	*DC*/ Possamai (2000)
		Aerial parts, leaves	Tea, ethanolic extract (for external use)	Pain	*EN*/ Sebold (2003)
		Leaves	Tea (for internal or external use)	Rheumatism	*AU*/ Kubo (1997)
			Tea	Abdominal pain	*SS*/ Fernandes (2001)
Mikania laevigata Sch. Bip. ex Baker	Guaco			Rheumatism	*SS*/ Leitzke (2003)
				Rheumatism	*CS*/ Ritter et al. (2002)
Pluchea sagittalis (Lam.) Cabrera	Arnica-do-banhado	Stem, leaves	Decoction, infusion, *chimarrão*, tincture	Pain	*DC*/ Casagrande (2009)
		Leaves	Infusion	Stomachache	*ES*/ Ceolin (2009)
		Inflorescences, aerial parts	Tea, ethanolic extract, plaster	Pain, Bellyache	*EN*/ Sebold (2003)
				Headache	Barbosa (2005)
				Toothache, headache	*CS*/ Ritter et al. (2002)
Sphagneticola trilobata (L.) Pruski	Insulina, arnica	-	-	Pain	*DC*/ Soares (2004)
		Leaves, flowers, stem, aerial parts, whole plant	Decoction, infusion, ethanolic extract	Sprain , leg pain	*LT*/ Marodin (2000)
Brassicaceae					
Lepidium didymum L.	Menstruz, mastruço	Aerial parts		Rheumatism	*DC*/ Vendruscolo (2004)
		Aerial parts, leaves, branches	Plaster, tincture, fresh (eating), decoction or infusion in milk or honey	Antiinflammatory, muscle ache	Casagrande (2009)
				Muscle, kidney pain, stomache	*ES*/ Zanandrea (2003)
		Aerial parts, leaves	Ethanolic extract, infusion, decoction	Leg pain	*LT*/ Marodin (2000)
		Aerial parts, flowers	Tea (internal or external use), ethanolic extract (external use), cataplasm	Pain	*EN*/ Sebold (2003)
		Whole plant	Tea, ethanolic extract (external use)	Rheumatism	*AU*/ Kubo (1997)
		Leaves, roots	Infusion, maceration in alcohol	Pain, antiinflammatory	*MS*/ Barros et al. (2007)
				Muscle, kidney pain, stomache	*ES*/ Zanandrea (2003)
		Aerial parts, leaves	Ethanolic extract, infusion, decoction	Leg pain	*LT*/ Marodin (2000)
Celastraceae					
Maytenus ilicifolia Mart. ex Reissek	Espinheira-santa, cancorosa	Leaves, roots	Decoction, *chimarrão*	Sore throat, backache, rheumatism	Casagrande (2009)
		Leaves	Infusion	Colics	*ES*/ Martha (2003)
		Leaves	Tea	Pain	*EN*/ Sebold (2003)
		Leaves, roots	Tea	Headache, stomachache	*AU*/ Kubo (1997)
		Leaves	Tea, powder	Stomachache, kidney inflammation	
					PM/ Garlet (2000)
Fabaceae					
Bauhinia forficata Link	Pata-de-vaca	Flowers, leaves	Tea	Backache	*EN*/ Sebold (2003)
Lamiaceae					
Cunila microcephala Benth.	Poejinho	Aerial parts		Bellyache	*DC*/ Vendruscolo (2004)
		Aerial parts, leaves	Decoction, infusion, syrup	Colics, pain	*LT*/ Marodin (2000)
		Leaves, stem	Tea	Baby'colics	*AU*/ Kubo (1997)
		Flowers, stem	Tea	Baby' colics	*PM*/ Garlet (2000)

(Cont.)

Chart 2 *cont.*

Family Species	Popular name	Used part	Prepare form	Symptom or claim	References (Regions/ Authors)
Lythraceae					
Cuphea carthagenensis (Jacq.) J. Macbr		Aerial parts		Stomachache, leg pain	*DC*/ Vendruscolo (2004)
	Sete-sangrias	Aerial parts	Tea	Bellyache	*EN*/ Sebold (2003)
				Bellyache	Barbosa (2005)
Malvaceae					
Luehea divaricata Mart. and Zucc.	Açoita-cavalo		Tea, gargle, bath, cataplasm	Antiinflammatory, toothache	*SS*/ Leitzke (2003)
				Rheumatism	*CS*/ Ritter et al. (2002)
Sida rhombifolia L.	Guanxuma			Antiinflammatory, pain due to insect bite	*ES*/ Zanandrea (2003)
		Roots	Compound tea with "Unha-de-gato"	Headache	*AU*/ Kubo (1997)
		Leaves, roots		Antiinflammatory, colics	*SS*/ Leitzke (2003)
Myrtaceae					
Eugenia uniflora L.	Pitangueira	Barks, leaves, shoots		Colics, bellyache	*DC*/ Vendruscolo (2004)
		Leaves	Decoction, infusion	Migraine, pain, colics, sore throat, bellyache	Possamai (2000)
		Fruits, leaves, roots	Decoction, infusion, fresh (eating or chewing leaves), bath	Bellyache	Casagrande (2009)
		Fruits, leaves	Infusion	Colics	*ES*/ Martha (2003)
		Leaves		Rheumatism	Zanandrea (2003)
		Leaves, shoots	Infusion	Pain, bellyache	Ceolin (2009)
		Leaves, stem	Decoction, infusion	Leg pain	*LT*/ Marodin (2000)
		Leaves		Rheumatism	Haas (2003)
		Leaves	Tea	Bellyache	*EN*/ Sebold (2003)
				Bellyache	Barbosa (2005)
		Leaves	Tea	Bellyache	*AU*/ Kubo (1997)
				Rheumatism	Löwe (2004)
		Fruits, leaves		Colics, rheumatism	*SS*/ Leitzke (2003)
		Leaves, shoots	Decoction, infusion	Colics, pain	*MS*/ Barros et al. (2007)
				Colics	*CS*/ Ritter et al. (2002)
		Leaves	Tea	Colics	*PM*/ Garlet (2000)
				Headache	*CS*/ Ritter et al. (2002)
Phyllantaceae					
Phyllanthus niruri L.	Quebra-pedra			Backache	*DC*/ Soares (2004)
		Whole plant, leaves		Antiinflammatory (kidney), muscle ache, rheumatism, backache	*SS*/ Leitzke (2003)
				Kidney pain	*CS*/ Ritter et al. (2002)
Plantaginaceae					
Plantago australis Lam.	Tansagem, tanchagem	Leaves	Infusion	Sore throat, headache	*DC*/Martha (2003)
		Leaves, roots	Decoction, infusion	Sore throat, antiinflammatory	Ceolin (2009)
		Leaves, whole plant, spike	Decoction, infusion, ethanolic extract, bath, compress	Sore throat, antiinflammatory	*LT*/ Marodin (2000)
		Roots, leaves	Tea, ointment	Antiinflammatory, sore throat, stomachache, rheumatism	*AU*/ Kubo (1997)
				Antiinflammatory	*CS*/ Ritter et al. (2002)
Polygonaceae					
Muehlenbeckia sagittifolia (Ortega) Meisn.	Salsa parrilha	Aerial parts		Rheumatism	*DC*/ Vendruscolo (2004)
				Rheumatism	*CS*/ Ritter et al. (2002)

