

Revisión / Review

Medicinal plants for digestive disorders: A review of ethnobotanical studies conducted in southern Brazil

[Plantas medicinales para los trastornos digestivos:
Una revisión de estudios etnobotánicos realizados en el sur de Brasil]

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Abstract: This review focuses on plant species traditionally used in Rio Grande do Sul, Santa Catarina and Paraná states (southern Brazil) for the relief of digestive disorders. Fifty ethnobotanical studies were compiled, resulting in 384 species mentioned, of which those cited in common to every state were selected. The search retrieved 63 native species used to alleviate gastrointestinal disorders, distributed in 21 botanical families, mainly Asteraceae, Lamiaceae and Myrtaceae. The most cited species include *Achyrocline satureioides* (82%), *Eugenia uniflora* (70%), *Baccharis crispa* (46%), *Psidium cattleianum* (36%), *Solanum paniculatum* (36%) and *Monteverdia ilicifolia* (34%). Scientific studies have corroborated their popular use for the relief the gastrointestinal disorders, but most of them are preclinical and mainly exploratory. In conclusion, the folk use of medicinal species with therapeutic purposes is widespread in southern Brazil, but further studies are needed to guarantee their efficacy and safety.

Keywords: Ethnobotany; Folk Medicine; Ethnobotanical Surveys; Gastrointestinal disorders; Toxicity

Resumen: Esta revisión presenta especies de plantas utilizadas en Rio Grande do Sul, Santa Catarina y Paraná (Sur de Brasil) con enfoque en el alivio de los trastornos digestivos. Se recopilaron 50 estudios etnobotánicos en los que se mencionaron un total de 384 especies, siendo seleccionadas las especies en común a todos los estados. La búsqueda recuperó 63 especies nativas citadas como utilizadas para aliviar trastornos gastrointestinales, distribuidas en 21 familias botánicas, principalmente Asteraceae, Lamiaceae y Myrtaceae. Las especies con mayor frecuencia de citación fueron: *Achyrocline satureioides* (82%), *Eugenia uniflora* (70%), *Baccharis crispa* (46%), *Psidium cattleianum* (36%), *Solanum paniculatum* (36%) y *Monteverdia ilicifolia* (34%). Los estudios científicos han corroborado el uso de especies para el alivio de los trastornos gastrointestinales, pero la mayoría de ellos son preclínicos y principalmente exploratorios. En conclusión, el uso popular de especies medicinales con fines digestivos está muy extendido en el sur de Brasil, pero aún se necesitan estudios científicos para garantizar la eficacia y seguridad de estas plantas.

Palabras clave: Etnobotánica; Medicina popular; Estudios etnobotánicos; Desórdenes gastrointestinales; Toxicidad

INTRODUCTION

Gastrointestinal disorders comprehend a number of unpleasant, common and complex abnormalities affecting the absorption of food and liquids, motility, digestion, and/or excretion processes (Neamsuvam *et al.*, 2012). These effects are manifested in the form of gastric and peptic ulcers, inflammation, diarrhea, constipation and abdominal pain (Greenwood-Van Meerveld *et al.*, 2017). Motor and sensorial dysfunctions of intestines, stomach and liver share a multifactorial pathogenesis, including genetic and environmental causes, microbiome growth, aging and chronic stress (Drossman, 2005; Holtmann *et al.*, 2017). Consequently, such disorders may be highly prevalent and associated with deficits in quality of life, causing mortality and generating substantial costs for health systems (Peery *et al.*, 2015).

Functional dyspepsia, popularly known as indigestion, is the most prevalent digestive syndrome, characterized by epigastric pressure, nausea, bloating, flatulence, diarrhea and abdominal pain (Capasso *et al.*, 2003). These symptoms may be associated with a dysfunction (deficient bile production, ulcer or gastritis) and/or psychosocial factors, including meal ingestion habits and lifestyle (Talley *et al.*, 2006; Hunt *et al.*, 2015). According to the World Gastroenterology Organization, gastroesophageal reflux disease is highly predominant in Western countries, affecting 25% of the population (WGO, 2021). Additionally, the Brazilian Federation of Gastroenterology estimates that nearly half of the population in the country reports dyspeptic symptoms (FBG, 2021).

Despite the efforts of pharmaceutical industry on the development of more effective medicines, few novel therapies have been recently introduced in the clinical practice, and the most available agents only aim to relieve the symptoms of dyspepsia (Madisch *et al.*, 2004). The current management for dyspepsia includes a therapeutic arsenal restricted to antacids, histamine H₂-receptor antagonists and proton pump inhibitors agents, all sharing a significant number of safety concerns related to their use (Tack *et al.*, 2006; Tack *et al.*, 2018).

Herbal medications are widely used in many countries as digestive agents, but controlled data supporting their efficacy are generally lacking. Nevertheless, the folk use of plants in primary health care for the treatment of acute and chronic diseases has attracted the attention of academia, pharmaceutical companies and regulatory agencies, leading to the study of local native species and their

active principles, and supporting the safety and efficacy of traditional herbal drugs or phytomedicines with therapeutic purposes (Dutra *et al.*, 2016).

The Committee on Herbal Medicinal Products (HMPC-EMA) and the European Scientific Cooperative on Phytomedicines (ESCOP) established a number of monographs of effective medicinal plants for the treatment of gastrointestinal complaints (Kelber *et al.*, 2017). The compendia include cholagogue/choleretic drugs (e.g. *Cynara cardunculus* L. leaves), carminatives (e.g. *Pimpinella anisum* L. seeds), anti-dyspeptics (e.g. *Matricaria chamomilla* L. flowers), antikinetic (e.g. *Zingiber officinale* Roscoe rhizomes) and laxatives (e.g. *Senna alexandrina* Mill. leaves).

Considering the huge biodiversity and the ethnically orientated use of medicinal plants, the Brazilian National Health Surveillance Agency (Anvisa) recognizes the traditional herb drugs as medicines, publishing several directives to indicate secure and effective plant species through a simplified registration (Brasil, 2014). Among these, *Glycyrrhiza glabra* L., *Matricaria chamomilla* L., *Melissa officinalis* L., *Monteverdia ilicifolia* (Mart. ex Reissek) Biral, *Monteverdia aquifolia* (Mart.) Biral, *Peumus boldus* Molina, and *Silybum marianum* (L.) Gaertn. are referred for the treatment of gastrointestinal disorders.

Ethnobotanical studies, as those demonstrating the popular use of plants for digestive ailments in southern Brazil (Ritter *et al.*, 2002; Meyer *et al.*, 2012; Staniski *et al.*, 2014), can be considered as systematized repositories of medicinal plant informations and cultural knowledge of local communities. Additionally, the resulting data can work as a pre-selection of specific plants to be investigated in therapeutics, in order to validate their folk use (Matos, 1989). Keeping in mind the above, this article will focus on a compilation of ethnobotanical studies conducted in the three Brazilian southern states: Paraná (PR), Santa Catarina (SC) and Rio Grande do Sul (RS), regarding the botanical, geographical, pharmacological and toxicological data for medicinal plants used for the management of gastrointestinal disorders, with emphasis on native species.

