Chapter 19
Innovation and Knowledge of Prospective Studies on the Genus *Baccharis*

Mariana Bonifácio Amancio, Yumi Oki, G. Wilson Fernandes, Carla Rago, Aristóteles Góes-Neto, and Vasco Ariston de Carvalho Azevedo

Abstract *Baccharis* species are well known for their secondary metabolites used in the treatment of several diseases and for having great potential of use in various industries. In order to identify the current status of innovation in which species of this genus are found, an assessment on scientific and technological productions was carried out, as well as on the collaboration of those involved in the generation of scientific knowledge and/or in the production of products and processes. This analysis aimed to measure the contributions of science and technology to society. As of December 2019, about 991 articles and 223 patents on the genus *Baccharis* were registered. Brazil, which harbors a great diversity of species of this genus (178 species), stands out in the number of published scientific articles (45.22%). Moreover, the United States with 21 native *Baccharis* species excels as the country with the highest number of patents for products and processes of this genus (48.02%). Nonetheless, it is worth mentioning that the majority of patents are not for *Baccharis* species from this country. When analyzing the species found in patents and scientific articles, the presence of 21 species of common interest was observed, mostly associated with the biological activity of their secondary metabolites. *Baccharis* patents are focused on the production of drugs for various medicinal applications. Although some scientific articles also deal with this topic, the authors focus on the chemical analysis of different species of *Baccharis*. Among the 401 inventors and 100 authors, only four turned out to be both patent filers and authors of scientific articles. These findings indicate a great difference between the production of articles and patents on *Baccharis*, which consequently, may represent a loss in economic development and performance, and international competitiveness.

Keywords Bioeconomy · Science · Economy · Pharmacology · Innovation · Patents

M. B. Amancio · Y. Oki · G. W. Fernandes (✉) · C. Rago · V. A. de Carvalho Azevedo (✉)
Departamento de Genética, Ecologia & Evolução, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

A. Góes-Neto
Departamento de Microbiologia, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

G. W. Fernandes et al. (eds.), *Baccharis*,
https://doi.org/10.1007/978-3-030-83511-8_19

1 Introduction

Over the last few years, the interest in science-technology relations has increased due to the relevance of knowledge and innovation for economic development and social benefits (Looy et al. 2006). It is an approach worth highlighting, especially in periods of economic recession and questioning of public expenses (Meyer 2000). Works such as those by Narin (1995) and Narin et al. (1997), in which analyses of patents and research activities (articles) were performed, underlined an increasing relationship between science and technology, especially in high-tech areas in the United States. Although technological production is associated with knowledge, this relationship is not always direct and clear. It can vary with the degree of science, and social interest and economic applicability.

Baccharis is one of the genera that aggregates a diversity of economic applications, and, among them, the control of soil erosion (Martinez et al. 2015; Vessella et al. 2015; Woolsey et al. 2018), ornamental use (Tognon and Cuquel 2016), food supplement (Navares et al. 2010), raw material for the development of cosmetics and pharmaceutical products (Sousa et al. 2011; Mejía-Giraldo et al. 2016; Casagrande et al. 2018), source of raw material for bees in propolis production (Souza et al. 2019), and products of botanical origin. Such prominence in the area of natural products is due to its diverse pharmacological properties in the treatment of several diseases such as ulcers, gastrointestinal diseases, diabetes, cancer, inflammations, and bacterial-fungal infections (e.g., Corrêa 1984; Carneiro and Fernandes 1996; Claudino 2013; Silva et al. 2019). These uses have favored studies on the propagation of some species of *Baccharis*. Furthermore, all of these attributions provided by *Baccharis* fall within the paradigm of bioeconomics, which describes the way in which a set of economic activities obtains latent value from biological processes and renewable bioresources to develop and promote better health, growth, and sustainability conditions (Vivien et al. 2019).

Baccharis' scientific knowledge and potential for innovation are high. In this research, we verify the existence of more than 900 published articles and 200 patent applications, as we shall see below. On the other hand, tropical countries such as Brazil, which exhibit a great diversity of species of this genus, do not always present a parallel relationship with scientific production nor are associated with the generation of patents. The challenges of many of these countries involve the ease and success of filing patents (França and Vasconcelos 2018) since the current relationship between science and technology may also help to better diagnose problems and to propose solutions that favor economic development.

2 Scope and the Database

Currently, prospective studies have shown to be a way of stimulus for organizations of innovation systems as it contemplates the interaction between science and technology. The publication of research results is seen as a direct representation of science itself in the form of scientific articles while technology is portrayed through the application of knowledge obtained from the creation of processes and products, represented by patents (Meyer and Batthacharya 2004). Thus, in order to seek comprehension of *Baccharis*' science-technology interaction, this chapter sought to analyze the profile of registered patents and articles on this genus available on virtual databases over the last six decades (1940–2019). To this end, the chapter was divided into five sections. The first section approaches an analysis of the profile of patents and articles on species of the genus *Baccharis*. In this section, we present the chronology, species of interest, and the origin of patents and articles. The second section addresses the processes, products, and international classification of patents that involves the genus. The third section discusses areas of interest and applications of patents and articles. The fourth section deals with the network of authors and inventors involved in patents and articles. Finally, the last section presents remarks on science-technology relations developed with *Baccharis* and their contributions to society.

The database used for patents was Google Patents, United States Patent and Trademark Office (USPTO), Espacenet (developed by the European Patent Office (EPO) together with member states of the European Patent Organization), Instituto Nacional da Propriedade Industrial (INPI), DISCUS, and World Intellectual Property Organization (WIPO). The data searches used for scientific productions was Web of Science.

3 Profile of Patents and Articles of the Genus *Baccharis*

Chronology of Publications and Patent Filings of Species of the Genus Baccharis

The first patent on *Baccharis* registered in the main available patent basis was in 1942. This first order was placed by the private company American District Telegraph Company and entitled "Radiant energy receiving system" (Lindsay and Pearson 1942). The purpose of this patent application was to create an antitheft system equipped with a sensor coupled to the alarm, and the main differential was the high capacity for protection regardless of weather conditions. One of the materials of interest described in this document is the fiber of *Baccharis* sp. (with no species identification), which is presented as one of the materials used in the sensor assembly once this fiber has a high adsorption capacity. Although the first patent

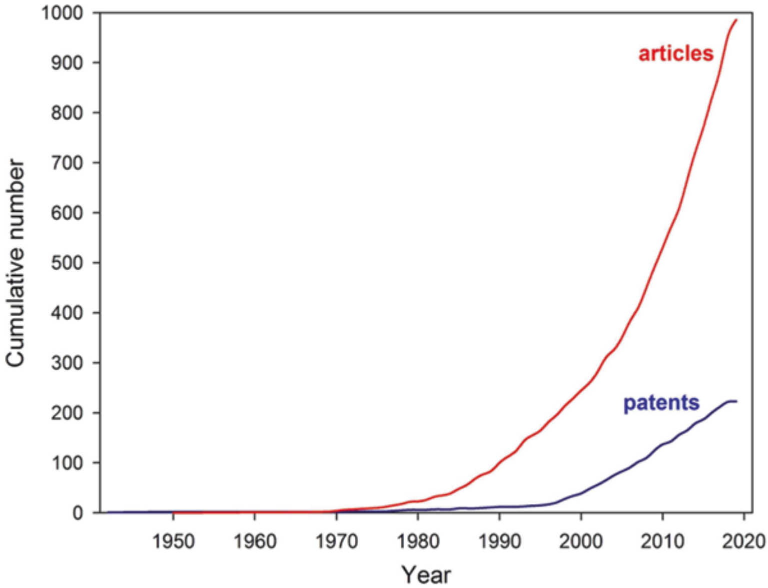

Fig. 19.1 Number of patent filings and publications of scientific articles on species of the genus *Baccharis* until 2019

filing focused on the use of *Baccharis* in the composition of a sensor, no other patent or article with the same purpose was developed afterward.

The first patent registrations occurred in a timid and inconsistent way during 1942 to 1995 (Fig. 19.1). Before that period, the patenting of pharmaceutical products was historically not permitted in many countries. Only in the late twentieth century, mandatory pharmaceutical patent protection was established for all members of the World Trade Organization (WTO) (Shadlen et al. 2019). Since then, registrations have increased rapidly, reaching a total of 223 registrations in 2019. The recent increase is so clear that in the last 10 evaluated years, almost half (98 patents) of *Baccharis* patents were registered.

The first article on *Baccharis* according to the Web of Science (1945–2019) was published in 1961 by Dolejs and collaborators (1961), with the title "Sesquiterpenic compounds of *Baccharis genistelloides* Pers – Structure of palustrol" in the journal *Collection of Czechoslovak Chemical Communications*. This publication analyzed secondary substances in the aerial part of *B. genistelloides*, focusing on the δ-cadinene sesquiterpenes. To date, this phytochemical interest in *Baccharis* species continues, particularly focused on the extraction and identification of chemical compounds (Bettucci et al. 2020).

Unlike patents, the publication of scientific articles on *Baccharis* only displayed a boost almost 10 years after the first scientific article had been published in 1961. Although the publication of articles started slightly later than patents, there has been a substantial growth reaching about 991 articles in 2019. Comparatively, the number of articles represents about 4.5 times more than the number of patents.

One of the factors that influence this variation between numbers of patents and articles is related to differences in the time of evaluation and concession between them. Most articles (67%) take 6 months to 2 years to finalize publication (Noorden 2016). However, even when an author needs to wait a long time for the article to be published, that time is much shorter than one required for a patent to be filed. Moreover, it is also important to highlight that article publication or even a lecture in any type of event before the secrecy period (1–5 years) can make patenting unfeasible. This condition imposes a choice that is not always feasible for the researcher who is being evaluated for his production of articles, and little for the number of patents.

Additionally, a patent application request does not mean that the patent will be granted (França and Vasconcelos 2018). In an analysis of the technological field of herbal medicines in Brazil, where there is the largest number of published articles, from a total of 876 analyzed patent applications, only 12 (1.3%) were granted (Vasconcellos et al. 2004). Therefore, the fact that the patent is granted does not mean that it will be licensed or even exploited in any way. This topic is complex, and the information gathered only outlines some of the many factors present in the context of the comparative and competitive relationship between the basic research of scientific articles and the generation of patent products and/or processes. The incentive to innovation based on basic research represents the entrepreneurial continuity of organizations, taking into account such important issues in the conduction of economic and social growth within companies and universities.

Currently, incentives and guidelines for the effective granting of patent deposits are not uniform across countries. Many developing countries have few incentives, and institutions that assist in the patenting process guarantee sooner success in patent grant (Moreira et al. 2016). Many research institutions validate various pharmacological data every day, but the lack of a culture of protection, or even the lack of knowledge about intellectual property, makes it impossible for these results to promote financial return (Dundas 2012; Fisch et al. 2015; Arqué-Castells et al. 2016).

