Research, Society and Development, v. 10, n. 14, e333101422076, 2021
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v10i14.22076

Technological prospection: the genus *Mikania* in therapeutic use

Prospecção tecnológica: o gênero *Mikania* em uso terapêutico

Prospección tecnológica: el género *Mikania* em uso terapéutico

Received: 10/20/2021 | Reviewed: 10/29/2021 | Accept: 11/01/2021| Published: 11/03/2021

Nathália Andrezza Carvalho de Souza
ORCID: https://orcid.org/0000-0003-1126-0126
Federal University of São Francisco Valley, Brazil
E-mail: nathaliaacsouza@gmail.com
Victória Laysna dos Anjos Santos
ORCID: https://orcid.org/0000-0001-5906-8227
Federal University of São Francisco Valley, Brazil
E-mail: vic.anjos@gmail.com
Tarcísio Cícero de Lima Araújo
ORCID: https://orcid.org/0000-0003-4376-9912
Federal Rural University of Pernambuco, Brazil
E-mail: tarcisiocla62@gmail.com
Pedrita Alves Sampaio
ORCID: https://orcid.org/0000-0003-2955-6873
Federal Rural University of Pernambuco, Brazil
E-mail: sampaiopedrita@gmail.com
Renata Rivelli Menezes de Souza
ORCID: https://orcid.org/0000-0003-0220-3656
Federal University of São Francisco Valley, Brazil
E-mail: renatarivelli1@hotmail.com
Pedro José Rolim Neto
ORCID: https://orcid.org/0000-0003-0723-2587
Federal University of Pernambuco, Brazil
E-mail: rolim.pedro@gmail.com
Rodolfo Hideki Vicente Nishimura
ORCID: https://orcid.org/0000-0002-3971-142X
Federal University of São Francisco Valley, Brazil
E-mail: rodolfo_hvn@yahoo.com.br
Larissa Araújo Rolim
ORCID: https://orcid.org/0000-0002-2403-1026
Federal University of São Francisco Valley, Brazil
E-mail: larissa.rolim@univasf.edu.br

Abstract
The genus *Mikania* (Asteraceae) comprises about 450 species of these, 203 are found in Brazil and present several chemical and biological activities. Considering the variety of species and their therapeutic properties, the present study aimed to perform technological prospecting of this genus, since this approach aims to contribute to technological, scientific and innovation research. For this purpose, the patent documents were analyzed, regarding the applicant countries, year of filing and the international classification of patents of the genus *Mikania*. The search was conducted in the databases World Intellectual Property Organization (WIPO), European Patent Office (EPO) and the National Institute of Industrial Property (INPI) in October 2020, using the descriptor "*Mikania*"; present in the title and/or abstract in addition, documents that included medicinal approaches were selected. Thus, taking into consideration the filing countries, Japan, Brazil and the United States led the patent deposits, with the first document filed in 1991 and the largest number of applications in the years 2000 and 2010. The data concerning the international patent classification are concentrated in subclass A61K, which deals with preparations for medical, dental or hygienic purposes. These results demonstrated the therapeutic and technological potential of the *Mikania* species and thus which can be evidenced the potential of this study.
Keywords: *Mikania;* Innovation; Intellectual property.

Resumo
O gênero *Mikania* (Asteraceae) compreende cerca de 450 espécies, destas, 203 são encontradas no Brasil e apresentam várias atividades químicas e biológicas. Considerando a variedade de espécies e as suas propriedades terapêuticas, o presente estudo teve como objetivo realizar a prospecção tecnológica deste gênero, uma vez que esta abordagem visa contribuir para a investigação tecnológica, científica e de inovação. Para isto, foram analisados os documentos de patentes, relativos aos países candidatos, ano de depósito e a classificação internacional de patentes do