MATERIALS AND METHODS

Fifty ethnobotanical studies comprising data from local communities (including original articles, thesis, dissertations and monographs) performed by researchers in RS, SC and PR states, Brazil were

consulted. These studies were assessed from virtual databases (PubMed – <http://www.pubmed.com>, SciELO – <http://www.sciELO.com> and Portal de Periódicos CAPES – <http://periodicos.capes.gov.br>), digital university repositories or regional university libraries (Stolz *et al.*, 2014). The keywords used were in both English and Portuguese: folk medicine and *medicina popular*, ethnobotany and *etnobotânica*; all combined with Rio Grande do Sul, Santa Catarina, Paraná, southern Brazil and *sul do Brasil*. The criteria

for the selection of ethnobotanical studies included: accessibility, presence of a botanist in the identification of plant species or in the team of authors, and publication interval up to and including December 2020. These studies were grouped according to each mesogeographical region of the abovementioned states, according to the Brazilian Institute of Geography and Statistics (IBGE) classification (IBGE, 2009), as listed in Table No. 1

Table No. 1

Mesogeographic regions of Southern Brazil states, as defined by IBGE (2009), including the studies found for each region and the municipalities investigated

Rio Grande do Sul State		
Mesogeographic regions	Municipalities	Studies
Centro-Occidental Riograndense	Santa Maria	(1) Somavilla & Canto-Dorow, 1996
	São João do Polêsine	(2) Soares <i>et al.</i> , 2004
Centro-Oriental Riograndense	Teutônia	(3) Schwambach, 2007
Metropolitana de Porto Alegre	Campo Bom	(4) Sebold, 2003
	Dom Pedro de Alcântara	(5) Marodin & Baptista, 2001
	Mariana Pimentel	(6) Possamai, 2000
	Nova Santa Rita	(7) Souza, 2007
	Porto Alegre	(8) Vendruscolo & Mentz, 2006; (9) Baldauf <i>et al.</i> , 2009; (10) Baptista <i>et al.</i> , 2013
	Rio Grande	(11) Borges, 2010
Nordeste Riograndense	Riozinho	(12) Koch, 2000
	Caxias do Sul	(13) Piva, 1998
Noroeste Riograndense	Ipê	(14) Ritter <i>et al.</i> , 2002
	Coronel Bicaco	(15) Kubo, 1997; (16) Magalhães, 1997
	Cruz Alta	(17) Garlet & Irgang, 2001
	Erebango	(18) Coan & Matias, 2014
Sudeste Riograndense	Palmeira das Missões	(19) Battisti <i>et al.</i> , 2013
	São Luiz Gonzaga	(20) Barros <i>et al.</i> , 2007
	Arroio do Padre, Canguçu, Morro Redondo, Pelotas and São Lourenço do Sul	(21) Borba, 2008; (22) Ceolin <i>et al.</i> , 2011
Sudoeste Riograndense	São Gabriel	(23) Löbner <i>et al.</i> , 2014
Santa Catarina State		
Grande Florianópolis	Florianópolis	(24) Melo <i>et al.</i> , 2008; (25) Giraldi & Hanazaki, 2010
Norte Catarinense	Itapoá	(26) Meretika, 2008
Oeste Catarinense	No studies were found	
Serra Catarinense	Anita Garibaldi, Campo Belo do Sul, Cerro Negro, Lages and São José do Cerrito	(27) Duarte <i>et al.</i> , 2020
	Lages	(28) Amorim, 2010

	Anita Garibaldi, Bocaina do Sul, Bom Jardim da Serra, Bom Retiro, Campo Belo do Sul, Capão Alto, Cerro Negro, Correia Pinto, Lages, Otacílio Costa, Paniel, Palmeira, Ponte Alta, Rio Rufino, São Joaquim, São José do Cerrito, Urubici and Urupema	(29) Fernandes, 2014
Sul Catarinense	Araranguá	(30) Aguiar, 2013
	Criciúma	(31) Tomazi <i>et al.</i> , 2014
	Imbituba, Garopaba	(32) Avila, 2012
Vale do Itajaí	Apiúna	(33) Tribess <i>et al.</i> , 2015
	Ascurra	(34) Meyer <i>et al.</i> , 2012
	Blumenau	(35) Zeni & Bosio, 2011
	Gaspar	(36) Pereira <i>et al.</i> , 2011
Paraná State		
Centro-Oriental Paranaense	Ponta Grossa	(37) Staniski <i>et al.</i> 2014
Centro-Sul Paranaense	Laranjal, Laranjeiras do Sul, Nova Laranjeiras, Palmital, Porto Barreiro and Rio Bonito do Iguaçu	(38) Rauber, 2016
Metropolitana de Curitiba	Adrianópolis	(39) Spisla, 2017
	Almirante Tamandaré	(40) Oliveira, 2004
	Campo Largo	(41) Gonçalves, 2017
	Doutor Ulysses	(42) Lopes, 2010
	Guaraqueçaba	(43) Lima, 1996; (44) Nogata, 2002
	Guaratuba	(45) Negrelle & Fornazzari, 2007a
	Matinhos	(46) Silva <i>et al.</i> , 2015
Norte-Central Paranaense	No studies were found	
Norte-Pioneiro Paranaense	Bandeirantes	(47) Fuck <i>et al.</i> , 2005
Noroeste Paranaense	No studies were found	
Oeste Paranaense	Cascavel	(48) Tomazzoni, 2004; (49) Negrelle <i>et al.</i> , 2007b
	São Pedro do Iguaçu	(50) Bolson <i>et al.</i> , 2015
Sudeste Paranaense	No studies were found	
Sudoeste Paranaense	No studies were found	

The native and exotic species cited in common for every state among the fifty ethnobotanical studies were listed; furthermore, those mentioned as useful for gastrointestinal disorders were selected. Reports that provided only the genus or popular names were not considered for further analysis. The search terms used to the classification of the species as helpful to digestive disorders were: stomachache, bellyache, gases, gastritis, ulcer, congestion, laxative, diarrhea, dysentery, digestive,

bad digestion, liver disturbances; liver and related ones, like stomach, liver and intestines, including the corresponding words in Portuguese. The native species with at least one common citation among the states of RS, SC and PR were selected to analyze the available scientific information regarding chemical composition, biological and pharmacological properties and toxicity.

Clinical and preclinical studies were searched in SciELO (<http://www.sciELO.com>), PubMed

(<http://pubmed.com>) and Portal de Periódicos CAPES (<http://periodicos.capes.gov.br>). The scientific name of each plant was combined with the terms digestive (*digestivo*), congestion (*congestão*), liver (*fígado*), toxicity (*toxicidade*), chemical composition (*composição química*) and biological activity (*atividade biológica*). Additionally, the total number of publications for each species found in PubMed and SciELO were registered. The number of Theses found in the Catálogo de Teses & Dissertações - CAPES (<http://catalogodeteses.capes.gov.br>) was considered.

The popular names mentioned for the species were compiled and preserved in our work. The valid scientific name of the species and the authors, possible synonymies and origin (native or exotic) were confirmed using The Plant List (2021), and Flora do Brasil 2020 (2021). Citation frequency was calculated as follows: number of studies that cite the species $\times (100) /$ total number of studies. The botanical families were updated based on the APG IV classification system (Stevens, 2017).

RESULTS AND DISCUSSION

From the fifty ethnobotanical studies consulted, 384 species indicated to treat gastrointestinal dysfunctions were collected, confirming that digestive complaints represent an important health concern in southern Brazil. All species mentioned in at least one study belonging to one state were listed, and some of them were cited in more than one study, resulting in a total of 1524 plant citations distributed among the states of RS (54.1%), PR (23.9%) and SC (22%).

Sixty-three species (natives, exotics and subsponaneous) were mentioned as having some common traditional use in all southern states, which constitutes 56.7% (864) of the total citations (Chart No. 2). Sixty-eight percent of the cited species are exotic and 32% native. The use of medicinal exotic species is frequent in Brazil, as previously described (Stolz et al., 2014; Gross et al., 2019). Many species of the families Asteraceae and Lamiaceae are exotic and cultivated in domestic and medicinal gardens. The herbaceous species, predominant in these families, are more easily cultivated and collected by the population.

The compiled species indicated for gastrointestinal dysfunctions were identified as members of 21 botanical families, with Asteraceae (n=16) as the most frequently cited, followed by Lamiaceae (n=12) and Myrtaceae (n=5). These results are in accordance with previous

ethnobotanical studies conducted in others regions of Brazil (Sousa et al., 2010; Brito & Senna-Valle, 2011; Pereira et al., 2012; Gois et al., 2016). According to Gomes & Lima (2017), the predominant use of species from Asteraceae and Lamiaceae is probably because they adapt to both tropical and temperate environments.

In Chart 1, the studies performed in each municipality located in RS (23), SC (13) and PR (14) were classified by their corresponding mesogeographic regions. It should be noted that the metropolitan regions of Curitiba and Porto Alegre concentrate 34% of the studies. Most of them were conducted in municipalities located in the Atlantic Forest biome, which encompasses the southern states of Brazil, characterized by its rich biodiversity (Pinto et al., 2006). According to Ritter et al. (2015), a greater number of ethnobotanical studies conducted in this ecosystem is related as a direct consequence of the proximity of the most important universities.