(Cont.)

Chart 2 *cont.*

Family Species	Popular name	Used part	Prepare form	Symptom or claim	References (Regions/ Authors)
Polygonum punctatum Elliot.	Erva-de-bicho	-	-	Bellyache	*DC*/ Soares (2004)
		Leaves, whole plant	Decoction, sitz bath	Leg pain	*LT*/ Marodin (2000)
Salicaceae					
Casearia sylvestris Sw.	Chá-de-bugre	Leaves	Decoction, infusion, *chimarrão*, bath	Rheumatism	*DC*/ Possamai (2000) Casagrande (2009)
		Leaves	Decoction (12 leaves/litter), infusion, powder	Rheumatism, pain	
				Rheumatism, antiinflammatory	*ES*/ Zanandrea (2003)
		Leaves	Infusion in alcohol	Rheumatism, pain	*LT*/ Haas (2003)
				Rheumatism, antiinflammatory	Leitzke (2003)
Solanum paniculatum L.	Juruveva	Leaves, roots, flowers		Headache, stomachache	*DC*/ Vendruscolo (2004)
		Leaves, roots, flowers, stem	Tea	Stomachache	Casagrande (2004)
		Leaves	Infusion	Migraine	*ES*/ Martha (2003)
		Leaves		Colics	*LT*/ Haas (2003)
Verbenaceae					
Lippia alba (Mill.) N.E.Br. ex Britton and P. Wilson	Erva-cidreira, salva	Leaves	Decoction	Migraine, pain	*DC*/ Possamai (2000)
		Aerial parts, leaves	Decoction, infusion, syrup	Stomachache, sore throat	*LT*/ Marodin (2000)
Stachytarpheta cayennensis (Rich.) Vahl.	Gervão-roxo	Leaves		Antiinflammatory, pain	*DC*/ Vendruscolo (2004)
		Leaves	Decoction, infusion, syrup	Backache	Possamai (2000)
		Leaves, roots	Tea with water or late, syrup	Antiinflammatory, toothache	Casagrande (2004)
		Aerial parts	Compress, cataplasm	Toothache, rheumatism	*ES*/ Martha (2003)
		Leaves		Stomachache	Ceolin (2009)
		Leaves, flowers		Colics	*LT*/ Haas (2003)

popularly known as *pitanga*, was the only one mentioned for pain relief in all studied regions, demonstrating its widespread folk use.

Table 1
Number of scientific studies on *Eugenia uniflora*, *Achyrocline satureioides*, *Maytenus ilicifolia*, *Baccharis articulata*, *Baccharis trimera* and *Coronopus didymus* indexed in Brazilian (*Banco de Teses* CAPES and SciELO Brazil) and international (PubMed) databases.

Species	Scientific literature (publication number)		
	Banco de Teses CAPES	SciELO Brazil	PubMed
Achyrocline satureioides	52	16	40
Baccharis articulata	12	5	6
Baccharis crispa	70	33	21
Lepidium didymum	4	8	11
Eugenia uniflora	118	66	54
Maytenus ilicifolia	87	46	61

A brief numerical analysis of the scientific data regarding the six species above-mentioned (Table 1) has shown that the majority of studies are indexed in the Banco de Teses CAPES, a Brazilian database that embraces all theses and dissertations submitted throughout the country. Only part of these studies is indexed in the Brazilian database SciELO as well as in the international database PubMed.

In the next paragraphs we present a summary of the scientific studies (related to pain and toxicity) on these species indexed in the consulted databases.

Achyrocline satureioides (Lam.) DC.

A. satureioides is widely used in southern Brazil, as it is in South America since ancient times (Mercosur, 1993). This species is described in The Brazilian Pharmacopoeia (Farm. Bras., 2001) and is considered the medicinal plant, symbol of Rio Grande do Sul (Assembléia Legislativa do Estado do Rio Grande do Sul, 2002). It is known as "*marcela/macela*", traditionally used to treat several diseases besides pain and inflammation. Anti-inflammatory, analgesic, antispasmodic and myorelaxant properties of aqueous (macerate and decoction) and ethanolic extracts of inflorescences, leaves and stems were demonstrated by pre-clinical studies (Langeloh and Schenkel, 1985; Simões et al., 1986a, 1988a, 1988b; Filot da Silva and Langeloh, 1994;

De Souza et al., 2007); these effects were attributed to the flavonoids, especially quercetin, 3-O-methylquercetin and luteolin (Simões et al., 1986a, 1988c; De Souza et al., 2007). Several reports demonstrate that *A. satureoides* does not seem to be associated with toxicity (Carney et al., 2002; Arredondo et al., 2004; Bettega et al., 2004; Polydoro et al., 2004; Rivera et al., 2004; Fachinetto et al., 2007). Nevertheless, European standards prohibit its use in food products (EFSA, 2007; 2009). A review regarding phytochemical and pharmacological data on *A. satureioides* was published by Retta et al. (2012). Clinical studies were not found.