gênero *Mikania*. A pesquisa foi conduzida nas bases de dados da Organização Mundial da Propriedade Intelectual (WIPO), Instituto Europeu de Patentes (EPO) e Instituto Nacional da Propriedade Industrial (INPI) em outubro de 2020, utilizando o descritor "*Mikania*" presente no título e/ou resumo, foram selecionados documentos que incluíam abordagens medicinais. Assim, levando em consideração os países depositários, Japão, Brasil e Estados Unidos lideraram os depósitos de patentes, com o primeiro documento depositado em 1991 e o maior número de pedidos nos anos 2000 e 2010. Os dados relativos à classificação internacional de patentes concentram-se na subclasse A61K, que trata de preparações para fins médicos, dentários ou higiênicos. Estes resultados demonstraram o potencial terapêutico e tecnológico da espécie *Mikania* e podem, assim, ser evidenciadas as potencialidades deste estudo.
Palavras-chave: *Mikania*; Inovação; Propriedade intelectual.

Resumen
El género *Mikania* (Asteraceae) comprende unas 450 especies, de las cuales 203 se encuentran en Brasil y presentan diversas actividades químicas y biológicas. Teniendo en cuenta la variedad de especies y sus propiedades terapéuticas, el presente estudio tuvo como objetivo realizar la prospección tecnológica de este género, ya que este enfoque pretende contribuir a la investigación tecnológica, científica y de innovación. Para ello, se analizaron los documentos de patentes, relativos a los países candidatos, el año de presentación y la clasificación internacional de patentes del género *Mikania*. La búsqueda se realizó en las bases de datos de la Organización Mundial de la Propiedad Intelectual (WIPO), la Oficina Europea de Patentes (EPO) y el Instituto Nacional de la Propiedad Industrial (INPI) en octubre de 2020, utilizando el descriptor "*Mikania*" presente en el título y/o el resumen, se seleccionaron los documentos que incluían enfoques medicinales. Así, teniendo en cuenta los países depositantes, Japón, Brasil y Estados Unidos lideraron la presentación de patentes, con el primer documento presentado en 1991 y el mayor número de solicitudes en los años 2000 y 2010. Los datos relativos a la clasificación internacional de patentes se concentran en la subclase A61K, que trata de las preparaciones para fines médicos, dentales o higiénicos. Estos resultados demostraron el potencial terapéutico y tecnológico de la especie *Mikania*, por lo que se puede evidenciar el potencial de este estudio.
Palabras clave: *Mikania;* Innovación; Propiedad intelectual.

1. Introduction

Mikania Willd. is a genus belonging to the family Asteraceae (Compositeae) and largest representative of the tribe Eupatorieae, comprising about 450 species (Coutinho, Gonçalves, & Marcucci, 2020; Honório, Quaresma, Oliveira, & Loiola, 2019). In Brazil there are 203 species, which are distributed in all regions and phytogeographic domains (Ritter, Gandara, Simão-Bianchini, Souza-Buturi, & Abreu, 2020; Silva, Owiti, & Barbosa, 2018).

Some secondary metabolites that present pharmacological activities have already been identified in several parts of *Mikania*. Among the main chemical classes present in this genus, the following stand out coumarins and derivatives, sesquiterpenes, sesquiterpene lactones, diterpenes, phytosterols/terpenoids and flavonoids (Rufatto, Gower, Schwambach, & Moura, 2012).

Pharmacological studies show that *Mikania* species have activities in the respiratory tract, anti-inflammatory, hypoglycemic, antioxidant, antiallergic, analgesic (Coutinho et al., 2020; Silva et al., 2018). The proof of the therapeutic potential of the genus facilitates research strategies and investigation of applicability in the areas of innovation and biotechnology. The survey of patents and publications enables the direction of knowledge for production and technological, scientific and economic development, in addition to issues that facilitate decision making (Correia, Júnior, Spósito, & Pungartnik, 2020; Pires, Ribeiro, & Quintella, 2020).

In this context, the objective of this study was to carry out a technological prospection on the *Mikania* genus, in order to verify the market trends of pharmaceutical products developed from its species, as well as to relate the patent deposits found with other scientific productions on this genus.