Regarding plant habit, 58.7% of the species (n=37) were herbaceous, 22.3% (n=14) were arboreal and 19% (n=12) were shrubby. Leaves are the most frequently used parts (94%), while 36.5% of the plants have the flowers or inflorescences used. Additionally, 41.2% of the cited species had their aerial parts used and 27% had the whole plant used. The majority of species used as medicinal plants are perennial, which favors the use of their leaves throughout Brazil (Santos et al., 2008; Pereira et al., 2009; Sousa et al., 2010; Brito & Senna-Valle, 2011).

The predominant form of preparation cited in the studies was “tea”, the standardized term employed for both infusion and decoction (98.4%), followed by water maceration (33.3%), alcoholatures (22.2%), food (20.6%), syrup (14.3%) and tinctures (8%). Besides, the use of plants associated with *chimarrão* (20.6%), a typical aqueous South American beverage of *Ilex paraguariensis* St. Hill. leaves, was also mentioned. Some reports described the common combination of other plants with *chimarrão*, either as medicinal or to flavor the drink. It is interesting to note that this use is reported by descendants of the *gauchos*, who maintain this social habit in other Brazilian regions, including the states of Rondônia (Santos et al., 2008) and Mato Grosso do Sul (Cunha & Bortolotto, 2011).

Eight species were cited in more than half of the studies surveyed: *Achyrocline satureioides* (82%), *Plectranthus barbatus* (80%), *Artemisia absinthium* and *Foeniculum vulgare* (74%), *Eugenia uniflora* (70%), *Matricaria chamomilla* and *Psidium guajava*

(62%) and *Punica granatum* (58%). Of these, only *A. satureioides* and *E. uniflora* are native to the Brazilian flora. The common use indicated for these eight species was digestive, in order to relief dyspepsia, bellyache, heartburn, nausea and diarrhea. Of note, the most frequently cited exotic species for digestive disorders was *Plectranthus barbatus*, which is widely used in southern Brazil and shares a high number of citations in ethnobotanical surveys conducted among the other regions of Brazil (Pilla *et al.*, 2006; Zucchi *et al.*, 2013; Fiebig & Pasa, 2016). It is known as “*boldo/falso-boldo*”, indicated by the Pharmacotherapeutic Formulary of the Brazilian Pharmacopoeia (PFBP) as an antidyspeptic (infusion, alcoholature and tincture), with the warning that the continuous use may induce toxicity and gastric irritation (Brasil, 2021).

The native species (n=20) more frequently mentioned for treating gastrointestinal disorders in southern Brazil were cited in the studies as being hepatoprotective, antispasmodic, antiulcer, gastroprotective and antidiarrheal. However, despite the wide folk use of these species, there is a lack of preclinical and, mainly, clinical studies to validate some of the pharmacological activities regarding their effects on the digestive system. A brief numerical analysis of the scientific data about the abovementioned native species (Table No. 1) has shown that the majority of the studies are indexed in the Catálogo de Teses e Dissertações CAPES, a Brazilian database. Additionally, a careful examination of pharmacological studies on medicinal plants in Brazil revealed that most investigations were conducted with crude extracts, with few clinical trials or studies on the toxicology, pharmacokinetics, and mechanisms of action using isolated compounds (Dutra *et al.*, 2016). Because the bioactive constituents are still unknown for most of the plants, the native species listed in Table No. 3 were subdivided into three different categories, according to the phytocomplex described for each of them.

The largest group of plants contains phenolic compounds as the main constituents, including flavonoids, tannins, phenolic acids and iridoids. Flavonoids are highlighted, since they are widely distributed and share a spectrum of relevant biological activities that may explain the beneficial actions on the digestive system, including antioxidant, anti-inflammatory and spasmolytic (Kelber *et al.*, 2017). Among these species, *Achyrocline satureioides*, *Baccharis crispa*, *Baccharis articulata* and *Bauhinia forficata*, share

preclinical gastrointestinal activities described in animal models, related to their content in flavonoids.

Infusions of *Achyrocline satureioides* inflorescences are indicated by the PFBP as antispasmodic, antidyspeptic and anti-inflammatory (Brasil, 2021). Quercetin is the main constituent of the total flavonoid content of the plant drug, accounting for at least 0.8% of its composition (Brasil, 2019). Studies conducted with hydroalcoholic extracts from *A. satureioides* aerial parts demonstrated antiulcer effect with no signs of toxicity in rats (Santin *et al.*, 2010) and antispasmodic effect on isolated rat-isolated jejunum (Silva & Langeloh, 1994). Preclinical assays confirmed the anti-inflammatory and immunomodulatory properties of the aqueous and ethanolic extracts obtained from aerial parts, leaves and flowers (Santos *et al.*, 1999; Cosentino *et al.*, 2008; Barioni *et al.*, 2013). Of interest, it was found that quercetin protects against gastric inflammation and apoptosis associated with *Helicobacter pylori* infection (Zhang *et al.*, 2017). Clinical studies are not available.

Baccharis crispa winged stems are indicated in the PFBP (infusion and tincture) as antidyspeptic, with the warning that they should not be used chronically due to the risk of leukopenia (Brasil, 2021). The gastroprotective and curative effects of a *B. crispa* hydroalcoholic extract were demonstrated in rats, attributed to the presence of flavonoids and caffeoylquinic acids (Lívero *et al.*, 2016). The antacid and antiulcer effects of an aqueous extract and isolated polyphenols were verified on rats and mice (Biondo *et al.*, 2011). Both *B. crispa* and *B. articulata* are popularly known as carquejas and used as hepatoprotective homemade remedies in South Brazil (Simões *et al.*, 1998), but only the former was investigated in preclinical studies (Pádua *et al.*, 2014; Rabelo *et al.*, 2018). Additionally, both species were mentioned for treating stomachache, bellyache and colics, but only *B. articulata* was found to be effective as an antispasmodic in mice (Toso & Boeris, 2010). No clinical studies were not found for the species.

Bauhinia forficata, known as *pata-de-vaca*, is traditionally used to treat several diseases, among them diabetes (Trojan-Rodrigues *et al.*, 2012). The hypoglycemic effect of the extracts obtained from leaves has been extensively demonstrated in animal models and clinical studies, showing few measurable toxic parameters (Pepato *et al.*, 2004; Damasceno *et al.*, 2004; Cunha *et al.*, 2010; Mariángel *et al.*, 2019);

the high content of flavonoids in the derived preparations seem to contribute to such an effect (Ferrerres *et al.*, 2012). Mazzeo *et al.* (2015) described the gastroprotective effect of an infusion of *B.*

forficata leaves in rodents, supporting its folk use as a remedy for stomach disorders and bad digestion, as mentioned in the ethnobotanical studies.

Table No. 2
Number of scientific studies indexed in Brazilian (Banco de Teses Capes and SciELO) and international (PubMed) databases on selected native species

Species	Scientific literature (number of publications)		
	Banco de Teses CAPES	SciELO	PubMed
<i>Achyrocline satureioides</i>	92	27	75
<i>Aloysia gratissima</i>	25	15	14
<i>Alternanthera brasiliana</i>	35	10	16
<i>Baccharis articulata</i>	19	13	9
<i>Baccharis crispa</i>	135	58	56
<i>Bauhinia forficata</i>	117	54	62
<i>Campomanesia xanthocarpa</i>	100	34	43
<i>Cuphea carthagenensis</i>	19	6	16
<i>Echinodorus grandiflorus</i>	37	16	24
<i>Eugenia uniflora</i>	305	138	140
<i>Lippia alba</i>	262	140	121
<i>Monteverdia aquifolia</i>	7	3	4
<i>Monteverdia ilicifolia</i>	126	63	85
<i>Plantago australis</i>	7	5	5
<i>Psidium cattleianum</i>	47	27	11
<i>Plinia peruviana</i>	9	5	8
<i>Sida rhombifolia</i>	66	73	35
<i>Solanum paniculatum</i>	75	24	30
<i>Stachytarpheta cayennensis</i>	23	19	10
<i>Zanthoxylum rhoifolium</i>	41	17	20

Table No. 3

Medicinal plants used for the relief of gastrointestinal disorders mentioned in the ethnobotanical studies in Rio Grande do Sul State (RS), Santa Catarina State (SC) and Paraná State (PR) – Brazil, distributed by family, parts of plant used and preparation form reported, with references.