Baccharis articulata (Lam.) Pers. and *Baccharis crispa Spreng*

Species of the *Baccharis* genus, popularly known as *carqueja*, are traditionally used in folk medicine of southern Brazil, Uruguay and Argentina (Simões et al., 1986b). The *Baccharis* genus comprises around 400 species (Bremer, 1984), and the differentiation between species is somewhat complex due to the presence of winged stems and branches (Barroso and Bueno, 2002). This fact leads people to indiscriminately use *Baccharis* species as medicinal plants (Gianello et al., 2000).

Scientific reports on analgesic or anti-inflamatory properties of *B. articulata* were not found. Recently, some authors demonstrated that the aqueous extract of aerial parts of *B. articulata* increases the number of micronucleated human peripheral blood mononuclear cells (PBMC) *in vitro* and exerts low mutagenic effects in mice (Cariddi et al., 2010). Also, aqueous extract of the aerial parts of *B. articulata* induces apoptosis in human PBMC *in vitro* and genotoxic effects on erythrocytes from bone marrow of mice (Cariddi et al., 2012). These results suggest that *B. articulata* should be used with caution as it may cause cell damage.

B. crispa is cited in the Brazilian Pharmacopoeia (Farm. Bras., 2010) and in the RENISUS (MS, 2009). It is popularly used to treat gastrointestinal, liver and kidney diseases, and inflammation (Verdi et al., 2005). The antinociceptive and anti-inflammatory properties of the crude aerial parts aqueous extract (Gené et al., 1996; Paul et al., 2009) and butanolic fraction (Nogueira et al., 2011) of *B. crispa* were demonstrated in pre-clinical studies. It has been proposed that these properties may be related to the presence of saponins (echinocystic acid), rutin and other phenolic compounds (Gené et al., 1996; Oliveira et al., 2012). No mutagenic effect of aqueous extract and ethanolic fraction of the aerial parts of *B. crispa* was observed on the *Salmonella typhimurium* microsomal activation assay (Nogueira et al., 2011). However, mice treatment with the same extracts induced *in vivo* and *in vitro* toxicological effects to kidney cells (Nogueira et al., 2011). Likewise, the aqueous extract of the aerial parts of *B. crispa* increased the frequency of micronucleated cells in bone marrow of treated mice, indicating a mutagenic effect at chromosomal level (Rodrigues et al., 2009). Moreover, the hydroethanolic extract of *B. crispa* aerial parts was toxic kidney and liver cells in pregnant rats, but did not cause changes in hematological parameters nor in maternal body weight (Grance et al., 2008). Pinho et al. (2010) demonstrated that aerial parts infusion of *B. crispa* presented dose-dependent mutagenic effects in the *Allium cepa* L. assay and induced chromosomal aberrations in human lymphocytes cultures. Also, the essential oil inhibits the differentiation of neuronal cells *in vitro* and reduces the survival of neurons as well as glial cells proliferation (Losqui et al., 2009). However, clinical studies were not found.

Lepidium didymum L.

L. didymum is popularly known as *mentruz, mastruço* or *mentruz-rasteiro*. It is used in folk medicine to treat several diseases, among them rheumatism (Mahmood et al., 2011) and headache (Rajan et al., 2005); it has been also reported antipyretic, wound healing and anti-inflammatory activities (Prabhakar et al., 2002; Mantena et al., 2005). The anti-inflammatory effect of *L. didymum* seems to be linked to several mechanisms, including the inhibition of enzymes (myeloperoxidase and adenosine-deaminase) and action on mediators (bradykinin, histamine, substance P, prostaglandin E2 and nitric oxide) (Busnardo et al., 2010). The hepatoprotective effect of *L. didymum* in rats has demonstrated to reverse the elevation in plasma alanine aminotransferase (ALT), aspartate aminotransferase (AST) and hepatic lipid peroxide levels induced by CCl4 hepatotoxin. These activities may be due to the presence of flavonoids, saponins and tannins (Mantena et al., 2005). However, clinical studies were not found.

Eugenia uniflora L.

This species is cited in the RENISUS (MS, 2009) list. Pre-clinical data suggest the efficacy of *pitanga* leaves infusion (Schapoval et al., 1994) and essential oil (Amorim et al., 2009) as antinociceptive; terpenoids (furanosesquiterpenes) seem to contribute to this effect (Amorim et al., 2009). Schapoval et al. (1994) also demonstrated the potential of *E. uniflora* leaves infusion as anti-inflammatory in the carrageenan induced rat paw edema test.

The aqueous extract of *E. uniflora* leaves did not display genotoxic nor clastogenic effects in the *Allium cepa* L. assay (Yajía et al., 1997). Nevertheless, Lora (2007) demonstrated the hydroethanolic extract of *E. uniflora* leaves induces hepatotoxicity in mice. In addition, the crude ethanol extract and ethyl acetate, *n*-hexane and chloroform fractions obtained from *E. uniflora* leaves, induced vasodilation, vascular congestion and toxicity in the hepatopancreas of *Oreochromis niloticus* L. (Fiuza et al., 2009). However, clinical studies were not found.