2. Methodology

The search was conducted in the databases of the World Intellectual Property Organization (WIPO), the European Patent Office (EPO) and the Brazilian National Institute of Industrial Property (INPI), considering all patent filings until

October 2020. The term "*Mikania*" was used as a descriptor, and the patents that presented the descriptor in the title or abstract were analyzed. In order to refine the search results, only patents with a medicinal approach were included, as well as pharmaceuticals and cosmetics. Duplicate patents within the same database were excluded (Silva et al., 2015).

The patents obtained were analyzed according to the country of origin, year of publication, International Patent Classification (IPC) and the *Mikania* species used. The data obtained were presented in graphs and figures processed in the Origin® software, version 8.0.

3. Results and Discussion

Using the descriptor "*Mikania*" and the preliminary criteria established, 234 patents were identified, 108 patents in WIPO, 119 in EPO and 07 in INPI. After analyzing the patents found and including only those with a medicinal approach, 34 patents were selected for this technological prospection study (WIPO - 21 patents; EPO - 10 patents; and INPI - 03 patents).

3.1 *Analysis of the WIPO database data*

Of the 21 selected patents, it was observed that one patent was duplicated, but with different CIP and filing countries. For the purposes of this technological prospection, only the patent with the oldest filing date was considered, resulting in 20 patents found in WIPO. Thus, Table 1 describes the title, identification number, a brief description of the patents and the *Mikania* species analyzed in each patent found in WIPO.

Table 1 - Results and summarized description obtained from the term *Mikania* at WIPO.