Origin: E=exotic, N= native. Habit: H=herb, S=shrub, T=tree. Prepare form: A=alcoholature, C=condiment, CH=*chimarrão*, F=food, M=maceration in water, S=syrup, T=tea, TN=tincture. Used parts: AP=aerial parts, B=barks, BR=branches, F=flowers, FR=fruit, I=inflorescences, L=leaves, P=fruit peel, R=roots, S=seeds, SH=shoots, ST=stems, T=tuber, WP=whole plant

Frequency	Species/ Family/ Popular name	Origin	Habits	Prepare form	Used parts	References
82%	<i>Achyrocline satureioides</i> (Lam.) DC./ Asteraceae/ Marcela	N	H	CH, T	AP, F, I, WP	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Piva, 1998; Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Sebold, 2003; Oliveira, 2004; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Vendruscolo & Mentz, 2006; Negrelle <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Schwambach, 2007; Souza, 2007; Borba, 2008; Melo <i>et al.</i> , 2008; Meretika, 2008; Baldauf <i>et al.</i> , 2009; Amorim, 2010; Borges, 2010; Lopes, 2010; Ceolin <i>et al.</i> , 2011; Pereira <i>et al.</i> , 2011; Zeni & Bosio, 2011; Avila, 2012; Meyer <i>et al.</i> , 2012; Aguiar, 2013; Baptista <i>et al.</i> , 2013; Battisti <i>et al.</i> , 2013; Coan & Matias, 2014; Fernandes, 2014; Löbler <i>et al.</i> , 2014; Staniski <i>et al.</i> 2014; Bolson <i>et al.</i> , 2015; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016; Duarte <i>et al.</i> , 2020
80%	<i>Plectranthus barbatus</i> Andr./ Lamiaceae/ Boldo	E	H	M, T	L, R, ST, WP	Lima, 1996; Somavilla & Canto-Dorow, 1996; Kubo, 1997; Piva, 1998; Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Nogata, 2002; Ritter <i>et al.</i> , 2002; Sebold, 2003; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Fuck <i>et al.</i> , 2005; Vendruscolo & Mentz, 2006; Barros <i>et al.</i> , 2007; Negrelle <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Schwambach, 2007; Souza, 2007; Borba, 2008; Meretika, 2008; Baldauf <i>et al.</i> , 2009; Giraldi & Hanazaki, 2010; Lopes, 2010; Ceolin <i>et al.</i> , 2011; Pereira <i>et al.</i> , 2011; Zeni & Bosio, 2011; Meyer <i>et al.</i> , 2012; Aguiar, 2013; Baptista <i>et al.</i> , 2013; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Löbler <i>et al.</i> , 2014; Staniski <i>et al.</i> 2014; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016; Gonçalves, 2017; Spisla, 2017; Duarte <i>et al.</i> , 2020
74%	<i>Artemisia absinthium</i> L./ Asteraceae/ Losna	E	H	M, S, T	AP, BR, F, L, R	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Piva, 1998; Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Nogata, 2002; Ritter <i>et al.</i> , 2002;

						Sebold, 2003; Oliveira, 2004; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Vendruscolo & Mentz, 2006; Barros <i>et al.</i> , 2007; Negrelle <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Schwambach, 2007; Souza, 2007; Borba, 2008; Meretika, 2008; Borges, 2010; Giraldi & Hanazaki, 2010; Ceolin <i>et al.</i> , 2011; Pereira <i>et al.</i> , 2011; Zeni & Bosio, 2011; Avila, 2012; Meyer <i>et al.</i> , 2012; Aguiar, 2013; Baptista <i>et al.</i> , 2013; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Staniski <i>et al.</i> , 2014; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016; Duarte <i>et al.</i> , 2020
74%	<i>Foeniculum vulgare</i> Mill. / Apiaceae/ Funcho	E	H	CH, F, M, T, TN	AP, BR, L, R, SD, ST, WP	Lima, 1996; Somavilla & Canto-Dorow, 1996; Kubo, 1997; Magalhães, 1997; Piva, 1998; Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Sebold, 2003; Oliveira, 2004; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Vendruscolo & Mentz, 2006; Barros <i>et al.</i> , 2007; Negrelle <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Souza, 2007; Borba, 2008; Meretika, 2008; Baldauf <i>et al.</i> , 2009; Borges, 2010; Giraldi & Hanazaki, 2010; Lopes, 2010; Ceolin <i>et al.</i> , 2011; Pereira <i>et al.</i> , 2011; Avila, 2012; Meyer <i>et al.</i> , 2012; Aguiar, 2013; Baptista <i>et al.</i> , 2013; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Löbler <i>et al.</i> , 2014; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016; Gonçalves, 2017
70%	<i>Eugenia uniflora</i> L./ Myrtaceae/ Pitangueira	N	T	F, M, S, T	AP, B, L, FR, SH, ST	Lima, 1996; Somavilla & Canto-Dorow, 1996; Kubo, 1997; Piva, 1998; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Nogata, 2002; Ritter <i>et al.</i> , 2002; Sebold, 2003; Soares <i>et al.</i> , 2004; Vendruscolo & Mentz, 2006; Barros <i>et al.</i> , 2007; Negrelle <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Souza, 2007; Borba, 2008; Melo <i>et al.</i> , 2008; Baldauf <i>et al.</i> , 2009; Borges, 2010; Giraldi & Hanazaki, 2010; Lopes, 2010; Ceolin <i>et al.</i> , 2011; Zeni & Bosio, 2011; Avila, 2012; Meyer <i>et al.</i> , 2012; Baptista <i>et al.</i> , 2013; Battisti <i>et al.</i> , 2013; Coan & Matias, 2014; Tomazzoni, 2004; Bolson <i>et al.</i> , 2015; Silva <i>et al.</i> , 2015; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016; Gonçalves, 2017

62%	<i>Matricaria chamomilla</i> L./ Asteraceae/ Camomila	E	H	A, CH, T	AP, F, I, L	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Piva, 1998; Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Nogata, 2002; Ritter <i>et al.</i> , 2002; Sebold, 2003; Oliveira, 2004; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Barros <i>et al.</i> , 2007; Negrelle <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Souza, 2007; Giraldi & Hanazaki, 2010; Pereira <i>et al.</i> , 2011; Zeni & Bosio, 2011; Avila, 2012; Aguiar, 2013; Battisti <i>et al.</i> , 2013; Coan & Matias, 2014; Fernandes, 2014; Löbler <i>et al.</i> , 2014; Rauber <i>et al.</i> , 2016; Gonçalves, 2017; Spisla, 2017; Duarte <i>et al.</i> , 2020
62%	<i>Psidium guajava</i> L./ Myrtaceae/ Goiabeira	E	T	F, T	FR, L, P, SH	Lima, 1996; Somavilla & Canto-Dorow, 1996; Kubo, 1997; Piva, 1998; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Sebold, 2003; Soares <i>et al.</i> , 2004; Vendruscolo & Mentz, 2006; Barros <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Souza, 2007; Borba, 2008; Melo <i>et al.</i> , 2008; Meretika, 2008; Baldauf <i>et al.</i> , 2009; Borges, 2010; Giraldi & Hanazaki, 2010; Ceolin <i>et al.</i> , 2011; Pereira <i>et al.</i> , 2011; Zeni & Bosio, 2011; Avila, 2012; Meyer <i>et al.</i> , 2012; Aguiar, 2013; Baptista <i>et al.</i> , 2013; Silva <i>et al.</i> , 2015; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016; Gonçalves, 2017
58%	<i>Punica granatum</i> L./ Lythraceae/ Romã	E	T	F, T	F, FR, R, S, ST	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Piva, 1998; Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Sebold, 2003; Oliveira, 2004; Soares <i>et al.</i> , 2004; Fuck <i>et al.</i> , 2005; Vendruscolo & Mentz, 2006; Barros <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Souza, 2007; Borba, 2008; Baldauf <i>et al.</i> , 2009; Borges, 2010; Ceolin <i>et al.</i> , 2011; Zeni & Bosio, 2011; Avila, 2012; Baptista <i>et al.</i> , 2013; Battisti <i>et al.</i> , 2013; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016; Gonçalves, 2017; Duarte <i>et al.</i> , 2020
46%	<i>Baccharis crispa</i> Spreng./ Asteraceae/ Carqueja	N	S	M, T	AP, L, R, WP	Lima, 1996; Piva, 1998; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Nogata, 2002; Sebold, 2003; Vendruscolo & Mentz, 2006; Negrelle & Fornazzari, 2007; Borba, 2008; Meretika, 2008; Amorim, 2010; Lopes, 2010; Ceolin <i>et al.</i> , 2011; Zeni & Bosio, 2011; Meyer <i>et al.</i> , 2012; Aguiar, 2013; Coan & Matias, 2014; Fernandes, 2014; Löbler <i>et al.</i> , 2014; Tribess <i>et</i>