Maytenus ilicifolia Mart. ex Reissek

M. ilicifolia is cited in the RENISUS (MS, 2009) list. It is known as *espinheira-santa* or *cangorosa,* found in the southern region of Brazil (Tropical Atlantic Forest), Paraguay, Uruguay and Argentina. Traditionally it is used as anti-inflammatory, analgesic and antiulcerogenic. The main compounds identified were phenolic metabolites, such as terpenoids (Shirota et al., 1994; Ohsaki et al., 2004; Gutiérrez et al., 2007), tannins (Gonzalez et al., 2001) and flavonoids (Leite et al., 2001). The pre-clinical studies showed that extract of *M. ilicifolia* has an anti-inflammatory effect in carrageenan or formaldehyde induced rat paw edema test (Jorge et al., 2004). The anti-inflammatory activity was associated to friedelin, a terpenoid isolated to *M.*

ilicifolia (Schimizu and Tomoo, 1994), and according to Oliveira et al. (1991) the acute and chronic extract administration did not induce any apparent toxicity. In pregnant rodents, the extract caused a pre-implantation embryonic loss, but had no effect on implantation or organogenesis; did not induce morphological alterations of the reproductive system, embryotoxic effects, nor external malformations; and it did not alter the development of the pups (righthing reflex, ambulation, eye-opening), general activity and learning when adults (Oliveira et al., 1991; Montanari and Bevilacqua, 2002). Clinical studies were not found.

As far as we know this is the first study aiming at gathering the use of native species for pain treatment in southern Brazil. It agrees with other reports that document the widespread use of native species as homemade remedies (ethnobotanical studies came from nine out of eleven physiographic regions) that integrate a portrait of the main medicinal plants popularly used for treating pain in the state of Rio Grande do Sul, Brazil. It might contribute to the selection of plants to further studies or include in programs of drug development and public health system. *A. satureioides, B. articulata, B. crispa, L. didymum, E. uniflora* and *M. ilicifolia* were the native species most cited for pain relief purposes. However, scientific data are still insufficient to guarantee the efficacy and safety of these plants.

Authors' contributions

EDS and LGM contributed in selection of ethnobotanical studies, search in virtual database, analysis of the data and manscript preparation. MT-R and EB contributed to selection of ethnobotanical studies. MRR and SMKR supervised the work and contributed to the manuscript preparation. All the authors have read the final manuscript and approved the submission.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgment

The authors thank CAPES and CNPq Brazilian agencies for the financial aid. This paper is the contribution number seven supported by CAPES/PNADB through the project "Knowledge, use and conservation of plant biodiversity in Atlantic Forest and Caatinga" (UFSC/UFRPE/UFRGS).

REFERENCES

Agra, M.F., Freitas, P.F., Barbosa Filho, J.M., 2007. Synopsis of the plants known as medicinal and poisonous in Northeast of Brazil. Rev. Bras. Farmacogn. 17, 114-140.

Amorim, A.C.L., Lima, C.K.F., Hovell, A.M.C., Miranda, A.L.P., Rezende, C.M., 2009. Antinociceptive and hypothermic evaluation of the leaf essential oil and isolated terpenoids from *Eugenia uniflora* L. (Brazilian Pitanga). Phytomedicine 16, 923-928.

Anvisa, 2010. Resolução da Diretoria Colegiada (RDC) nº 10, de 9 de março de 2010. Agência Nacional de Vigilância Sanitária, Published in DOU 10.03.2010.

Anvisa, 2014. Resolução da Diretoria Colegiada (RDC) nº 26, de 13 de maio de 2014. Agência Nacional de Vigilância Sanitária, Published in DOU 14.05.2014.

Arredondo, M.F., Blasina, F., Echeverri, C., Morquio, A., Ferreira, M., Abin-Carriquiry, J.A., Lafon, L., Dajas, F., 2004. Cytoprotection by *Achyrocline satureioides* (Lam.) DC. and some of its main flavonoids against oxidative stress. J. Ethnopharmacol. 91, 13-20.

Assembleia Legislativa do Estado do Rio Grande do Sul, Brazil 2002. Lei nº 11.858, de 5 de dezembro de 2002. Published in DOE 6.12.2002.

Banco de Teses CAPES. http://www1.capes.gov.br/bdteses/

Barbosa, J.F., 2005. Estudo etnobotânico das plantas de uso medicinal e místico utilizadas na comunidade quilombola de Nova Real, Bom Retiro do Sul, estado do Rio Grande do Sul. São Leopoldo, 53 p. Undergraduate Monograph, Universidade do Vale do Rio dos Sinos.

Barros, F.M.C., Pereira, K.N., Zanetti, G.D., Heinzmann, B.M., 2007. Plantas de uso medicinal no município de São Luiz Gonzaga, RS, Brasil. Lat. Am. J. Pharm. 26, 652-662.

Barroso, G.M., Bueno, O.L. 2002. Compostas: Subtribo Baccharidinae. Flora Ilustrada Catarinense. Itajaí: Herbário Barbosa Rodrigues.

Bettega, J.M.R., Teixeira, H., Bassani, V.L., Barardi, C.R.M., Simões, C.M.O., 2004. Evaluation of the antiherpetic activity of standardized extracts of *Achyrocline satureioides*. Phytother. Res. 18, 819-823.

Borba, A.M., Macedo, M., 2006. Plantas medicinais usadas para a saúde bucal pela comunidade do bairro Santa Cruz, Chapada dos Guimarães, MT, Brasil. Acta Bot. Bras. 20, 771-782.

Brandão, M.G., Zanetti, N.N., Oliveira, P., Grael, C.F., Santos, A.C., Monte-Mór, R.L., 2008. Brazilian medicinal plants described by 19th century European naturalists and in the Official Pharmacopoeia. J. Ethnopharmacol. 120, 141-148.

Bremer, K., 1984. Asteraceae. Cladistics and classification. Portland: Timber Press.

Brunton, L.L., Blumenthal, D.K., Murri, N., Dandan, R.H., Knollmann, B.C., 2011. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 12th ed. New York: McGraw-Hill.

Busnardo, T.C.P.M., Padoani, C., Mora, T.C., Biavatti, M.W., Fröde, T.S., Bürger, C., Claudino, V.D., Dalmarco, E.M., Souza, M.M., 2010. Anti-inflammatory evaluation of *Coronopus didymus* in the pleurisy and paw oedema models in mice. J. Ethnopharmacol. 128, 519-525.