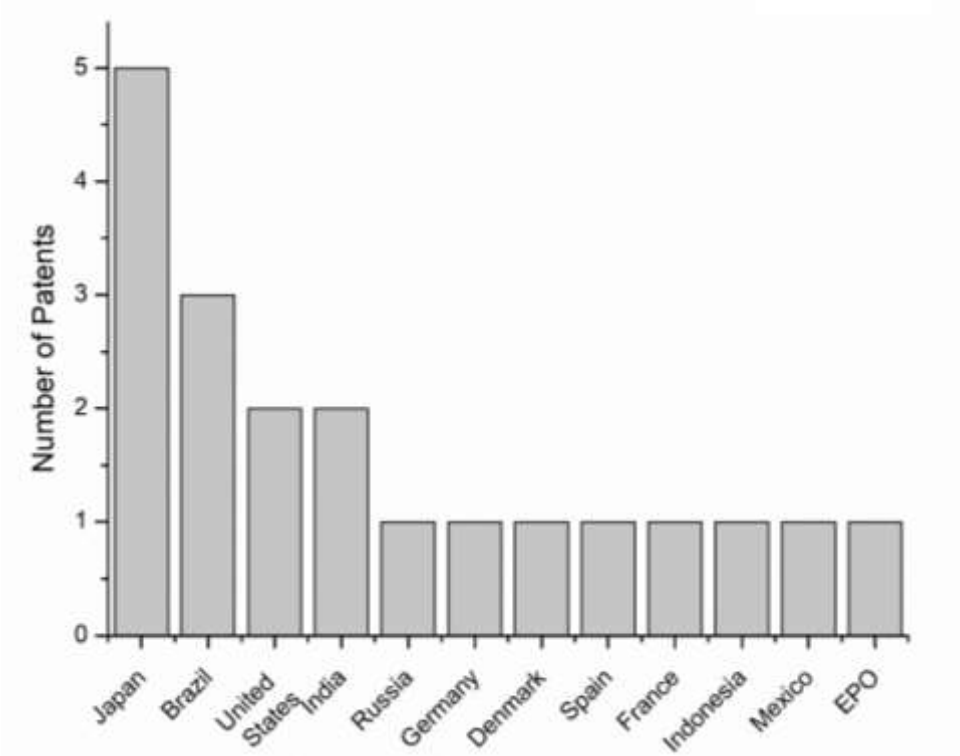
Title[a]	Patent Description[b]	Species
Aerosol cosmetic	Cosmetic suppression in aerosol with vegetal extracts and with excellent stability.	*Mikania sp.*
Antioxidative stress agent	Antirust stressing agent derived from the natural product that accelerates the improvement activities of the Antioxidant Response Element (ARE) in a path Erythroid-2 Nrf2/ARE related nuclear factor participating in the oxidative stress, thus inducing the expression of an antioxidative enzyme to mitigate the oxidative stress.	*M. glomerata*
Composicion farmaceutica y metodo de tratamento utilizando dicha composicion	Extract derived from plants that have active components capable of inhibiting the lethal effects of a poisonous animal poison, the extracts being combined with an acceptable pharmaceutical vehicle and combined in an effective proportion to inhibit the lethal effects of the poison.	*M. guaco*
Composition for suppressing emission of odor	Odor emission suppressive composition is formulated with plants of several genres.	*M. lindleyana*
Formulações farmacêuticas a partir do extrato etanólico das folhas de *Mikania glomerata* Sprengel	Production of an anxiolytic agent and central nervous system depressant, obtained from the ethanolic extract of the leaves of the plant *M. glomerata* Sprengel.	*M. glomerata*
Fremgangsmåde til fremstilling af mikania-ekstrakter, som indeholder mikanolid og dihydromikanolid, og anvendelse i behandlingen af prolifererende sygdomme	Inhibitors of DNA polymerase, extracts enriched with mikanolide and dihydromikanolide or mixtures that can be used for the preparation of drugs for the treatment of proliferative diseases, particularly cancer, viral diseases, or parasitic diseases caused by protozoa or protists.	*Mikania sp.* *(not specified)*
Heatoproblective activity of *Mikania scandens* (l) Willd. against thisaccta mide induced hepato toxicity	Composition of synergistic herbs for the hepatoprotective activity. Preparation process of 4-(l-Carboxy-ethyl)-8-9-dimethyl-cyclodeca-2, carboxylic acid of 5 diene of *M. scandens* (L.) Willd.	*M. scandens*
Herbal compositions for management of bone disorders and methods thereof	Pharmaceutical phytotherapic preparation to natural treatment and management of metabolic bone disorders with anti-osteotetotic potential composed of *M. micrantha* and *Zinziber officinale* as active ingredient and at least one acceptable pharmaceutical excipient. The herbal preparation of this publication is economical and exhibits minimal side effects.	*M. micrantha*
Methods for inhibiting conversion of choline to trimethylamine (TMA)	Plant extracts from the genus *Mikania* inhibit choline metabolism through the intestine or microbiota of the digestive tract, resulting in reduced trimethylamine formation (TMA). Extracts of *M. guaco* Bonpl. inhibit the conversion of choline into TMA, *in vivo* and *in vitro* and reduce it to trimethylamine oxide (TMAO), providing a composition composed of an extract of *Mikania*	*M. guaco* Bonpl.
Mikanolide and dihydromikanolide as inhibitors of DNA-polymerases	Mikanolide and dihydromikanolide are used to treat proliferative and parasitic diseases. In addition, the invention concerns a medicinal agent containing plant extract.	*M. cordata* *M. micrantha* *M. scandens*
Neurite outgrowth agent	The neuritis growth agent comprises compounds of various plants. A preventive/therapeutic agent for neurodegenerative diseases, a preventive/therapeutic agent for Alzheimer's and dementia diseases and food are provided, each comprising the neuritis growth agent.	*M. glomerata*
New 11-membered ring compound	New 11-member ring compound expressed by a specific and useful structural formula as a carcinostatic agent, among others. The compound can be produced by extracting the dry leaf and stalk of M. hirsutissima with ethanol, concentrating the extract under reduced pressure and purifying the concentrate by column chromatography.	*M. hirsutisima*
Un nouveau medicament, le dihydromikanolide, son obtention par extraction de la plante *Mikania* micrantha et son utilisation comme agent anti-proliferatif	Anti-proliferative agent, from dihydromikanolide-enriched extracts as well as dihydromikanolide. It is also intended to obtain them by extraction of the plant *M. micrantha*.	*M. micrantha*