Species of Interest for Patents and Articles

Baccharis is considered the largest genus that belongs to the Asteraceae family, covering formally 442 species (Fielding 2001; Giuliano 2001; Heiden and Pirani 2016). *Baccharis* has a wide geographic distribution occuring from Canada to the southern tip of Argentina and Chile (Barroso 1976; Fielding 2001; Verdi et al. 2005; Heiden et al. 2006). In patent filing applications, 43 species of this genus were identified. However, patent filing requests without identification at the species level reached 15.7%. In scientific articles, the number of investigated species was greater, 192 studied species (43.4% of the genus). Approximately 10% of published articles present only the genus, without species determination. Those of common interest

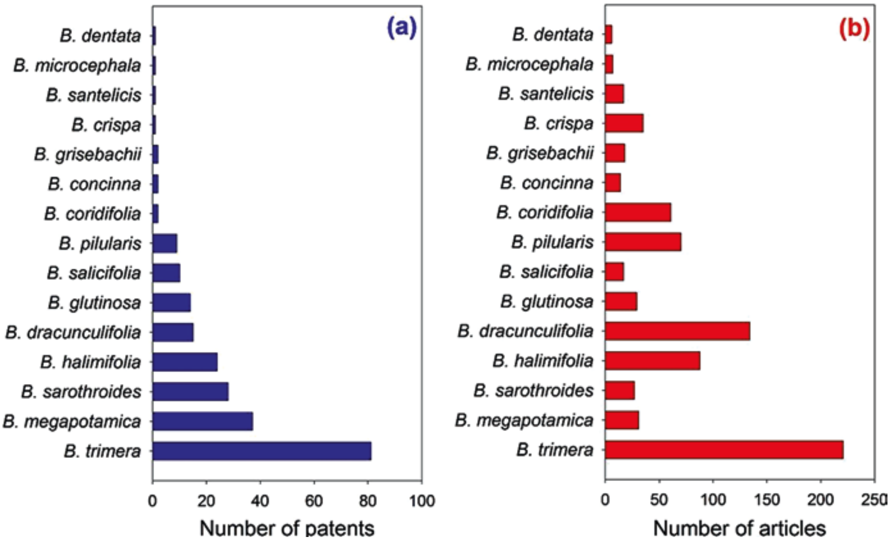

Fig. 19.2 Number of (**a**) patents and (**b**) scientific articles of the most cited species of the genus *Baccharis*

found in articles and patents are: *B. concinna, B. coridifolia, B. cutervensis, B. crispa, B. dentata, B. dracunculifolia, B. erioclada, B. glaziovii, B. glutinosa, B. grisebachii, B. halimifolia, B. megapotamica, B. microcephala, B. pilularis, B. pseudotenuifolia, B. salicifolia, B. santecilis, B. sarothroides, B. stenocephala, and B. trimera* (Fig. 19.2).

The most cited species of the most cited patents are *B. trimera* (36.3%), *B. megapotamica* (16.6%), and *B. sarothroides* (12.6%) (Fig. 19.2). *Baccharis trimera* is considered one of the most studied plant species in botanical, pharmacological, and chemical terms and is present in the list and described in the sixth Edition of the Brazilian Pharmacopoeia (Karam et al. 2013; ANVISA 2019). It has a wide distribution in Brazil, occurring in the Cerrado (Rodrigues and Carvalho 2001), Atlantic Forest (Pavan-Fruehauf 2000; Vieira and Silva 2002), and Pampa (Ritter and Baptista 2005; Caporal and Boldrini 2007) biomes, and can even be found in many ruderal environments (Brandão and Oliveira 1995; Macedo 1995; Vieira and Silva 2002), whereas *B. megapotamica* inhabits wetlands from Brazil and Argentina (Tokarnia et al. 1992; Carneiro and Irgang 2005). This shrub stands out for the presence of a series of potent cytotoxic agents that belong to the trichothecene antibiotics complex. In addition, trichothecenes have exceptionally high toxicity for eukaryotic organisms, including high phytotoxicity (Ueno 1983; Bamburg 1983; Snyder 1986). Among the analyzed chemical compounds, macrocyclic trichothecenes (roridins, verrucarins, and baccharinoids) proved to be among the most potent phytotoxic agents (Cutler and Jarvis 1985). The species *B. sarothroides* has its origin in the desert regions of the United States, and its notoriety is mainly focused on its concentration of flavonoids with proven cytotoxic activity such as centauredin and 3,4′-di-methoxy −3′,5,7-trihydroxy-flavone (Kupchan and Baverschmidt 1971).

The most cited species in articles are *B. trimera* (22.3%), *B. dracunculifolia* (13.5%), and *B. halimifolia* (8.87%). *Baccharis dracunculifolia* is a dioecious shrub whose distribution ranges from southeastern to southern Brazil, reaching Argentina, Uruguay, Paraguay, and Bolivia (Gomes and Fernandes 2002). This species is a facilitator of other species in Cerrado, as it houses a wide network of interactions (Fagundes et al. 2005; Neves et al. 2016; Barbosa et al. 2019; Monteiro et al. 2020; Rodrigues et al. 2020), especially with the Africanized bees *Apis mellifera* that collect their resins for propolis manufacturing (Fernandes et al. 2018; Rodrigues et al. 2020). It is also known for its pharmacological properties and for the treatment of several microbial and fungal diseases, ulcers, leishmania, schistosomiasis, and cancer, among others (e.g., Park et al. 2004; Silva-Filho et al. 2009; Parreira et al. 2010). The shrub species *B. halimifolia*, known for its complex network of interactions, is native to salt marshes and dunes along the Atlantic and North American Gulf Coast (Krischik and Denno 1990; Egerova et al. 2003). It is considered an invasive species in Australia and especially in Europe (Sims-Chilton et al. 2010; Caño et al. 2013, 2016). In the past hundred years, *B halimifolia* has invaded almost all of Europe's estuaries (Caño et al. 2016).

Origin of Patent Filings and Articles

The origin of *Baccharis*' patents is distributed in 53 countries, and the articles have been originated from 174 countries (Fig. 19.3a, b). Despite being a genus of origin in the Americas (Heiden and Pirani 2016), only 5.73% of patent deposits were generated in this region (Fig. 19.3). This number is significantly lower than the frequency of articles published in the same region, which was approximately 67.5%. These results also show that the potential to generate patents with *Baccharis* is not being explored by the countries of origin. Consequently, these countries are not being favored by the economic advantages that patents can bring such as market monopoly for a certain period of time (Moir 2008). This way, these countries through patents could have higher income and profitability indicators.

The country with the highest number of patents (95 patents, 48.02% of patents) for *Baccharis* was the United States (Fig. 19.3a). The country is home to 21 native species (Kupchn and Baverschmidt 1971), of which only six have patents (28.6% of native species in the United States): *B. dioica*, *B. emoryi*, *B. glutinosa*, *B. halimifolia*, *B. pilularis*, and *B. sarothroides*. It is noted; however, that about 50% of the patents in the United States correspond to two non-native species: *B. trimera* (26.3% of the United States patents) and *B. megapotamica* (24.2% of the patents) (Fig. 19.4). *B. trimera* patents are associated with the development of cosmetics (69.23% of patents), pharmacological products (23.08%), and chemical extraction (7.69%), while *B. megapotamica* patents are mostly directed to pharmacology (91.30%). The United States has been known for its mastery in the pharmacological field since the

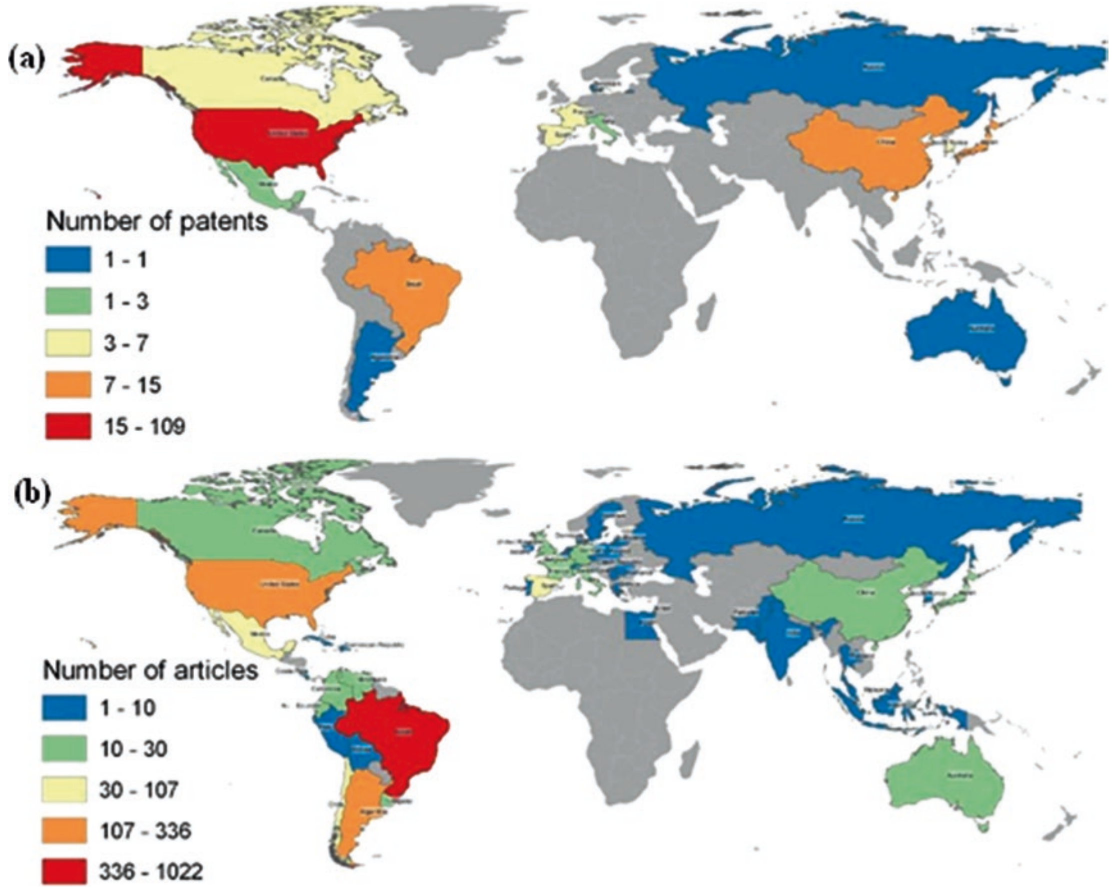

Fig. 19.3 Geographic distribution of the (**a**) number of filed patents and (**b**) published scientific articles related to the genus *Baccharis*

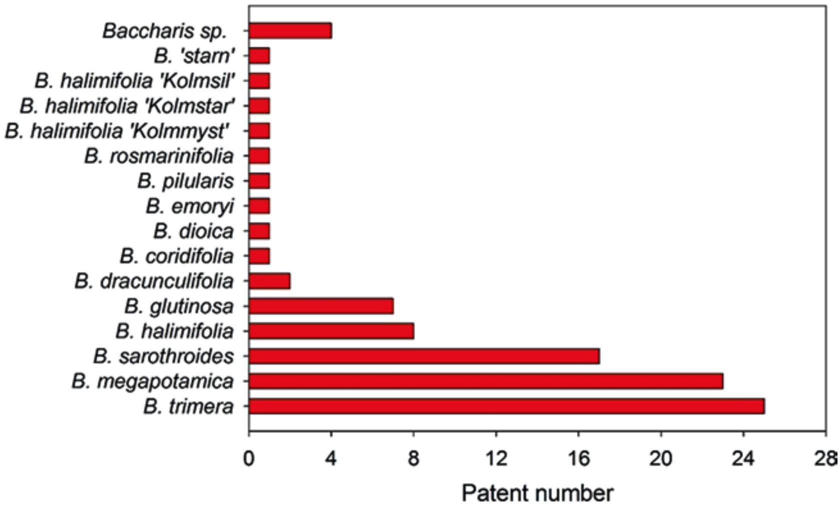

Fig. 19.4 Distribution of the number of patents in the United States (95 patents) per species of *Baccharis*. *Baccharis* sp.* – identification presented in the patent only at gender level

nineteenth century by means of pharmaceutical researches based on the extraction, purification, and isolation of natural products (Radaelli 2007).