Calixto, J.B., 2000. Efficacy, safety, quality control, marketing and regulatory guidelines for herbal medicines (phytotherapeutic agents). Braz. J. Med. Biol. Res. 33, 179-189.

Cariddi, L., Escobar, F., Sabini, C., Torres, C., Reinoso, E., Cristofolini, A., Comini, L., Montoya, S.N., Sabini,, L., 2012. Apoptosis and mutagenicity induction by a characterized aqueous extract of *Baccharis articulata* (Lam.) Pers. (Asteraceae) on normal cells. Food Chem Toxicol. 50, 155-161.

Cariddi, L.N., Escobar, F.M., Sabini, M.C., Torres, V.C., Zygadlo, J.A., Sabini, L.I., 2010. First approaches in the study of cytotoxic and mutagenic damage induced by cold aqueous extract of *Baccharis articulata* on normal cells. Mol. Med. Chem. 21, 4-7.

Carney, J.R., Krenisky, J.M., Williamson, R.T., Luo, J., 2002. Achyrofuran, a new antihyperglycemic dibenzofuran from

the South American medicinal plant *Achyrocline satureioides*. J. Nat. Prod. 65, 203-205.

Casagrande, A., 2009. *Plantas medicinais e ritualísticas utilizadas pela comunidade do Morro da Cruz, Porto Alegre – RS*. Porto Alegre, 139 p. Undergraduate Monograph, Universidade Federal do Rio Grande do Sul.

Ceolin, T., 2009. *Conhecimento sobre plantas medicinais entre agricultores de base ecológica da Região Sul do Rio Grande do Sul*. Pelotas, 108 p. Master Thesis. Universidade Federal de Pelotas.

Conde, R., Corrêa, V.S., Carmona, F., Contini, S.H., Pereira, A.M., 2011. Chemical composition and therapeutic effects of *Lippia alba* (Mill.) N. E. Brown leaves hydro-alcoholic extract in patients with migraine. Phytomedicine 18, 1197-1201.

De Souza, K.C.B., Bassani, V.L., Schapoval, E.E.S., 2007. Influence of excipients and technological process on anti-inflammatory activity of quercetin and *Achyrocline satureioides* (Lam.) DC. extracts by oral route. Phytomedicine 14, 102-108.

Dhanani, N.M., Caruso, T.J., Carinci, A.J., 2011. Complementary and alternative medicine for pain: an evidence-based review. Curr. Pain Headache R. 15, 39-46 .

Di Stasi, L.C., 2002. Plantas medicinais na Amazônia e na Mata Atlântica, 2nd ed. São Paulo: Unesp.

EFSA, 2007. Draft Guidance Document of the Scientific Committee. European Food Safety Authority.

EFSA, 2009. EFSA Compendium of botanicals that have been reported to contain toxic, addictive, psychotropic or other substances of concern. EFSA J. 7, 281.

Fachinetto, J.M., Bagatini, M.D., Durigon, J., da Silva, A.C.F., Tedesco, S.B., 2007. Efeito anti-proliferativo das infusões de *Achyrocline satureioides* DC. (Asteraceae) sobre o ciclo celular de *Allium cepa*. Rev. Bras. Farmacogn. 17, 49-54.

Farm. Bras., 2001. Farmacopeia Brasileira, 4th ed. São Paulo: Atheneu.

Farm. Bras., 2010. Farmacopeia Brasileira, 5th ed. http://www.anvisa.gov.br/hotsite/cd_farmacopeia/index.htm, accessed in March, 2013.

Fernandes, A.A., 2001. *Levantamento etnobotânico* na região da Pedra do Segredo, Caçapava do Sul, RS. Pelotas, 54 p. Undergraduate Monograph, Universidade Federal de Pelotas.

Figueredo, S.M., do Nascimento, F.P., Freitas, C.S., Baggio, C.H., Soldi, C., Pizzolatti, M.G., de Ibarrola Mdel, C., de Arrua, R.L., Santos, A.R., 2011. Antinociceptive and gastroprotective actions of ethanolic extract from *Pluchea sagittalis* (Lam.) Cabrera. J. Ethnopharmacol. 135, 603-609.

Filot da Silva, L., Langeloh, A., 1994. A comparative study of antispasmodic activity of hydroalcoholic 80% (v/v) extracts of *Achyrocline satureioides* (Lam.) DC. (Asteraceae) with papaverine and atropine on rat isolated jejunum. Latin Am. J. Pharm. 13, 35-40.

Fiuza, T.S., Silva, P.C., De Paula, J.R., Tresvenzol, L.M., Sabóia-Morais, S.M., 2009. Bioactivity of crude ethanol extract and fractions of *Eugenia uniflora* (Myrtaceae) in the hepatopancreas of *Oreochromis niloticus* L. Biol. Res. 42, 401-414.

Fortes AB 1959. Geografia física do Rio Grande do Sul. Porto Alegre: Editora Globo.

Galeotti, N., Vivoli, E., Bilia, A.R., Bergonzi, M.C., Bartolini, A., Ghelardini, C., 2010. A prolonged protein kinase C-mediated, opioid-related antinociceptive effect of St John's Wort in mice. J. Pain 11, 149-159.

Garlet, T.M.B., 2000. *Levantamento das plantas medicinais utilizadas no município de Cruz Alta, RS, Brasil*. Porto Alegre, 211 p. Master Thesis. Universidade Federal do Rio Grande do Sul.

Gené, R.M., Cartaña, C., Adzet, T., Marín, E., Parella, T., Cañigueral, S., 1996. Anti-inflammatory and analgesic activity of *Baccharis trimera:* identification of its active constituents. Planta Med. 62, 232-235.