Pharmaceutical composition and method of treatment utilizing the composition	An antivenom composition composed of extracts of active components of the plants combined in effective proportions; the method of elaboration of this composition; the pharmaceutical products derived from these extracts of active components; and a method of treatment of snake bites, scorpion bites and similar using this composition.	*M. guaco*
Procedimiento de preparacion de extractos de *Mikania* que contienen mikanolida y dihidromikanolida y utilizacion en el tratamiento de enfermedades proliferativas	Drugs as antiproliferative agents, extracts enriched with dihydromikanolide, obtained by extraction of *M. micrantha*. The effects of a treatment using the compounds of the invention in the incorporation of cytosine marked with 32P to a presence of DNA of DNA polymerase (acellular system); the incorporation of tritiated thymidine in the DNA of the tumor cells in division for a short period of time (cellular system); proliferation of two human cellular lines Mia-Paca2 and Du145.	*M. cordata* *M. micrantha* *M. scandens*
Process for preparing *Mikania* extracts containing mikanolide and dihydromikanolide and use in the treatment of proliferative disorders	Polymeric DNA inhibitors, i.e., mikanolide, dihydromikanolide and dihydromikanolide-enriched extracts. These compounds or mixtures can be used to prepare drugs for the treatment of proliferative diseases such as cancer, viral diseases, or parasitic diseases caused by protozoa or prothesisists.	*M. cordata* *M. micrantha* *M. scandens*
Verfahren zur herstellung von *Mikania* extrakten enthaltend mikanolide und dihydromikanolide und verwendung in der behandlung proliferativer erkrankungen	Dihydromikanolide-enriched extracts in the form of drugs and, in particular, in the form of antiproliferative agents from preparation by extraction of the plant *M. micrantha*.	*M. cordata* *M. micrantha* *M. scandens*
Processo de preparação de extratos secos padronizados de *Mikania* sp., Asteraceae (Guaco), extratos secos padronizados assim obtidos e aplicações	Standardized dry vegetal extract in coumarin and *o*-cumaric acid, elaborated from the extraction, characterization, standardization, and drying of a guaco extract. The dry extract showed antiulcerogenic activity in the model and Indometacin-induced ulcers. The production of dry extracts by spray drying from the leaves of *Mikania* sp. can be an interesting and promising alternative to obtain this raw material.	*Mikania* sp.
Processo para extração de frações do extrato hidro-alcoólico da *Mikania glomerata*; fração MG1 obtida pelo processo; composição farmacêutica contendo a dita fração e uso terapêutico da composição em doenças respiratórias em geral	Obtaining fractions from the hydro-alcoholic extract of *M. glomerata* leaves with dilating activity of the respiratory smooth, anti-edema and anti-allergic musculature. The organic fraction presented great dilating activity of the respiratory smooth muscle much more intense than the dry residue of the hydro-alcoholic extract. The inorganic fraction also presented anti-edema activity in mice and anti-allergic action in rats. From the inorganic fraction, gelatinous capsules containing this fraction were prepared and when tested in chronic asthmatic patients it showed anti-asmatic activity.	*M. glomerata*
Sirompas para (*Mikania micrantha*) sebagai salah satu alternatif obat ramuan pada pengobatan malaria	Plants that have the potential to be developed as antimalarial alternatives: *M. micrantha* leaf ethanol extract shows no significant signs of poisoning and death until the highest dose of the test is 5000 mg/kg. *M. micrantha* Kunth ethanol extract is categorized as practically non-toxic or mild toxicity. From these results, it can be affirmed that the treatment with doses of 100 mg/kg, 200 mg/kg, and 400 mg/kg has potential for antimalarial activity.	*M. micrantha*

Legend: a.The titles are presented in the language in which they were published; b.The descriptions were translated into English;
Source: Authors (2021).

Analyzing the distribution of patents per country, Japan and Brazil stand out as the largest holders of registered patents involving the genus *Mikania* for medicinal application with 5 and 3 patents, respectively (Figure 1).

Figure 1 - Distribution of patents in WIPO by country.



Source: Authors (2021).