The United States' leadership in the number of *Baccharis* patents may be associated with its oldest patent on record as of 1790 and its stronger and facilitative structure in patent generation (Khan 2005). A different profile of countries in South America, such as Brazil, which harbors 178 species of *Baccharis* (about 36% of *Baccharis* species; Heiden et al. 2019), leads the list of countries with the largest number of scientific publications on species of this genus with a frequency of 45.22% (448 articles) among published studies (Fig. 19.3b). Brazil has 12 patents for 30 species of *Baccharis* (30 species out of 175 registered species: 17% of the existing species in the country). Part of this difference may be associated with the country's patent history. Until 1996, pharmaceutical products were excluded from patent protection in the country (Nogués 1990). Currently, unfortunately, the vast majority of patent rights granted in Brazil belong to foreign business groups, especially from the United States (Marques 2000).

Additionally, an analysis on the patents' origin countries of the three most cited *Baccharis* species (*B. trimera*, *B.megapotamica*, *B. dracunculifolia*) indicates that over 50% of the patents were developed outside their countries of origin (Fig. 19.5). About 88% of *B. trimera* patents came from where it is not native: Canada, China, EPO, Spain, United States, France, Japan, United Kingdom, and WIPO (Fig. 19.6). While for *B. megapotamica*, no patent was found for its origin locations. About 53.9% of *B. dracunculifolia* patents were carried out outside their countries of origin: United States, EPO, Japan, and WIPO (Fig. 19.6). In contrast, the origin of studies developed for publication of articles on *B. trimera*, *B. megapotamica*, and *B. dracunculifolia* are, in their majority (over 50%), in the countries where they are native.

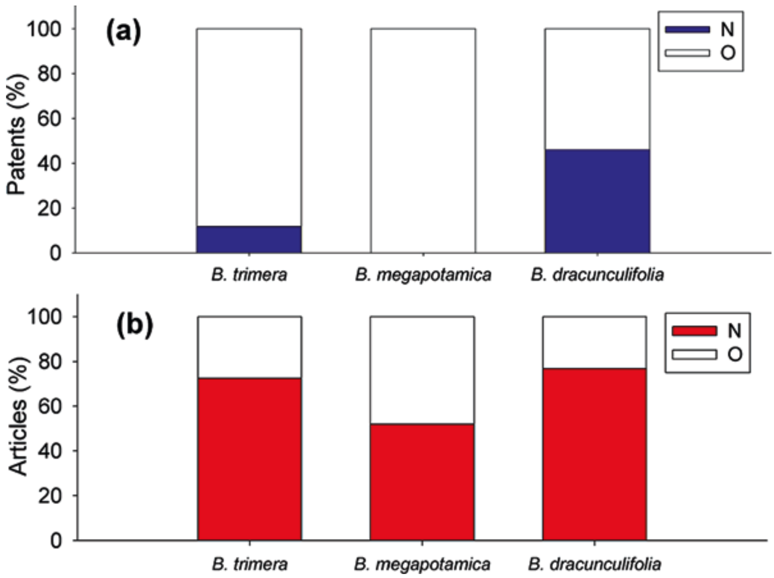

Fig. 19.5 Frequency of patents (**a**) and articles (**b**) found inside (N) and outside (O) their country of origin for *Baccharis trimera*, *Baccharis megapotamica*, and *Baccharis dracunculifolia*

Plant Parts Explored in Patents and Articles

Plants exhibit a wealth of chemical substances that can vary not only among species or plant gender but also according to the plant organ (Ferracini et al. 1995; Muller-Riebau et al. 1997; Perri et al. 1999; Vesela et al. 1999; Lago et al. 2008; Manurung et al. 2017; Feduraev et al. 2019). These chemical differences in composition and contents found among plant organs have been generally considered in studies and scientific innovations. Other environmental factors may influence plant production of chemical compounds such as seasonality, geographical distribution, and the level of stress that they are subjected to (Perri et al. 1999; Carvalho-Filho et al. 2006; Edreva et al. 2008). These factors, regardless of their importance, are hardly explored in patents but practically only in scientific publications.

In patents, pollen represents the part of the plant of greatest interest (37.3%), followed by the use of leaves (25.5%), aerial part as a whole (13.7%), and whole plant (11.8%) (Fig. 19.7). Other organs such as branches, roots, and cladodes are less explored in patents.

The majority of the patents of *Baccharis* pollen is associated with the health benefits it brings, such as nutritional supplementation (Cho et al. 2017), physical vigor, and immune-strengthening (Kroyer and Hegedus 2001). Pollen has been incorporated for the development of patents that involve immunotherapy of allergies and vaccines and administration of immunomodulatory compounds in order to increase immune response or sensitivity of patients with cancer or autoimmune diseases (Graça and Água-Doce 2010; Bartlett et al. 2014; Santos et al. 2014; Zhu

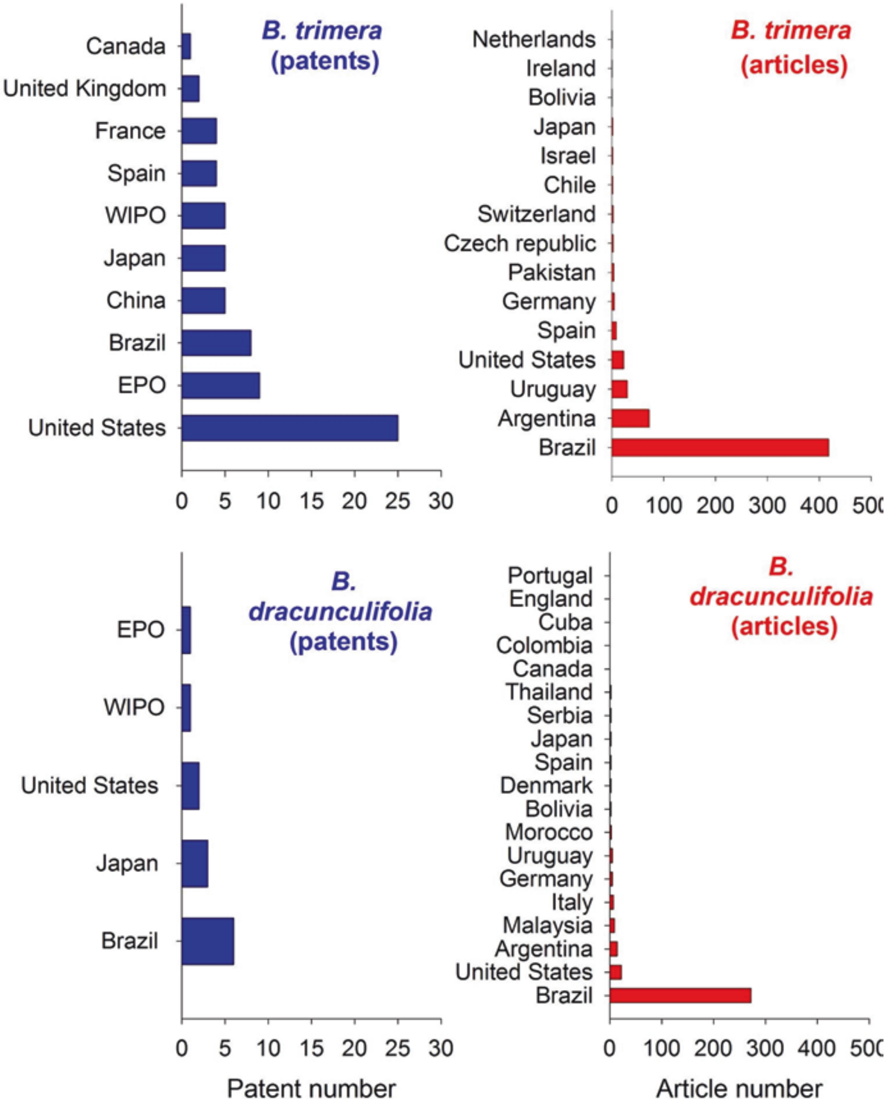

Fig. 19.6 Number of patents and published articles for the species *B. trimera* and *B. dracunculifolia*

2015; Fleisner 2016). Another highlight of the use of pollen in patents, for *B. sarothroides* in this matter, is related to the improvement of immune responses during the treatment of complications derived from transplant and graft rejection. Most of the patents that use pollen as a raw material are for *B. sarothroides* and *B. halimifolia*. *Baccharis halimifolia* is native to Nova Scotia, eastern and southern United States, eastern Mexico, Bahamas, and Cuba (Heering 1907; Hitchcock and Standley 1919; Sánchez and Cano 1983).

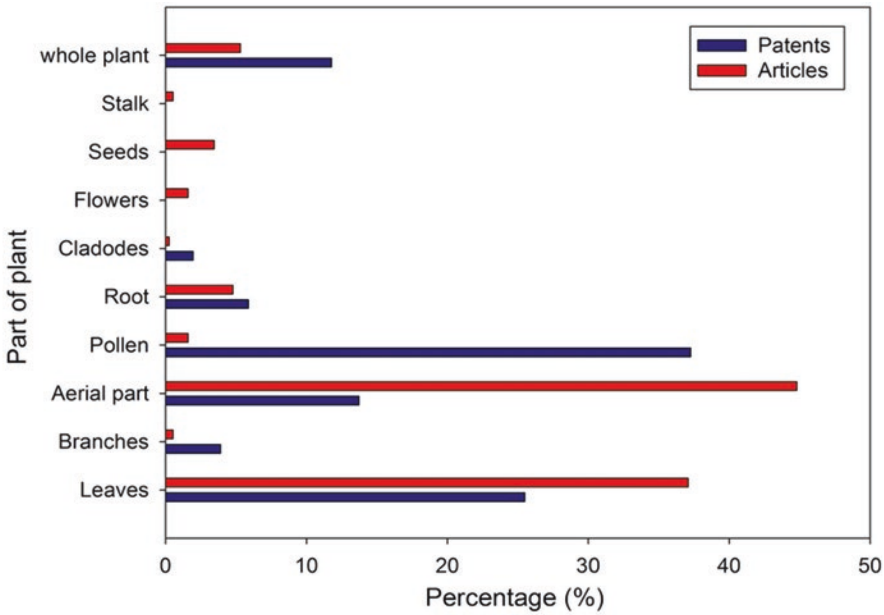

Fig. 19.7 Percentage of patents and articles on plant parts of species of the genus *Baccharis*

In articles, the aerial part as a whole (leaves and branches) was mainly used for studies (44.8%), while the specific use of leaves was found in 37% of the articles (Fig. 19.7). The other parts of research interest were roots, seeds, flowers, pollen, branches, and cladodes, each presenting less than 5% of the articles herein analyzed (Fig. 19.7). *Baccharis* is a genus with a great richness of secondary compounds in leaves, such as flavonoids, phenolics, and, especially, essential oils, which release a distinctive odor that attracts insects (Ferracini et al. 1995; Moreira et al. 2019). Two species of *Baccharis* stand out for the exploration of all plant parts: *B. trimera*, and *B. dracunculifolia*.