Gianello, J.C., Ceñal, J.P., Giordano, O.S., Tonn, C.E., Petenatti, M.E., Petenatti, E.M., Del Vitto, L.A., 2000. Medicamentos herbários en el centro-oeste argentino. II. "Carquejas": control de calidad de lãs drogas oficiales y sustituyentes. Acta Farm. Bonaer. 19, 99-103.

Giulietti, A.M., Harley, R.M., Queiroz, L.P., Wanderley, M.G.L., Van den Berg, C., 2005. Biodiversidade e conservação das plantas no Brasil. Megadiversidade 1, 52-61.

Gonzalez, F.G., Portela, T.Y., Stipp, E.J., Di Stasi, L.C., 2001. Antiulcerogenic and analgesic effects of *Maytenus aquifolium, Sorocea bomplandii* and *Zolernia ilicifolia*. J. Ethnopharmacol. 77, 41-47.

Grance, S.R., Teixeira, M.A., Leite, R.S., Guimarães, E.B., de Siqueira, J.M., de Oliveira Filiu, W.F., de Souza Vasconcelos, S.B., do Carmo Vieira, M., 2008. *Baccharis trimera*: effect on hematological and biochemical parameters and hepatorenal evaluation in pregnant rats. J. Ethnopharmacol. 117, 28-33.

Gutiérrez, F., Estévez-Braun, A., Ravelo, A.G., Astudillo, L., Zárate, R., 2007. Terpenoids from the Medicinal Plant *Maytenus ilicifolia*. J. Nat. Prod. 70, 1049-1052.

Haas, A.P.S., 2003. *Categorização tóxico-terapêutica de plantas medicinais usadas no município de Maquiné-Rio Grande do Sul*. Porto Alegre, 56 p. Internship Undergraduate Monograph, Universidade Federal do Rio Grande do Sul.

Haas, J.S., Stolz, E.D., Betti, A.H., Stein, A.C., Schripsema, J., Poser, G.L., Rates, S.M.K., 2011. The anti-immobility effect of hyperoside on the forced swimming test in rats is mediated by the D2-like receptors activation. Planta Med. 77, 334-339.

Hruby, J.V., Porreca, F., Yamamura, H.I., Tollin, G., Agnes, R.S., Lee, Y.S., Cai, M., Alves, I., Cowell, S., Varga, E., Davis, P., Salamon, Z., Roeske, W., Vanderah, T., Lai, J., 2006. New paradigms and tools in drug design for pain and addiction. AAPS J. 8, E450-E460.

IASP, 1986. Classification of chronic pain. Descriptions of chronic pain syndromes and definitions of pain terms. International Association for the Study of Pain. Pain Suppl 3, S1-S225.

Jorge, R.M., Leite, J.P.V., Oliveira, A.B., Tagliati, C.A., 2004. Evaluation of antinociceptive, anti-inflammatory and antiulcerogenic activities of *Maytenus ilicifolia*. J. Ethnopharmacol. 94, 93-100.

Kubo, R., 1997. *Levantamento das plantas de uso medicinal em Coronel Bicaco, RS*. Porto Alegre, 163 p. Master Thesis, Universidade Federal do Rio Grande do Sul.

Kumar, S., Kumar, R., Khan, A., 2011. Medicinal plant resources: manifestation and prospects of life-sustaining healthcare system. Cont. J. Biol. Sci. 4, 19-29.

Langeloh, A., Schenkel, E.P., 1985. Atividade antiespasmódica do extrato alcoólico de marcela (*Achyrocline satureoides* (Lam.) DC., Compositae) sobre a musculatura lisa genital de ratos. Cad. Farm. 1, 38-44.

Leite, J.P., Rastrelli, L., Romussi, G., Oliveira, A.B., Vilegas, J.H., Vilegas, W., Pizza, C., 2001. Isolation and HPLC quantitative analysis of flavonoid glycosides from Brazilian beverages (*Maytenus ilicifolia* and *M. aquifolium*). J. Agr. Food Chem. 49, 3796-3801.

Leitzke, Z.C.S., 2003. *Levantamento das plantas medicinais da comunidade Nossa Senhora da Conceição – Canguçu-RS*. Pelotas, 128 p. Undergraduate Monograph, Universidade Federal de Pelotas.

Lessa, L.C.B., 1986. História do chimarrão. Porto Alegre: Sulina.

Lista de Espécies da Flora do Brasil. Jardim Botânico do Rio de Janeiro. http://floradobrasil.jbrj.gov.br/

Lora, J., 2007. *Avaliação da toxicidade aguda do extrato hidroalcoólico de folhas de Eugenia uniflora L. (Myrtaceae*) 2007. Criciuma, 58 p. Master Thesis, Universidade do Extremo Sul Catarinense.

Losqui, Y.R., Rozete, F.S.S., Almeida, M.B., Bittencourt, A.H.C., Pereira, S.P.F., 2009. Activity of *Baccharis trimera* (Less.) DC. Asteraceae on culture of retinal ganglion cells in vitro. Rev. Bras. Farmacogn. 19, 931-936.

Löwe, T.R., 2004. *Estudo etnobotânico em uma área rural do município de Três de Maio, RS*. Pelotas, 45 p. Undergraduate Monograph, Universidade Federal de Pelotas.

Mahmood, A., Qureshi, R.A., Mahmood, A., Sangi, Y., Shaheen, H., Ahmad, I., Nawaz, Z., 2011. Ethnobotanical survey of common medicinal plants used by people of district Mirpur, AJK, Pakistan. J. Med. Plants Res. 5, 4493-4498.

Mantena, S.K., Mutalik, S., Srinivasa, H., Subramanian, G.S., Prabhakar, K.R., Reddy, K.R., Srinivasan, K.K., Unnikrishnan, M.K., 2005. Antiallergic, antipyretic, hypoglycemic and hepatoprotective effects of aqueous extract of *Coronopus didymus* LINN. Biol. Pharm. Bull. 28, 468-472.