						<i>al.</i> , 2015; Rauber <i>et al.</i> , 2016; Duarte <i>et al.</i> , 2020
46%	<i>Cynara cardunculus</i> L./ Asteraceae/ Alcachofra	E	H	A, CH, F, M, T	F, L, R, ST	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Piva, 1998; Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Sebold, 2003; Oliveira, 2004; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Negrelle <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Schwambach, 2007; Giraldi & Hanazaki, 2010; Ceolin <i>et al.</i> , 2011; Avila, 2012; Battisti <i>et al.</i> , 2013; Löbler <i>et al.</i> , 2014; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016; Gonçalves, 2017; Duarte <i>et al.</i> , 2020
42%	<i>Tanacetum vulgare</i> L./ Asteraceae/ Catinga-de-mulata	E	H	A, M, T, TN	AP, F, L, ST, R, S	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Piva, 1998; Koch, 2000; Possamai, 2000; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Sebold, 2003; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Vendruscolo & Mentz, 2006; Barros <i>et al.</i> , 2007; Negrelle <i>et al.</i> , 2007; Meretika, 2008; Borges, 2010; Ceolin <i>et al.</i> , 2011; Avila, 2012; Fernandes, 2014; Rauber <i>et al.</i> , 2016; Gonçalves, 2017; Duarte <i>et al.</i> , 2020
38%	<i>Rosmarinus officinalis</i> L./ Lamiaceae/ Alecrim	E	S	A, C, M, T	AP, L, ST, R	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Piva, 1998; Koch, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Soares <i>et al.</i> , 2004; Vendruscolo & Mentz, 2006; Schwambach, 2007; Borges, 2010; Barros <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Pereira <i>et al.</i> , 2011; Avila, 2012; Fernandes, 2014; Löbler <i>et al.</i> , 2014; Staniski <i>et al.</i> , 2014; Silva <i>et al.</i> , 2015
36%	<i>Psidium cattleianum</i> Sabine/ Myrtaceae/ Araçá	N	T	T	B, FR, L, SH	Lima, 1996; Possamai, 2000; Marodin & Baptista, 2001; Nogata, 2002; Ritter <i>et al.</i> , 2002; Sebold, 2003; Oliveira, 2004; Vendruscolo & Mentz, 2006; Souza, 2007; Meretika, 2008; Borges, 2010; Giraldi & Hanazaki, 2010; Avila, 2012; Baptista <i>et al.</i> , 2013; Tomazi <i>et al.</i> , 2014; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016; Gonçalves, 2017
36%	<i>Gymnanthemum amygdalinum</i> (Delile) Sch. Bip. ex Walp./Asteraceae/ Boldo-da-folha-lisa	E	T	M, T	L	Lima, 1996; Possamai, 2000; Garlet & Irgang, 2001; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Negrelle <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Meretika, 2008; Giraldi & Hanazaki, 2010; Pereira <i>et al.</i> , 2011; Zeni & Bosio, 2011; Avila, 2012; Meyer <i>et al.</i> , 2012; Aguiar, 2013; Baptista <i>et al.</i> , 2013; Battisti <i>et al.</i> , 2013; Rauber <i>et al.</i> , 2016; Spisla, 2017

36%	<i>Solanum paniculatum</i> L./ Solanaceae/ Jurubeba	N	S	A, S, M, T, X	AP, F, FR, L, R, ST, WP	Magalhães, 1997; Piva, 1998; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Nogata, 2002; Soares <i>et al.</i> , 2004; Vendruscolo & Mentz, 2006; Souza, 2007; Borba, 2008; Baldauf <i>et al.</i> , 2009; Borges, 2010; Pereira <i>et al.</i> , 2011; Avila, 2012; Meyer <i>et al.</i> , 2012; Battisti <i>et al.</i> , 2013; Bolson <i>et al.</i> , 2015; Tribess <i>et al.</i> , 2015
34%	<i>Monteverdia ilicifolia</i> (Mart. ex Reissek) Biral/ Celastraceae/ Espinheira-santa	N	T	CH, T	AP, L, R	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Koch, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Sebold, 2003; Oliveira, 2004; Tomazzoni, 2004; Fuck <i>et al.</i> , 2005; Negrelle <i>et al.</i> , 2007; Schwambach, 2007; Meretika, 2008; Amorim, 2010; Pereira <i>et al.</i> , 2011; Battisti <i>et al.</i> , 2013; Rauber <i>et al.</i> , 2016
32%	<i>Aloysia gratissima</i> (Gillies & Hook.) Tronc./ Verbenaceae/ Erva-santa, erva-cidreira	N	S	A, T	B, L, ST	Somavilla & Canto-Dorow, 1996; Koch, 2000; Marodin & Baptista, 2001; Sebold, 2003; Soares <i>et al.</i> , 2004; Vendruscolo & Mentz, 2006; Schwambach, 2007; Souza, 2007; Borges, 2010; Avila, 2012; Meyer <i>et al.</i> , 2012; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Löbler <i>et al.</i> , 2014; Gonçalves, 2017
32%	<i>Plectranthus ornatus</i> Codd/ Lamiaceae/ Boldinho	E	H	M, T	F, L	Sebold, 2003; Oliveira, 2004; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Vendruscolo & Mentz, 2006; Barros <i>et al.</i> , 2007; Negrelle <i>et al.</i> , 2007; Meretika, 2008; Borges, 2010; Giraldo & Hanazaki, 2010; Pereira <i>et al.</i> , 2011; Zeni & Bosio, 2011; Meyer <i>et al.</i> , 2012; Baptista <i>et al.</i> , 2013; Rauber <i>et al.</i> , 2016; Gonçalves, 2017
32%	<i>Stachytarpheta</i> <i>cayennensis</i> (Rich.) Vahl/ Verbenaceae/ Gervão- roxo	N	S	S, T	AP, B, F, L, R, ST, WP	Magalhães, 1997; Piva, 1998; Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Sebold, 2003; Negrelle & Fornazzari, 2007; Borba, 2008; Meretika, 2008; Borges, 2010; Ceolin <i>et al.</i> , 2011; Pereira <i>et al.</i> , 2011; Avila, 2012; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Bolson <i>et al.</i> , 2015
30%	<i>Achillea millefolium</i> L./ Asteraceae/ Ponto-alívio, mil-em-ramas	E	S	CH, T	F, L, R, ST, WP	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Soares <i>et al.</i> , 2004; Barros <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Souza,