4 Processes and Products and the International Classification of Patents

Patents are classified into products, processes, or products and processes (found in a single patent application). The differentiation between product and process can be summarized as follows: the product is directly related to the customer's needs and desires, whereas the process pursues to define how produced items or services can be presented in the most optimized possible way.

As an exemplification of a product patent, there is the first patent application for a body sunscreen that utilized the photo-absorbent chemical compounds of *B.*

sarothroides in the cosmetic composition (Unger and Creery 1998). This application was dated in 1998 by an American company, and the patent was entitled "Sunscreen agents from natural sources". It is known that *B. sarothroides* possesses a high concentration of centaureidin. According to Saeki et al. (2003), centaureidin is able to inhibit the growth of melanocyte dendrites, which reduces epidermal pigmentation. A combination of chemical compounds of natural origin and their proven effectiveness, such as centaureidin, presents an opportunity to create exclusive cosmetic products applied precisely in skin darkening or lightening (Tada et al. 2006).

As to exemplify a process patent, we can reference "Method for obtaining extracts of *Baccharis glutinosa* with antifungal activity" (Rosa-Burgos et al. 2011). This patent, filed in 2015, is the most recent among the reviewed documents in the pharmacology field of plants of the genus *Baccharis* with interest in the development of extraction methods, more specifically of *B. glutinosa* chemical compounds.

Moreover, in product and process patents, the technical formulation characteristics of a given product as well as the methodology used to produce it are described in the same patent application. A good example of this type of patent is "Combination of vegetable extracts modifies immune response and is effective against e.g. multiple sclerosis" (Carreiras 2001). This application fits in the area of oncology and autoimmune diseases. It is a Spanish patent from 2001, which contains in its claims the extraction description of root chemical compounds of several plant species, among them *B. trimera*, followed by the drug formulation and its description as a pharmaceutical product.

In general, about 59.2% of *Baccharis* patents refer to products and processes, 26.3% refer to products, and 14.5% aim at the creation of processes only (Fig. 19.8).

Regardless of the type of patent (product or process), a specific classification is designated. All applications are classified in accordance with the International Patent Classification (IPC) according to their technological area. The assessment of this classification by the users promotes the establishment of yet another effective

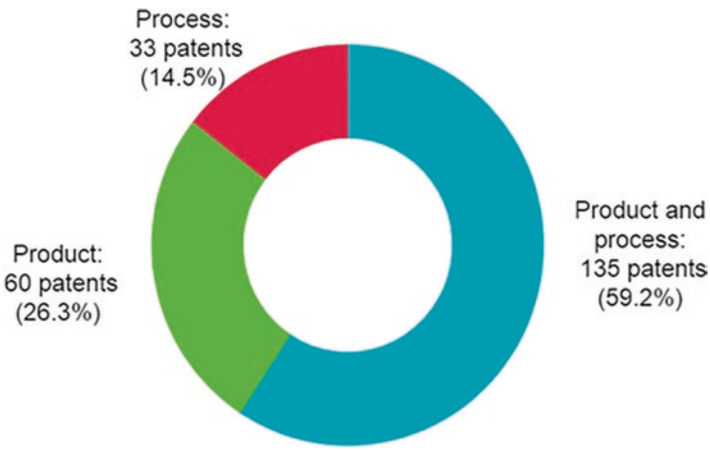

Fig. 19.8 Percentage of *Baccharis* patents classified as product, process, and product and process

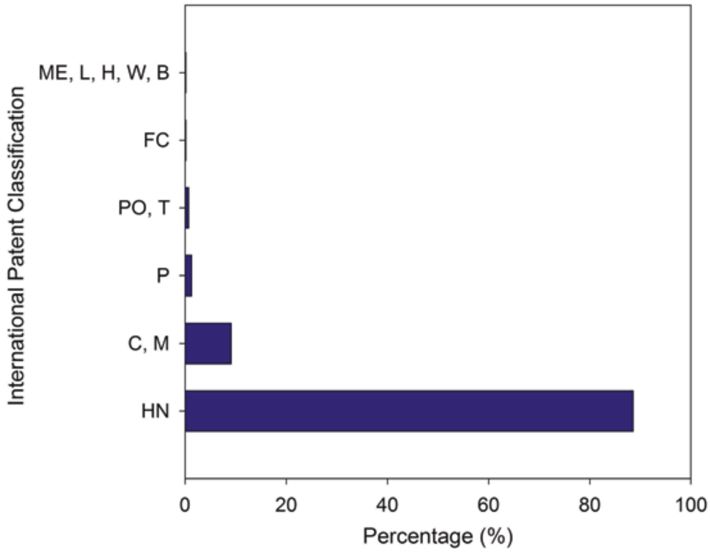

Fig. 19.9 International Patent Classification (IPC) referring to species of the genus *Baccharis*. Abbreviations: *ME* Mechanical Engineering, *L* Lighting, *H* Healting, *W* Weapons, *B* Blasting, *FC* Fixed Constructions, *PO* Performing Operations, *T* Transporting, *P* Physics, *C* Chemistry, *M* Metallurgy, *HN* Human necessities

search tool for the retrieval of patent documents. Statistical analysis of patent filing activity is one of the most used methodologies in technological monitoring (Weid et al. 2018); therefore, IPC can be used as a database for the elaboration of statistics aimed at the industrial property, which allows the assessment of technological development in several areas (OECD 2005). Human needs represent the area of greatest interest for patents of species of the genus *Baccharis* with a frequency of 88.6% (Fig. 19.10). This class of patents encompasses subclasses that involve agriculture, food or food products, articles for personal household use, as well as health and recreation.

5 Areas of Interest and Applications of Patents and Articles

Patents

Baccharis' product and process patents were found in the following application areas: cosmetics, pharmacology, methods of chemical compounds extraction, nutrition, sensors, veterinary, agronomy, environment, and labeling. For *Baccharis*' product patents, the main areas of interest are cosmetics (63.75%) and pharmacology (24.35%) (Fig. 19.9a, Table 19.1). *Baccharis* patents for cosmetic products are

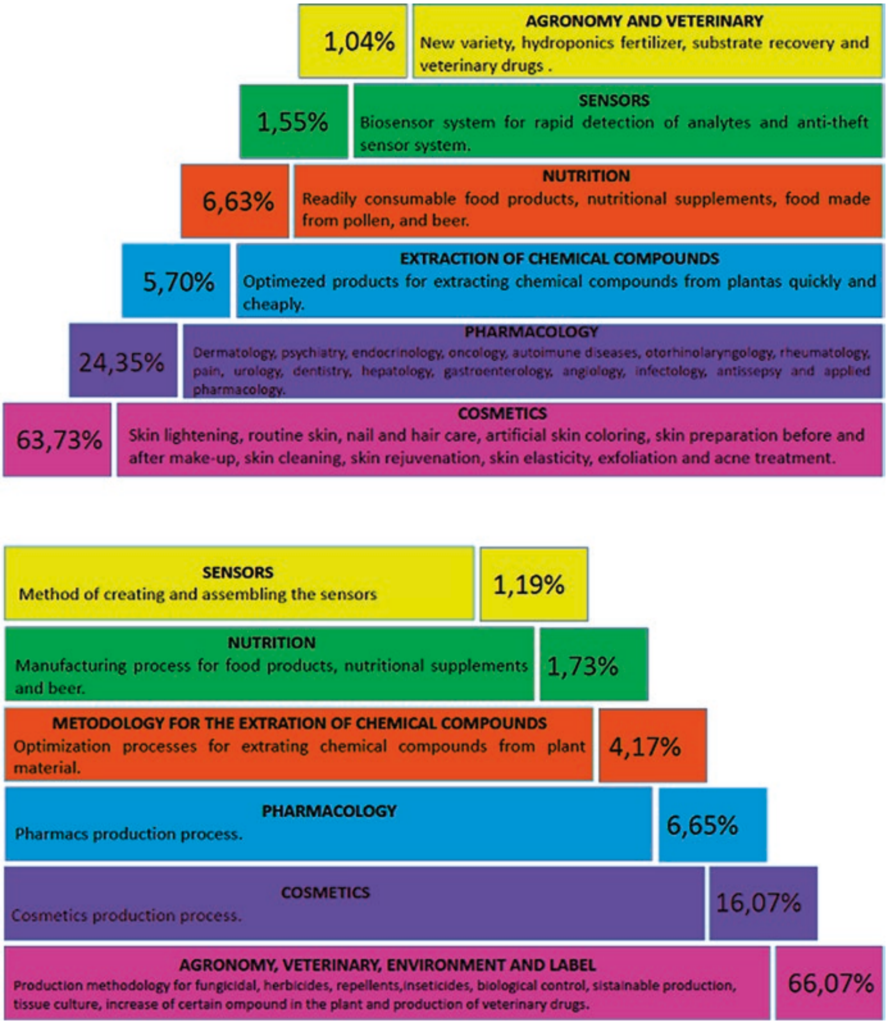

Fig. 19.10 Frequency of patent applications for products (**a**) and processes (**b**) of the genus *Baccharis*, separated by areas of interest

mostly aimed at dermatological treatments, such as hair loss, prevention and treatment of signs caused by age, scar treatment, exfoliating, and others. As for pharmacology, product patents were found for administration and production of drugs in the following areas: psychiatry, endocrinology, oncology, autoimmune diseases, otolaryngology, rheumatology, pain, urology, dentistry, hepatology, gastroenterology, infectology, and applied pharmacology (release of drugs) (Table 19.1). About 18% of patents aimed at oncology draw on the species *B. glutinosa*, *B. megapotamica*, *B. sarothroides*, and also on documents in which the species has not been described at species level, reaching 21% of the analyzed results. Process patents

Table 19.1 (a) Products and (b) processes generated from species of *Baccharis* in the areas of pharmacology and cosmetology