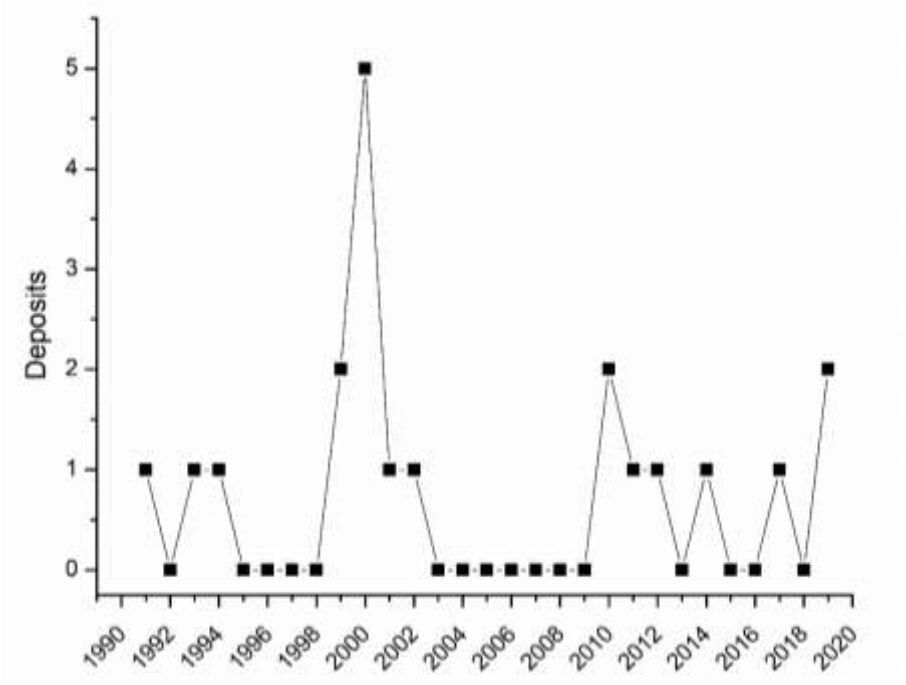
Japan ranks 15th in the Global Innovation Index (2019), with the number of patent filings in a wide range of areas standing out. Considering the number of patent filings in healthcare, during the years 2010-2017, Japan ranked 3rd in biotechnology and pharmaceuticals, with the filing of 33,818 and 45,850 patents, respectively (Dutta, Lanvin, & Wunsch-Vincent, 2019).

Brazil has the largest plant biodiversity on the planet, with more than 20% of the total number of species on planet Earth (Brazil & Environment, 2021). Thus, the country presents a great innovative potential in the areas of natural products and biotechnology, and can promote innovation in different areas, such as biopharmaceuticals (Bittencourt et al., 2020; Dutta et al., 2019).

In the 2019 Global Innovation Index Rankings, Brazil ranked 66th, losing two positions from 2018. With a total investment of $41 billion in public and private R&D spending, the country ranked 9th in 2017. Regarding innovation performance at different income levels, Brazil is in line with expectations regarding the level of development (Dutta et al., 2019).

Considering the year of patent filing (Figure 2), patent filings were observed in the period from 1991 to 2019. The year 2000 presented the highest number of patents filed, with 5 patents. In the following years there was a decrease in deposits, followed by stability until the year 2019, where a brief increase in deposits was observed, with 2 patents.