Marodin, S.M., 2000. *Plantas utilizadas como medicinais no município de Dom Pedro de Alcântara, Rio Grande do Sul*. Porto Alegre, 415 p. Master Thesis, Universidade Federal do Rio Grande do Sul.

Martha, E.M., 2003. *O uso das plantas medicinais pela comunidade da associação dos agricultores construtores da Palma – assentamento Vinte e Quatro de Novembro*. Pelotas, 79 p. Undergraduate Monograph, Universidade Federal de Pelotas.

Matos, F.J.A., 2007. Plantas Medicinais: Guia de Seleção e Emprego de Plantas Usadas em Fitoterapia no Nordeste do Brasil, 3rd ed. Fortaleza: Imprensa Universitária.

Mercosur (Mercado Común del Sur), GMC (Grupo Mercado Común) 1993. Resolución nº 46, de 24 de novembro de 1993. Published in GMC acta - 03/1993.

MS, 2009. Relação Nacional de Plantas Medicinais de Interesse ao Sistema Único de Saúde (RENISUS), Ministério da Saúde, http://portal.saude.gov.br/portal/arquivos/pdf/RENISUS.pdf, accessed March 2013.

Montanari, T., Bevilacqua, E., 2004. Effect of *Maytenus ilicifolia* Mart. on pregnant mice. Contraception 65, 171-175.

MTG, 2014. Folclore: Chimarrão. Movimento Tradicionalista Gaúcho. http://www.mtg.org.br/site/fol_chimarrao.php, accessed December 2013.

Nogueira, N.P., Reis, P.A., Laranja, G.A., Pinto, A.C., Aiub, C.A., Felzenszwalb, I., Paes, M.C., Bastos, F.F., Bastos, V.L., Sabino, K.C., Coelho, M.G., 2011. J. Ethnopharmacol. 138, 513-522.

Ohsaki, A., Imai, Y., Naruse, M., Ayabe, S.I., Komiyama, K., Takashima, J., 2004. Four new triterpenoids from *Maytenus ilicifolia*. J. Nat. Prod. 67, 469-471.

Oliveira, C.B., Comunello, L.N., Lunardelli, A., Amaral, R.H., Pires, M.G.S., Silva, G.L., Manfredini, V., Vargas, C.R., Gnoatto, S.C.B., de Oliveira, J.R., Gosmann, G., 2012. Phenolic enriched extract of *Baccharis trimera* presents anti-inflammatory and antioxidant activities. Molecules 17, 1113-1123.

Oliveira, M.G., Monteiro, M.G., Macaúbas, C., Barbosa, V.P., Carlini, E.A., 1991. Pharmacologic and toxicologic effects of two *Maytenus* species in laboratory animals. J. Ethnopharmacol. 34, 29-41.

Paul, E.L., Lunardelli, A., Caberlon, E., de Oliveira, C.B., Santos, R.C., Biolchi, V., Bastos, C.M., Moreira, K.B., Nunes, F.B., Gosmann, G., de Oliveira, J.R., 2009. Anti-inflammatory and immunomodulatory effects of *Baccharis trimera* aqueous extract on induced pleurisy in rats and lymphoproliferation *in vitro*. Inflammation 32, 419-425.

Phillipson, J.D., 2007. Phytochemistry and pharmacognosy. Phytochemistry 68, 2960-2972.

Pinho, D.S., Sturbelle, R.T., Martino-Roth, M.G., Garcias, G.L., 2010. Evaluation of mutagenic activity resulting from the infusion *Baccharis trimera* (Less.) DC. using the *Allium cepa* test and a chromosomal test for aberrations in human lymphocytes. Rev. Bras. Farmacogn. 20, 165-170.

Polydoro, M., de Souza, K.C.B., Andrades, M.E., Da Silva, E.G.B., Bonatto, F., Hey-drichb, J., Dal-Pizzola, F., Schapoval, E.E.S., Bassani, V.L., Moreira, J.C.F., 2004. Antioxidant, pro-oxidant and cytotoxic effects of *Achyrocline satureioides* extracts. Life Sci. 74, 2815-2826.

Portal de Periódicos CAPES. http://www.periodicos.capes.gov.br

Possamai, R.M. 2000. *Levantamento etnobotânico das plantas de uso medicinal em Mariana Pimentel, Rio Grande do Sul*. Porto Alegre, 108 p. Master Thesis, Universidade Federal do Rio Grande do Sul.

Prabhakar, K,R,, Srinivasan, K,K,, Rao, P.G.M., 2002. Chemical investigation, anti-inflammatory and wound healing properties of *Coronopus didymus*. Pharm. Biol. 40, 490-493.

PubMed. http://www.pubmed.com

Radulovic, N., Dorđevic, N., Denic, M., Pinheiro, M.M., Fernandes, P.D., Boylan, F., 2012. A novel toxic alkaloid from poison hemlock (*Conium maculatum* L., Apiaceae): Identification, synthesis and antinociceptive activity. Food Chem. Toxicol. 50, 274-279.

Rajan, S., Jayendran, M., Sethuraman, M., 2005. Folk herbal practices among Toda tribe of the Nilgiri Hills in Tamil Nadu, India. J. Nat. Remedies 5, 52-58.

Rates, S.M.K., 2001. Plants as source of drugs. Toxicon 39, 603-613.

Retta, D., Dellacassa, E., Villamil, J., Suárez, S.A., Bandoni, A.L., 2012. Marcela, a promising medicinal and aromatic plant from Latin America: A review. Ind. Crop Prod. 38, 27-38.

Ritter, M.R., Sobierajski, G.R., Schenkel, E.P., Mentz, L.A., 2002. Plantas Utilizadas como medicinais no município de Ipê, RS, Brasil. Rev. Bras. Farmacogn. 12, 51-62.

Rivera, F., Gervaz, E., Serec, C., Dajas, F., 2004. Toxicological studies of the aqueous extract from *Achyrocline satureioides* (Lam.) DC. (Marcela). J. Ethnopharmacol. 95, 359-362.