(a) Products
a.1) Dermatology
Skin clarification
Inhibit or restore skin damage caused by dryness
Artificial skin coloration
Cosmetic with anti-inflammatory property
Hair cleaning and hydration
Hair loss treatment
Prevention and cure of gray hair
Sunscreen
Antiperspirant
Routine skin, hair and/or nail care
Skin preparation
Skin protection for diaper wearers
Prevention and treatment for aging
Protection against skin lesions
Artificial skin coloration
Composition for treatment of herpes and cold sores
Diaper rash treatment
Exfoliating
Products for better appearance or health of lips and facial skin
Dehydroascorbic acid or its derivatives for skin coloration; care and/or makeup methods
Wound care
a.2) Psychiatry
Treatment and prevention of cognitive decline and age-related memory impairments
Addiction treatment
a.3) Endocrinology
Sweeteners, promoters, or enhancers of sweeteners
Drug for prevention and treatment of diseases and conditions induced by carbohydrates
Treatment of diabetes, obesity, and other metabolic diseases
Product to promote weight loss
a.4) Oncology and autoimmune diseases
Kit with presegmentation compounds
Treatment or prevention of autoimmune disease, allergic reaction, transplant-related complication, graft rejection
Treatment of infectious diseases, cancer, inflammation, tissue damage, etc.
Induction of immune tolerance
Vaccine to improve immune response
Immunotherapy and vaccine
Immunotherapy and allergy
Treatment of angiogenesis and metastasis
Fc coupled to compositions and methods of its use

(continued)

Table 19.1 (continued)

Product that prevents or limits the effects of chemotherapy
Oncology and autoimmune diseases
a.5) Otorhinolaryngology and allergy
Treatment of one or more nasal or sinus conditions
Composition to prevent and treat type I allergy
Expandable devices for nasal polyps treatment
Treatment for allergies and asthma
Methods and compositions for allergens dosage
Method and device for testing and allergy treatment
a.6) Rheumatology
Treatment for arthritis-associated deformity, including pain and for prevention or treatment of stiffness or inflammation
Prevention, therapy, and osteoporosis treatment
a.7) Ache
Therapeutic inhibitor of vascular smooth muscle cells
Anti-inflammatory (potent COX-2 inhibitors)
a.8) Urology
Treatment of urinary system diseases
a.9) Dentistry
Prevention and treatment of oral diseases
Aroma for oral products
Oral health products
a.10) Hepatology
Compound for hepatitis treatment
a.11) Gastroenterology
Intestinal regulator
Treatment to reverse symptoms of constipation
a.12) Angiology
Treatment of homeostatic instability conditions
Treatment for vascular trauma
Treatment for thrombosis
a.13) Infectology
Malaria treatment
Treatment of diseases related to coronavirus infection (pneumonia and gastroenteritis)
a.14) Applied pharmacology
Product and method for oral administration of nutraceuticals
Promoter of vitamin C transporter production
Drug delivery and release
Antibiotics
a.15) Antisepsis
Paints, coatings, and polymers containing phytochemicals
Paint to apply on surface and inhibit the colonization of organism-painted surfaces
Product with sanitizing, antiseptic, and/or disinfectant function for objects, food, and skin

(continued)

Table 19.1 (continued)

Filtering materials with biocidal phytochemicals
Skin sanitizers (durable)
Hand sanitizer
Antimicrobial film
(b) Processes
b.1) Dermatology
Assessment method of dry skin state
Process for artificial skin coloration
Tanning techniques
Fast and economical process for preparing substituted phenylaldehydes (raw material for the preparation of a large number of aromatic compounds useful in the perfume industry)
b.2) Extraction of compounds
Methodology of secondary metabolites extraction
Identification of compounds found in propolis
Acquisition of propolis extract
Methodology of artepilin C extraction
Process of acquisition of plant extracts and compositions comprising extracellular protease inhibitors
Extraction and use of propolis extracts in products
b.3) Quality control
Methodology for quality control of propolis and extracts of *B. dracunculifolia*
b.4) Antisepsis
Active oxygen scavenger
b.5) Applied pharmacology
Isolation of autoantibodies (autoimmune diseases)
Methodology of product/medicine preparation

focused on pharmacology generally describe the way a certain product was produced or even optimized, the extraction of its compounds, or even the evaluation methods for dermatological problems (Table 19.1).

The greatest highlight in the agronomy, veterinary, and environment fields (about 1% of product patents) is among phytosanitary products formulated with secondary compounds of *Baccharis* species, which have a natural-based formulation and, for this reason, present shorter retention time in the cultivated area and low level of soil and water contamination. Another interesting application is related to hybrid species, that is, the result of natural crossing between genetically similar species, such as the following species: *Baccharis hybris* 'Starn', *Baccharis halimifolia* 'Kolmmyst' (Kolster 2003a), *Baccharis halimifolia* 'Kolmstar' (Kolster 2003b), and *Baccharis halimifolia* 'Kolmsil' (Kolster 2003c). The particularity of these species is their high potential in the recovery of degraded areas due to their morphological characteristics such as deep root system and voluminous aerial part.

Considering the areas of interest of process patents (Fig. 19.9b), cosmetics and pharmacology occupy second and third places with a frequency of 16.07% and 6.55%, respectively. In first place, with 66.07% of frequency, there are processes

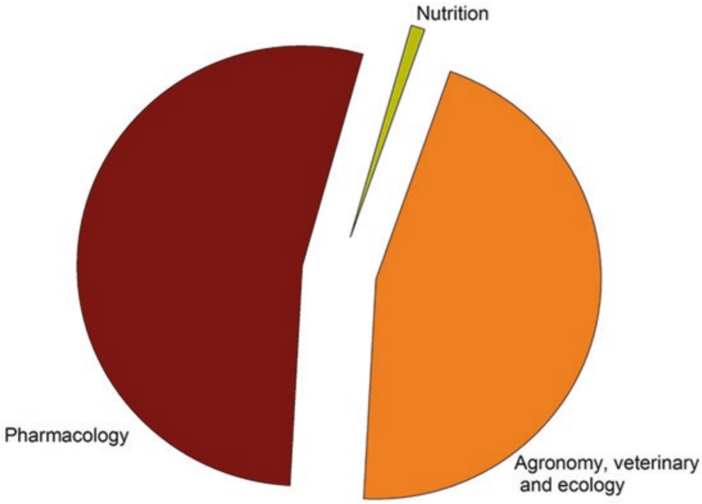

Fig. 19.11 Areas of interest of scientific articles on *Baccharis*

aimed at agronomy and environment, mostly associated with damage reduction caused by herbivores and phytopathogens, but also weed control.

Process patents, when compared to product patents, have been particularly evaluated at a lower economic value, partly due to the difficulty of screening (Kartal 2007). In addition, many product patents are frequently filed with the same methodologic process (Kartal 2007).

Articles

The scientific articles on *Baccharis* can be grouped into three large groups in accordance with similarity of interests: pharmacology (54.5%), agronomy, veterinary and ecology (45.5%), and nutrition (1%) (Fig. 19.11). Within the great area of pharmacology, there are studies focused on the extraction of chemical compounds, taking into account the following aspects: types of solvents, concentration and chemical composition, and according to the plant part, optimization of extraction processes, chromatographic analysis of compounds, and others. In studies that involved tests of medicinal interest, extracted chemical compounds were tested in vivo and in vitro experiments.

Many in vivo and in vitro experiments carried out with *Baccharis* coincide with the testing objectives of patent applicants, such as compounds with carcinogenic, analgesic, anticonvulsant, anti-inflammatory, antihyperglycemic, and antihyperlipidemic functions and antioxidants among others. This similarity suggests an interaction between articles and patents with regard to the knowledge generated on *Baccharis*' biological activities of pharmacological interest, especially those associated with carcinogenic activity of chemical compounds of *Baccharis* (Galvão et al. 2012; González et al. 2018; Jaramillo-García et al. 2018). The species that stood out the most in carcinogenesis studies were *B. coridifolia* and *B. dracunculifolia*. However, within pharmacology scientific articles, 68% refer to biocidal activities found in some *Baccharis.* Some of these articles aim to apply the *Baccharis* compounds to bacteria and fungi responsible for human diseases. In the meantime, no antibiotic product or fungicide with the same activity was observed in patents, only just fungicide patents for the protection of agricultural crops, such as the patent by Burgos and Rocha (2014).

It was also noted that some biological activities, such as the antimalarial action of *Baccharis* species, were more significantly evaluated in articles than in patents. Oliveira et al. (2012) were the inventors of a patent on the use of antimalarial chemical compounds (diterpenes), but the species has not been described at species level. While, in articles found on the same subject, the following *Baccharis* species were used in the tests: *B. microdonta*, B. *paucifloculosa*, *B. punctulata*, *B. reticularioides*, *B. stenocephala*, and *B. genisteloides* (Henning et al. 2011; Budel et al. 2018a, b). *Baccharis*' biological activities for Leishmaniasis treatment (Grecco et al. 2010, 2012; Parreira et al. 2010; Passero et al. 2011; Neto et al. 2019) and Chagas disease (Grecco et al. 2010; Vanini et al. 2012; Guerreiro et al. 2018; Ueno et al. 2018) were only addressed in scientific articles. The species *B. uncinella* and *B. dracunculifolia* showed activity to treat Leishmaniasis and Chagas disease. For Chagas disease treatment, the species *B. semiserrata* and *B. retusa* also showed activity. This lack of interaction between science and technology is aimed at curing neglected diseases, although in 2009, they were considered priorities by the World Health Organization (2004).

In the veterinary field, studies focused on species that cause animal poisoning, with emphasis on *B. megapotamica*. Reports on the intoxication of whole herds, induced resistance, experimental intoxication, and animal testing with the purpose to prevent intoxication were found in the studies. Another information only found in articles is related to the antiophidic capacity that the leaves of *B. crispa* present (Costa 2010).

Baccharis friburguensis was the species of interest in only one scientific article; however, this same species has been pointed out to be used as a natural sweetener. In the four remaining scientific articles involving plants of the genus *Baccharis* in the area of nutrition, there are nutritional analyses in search of carbohydrate sources.

In our study, a total of 85 articles involves morpho-anatomical study areas of the species, taxonomic classification, and floristic surveys (involving native, pioneer, endemic, dominant, weed species, etc.). Specifically, inside ecology, studies with *Baccharis* were carried out on the recovery of degraded areas (e.g., Perea et al. 2019), phytoremediation (Haque et al. 2008), and insect–plant interaction (e.g., Fagundes et al. 2005; Fernandes et al. 2014; Monteiro et al. 2020), mainly with gall-inducing insects (e.g., Arduin et al. 2005; Espirito-Santo et al. 2012; Agudelo et al. 2018).

6 Collaborative Network Among Those Involved in the Patents and Articles

Other aspects related to the study of science–technology interaction start from the analysis of coauthorship. One hundred of scientific articles authors were found in this survey, a number far lower than the number of patent applicants for the genus *Baccharis*: four hundred and four. A survey was carried out with ten patent inventors and scientific article authors (Table 19.2). Bastos JK is the author of the largest number of published scientific articles, with 40 publications. Bastos is a Pharmacognosy professor in the Department of Pharmaceutical Sciences at the Faculty of Pharmaceutical Sciences, University of São Paulo. His research is focused on the organic chemistry of natural products, mainly on secondary metabolites of higher plants and propolis, in which species of the genus *Baccharis* lie, with emphasis on *B. dracunculifolia*. The inventor Reno JM stood out in the ranking of the most frequent inventors, with 20 patent applications. All of Reno' patents were applied by the private company Neorx Corporation. The high number of patents invented by Reno draws attention mainly due to the fact that the other inventors present a frequency of 1 to 3 deposits.