						2007; Giraldi & Hanazaki, 2010; Meyer <i>et al.</i> , 2012; Fernandes, 2014; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016
30%	<i>Bidens pilosa</i> L./ Asteraceae/ Picão-preto	E	H	F, T, TN	AP, F, L, R, WP	Lima, 1996; Somavilla & Canto-Dorow, 1996; Piva, 1998; Possamai, 2000; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Sebold, 2003; Oliveira, 2004; Vendruscolo & Mentz, 2006; Negrelle & Fornazzari, 2007; Meretika, 2008; Amorim, 2010; Bolson <i>et al.</i> , 2015; Tribess <i>et al.</i> , 2015; Spisla, 2017
30%	<i>Cymbopogon citratus</i> (D C.) Stapf/ Poaceae/ Capim-cidró, cidreira	E	H	F, CH, T, X	L, R, WP	Somavilla & Canto-Dorow, 1996; Magalhães, 1997; Piva, 1998; Marodin & Baptista, 2001; Nogata, 2002; Sebold, 2003; Soares <i>et al.</i> , 2004; Negrelle & Fornazzari, 2007; Giraldi & Hanazaki, 2010; Pereira <i>et al.</i> , 2011; Avila, 2012; Baptista <i>et al.</i> , 2013; Battisti <i>et al.</i> , 2013; Löbler <i>et al.</i> , 2014; Silva <i>et al.</i> , 2015
30%	<i>Ocimum carnosum</i> (Spreng.) Link & Otto ex Benth./ Lamiaceae/ Anis, alfavaca, manjeriço-do- mato	E	H	A, CH, S, T	AP, L, R, S, ST	Somavilla & Canto-Dorow, 1996; Piva, 1998; Possamai, 2000; Garlet & Irgang, 2001; Sebold, 2003; Soares <i>et al.</i> , 2004; Vendruscolo & Mentz, 2006; Souza, 2007; Borges, 2010; Zeni & Bosio, 2011; Avila, 2012; Meyer <i>et al.</i> , 2012; Baptista <i>et al.</i> , 2013; Rauber <i>et al.</i> , 2016; Gonçalves, 2017
30%	<i>Salvia officinalis</i> L./ Lamiaceae/Sálvia	E	H	C, S, T	AP, L	Kubo, 1997; Piva, 1998; Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Ritter <i>et al.</i> , 2002; Sebold, 2003; Tomazzoni, 2004; Fuck <i>et al.</i> , 2005; Negrelle <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Schwambach, 2007; Giraldi & Hanazaki, 2010; Battisti <i>et al.</i> , 2013; Rauber <i>et al.</i> , 2016
28%	<i>Artemisia alba</i> Turra/ Asteraceae/ Canflor	E	S	A, M, T	AP, L, ST, R	Kubo, 1997; Magalhães, 1997; Piva, 1998; Garlet & Irgang, 2001; Nogata, 2002; Tomazzoni, 2004; Fuck <i>et al.</i> , 2005; Vendruscolo & Mentz, 2006; Negrelle <i>et al.</i> , 2007; Lopes, 2010; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Rauber <i>et al.</i> , 2016; Gonçalves, 2017
26%	<i>Plantago australis</i> Lam./ Plantaginaceae/ Tanchagem-miúda	N	H	CH, T	F, L, R, S, WP	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Nogata, 2002; Ritter <i>et al.</i> , 2002; Oliveira, 2004; Soares <i>et al.</i> , 2004; Meyer <i>et al.</i> , 2012; Aguiar,

						2013; Rauber <i>et al.</i> , 2016; Spisla, 2017
24%	<i>Baccharis articulata</i> (Lam.) Pers./ Asteraceae/ Carquejinha	N	S	CH, T	AP, F, R, ST, WP	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Sebold, 2003; Soares <i>et al.</i> , 2004; Barros <i>et al.</i> , 2007; Ceolin <i>et al.</i> , 2011; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Rauber <i>et al.</i> , 2016
24%	<i>Pimpinella anisum</i> L./ Apiaceae/ Erva-doce	E	H	CH, T	FR, L, S	Somavilla & Canto-Dorow, 1996; Sebold, 2003; Tomazzoni, 2004; Negrelle <i>et al.</i> , 2007; Giraldi & Hanazaki, 2010; Aguiar, 2013; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Löbler <i>et al.</i> , 2014; Staniski <i>et al.</i> , 2014; Silva <i>et al.</i> , 2015; Duarte <i>et al.</i> , 2020
24%	<i>Sida rhombifolia</i> L./ Malvaceae/ Guanxumabranca	N	H	T	AP, L, SH, R, ST, WP	Somavilla & Canto-Dorow, 1996; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Sebold, 2003; Soares <i>et al.</i> , 2004; Vendruscolo & Mentz, 2006; Baldauf <i>et al.</i> , 2009; Ceolin <i>et al.</i> , 2011; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Bolson <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016
22%	<i>Echinodorus grandiflorus</i> (Cham. & Schltr.) Micheli/ Alismataceae/ Chapéu-de-couro	N	H	A, M, T	L	Lima, 1996; Kubo, 1997; Garlet & Irgang, 2001; Nogata, 2002; Ritter <i>et al.</i> , 2002; Sebold, 2003; Negrelle & Fornazzari, 2007; Avila, 2012; Battisti <i>et al.</i> , 2013; Bolson <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016
22%	<i>Plantago major</i> L./ Plantaginaceae/ Tanchagem, tansagem	E	H	T	L, S, WP	Garlet & Irgang, 2001; Soares <i>et al.</i> , 2004; Vendruscolo & Mentz, 2006; Negrelle & Fornazzari, 2007; Souza, 2007; Borba, 2008; Meyer <i>et al.</i> , 2012; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Rauber <i>et al.</i> , 2016; Duarte <i>et al.</i> , 2020
22%	<i>Symphytum officinale</i> L./ Boraginaceae/ Confrei	E	H	T	L	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Possamai, 2000; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Sebold, 2003; Tomazzoni, 2004; Negrelle <i>et al.</i> , 2007; Meretika, 2008; Battisti <i>et al.</i> , 2013; Rauber <i>et al.</i> , 2016
20%	<i>Anethum graveolens</i> L./ Apiaceae/ Endro	E	H	CH, T	F, FR, L, S	Koch, 2000; Possamai, 2000; Garlet & Irgang, 2001; Marodin & Baptista, 2001; Sebold, 2003; Soares <i>et al.</i> , 2004; Giraldi & Hanazaki, 2010; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Rauber <i>et al.</i> , 2016
20%	<i>Artemisia verliotorum</i> Lamotte/ Asteraceae/ Incenso-da-horta,	E	S	M, T	L, ST	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Possamai, 2000; Garlet & Irgang, 2001; Ritter <i>et al.</i> , 2002; Soares <i>et al.</i> , 2004; Borges, 2010;

	infalivina					Ceolin <i>et al.</i> , 2011; Zeni & Bosio, 2011; Spisla, 2017
20%	<i>Chelidonium majus</i> L./ Papaveraceae/ Celidônia, codina	E	H	M, T	AP, L, R	Piva, 1998; Ritter <i>et al.</i> , 2002; Sebold, 2003; Oliveira, 2004; Tomazzoni, 2004; Negrelle <i>et al.</i> , 2007; Ceolin <i>et al.</i> , 2011; Battisti <i>et al.</i> , 2013; Fernandes, 2014; Duarte <i>et al.</i> , 2020
20%	<i>Lippia alba</i> (Mill.) N.E. Br. ex Britton & P. Wilson/ Verbenaceae/ Erva-cidreira, salva	N	S	S, T	AP, F, L	Kubo, 1997; Marodin & Baptista, 2001; Oliveira, 2004; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Negrelle <i>et al.</i> , 2007; Amorim, 2010; Pereira <i>et al.</i> , 2011; Fernandes, 2014; Bolson <i>et al.</i> , 2015
20%	<i>Melissa officinalis</i> L./ Lamiaceae/ Melissa	E	H	CH, M, T	AP, L	Lima, 1996; Somavilla & Canto- Dorow, 1996; Koch, 2000; Possamai, 2000; Marodin & Baptista, 2001; Soares <i>et al.</i> , 2004; Negrelle & Fornazzari, 2007 Giraldi & Hanazaki, 2010; Fernandes, 2014; Gonçalves, 2017
20%	<i>Origanum vulgare</i> L./ Lamiaceae/ Orégano	E	H	T	L, ST	Koch, 2000; Oliveira, 2004; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Negrelle <i>et al.</i> , 2007; Borba, 2008; Zeni & Bosio, 2011; Meyer <i>et al.</i> , 2012; Silva <i>et al.</i> , 2015; Duarte <i>et al.</i> , 2020
20%	<i>Taraxacum officinale</i> F.H. Wigg./ Asteraceae/ Dente-de-leão	E	H	A, F, M, T	L, R	Kubo, 1997; Piva, 1998; Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Sebold, 2003; Oliveira, 2004; Pereira <i>et al.</i> , 2011; Avila, 2012; Battisti <i>et al.</i> , 2013; Rauber <i>et al.</i> , 2016
18%	<i>Lavandula angustifolia</i> Mill./ Lamiaceae/ Alfazema, alfazema- miúda	E	H	C, T	L, ST	Somavilla & Canto-Dorow, 1996; Kubo, 1997; Tomazzoni, 2004; Vendruscolo & Mentz, 2006; Negrelle <i>et al.</i> , 2007; Borba, 2008; Avila, 2012; Meyer <i>et al.</i> , 2012
18%	<i>Tanacetum parthenium</i> (L.) Sch. Bip./ Asteraceae/ Camomila-romana, artemisia	E	H	A, T	F, L, R, ST, WP	Kubo, 1997; Sebold, 2003; Soares <i>et al.</i> , 2004; Tomazzoni, 2004; Negrelle <i>et al.</i> , 2007; Avila, 2012; Meyer <i>et al.</i> , 2012; Rauber <i>et al.</i> , 2016
16%	<i>Brassica oleracea</i> L./ Brassicaceae/ Couve	E	H	F, T	L, ST	Marodin & Baptista, 2001; Negrelle & Fornazzari, 2007; Borba, 2008; Pereira <i>et al.</i> , 2011; Avila, 2012; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016; Gonçalves, 2017
16%	<i>Ocimum basilicum</i> L./ Lamiaceae/ Manjerição	E	H	M, T	AP, L, ST	Somavilla & Canto-Dorow, 1996; Koch, 2000; Sebold, 2003; Oliveira, 2004; Vendruscolo & Mentz, 2006; Negrelle & Fornazzari, 2007; Zeni & Bosio, 2011; Silva <i>et al.</i> , 2015