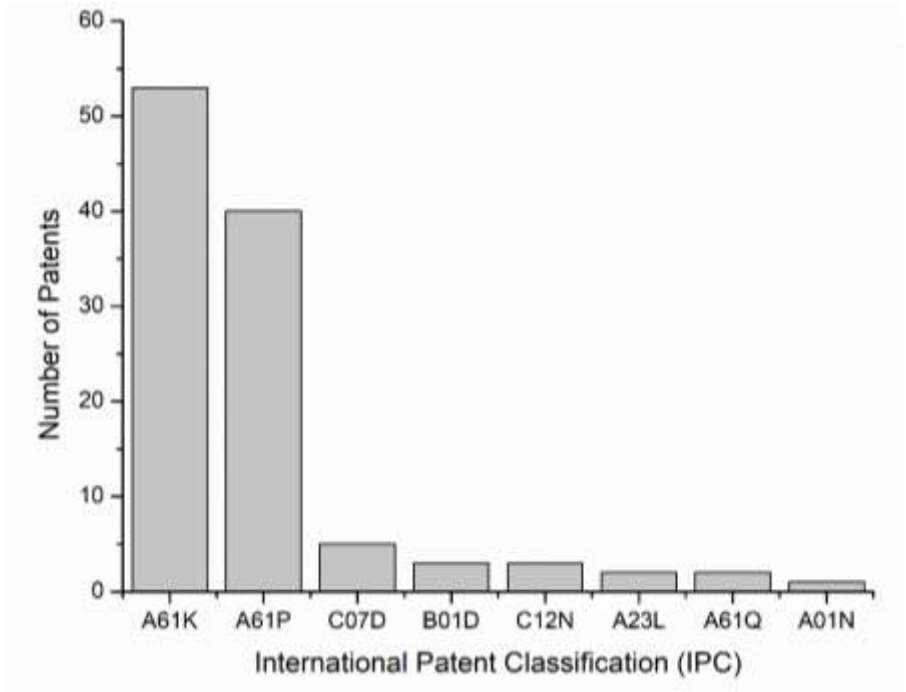
Figure 2 - Annual evolution of patents deposited at WIPO.



Source: Authors (2021).

With respect to IPC, section A (Human needs) had the largest number of patents filed, followed by section C (Chemistry; metallurgy) and B (Processing operations; transportation). It is worth noting that the 20 patents included in the survey presented more than one classification, with 55 assigned to subclass A61K (Preparations for medical, dental or hygienic purposes), and 44 patents appearing in subclass A61P (Specific therapeutic activity of chemical compounds or medicinal preparations), these two subclasses containing 86% of all patents filed (Figure 3).

Figure 3 - Distribution of patents deposited in WIPO by IPC



Source: Authors (2021).

The remaining deposits, in smaller numbers, were observed in subsections C07D (heterocyclic compounds), B01D (separation), C12N (microorganisms or enzymes; compositions thereof; propagating, preserving or maintaining microorganisms; mutation or genetic engineering culture media), A23L (food, foodstuffs or non-alcoholic beverages), A61Q (specific use of cosmetics or toilet preparations or the like) and A01N (preservation of bodies of humans or animals or plants or parts thereof).

3.2 Analysis of the EPO database data

After analysis and application of the inclusion criteria of the results obtained from the EPO database using the term "*Mikania*", 10 patents were selected (Table 2).

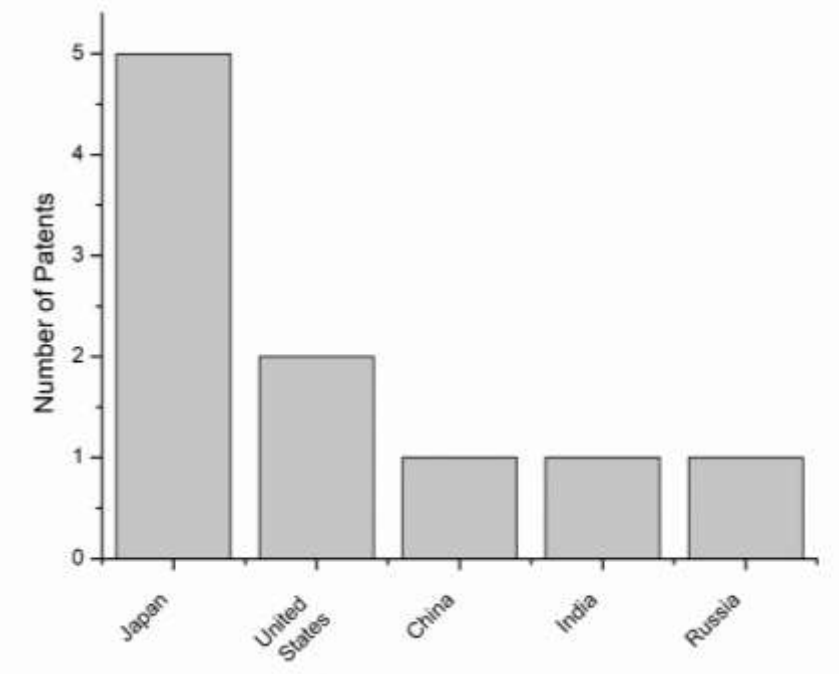
Table 2 - Results and summarized description obtained from the term *Mikania* at the EPO.