Bastos presented another very interesting feature, as he was one of the 4 patent inventors who also appear on the list of scientific article authors, the other three are Jarvis BB, Rosa-Burgos EC, and Cortez-Rocha MO. Bastos and Jarvis are inventors of one patent each; however, Bastos published 40 articles while Jarvis published 21. Rosa-Burgos and Cortez-Rocha filed two patent applications each, yet the first has seven scientific articles published, while the second has five. This amount of inventors–authors demonstrates how weak is the collaboration between professionals involved in the science and technology of species of the genus *Baccharis*. Pravdic and Oluic-Vukovic (1986) stated that more productive authors tend to form partnerships more frequently, and authors who work in multidisciplinary research exhibit the most frequent collaborative behavior with highly productive authors.

Table 19.2 Ranking of inventors and authors who most filed patents and published scientific articles on the genus *Baccharis*

Inventors	Number of patent deposits	Authors	Number of article publications
Reno JM	20	Bastos JK	40
Theodor LJ	13	Fernandes GW	35
Gustavson LM	10	Tonn CE	27
Axworthy DB	9	Giordano OS	24
Leroy Kunz LL	9	Budel JM	23
Portes P	9	Lago JHG	23
Gupta SK	9	Jarvis BB	21
Simonnet JT	8	Heiden G	20
Jia Q	8	Romoff P	19
Laboureau J	6	da Silva AA	18

The future perspective in which society can be favored by the range of benefits provided by species of the genus *Baccharis* focuses on the need of a deep stage of maturity related to interaction and collaboration of professionals interested in patent study and development. According to Moura (2012), authorship in scientific articles has been configured as an opening opportunity, mainly to compete or obtain funding to carry out their research, discussions between counterparts, and the researcher' scientific visibility in their area of expertise. In contrast, coinvention presents criteria of participation for authorship in technological production, different from those used in scientific production.

Collaborations between universities and companies have been growing in recent years (Cohen et al. 2002; Kon 2016). The knowledge generated by universities is extremely important for industrial development, especially high-tech sectors due to their proximity to the scientific knowledge basis (Klevorick et al. 1995). The financial resources derived from companies are pointed out as one of the advantages of partnership for universities (Lehmann and Menter 2016).

7 Final Considerations

Baccharis stands out for its great potential for science and technology, especially in the pharmacological area, with publications and patents that go beyond limits of origin. Patent filings on *Baccharis*; however, have been hampered due to legal reasons, required time for patenting, and difficulty in patent granting after application. These barriers have affected countries such as Brazil, which, although shows the greatest scientific contribution on *Baccharis*, does not have the greatest economic contribution in the form of patents. The largest number of *Baccharis* patent filings is led by the United States, which, throughout its history, has had great incentives and investments in the innovation sector.

Among the species *B. trimera* and *B. dracunculifolia* represent the species with more scientific studies. *Baccharis trimera* also appears at the top of the species of greatest interest to patent inventors, followed by *B. megapotamica*. This great scientific and market interest in *B. trimera* may be related to the use of secondary metabolites in the treatment of various diseases.

Unfortunately; however, *Baccharis*' scientific knowledge has not always contributed to the advance of the generation of patent filings. Published scientific articles could assist in generating patent filings, such as a potential antibiotic and antifungal for human diseases, treatment of various diseases (such as autoimmune diseases, cancers, among others) bringing innovation and economic incentives. The innovative discoveries evidenced in patents of this genus were also not reflected in the scientific deepening and development. There are no reports in the form of articles on the already patent work deposited, *Baccharis* fiber sensors, nor studies that explore the anticarcinogenic activity of the species *B. glutinosa*, *B. megapotamica*, and *B. sarothroides*.

Another aspect that reinforces the poor interaction between the knowledge generated by articles and patents is the low collaboration among authors of scientific articles (mostly researchers from higher education and research institutions) and patent applicants (mostly companies). These findings indicate an urgent need for greater exchange of knowledge generated from articles and patents, and collaborations between *Baccharis* researchers and applicants to promote science and technology. The application of research and technology helps to create new demands and new industries, which drive a future of economic growth and social development.

Acknowledgments We thank Frederico Oliveira for the development of the maps and the funding agencies CAPES, CNPq, Planta Ltda, and FAPEMIG for the scholarships granted to the authors involved.

References

Agência Nacional de Vigilância Sanitária (2019) Farmacopéia Brasília, vol I. Agência Nacional de Vigilância Sanitária, Brasília.

Agudelo I, Cogoi L, Filip R, Kuzmanich N, Wagner ML, Ricco RA (2018) Anatomy, histochemistry, and comparative analysis of hydroxycinnamic derivatives in healthy leaves and galls induced by *Baccharopelma* spp. (Hemiptera: Psyllidae) in *Baccharis spicata* (Lam) Baill (Asteraceae). Biochem Syst Ecol 77:22–30

Arduin M, Fernandes GW, Kraus JE (2005) Morphogenesis of galls induced by *Baccharopelma dracunculifoliae* (Hemiptera: Psyllidae) on *Baccharis dracunculifolia* (Asteraceae) leaves. Braz J Biol 65:559–571

Arqué-Castells P, Cartaxo RM, García-Quevedo J, Godinho MM (2016) Royalty sharing effort and invention in universities: evidence from Portugal and Spain. Res Policy 45:1858–1872

Bamburg JR (1983) Biological and biochemical actions of tricothecene mycotoxins. In: Hahn FE, Kopecko DJ, Müller EG (eds) Progress in Molecular and Subcellular Biology, vol 8. Springer-Verlag, Heidelberg, pp 41–110

Barbosa M, Fernandes GW, Morris RJ (2019) Interaction engineering: non-trophic effects modify interactions in an insect galler community. J Anim Ecol 8:1168–1177

Barroso GM (1976) Compositae – Subtribo Baccharidinae Hoffmann – Estudo das espécies ocorrentes no Brasil. Rodriguésia 28:1–273

Bartlett JB, Muller GW, Schafer PH, Galustian C, Dalgleish AC, Meyer B (2014) Immunologische Verwendungen von immunomodulatorischen Verbindungen zur Impfung und zur Therapie gegen Infektionskrankheiten. Applicant: Celgene Corporation. EP2301535B1. Priority data: 2005-09-01

Bettucci GR, Rodriguez MV, Ferretti M, Campagna MN, Monti J, Carnovale CE, Alvarez MJ, Martínez ML (2020) Choleretic properties of *Baccharis spicata* aerial parts extracts in male Wistar Rats. Rev Bras Farmacogn 30:54–60

Brandão M, Oliveira AK (1995) Plantas ruderais e subespontâneas do Município de Ouro Preto e sua utilização na Medicina Popular. Daphne 5:49–71

Budel JM, Raman V, Monteiro LM, Almeida VP, Bokek VB, Heiden G, Takeda IJM, Khan IA (2018a) Foliar anatomy and microscopy of six Brazilian species of *Baccharis* (Asteraceae). Microsc Res Tech 81:1–11

Budel JM, Wang M, Raman V, Zhao J, Khan SI, Rehman JU, Techen N, Tekwani B, Monteiro LM, Heiden G, Takeda IM, Farago PV, Khan IA (2018b) Essential oils of five *Baccharis* species: investigations on the chemical composition and biological activities. Molecules 23:1–19

Burgos ECR, Rocha MOC (2014) Method for obtaining extracts of *Baccharis glutinosa* with antifungal activity. Applicant: Universidade de Sonora. MX2014000932A. Priority data: 2013-12-13

Caño L, Campos JA, García-Magro D, Herrera M (2013) Replacement of estuarine communities by an exotic shrub: distribution and invasion history of *Baccharis halimifolia* in Europe. Biol Invasions 15:1183–1188

Caño L, Fuertes-Mendizabal T, García-Baquero G, Herrera M, González-Moro MB (2016) Plasticity to salinity and transgenerational effects in the nonnative shrub *Baccharis halimifolia*: insights into an estuarine invasion. Am J Bot 103:808–820

Caporal FJM, Boldrini II (2007) Florística e fitossociologia de um campo manejado na Serra do Sudeste, Rio Grande do Sul. Rev Bras Biocienc 53:37–44

Carneiro MAA, Fernandes GW (1996) Herbivoria. Ciência Hoje 20:35–39

Carneiro AM, Irgang BE (2005) Origem e distribuição geográfica das espécies ruderais da Vila de Santo Amaro, General Câmara, Rio Grande do Sul. Iheringia Ser Bot 60:175–188

Carreiras GJA (2001) Combinacion de extractos vegetales modificadora de la respuesta inmune. Applicants: Carreiras Garcia José Antônio ES2156694A1

Carvalho-Filho JLS, Blank AF, Alves PB, Ehlert PAD, Melo AS, Cavalcanti SCH, Arrigoni-Blank MF, Silva-Mann (2006) Influence of the harvesting time, temperature and drying period on basil (*Ocimum basilicum* L.) essential oil. Rev Bras Farmacogn 16:24–30

Casagrande M, Zanela J, Júnior AW, Busso C, Wouk J, Lurckevicz G, Montanher PF, Yamashita F, Malfatti CRM (2018) Influence of time, temperature, and solvente on the extraction of bioactive compounds of *Baccharis dracunculifolia*: in vitro antioxidante activity, antimicrobial potential, and phenolic compound quantification. Ind Crop Prod 125:207–219

Cho NJ, Jackman JÁ, Mundargi RC, Park JH, Potroz MG (2017) Microemcapsulation compounds into natural spores and pollen grains. Applicant: Nanyang Technological Universitu. WO2017010945A1. Priority data: 2015-07-16

Claudino CC (2013) *Baccharis trimera* (Less) DC. Estudo fitoquímico e avaliação da citotoxicidade com sulforrodamina B. Tese de Mestrado em Ciências Farmacêuticas, Faculdade de Ciências Farmacêuticas, Universidade Estadual Paulista

Cohen WM, Nelson RR, Walsh JP (2002) Links and impacts: the influence of public research on industrial R&D. Manag Sci 48:1–23

Corrêa MP (1984) Dicionário das plantas úteis do Brasil e das exóticas cultivadas. MINAGRI/IBDF, Rio de Janeiro

Costa PRR (2010) Produtos naturais como ponto de partida para a descoberta de novas substâncias bioativas: Candidatos a fármacos com ação antiofídica, anticâncer e antiparasitária. Rev Virtual Quim 1:58–66

Cutler HC, Jarvis BB (1985) Preliminary observations on the effects of macrocyclic trichothecenes on plant growth. Environ Exp Bot 25:115–128

Dolejs L, Herout V, Sorm F (1961) Sesquiterpenic compounds of *Baccharis genistelloides* Pers: structure of palustrol. Colln Czech Chem Commun Engl Edn 26:811–817

Dundas N (2012) Research intensity and knowledge transfer activity in UK universities. Res Policy 41:262–275

Edreva A, Velikova V, Tsonev T, Dagnon S, Gürel A, Aktaş L, Gesheva E (2008) Stress-protective role of secondary metabolites: diversity of functions and mechanisms. Gen Appl Plant Physiol 34:67–78