Rodrigues, C.R., Dias, J.H., de Mello, R.N., Richter, M.F., Picada, J.N., Ferraz, A.B., 2009. Genotoxic and antigenotoxic properties of *Baccharis trimera* in mice. J. Ethnopharmacol. 125, 97-101.

Sardella, A., Lodi, G., Demarosi, F., Tarozzi, M., Canegallo, L., Carrassi, A., 2008. *Hypericum perforatum* extract in burning mouth syndrome: a randomized placebo-controlled study. J. Oral Pathol. Med. 37, 395-401.

Sawynok, J., 2011. Methylxanthines and pain. Handb. Exp. Pharmacol. 200, 311-329.

SBED, 2012. Brazilian Society for Pain Studies, São Paulo. Available from: http://www.dor.org.br, accessed December 2012.

Schapoval, E.E.S., Silveira, S.M., Miranda, M.L., Alice, C.B., Henriques, A.T., 1994. Evaluation of some pharmacological activities of *Eugenia uniflora* L. J. Ethnopharmacol. 44, 137-142.

Schimizu, M., Tomoo, T., 1994. Anti-inflammatory constituients of topically applied crude drugs. V. Constituints and anti-inflammatory effect of Aoki, *Aucuba japonica* Thunb. Biol. Pharm. Bull. 17, 665-667.

SciELO - Scientific Electronic Library Online. http://www.SciELO.org/php/index.php.

Sebold, D.F., 2003. *Levantamento etnobotânico de plantas de uso medicinal no município de Campo Bom, Rio Grande do Sul, Brasil*. Porto Alegre, 107 p. Master thesis, Universidade Federal do Rio Grande do Sul.

Shirota, O., Morita, H., Takeya, K., Itokawa, H., 1994. Cytotoxic aromatic triterpenes from *Maytenus ilicifolia* and *Maytenus chuchuhuasca*. J. Nat. Prod. 57, 1675-1681.

Silva, K.A., Paszcuk, A.F., Passos, G.F., Silva, E.S., Bento, A.F., Meotti, F.C., Calixto, J.B., 2011. Activation of cannabinoid receptors by the pentacyclic triterpene α,β-amyrin inhibits inflammatory and neuropathic persistent pain in mice. Pain 152, 1872-1887.

Simões, C.M.O., 1988a. Anti-inflammatory action of *Achyrocline satureioides* extracts applied topically. Fitoterapia 59, 419-421.

Simões, C.M.O., Bauer, L., Petrovick, P., Bassani, V.L., 1988c. Analysis of flavonoids from *Achyrocline satureioides* (Lam.) DC. Compositae. Rev. Asociac. Argentina Farm. Bioquím. Ind. 28, 2626-2630.

Simões, C.M.O., Mentz, L.A., Schenkel, E.P., Irgang, B.E., Stehmann, J.R., 1986b. Plantas da medicina popular no Rio Grande do Sul. Porto Alegre: UFRGS.

Simões, C.M.O., Rech, N., Lapa, A.J., 1986a. Investigação farmacologica do extrato aquoso de folhas/caules de *Achyrocline satureioides* (Lam.) DC. Compositae, (Marcela). Cad, Farm. 1, 37-54.

Simões, C.M.O., Schenkel, E.P., Bauer, L., Langeloh, A., 1988b. Pharmacological investigations on *Achyrocline satureioides* (Lam.) DC., Compositae. J. Ethnopharmacol. 22, 281-293.

Soares, E.L.C., Vendruscolo, G.S., Eisinger, S.M., Záchia, R.A., 2004. Estudo etnobotânico do uso dos recursos vegetais em São João do Polêsine, RS, Brasil, no período de outubro de 1999 a junho de 2001. I- Origem do conhecimento. Rev. Bras. Pl. Med. 6, 69-95.

Stevens, P.F. (2001 onwards). Angiosperm Phylogeny Website. Version 12, July 2012 [and more or less continuously updated since]. will do. http://www.mobot.org/MOBOT/research/APweb/.

The Plant List. http://www.theplantlist.org/

Veiga, A.P.F., 2003. *Levantamento das espécies de plantas medicinais usadas pela população do bairro Cohab-Fragata e comparação entre os usos popular e científico da Macela* (Achyrocline satureioides), *Capim-limão* (Cymbopogon citratus) e *Camomila* (Matricaria chamomilla). Pelotas, 42 p. Undergraduate Monograph, Universidade Federal de Pelotas.

Vendruscolo, G.S., 2004. *Estudo etnobotânico das plantas utilizadas como medicinais por moradores do bairro Ponta Grossa, Porto Alegre, Rio Grande do Sul*. Porto Alegre, 276 p. Master Thesis, Universidade Federal do Rio Grande do Sul.

Verdi, L.G., Brighent, I.M.C., Pizzolatti, M.G., 2005. Gênero *Baccharis* (Asteraceae): aspectos químicos, econômicos e biológicos. Quim. Nova 28, 85-94.

WHO, 1992. Quality control methods for medicinal plants material. World Health Organization, Geneva.

WHO, 2007. WHO Normative Guidelines on Pain Management. World Health Organization, Geneva.

WHO, 2008. Traditional medicine. Fact sheet no. 134. World Health Organization, http://www.who.int/mediacentre/factsheets/fs134/en/, accessed February 2012.

Yajía, M.E., González, C.F., Lorca, C.L., Amat, A.G., De Battista, G.A., Sánchez-González, F., 1997. Toxicidad general y genotoxicidad de los extractivos de *Eugenia uniflora* L. (Myrtaceae). An. Soc. Argentina Investig. Prod. Arom. 15, 229-237.

Zanandrea, I., 2003. *Estudo etnobotânico das plantas medicinais mais utilizadas pelos moradores do bairro Santa Terezinha, Pelotas, RS*. Pelotas 68 p. Undergraduate Monograph, Universidade Federal de Pelotas.