14%	<i>Leonurus sibiricus</i> L./ Lamiaceae/ Erva-do-santo-filho	E	H	M, T	AP, F, L, R	Marodin & Baptista, 2001; Ritter <i>et al.</i> , 2002; Oliveira, 2004; Lopes, 2010; Fernandes, 2014; Rauber <i>et al.</i> , 2016; Gonçalves, 2017
14%	<i>Ruta graveolens</i> L./ Rutaceae/ Arruda	E	H	A, T	L, R	Piva, 1998; Nogata, 2002; Soares <i>et al.</i> , 2004; Barros <i>et al.</i> , 2007; Avila, 2012; Fernandes, 2014
12%	<i>Alternanthera brasiliana</i> (L.) Kuntze/ Amaranthaceae/ Erva-de-santa-maria, penicilina	N	S	T	AP, L, ST	Garlet & Irgang, 2001; Marodin & Baptista, 2001; Vendruscolo & Mentz, 2006; Negrelle <i>et al.</i> , 2007; Avila, 2012; Aguiar, 2013
12%	<i>Artemisia vulgaris</i> L./ Asteraceae/ Artemísia, infalivina	E	H	T	AP, F, L, R	Sebold, 2003; Barros <i>et al.</i> , 2007; Borges, 2010; Fernandes, 2014; Gonçalves, 2017; Duarte <i>et al.</i> , 2020
12%	<i>Bauhinia forficata</i> Link/ Fabaceae/ Pata-de-vaca	N	T	T, TN	B, F, L	Piva, 1998; Borba, 2008; Amorim, 2010; Bolson <i>et al.</i> , 2015; Silva <i>et al.</i> , 2015; Duarte <i>et al.</i> , 2020
12%	<i>Carica papaya</i> L./ Caricaceae/ Mamão, mamoeiro	E	T	T	F, FR, L, S	Somavilla & Canto-Dorow, 1996; Possamai, 2000; Vendruscolo & Mentz, 2006; Giraldi & Hanazaki, 2010; Meyer <i>et al.</i> , 2012; Rauber <i>et al.</i> , 2016
12%	<i>Citrus limon</i> (L.) Osbeck/ Rutaceae/ Lima, limeira	E	T	A, F, S, T	FR, L, P, S	Nogata, 2002; Oliveira, 2004; Vendruscolo & Mentz, 2006; Borges, 2010; Meyer <i>et al.</i> , 2012; Rauber <i>et al.</i> , 2016
12%	<i>Dysphania ambrosioides</i> (L.) Mosyakin & Clemants/ Amaranthaceae/ Erva-de-santa-maria, mentruz	E	H	M, T	AP, F, L, S, WP	Lima, 1996; Garlet & Irgang, 2001; Negrelle & Fornazzari, 2007; Aguiar, 2013; Fernandes, 2014; Bolson <i>et al.</i> , 2015
12%	<i>Monteverdia aquifolia</i> (Mart.) Biral/ Celastraceae/ Espinheira-santa, cancorosa	N	T	T, TN	B, L	Soares <i>et al.</i> , 2004; Avila, 2012; Bolson <i>et al.</i> , 2015; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016
10%	<i>Campomanesia xanthocarpa</i> (Mart.) O. Berg/ Myrtaceae/ Guabirola	N	T	M, T	FR, L, ST	Kubo, 1997; Sebold, 2003; Amorim, 2010; Bolson <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016
10%	<i>Citrus × aurantium</i> L./ Rutaceae/ Laranjeira-amarga	E	T	F, S, T	F, FR, L, P, S	Possamai, 2000; Marodin & Baptista, 2001; Vendruscolo & Mentz, 2006; Negrelle & Fornazzari, 2007; Giraldi & Hanazaki, 2010
10%	<i>Mentha × piperita</i> L./ Lamiaceae/ Hortelã-pimenta	E	H	T	L, ST, WP	Kubo, 1997; Barros <i>et al.</i> , 2007; Negrelle & Fornazzari, 2007; Pereira <i>et al.</i> , 2011; Staniski <i>et al.</i> 2014
10%	<i>Sedum dendroideum</i> DC./ Crassulaceae/ Bálsamo-miúdo, bálsamo-branco	E	H	F, T	L	Barros <i>et al.</i> , 2007; Ceolin <i>et al.</i> , 2011; Pereira <i>et al.</i> , 2011; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016
10%	<i>Cuphea carthagenensis</i> (Jacq.) J.F. Macbr./	N	H	T	AP, L, R, WP	Nogata, 2002; Sebold, 2003; Vendruscolo & Mentz, 2006;

	Lythraceae/ Sete-sangrias					Meretika, 2008; Fernandes, 2014
8%	<i>Mentha pulegium</i> L./ Lamiaceae/ Poejo	E	H	T	L	Borba, 2008; Meyer <i>et al.</i> , 2012; Aguiar, 2013; Rauber <i>et al.</i> , 2016
8%	<i>Petiveria alliacea</i> L./ Phytolaccaceae/ Guiné	E	S	A, T	L, R	Kubo, 1997; Avila, 2012; Fernandes, 2014; Rauber <i>et al.</i> , 2016
8%	<i>Plinia peruviana</i> (Poir.) Govaerts/ Myrtaceae/ Jabuticabeira	N	T	T	FR, L, P, SH	Lima, 1996; Sebold, 2003; Coan & Matias, 2014; Tribess <i>et al.</i> , 2015
8%	<i>Solanum tuberosum</i> L./ Solanaceae/ Batata- inglesa	E	H	F	R, T	Souza, 2007; Meretika, 2008; Avila, 2012; Gonçalves, 2017
8%	<i>Zanthoxylum rhoifolium</i> Lam./ Rutaceae/ Mamica-de- cadela	N	T	T	B, L	Somavilla & Canto-Dorow, 1996; Borges, 2010; Tribess <i>et al.</i> , 2015; Rauber <i>et al.</i> , 2016
6%	<i>Calendula officinalis</i> L./ Asteraceae/ Calêndula	E	H	T	F, L	Marodin & Baptista, 2001; Aguiar, 2013; Rauber <i>et al.</i> , 2016

Other species traditionally used for gastrointestinal disorders identified in this study include *Alternanthera brasiliana* and *Cuphea carthagenensis*, cited as useful to relieve diarrhea, bellyache, stomach and intestines. The *A. brasiliana* infusion obtained from leaves and inflorescences is indicated in the PFBP as an antipyretic for mild fever conditions (Brasil, 2021). The pharmacological activities described for these species seem to be associated with the high presence of flavonoids and polyphenols (Formagio *et al.*, 2012; Alencar Filho *et al.*, 2020; Santos *et al.*, 2020), although scientific studies on the digestive properties for the species were not found.

Tannins are polyphenols with the property to interact with proteins and polysaccharides, forming stable complexes and leading to the formation of a protective layer on the gastric mucosa, resistant to chemical or mechanical aggression (Mello & Santos, 2004). In addition, as free radicals are important contributing factors to produce ulcerative damage, the antiulcer properties of medicinal plants containing flavonoids and tannins point to their antioxidant effects (Donatini *et al.*, 2009). Likewise, *Monteverdia ilicifolia* and *Monteverdia aquifolia*, both known as *espinheira-santa* and popularly used to treat dyspepsia and gastric ulcers, are species included in this group and extensively investigated in preclinical and, more recently, clinical trials (Souza-Formigoni *et al.*, 1991; Gonzalez *et al.*, 2001; Jorge *et al.*, 2004; Tabach *et al.*, 2017). *M. ilicifolia* is indicated in the PFBP (decoction and capsules) as an antacid, with the warning that its use may cause nausea,

xerostomia and polyuria and that it should not be used chronically (Brasil, 2021).