Egerova J, Proffitt CE, Travis SE (2003) Facilitation of survival and growth of *Baccharis halimifolia* L. by *Spartina alterniflora* Loisel in a created Louisiana salt marsh. Wetlands 23:250–256

Espirito-Santo MM, Neves FS, Fernandes GW, Silva JO (2012) Plant phenology and absence of sex-biased gall attack on three species of *Baccharis*. PLoS One 10:e46896

Fagundes M, Neves FS, Fernandes GW (2005) Direct and indirect interactions involving ants, insect herbivores, parasitoids, and the host plant *Baccharis dracunculifolia* (Asteraceae). Ecol Entomol 30:28–35

Feduraev P, Chupakhina, Maslennikov P, Skrypnik L (2019) Variation in phenolic compounds content and antioxidant activity of different plant organs from *Rumex crispus* L. and *Rumex obtusifolius* L. at different growth stages. Antioxidants 8:1–15

Fernandes GW, Silva JO, Espírito-Santo MM, Fagundes M, Oki Y, Carneiro MAA (2014) *Baccharis*: a neotropical model system to study insect plant interactions. In: Fernandes GW, Santos JC (eds) Neotropical insect galls. Springer, Dordrecht, pp 193–219

Fernandes GW, Oki Y, Belmiro MS, Resende FM, Junior AC, de Azevedo JL (2018) Multitrophic interactions among fungal endophytes, bees, and *Baccharis dracunculifolia*: resin tapering for propolis production leads to endophyte infection. Arthropod Plant Interact 12:329–337

Ferracini VL, Paraiba LC, Leitao Filho HF, Da Silva AG, Nascimento LR, Marsaioli AJ (1995) Essential oils of seven Brazilian *Baccharis* species. J Essent Oil Res 7:355–367

Fielding RR (2001) *Baccharis*: a genus of the Asteraceae new to Canada. Proc Natl Sci Inst Sci 41:214–215

Fisch CO, Hassel TM, Sandner PG (2015) University patenting: a comparison of 300 leading universities worldwide. J Technol Transfer 40:318–345

Fleisner DC (2016) Methods and devices for allergy testing and treatment. Appicant: Spiriplex, Inc. US2016327567A1. Priority data: 2015-05-07

França E, Vasconcellos AG (2018) Patentes de fitoterápicos no Brasil: uma análise do andamento dos pedidos no período de 1995-2017. Cad Cienc Technol 35:329–359

Galvão LCC, Furletti VF, Bersan SMF, Cunha MG, Ruiz ALTC, Carvalho JE, Santoratto A, Rehder VLG, Figueira GM, Duarte MCT, Ikegaki M, Alencar SM, Rosalen PL (2012) Antimicrobial activity of essential oils against *Streptococcus mutans* and their antiproliferative effects. Evid Based Complement Alternat Med 2012:1–15

Giuliano DA (2001) Classificación infragenérica de las espécies Argentinas de *Baccharis* (Asteraceae, Astereae). Darwin 39:131–154

Gomes V, Fernandes GW (2002) Germination of *Baccharis dracunculifolia* DC (Asteraceae) achene. Acta Bot Bras 16:421–427

González ML, Joray MB, Laiolo J, Crespo MI, Palacios SM, Ruiz GM, Carpinella (2018) Cytotoxic activity of extracts from plants of Central Argentina on sensitive and multidrug-resistant leukemia cells: isolation of an active principle from *Gaillardia megapotamica*. Evid Based Complement Alternat Med 2018:1–13

Graça LRSS, Água-doce AMM (2010) The use of adjuvant to facilitate the induction of immune tolerance. Applicants: Água-doce AMM, Graça LRSS, Instituto de Medicina Molecular, Universidade de Lisboa. WO2010056143A1. Priority data: 2008-11-13

Grecco SS, Reimão JQ, Tempone AG, Sartorelli O, Romoff P, Ferreira MJP, Fávero AO, Lago JHG (2010) Isolation of an antileishmanial and antitrypanosomal flavanone from the leaves of *Baccharis retusa* DC. (Asteraceae). Parasitol Res 106:1245–1248

Grecco SDS, Ferreira MJ, Romoff P, Favero OA, Lago JHG (2012) Phenolic derivatives from *Baccharis retusa* DC (Asteraceae). Biochem Syst Ecol 42:21–24

Guerreiro AC, Cecati FM, Ardánáz CE, Donadel OJ, Tonn CE, Sosa ME (2018) Assessment of the insecticidal potential of the *Eupatorium buniifolium* essential oil against *Triatoma infestans* (Hemiptera: Reduviidae). A chiral recognition approach. Neotrop Entomol 47:418–428

Haque N, Peralta-Videa JR, Jones GL, Gill TE, Gardea-Torresdey JL (2008) Screening the phytoremediation potential of desert broom (*Baccharis sarothroides* Gray) growing on mine tailings in Arizona, USA. Environ Pollut 153:362–368

Heering WCA (1907) Symbolae Antillanae, seu, Fundamenta florae Indiae Occidentalis. editi Ignatius Urban, Germany, 243p

Heiden G, Pirani JR (2016) Taxonomy of *Baccharis* subgen. Tarchonanthoides (Asteraceae: Astereae: Baccharidinae), a group from the southeastern South American grasslands and savannas. Phytotaxa 241:1–70

Heiden G, Barbieri RL, Stumpf ER (2006) Considerações sobre o uso de plantas ornamentais nativas. Ornam Hortic 171:2–7

Heiden G, Antonelli A, Pirani JR (2019) A novel phylogenetic infrageneric classification of *Baccharis* (Asteraceae: Astereae), a highly diversified American genus. Taxon 68:1048–1081

Henning L, Garcia GM, Giannis A, Bussmann RW (2011) New constituents of *Baccharis genistelloides* (Lam.) Pers. ARKIVOC 2011:78–81

Hitchcock AS, Standley PC (1919) Flora of the district of Columbia and Vicinity (Contributions from the United States National Herbarium, vol 21). United States National Museum (Reprinted by Kessinger Publishing, LaVergne, Tennessee, 2010), Washington, pp 329 (+42 plates).

Jaramillo-García V, Trindade C, Lima E, Guecheva TN, Villela I, Martinez-Lopez W, Corrêa DS, Ferraz ABF, Moura S, Sosa MQ, da Silva J, Henriques JAP (2018) Chemical characterization and cytotoxic, genotoxic, and mutagenic properties of *Baccharis trinervis* (Lam. Persoon) from Colombia and Brazil. J Ethnopharmacol 213:210–220

Karam TK, Dalposso LM, Casa DM, de Freitas GBL (2013) Carqueja (*Baccharis trimera*): utilização terapêutica e biossíntese. Rev Bras Plant Med 15:280–286

Kartal M (2007) Intellectual property protection in the natural product drug discovery, traditional herbal medicine and herbal medicinal products. Phytother Res 21:113–119

Khan BZ (2005) The democratization of invention: patents and copyrights in American economic development, 1st edn. Cambridge University Press, New York

Klevorick AK, Levin RC, Nelson RR, Winter SG (1995) On the sources and significance of inter-industry differences in technological opportunities. Res Policy 24:185–205

Kolster PR (2003a) *Baccharis* planta named "Kolmmyst". Applicant: Gebr kolster BV. USPP13744P2. Priority data: 1998–01- 23

Kolster PR (2003b) *Baccharis* planta named "Kolmstar". Applicant: Gebr kolster BV. USPP1895P2. Priority data: 2006-03-17

Kolster PR (2003c) *Baccharis* planta named "Kolmsil". Applicant: Gebr kolster BV. USPP1895P2. Priority data: 1998-01-23

Kon A (2016) Ecossistemas de inovação: a natureza da inovação em serviços. RACEF 7:14–27

Krischik VA, Denno RF (1990) Patterns of growth, reproduction, defense, and herbivory in the dioecious shrub *Baccharis halimifolia* (Compositae). Oecologia 83:182–190

Kroyer G, Hegedus N (2001) Evaluation of bioactive properties of pollen extracts as functional dietary food supplement. Innov Food Sci Emer 2:171–174

Kupchan SM, Bauerschmidt E (1971) Cytotoic flavonols fron *Baccharis sarothroides*. Phytochemistry 10:664–666

Lago JHG, Romoff P, Favero OA, Souza FO, Soares MG, Baraldi PT, Corrêa AG (2008) Chemical composition of male and female *Baccharis trimera* (Less.) DC.(Asteraceae) essential oils. Biochem Syst Ecol 36:737–740

Lehmann EE, Menter M (2016) University–industry collaboration and regional wealth. J Technol Transfer 41:1284–1307

Lindsay MHA, Pearson HJ (1942) Radiant energy receiving system. Depositor: American District Telegraph Co. US2278936A. Deposit data: 25-04-1939

Looy BA, Callaert J, Debachere K (2006) Publication and patente behavior of academic researches: conflicting, reinforrcing or merely co-existing? Res Policy 35:596–608

Macedo JF (1995) Fenologia da floração das plantas invasoras no Campus-Pampulha da Universidade Federal de Minas Gerais. Daphne 5:15–27

Manurung H, Kustiawan W, Kusuma IW, Marjenah M (2017) Total flavonoid content and antioxidant activity of tabat Barito (*Ficus deltoidea* Jack) on different plant organs and ages. J Med Plant 5:120–125

Marques MB (2000) Patentes farmacêuticas e acessibilidade aos medicamentos no Brasil. Hist Cienc Saude-Manguinhos 8:7–21

Martinez EGA, Forero LML, Pérez FC (2015) Promoción del crecimiento de *Baccharis macrantha* (Asteraceae) con bacterias solubilizadoras de fosfatos asociadas a su rizosfera. Acta Biol Colomb 20:121–131

Mejía-Giraldo JC, Winkler R, Gallardo C, Sánchez-Zapata AM, Puertas-Mejía MA (2016) Photoprotective potential of *Baccharis antioquensis* (Asteraceae) as natural sunscreen. Photochem Photobiol 92:742–752

Meyer M (2000) Does science push technology? Patents citing science literature. Res Policy 29:409–434

Meyer M, Batthacharya S (2004) Commonalities and differences between scholarly and technical collaboration. Scientometrics 6:443–456

Moir HVJ (2008) Who benefits? an empirical analysis of Australian and US patent ownership. Centre for Governance of Knowledge and Development (CGKD) working paper. https://doi.org/10.2139/ssrn.1409502

Monteiro GF, Macedo-Reis LE, Dáttilo W, Fernandes GW, Siqueira de Castro F, Neves FS (2020) Ecological interactions among insect herbivores, ants and the host plant *Baccharis dracunculifolia* in a Brazilian mountain ecosystem. Austral Ecol 45:158–167

Moreira FGP, Torkomian ALV, Soares TJCC (2016) Exploration and firms' innovative performance. How does this relationship work? Rev Bras Gest Neg 18:392–415

Moreira X, Abdala-Roberts L, Nell CS, Vázquez-González C, Pratt JD, Keefover-Ring K, Mooney KA (2019) Sexual and genotypic variation in terpene quantitative and qualitative profiles in the dioecious shrub *Baccharis salicifolia*. Sci Rep 9:1–10

Moura AMM (2012) Motivação para a pesquisa, determinação de parcerias e divisão da coautoria e coinvenção: principais critérios utilizados pelos pesquisadores da área da Biotecnologia. Em Questão 18:29–45

Muller-Riebau FJ, Berger BM, Yegen O, Cakir C (1997) Seasonal variation in the chemical compositions of essential oils of selected aromatic plants growing in Turkey. J Agric Food Chem 45:4821–4825

Narin F (1995) Patents as indicators for the evaluation of industrial research output. Scientometrics 34:489–496

Narin F, Hamilton KS, Olivastro D (1997) The increasing linkage between US technology and public science. Res Policy 26:317–330

Navares N, Brosh A, Pittrof W (2010) Seasonal dynamics of nutritional quality of California chaparral species. Anim Feed Sci Technol 158:44–56

Neto RNM, Setúbal RFB, Higino TMM, Brelaz-de-Castro MCA., Silva LCN, Aliança ASDS (2019) Asteraceae plants as sources of compounds against leishmaniasis and Chagas disease. Front Pharmacol 10:1–20

Neves FS, Cornelissen T, Coelho MS, Barbosa M, Carneiro MAA, Ribeiro SP, Fernandes GW (2016) Antagonistic interactions in the rupestrian grasslands: new insights and perspectives. In: Fernandes GW (ed) Ecology and conservation of mountaintop grasslands in Brazil. Springer, Switzerland, pp 315–343

Nogués J (1990) Patents and pharmaceutical drugs: understanding the pressures on developing countries. J World Trade 24:81–104

Noorden RV (2016) Snail's pace: nature readers on their longest wait to get published. Nature 19375:1–2

OECD (2005) Annual Report 2005. OECD Publishing, Paris, 143 p

Oliveira AB, Varotti FP, Batista R. (2012) Composições farmacêuticas antimaláricas contendo derivados de diterpenos caurânicos. Applicants: Batista Ronan, Olivera Alaide Braga, Universidade Federal de Minas Gerais, Varotti Fernando de Pilla. WO2012083408A1. Priority data: 2010-12-23

Park YK, Paredes-Guzman JF, Aguiar CL, Alencar SM, Fujiwara FY (2004) Chemical constituents in *Baccharis dracunculifolia* as the main botanical origin of southeastern Brazilian propolis. J Agric Food Chem 52:1100–1103

Parreira NA, Magalhães LG, Morais DR, Caixeta SC, de Sousa JPB, Bastos JK, Cunha WR, Silva MLA, Nanayakkara NPD, Rodrigues V, Filho AAS (2010) Antiprotozoal, schistosomicidal, and antimicrobial activities of the essential oil from the leaves of *Baccharis dracunculifolia*. Chem Biodivers 7:993–1001

Passero LFD, Bomfim-Melo A, Corbett CEP, Laurenti MD, Toyama MH, Toyama DO, Ramoff P, Fávero AO, Grecco SSG, Zalewsky CY, Lago JHG (2011) Anti-leishmanial effects of purified compounds from aerial parts of *Baccharis uncinella* C. DC. (Asteraceae). Parasitol Res 108:529–536

Pavan-Fruehauf S (2000) Plantas medicinais de Mata Atlântica: manejo sustentado e amostragem. Annablume/FAPESP, São Paulo, 216p

Perea R, Cunha JS, Spadeto C, Gomes VM, Moura AL, Rúbia B, Fernandes GW (2019) Nurse shrubs to mitigate plant invasion along roads of montane Neotropics. Ecol Eng 136:193–196

Perri NB, Anderson RE, Brennan NJ, Douglas MH, Heaney AJ, McGimpsey JA, Smallfield BM (1999) Essential oils from dalmatian sage (*Salvia officinalis* L.): variations among individuals, plant parts, seasons, and sites. J Agric Food Chem 47:2048–2054

Pravdic N, Oluic-Vukovic V (1986) Dual approach to multiple authorship in the study of collaborator and scientific output relationship. Scientometrics 10:259–280

Radaelli V (2007) Etapas evolutivas da indústria farmacêutica: da formação à consolidação, expansão e hegemonia das grandes empresas. Pensam Real 20:59–77

Ritter MR, Baptista LRM (2005) Levantamento florístico da família Asteraceae na “Casa Ede Pedra” e áreas adjacentes, Bagé, Rio Grande do Sul. Iheringia Ser Bot 60:5–10

Rodrigues VEG, Carvalho DA (2001) Plantas medicinais no domínio do cerrados. UFLA, Lavras, 180p

Rodrigues DM, De Souza MC, Arruda C, Pereira RAS, Bastos JK (2020) The role of *Baccharis dracunculifolia* and its chemical profile on green propolis production by *Apis mellifera*. J Chem Ecol 46:150–162

Rosas-Burgos ECR, Cortez-Rocha MO, Plascenciajatomea M, Cinco-Moroyoqui FJ, Robles-Zepeda RE, Lópezcervantes J, Sánchez-Machado DI, Lares-Villa F (2011) The effect of *Baccharis glutinosa* extract on the growth of mycotoxigenic fungi and fumonisin B1 and aflatoxin B1 production. World J Microbiol Biotechnol 27:1025–1033

Saeki Y, Kanamaru A, Matsumoto K, Tada A (2003) PP01The inhibitory effects of centaureidin on the outgrowth of dendrites, melanosome transfer and melanogenesis in normal human melanocyte. Pigment Cell Res 16:593–593

Sánchez MS, Cano EFC (1983) Listados Floristicos de México. II. Flora de Quintana Roo. Universidad Nacional Autónoma de México, México

Santos CF, Popa-Mckiver M, McCord AM, Hirschel M (2014) Materials and methods for directing an immune response to an epitope. Applicant: Biovest International Inc. US20140140986A1. Priority data: 2010-11-08

Shadlen KC, Sampat BN, Kapczynsky A (2019) Patents, trade and medicines: past, present and future. Rev Int Polit Econ 27:75–97

Silva Filho AA, Resende DO, Fukui MJ, Santos FF, Pauletti PM, Cunha WR, Silva MLA, Gregório LE, Bastos JK, Nanayakkara NPD (2009) In vitro antileishmanial, antiplasmodial and cytotoxic activities of phenolics and triterpenoids from *Baccharis dracunculifolia* DC (Asteraceae). Fitoterapia 80:478–482

Silva CM, Caetano FH, Pereira FDC, Morales MAM, Sakane KK, Moraes KCM (2019) Cellular and molecular effects of *Baccharis dracunculifolia* D.C. and *Plectranthus barbatus* Andrews medicinal plant extracts on retinoid metabolism in the human hepatic stellate cell LX-2. BMC Complement Altern M 19:1–11

Sims-Chilton NM, Zalucki MP, Buckley YM (2010) Long-term climate effects are confounded with the biological control programme against the invasive weed *Baccharis halimifolia* in Australia. Biol Invasions 12:3145–3155

Snyder AP (1986) Qualitative, quantitative and technological aspects of the trichothecene mycotoxins. J Food Prot 49:544–569

Sousa JPB, Leite MF, Jorge RF, Resende DO, Silva Filho AA, Furtado NA, Soares AEE, Spadaro ACC, Magalhães PM, Bastos JK (2011) Seasonality role on the phenolics from cultivated *Baccharis dracunculifolia*. Evid Based Complement Alternat Med 2011:1–8

Souza ARS, Moraes SZC, Viana-Júnior AB, Araújo ED (2019) Toward a novel pharmacology and therapeutic understanding of Brazilian Propolis: a meta-analytical approach. Pharmacogn Rev 14:1–7

Tada A, Kanamaru A, Ito Y (2006) Control of melanosome transfer by promoting shrinkage or expansion of melanocyte dendrites. Int J Cosmet Sci 28:147–149

Tognon GB, Cuquel FL (2016) Ornamental potential use of *Baccharis milleflora* and *Baccharis tridentata* as ornamental cut foliage. Cien Rural 46:70–75

Tokarnia CH, Peixoto PV, Gava A, Barros CSL (1992) Intoxicação experimental por *Baccharis megapotamica* var. *megapotamica* e var. *weirii* (Compositae) em bovinos. Pesqui Vet Bras 12:19–31

Ueno Y (1983) Tricotecenes-chemical, biological and toxicological aspects. Elsevier, Amsterdam

Ueno AK, Barcellos AF, Costa-Silva TA, Mesquita JT, Ferreira DD, Tempone AG, Romoff P, Antar GM, Lago JHG (2018) Antitrypanosomal activity and evaluation of the mechanism of action of diterpenes from aerial parts of *Baccharis retusa* (Asteraceae). Fitoterapia 12:55–58

Unger EC, Creery TPM (1998) Sunscreen agents from natural sources. Applicant: Imarx Pharmaceutical Corp. US5824312A. Priority data: 1994-03-10

Vanini AB, Fleming AC, Santos TG, Purnhagen L (2012) Chemical characterization and antimicrobial evaluation of the essential oils from *Baccharis uncinella* DC and *Baccharis semiserrata* DC (Asteraceae). J Essent Oil Res 24:547–554

Vasconcellos AG, Esquibel MA, Lage CLS (2004) Proteção patentária de fitoterápicos no Brasil: um estudo sobre os depósitos de patente ao longo da década de 90. Rev Bras Plant Med 7:51–56

Verdi LG, Brighente IMC, Pizzolatti MG (2005) Gênero *Baccharis* (Asteraceae): aspectos químicos, econômicos e biológicos. Quim Nova 28:85–94

Vesela D, Sman D, Valteronová I, Vanek T (1999) Seasonal variations in the contents of taxanes in the bark of *Taxus baccata* L. Phytochem Anal 10:319–321

Vessella F, Sciré M, Salis A, Piovesan G (2015) Natural regeneration and gender-specific spatial pattern of *Taxus baccata* in an old-growth population in Foresta Umbra (Italy). Dendrobiology 73:75–90

Vieira RF, Silva SR (2002) Estratégias para conservação e manejo de recursos genéticos de plantas medicinais e aromáticas. Resultados da 1° reunião técnica. Embrapa/Ibama/MMA/CNPq, Brasília, 184p

Vivien FD, Nieddu M, Befert N, Debref R, Giampietro M (2019) The hijacking of the bioeconomy. Ecol Econ 159:189–197

Weid I von der, Santos, PR, Valadão ABG, Mayerhoff ZDVL (2018) Categorização do setor de biotecnologia baseada na Classificação Internacional de Patentes e análise do panorama de depósito de pedidos de patentes neste Setor, no Brasil (2012–2016). INPI, DIRPA, CEPIT, DIESP, Rio de Janeiro, 28p

Woolsey J, Hanna C, Mceachern K, Anderson S, Hartman BD (2018) Regeneration and expansion of *Quercus tomentella* (Island Oak) groves on Santa Rosa Island. West N Am Nat 78:758–767

World Health Organization (2004) The World Health Organization quality of life (WHOQOL) BREF 2012 revision. World Health Organization, Switzerland

Zhu X (2015) Fc coupled compositions and methods of their use. Applicant: University of Maryland. US2015004161A1. Priority data: 2013-07-01