Eugenia uniflora is widely used in folk medicine as an antidiarrheal, antispasmodic and for bellyache. The infusion of the *pitanga* leaves is indicated in the PFBP for the symptomatic relief of mild non-infectious diarrhea (Brasil, 2021). According to The Brazilian Pharmacopeia, *E. uniflora* leaves must contain at least 5% of tannins (Brasil, 2019). These compounds are characterized by their antidiarrheal effect, justifying the use of this plant in gastrointestinal disorders (Almeida *et al.*, 1995). Other tannin-containing species used in southern Brazil folk medicine for similar therapeutic purposes include *Psidium cattleyanum* (araçá), *Plinia peruviana* (jaboticaba) and *Campomanesia xanthocarpa* (guabiroba). Preclinical data suggest the antispasmodic effect of the *P. cattleyanum* aerial parts hydroalcoholic extract, with an absence of toxicity in mice (Rahman *et al.*, 2020). The oral administration of the hydroalcoholic extract from *C. xanthocarpa* leaves showed antiulcerogenic activity in rats (Markman *et al.*, 2004), while the fruits extract did not produce antidiarrheal effect in animal models (Souza-Moreira *et al.*, 2011).

Plants containing iridoids glycosides are known to have a bitter taste, displaying cholagogue and stimulatory effects on gastric secretion, thus facilitating digestion (Capasso *et al.*, 2003). *Stachytarpheta cayennensis*, *Echinodorus grandiflorus* and *Plantago australis* are examples, but only the first species has preclinical investigations describing its eupeptic activity. Penido

et al. (2006) showed the gastroprotective and anti-inflammatory effects of an ethanolic extract of *S. cayennensis* rich in ipolamiide and verbascoside in mice, while an aqueous extract from aerial parts (but not stems) promoted a mild-laxative effect, associated with a potent inhibition of gastric secretion in rodents (Mesia-Vela *et al.*, 2004).

Some of the native species listed in Chart 2 are classified as aromatic plants based on the main presence of essential oils, compounds recognized by their spasmolytic or stimulating effects on digestion and peristalsis (Kelber *et al.*, 2017). Among them, *Aloysia gratissima* and *Lippia alba*, both popularly known as *erva-cidreira*, are mentioned.

Infusions and alcoholic preparations made with *Aloysia gratissima* are traditionally used in South America due to their eupeptic properties, for nausea, abdominal pain and dizziness (Alonso & Desmarchelier, 2015). Guaiol and 1,8-cineol are described as the main constituents of the volatile oil of the plant (Garcia *et al.*, 2018). Aqueous extracts and tinctures of *A. gratissima* displayed spasmolytic activity in rat isolated ileum and duodenum, which may be associated to the presence of flavonoids (quercetin and hesperidin) and monoterpenes (carvone) (Consolini *et al.*, 2011). The gastroprotective effect of *A. gratissima* aqueous extract was demonstrated in rats after the administration of absolute ethanol as necrotizing agent (Bucciarelli *et al.*, 2007).

The infusion prepared from *Lippia alba* leaves and flowers is indicated in the PFBP as an antidyseptic, antispasmodic and mild anxiolytic, and that it may potentiate the effect of sedative drugs (Brasil, 2021). Blanco *et al.* (2013) compared the antispasmodic activity of the volatile oils obtained from two *L. alba* chemotypes that are rich in citral and linalool in isolated rat duodenum and ileum. The results demonstrated that the citral-rich oil chemotype inhibited more potently the muscarinic contractions. The antiulcerogenic effect of *L. alba* infusion was evaluated in rat gastric mucosa, showing efficacy in the short and long-term consume, without producing any apparent toxicity (Pascual *et al.*, 2001).

Finally, some native medicinal plants listed in Chart No. 2 as *Solanum paniculatum*, *Zanthoxylum rhoifolium* and *Sida rhombifolia* are characterized by the presence of alkaloids, bioactive compounds that exhibit spasmolytic effects (Kelber *et al.*, 2017). As alkaloids may also exhibit an important toxicity (Matsuura & Fett-Neto, 2015), some safety restrictions for phytopharmaceuticals or herbal drugs

containing these compounds were determined by ANVISA, including any *Solanum* species containing steroidal alkaloids, as specified by RDC 26/14 (Brasil, 2014).

Solanum paniculatum, known as *jurubeba*, is cited in the RENISUS (Brasil, 2009), being widely used in southern Brazil as a digestive and hepatoprotective remedy (Simões *et al.*, 1998). Studies conducted with extracts (aqueous or ethanolic) from *S. paniculatum* confirmed the liver protective effects *in vivo*, attributing such an effect to the steroidal alkaloids present in roots (Gazolla *et al.*, 2020) or to the phenolic compounds present in leaves (Souza *et al.*, 2019). Aqueous extracts of roots and stems were found to inhibit gastric acid secretion in pylorus-ligated mice, while fruits extract stimulated gastric secretion (Mesia-Vela *et al.*, 2002). The authors correlated the anti-secretory effects to the higher content of alkaloids in roots and stems, associated with an absence of toxicity observed after the oral administration. The ethanolic extracts of *S. paniculatum* leaves also displayed antiulcer effect in rats (Vieira Júnior *et al.*, 2015) and antidiarrheal activity in mice (Clementino-Neto *et al.*, 2015). However, no clinical studies were found.

Zanthoxylum rhoifolium, popularly known as *mamica-de-cadela*, is used in folk medicine as a digestive, for stomachache and hepatitis. The ethanolic extract from stem barks, rich in alkaloids and triterpenes, exhibited gastroprotective effect on different ulcer models in rodents and did not induce any apparent toxicity (Freitas *et al.*, 2011). Additionally, the antinociceptive activity was also confirmed for *Z. rhoifolium* stem bark extract and its fractions in mice (Pereira *et al.*, 2010).

Sida rhombifolia (*guanxuma*) is traditionally used as cholagogue, for bellyache, diarrhea, as a digestive and liver detoxifier. Chemical studies revealed a variety of compounds present in this species, including alkaloids, flavonoids and triterpenes (for a review, see Dinda *et al.*, 2015). A preclinical study showed that methanol and aqueous extracts of *S. rhombifolia* exhibited hepatoprotective activity in CCl₄, paracetamol and rifampicin-induced liver damage in rats (Kumar & Mishra, 1997). The infusion obtained from *S. rhombifolia* leaves demonstrated hepatoprotective activity in an experimental model of non-alcoholic steatohepatitis in mice (Thounaojam *et al.*, 2012). According to Thounaojam *et al.* (2010), the acute and chronic oral administration of the extracts did not induce any apparent toxicity.

It becomes evident that the bioactive compounds described for the abovementioned species, even if not fully identified, are able to exert synergic effects and consequently, potential toxic effects in the derived preparations (teas, tinctures, etc.). Indications regarding safety were found for most of the medicinal plants cited in the ethnobotanical studies, including some evidence of efficacy and safety from Brazilian official monographs, as the PFBP (Brasil, 2021). However, further investigations are needed to better explore their pharmacological profile, including mechanistic and clinical aspects.

CONCLUSION

The present study agrees with other reports documenting the extensive use of native species as home medicines that integrate a portrait of the main medicinal plants popularly used for the relief of gastrointestinal disorders in southern Brazil (the ethnobotanical studies came from 17 out of 22

mesogeographic regions from RS, SC and PR). Taken together, the results present potential evidences for the selection of plant species in programs of public health system and drug development. *Achyrocline satureioides*, *Eugenia uniflora*, *Baccharis crispa*, *Solanum paniculatum*, *Monteverdia ilicifolia*, *Stachytarpheta cayennensis*, *Alloysia gratissima*, *Lippia alba* and *Sida rhombifolia* were the native species sharing the highest number of preclinical studies corroborating folk indications for digestive purposes. However, scientific data are still insufficient to guarantee the efficacy and safety for most of them.

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