Title	Patent Description	Species
Aerosol cosmetic	Cosmetic suppression in aerosol with vegetal extracts and with excellent stability.	*Mikania* sp.
Antioxidative stress agent	Antioxidative stressing agent derived from the natural product that accelerates the improvement activities of the Antioxidant Response Element (ARE) in a path Erythroid-2 Nrf2/ARE related nuclear factor participating in the oxidative stress, thus inducing the expression of an antioxidative enzyme to mitigate the oxidative stress.	*M. glomerata*
Composition for suppressing emission of odor	Odor emission suppressive composition is formulated with plants of several genera	*M. lindleyana*
Heatoproblective activity of *Mikania* scandens (L) Willd. against thisaccta mide induced hepato toxicity	Composition of synergistic herbs for the hepatoprotective activity. More particularly, the present invention concerns the preparation process of 4-(l-Carboxy-ethyl)-8-9-dimethyl-cyclodeca-2, carboxylic acid of 5 diene from *M. scandens* (L.) Willd.	*M. scandens*
Medicament for treating cancer and preparation method thereof	The medicament is made from a formula with plants of several genera. The drug disseminated by the invention has the functions of cleaning heat, detoxifying, eliminating stagnation, relieving water retention, dispersing blood stasis, inducing diuresis, expelling wet wind, cleaning lung heat, expelling pus, detoxifying, stimulating menstrual flow, eliminating stagnant blood, regulating vital energy, reducing swelling, and treating multiple cancers. In addition, the raw material used in the invention drug is based on pure Chinese plants, so that the drug has low cost; and clinical applications indicate that the drug has a good treatment effect on breast cancer, liver cancer, lung cancer, and the like.	*Mikania* sp.
Neurite outgrowth agent	The neuritis growth agent comprises compounds of various plants. A preventive/therapeutic agent for neurodegenerative diseases, a preventive/therapeutic agent for Alzheimer's and dementia diseases, and a food are also provided, each comprising the neuritis growth agent.	*M. glomerata*
Methods for inhibiting conversion of choline to trimethylamine (TMA)	Plant extracts from the genus *Mikania* inhibit choline metabolism through the intestine or microbiota of the digestive tract, resulting in reduced trimethylamine formation (TMA). Extracts of *M. guaco* Bonpl. inhibit the conversion of choline into TMA, *in vivo* and *in vitro*, and reduce the trimethylamine oxide (TMAO) in an individual, providing a compound composed of a *Mikania* extract.	*M. guaco*
Mikanolide and dihydromikanolide as inhibitors of DNA-polymerases	Mikanolide and dihydromikanolide are used to treat proliferative and parasitic diseases. They are used as antiproliferative, antiviral and antiparasitic drugs, mikanolide, dihydromikanolide and extracts enriched with dihydromikanolide. The invention also refers to a method for its preparation by extraction from the *M. micrantha* plant. Besides, the dihydromikanolide and the mikanolide inhibit the replication of the DNA by inhibiting the enzymes of the polymerase of the DNA necessary for the reproduction of eukaryots.	*M. cordata* *M. micrantha* *M. scandens*
New 11-membered ring compound	Composed of an 11-member ring expressed by a specific structural formula and useful as a carcinostatic agent, among others. The compound can be produced by extracting the dry leaf and stalk of *M. hirsutissima* with ethanol, concentrating the extract under reduced pressure and purifying the concentrate by column chromatography.	*M. hirsutissima*
Pharmaceutical composition and method of treatment utilizing the composition	An antivenom composition composed of extracts of active components of the plants combined in effective proportions; the method of elaboration of this composition; the pharmaceutical products derived from these extracts of active components; and a method of treatment of snake bites, scorpion bites, and the like using this composition.	*M. guaco*

Legend: a.The titles are presented in the language in which they were published; b. The descriptions were translated into English.
Source: Authors (2021).

Regarding the depositing countries, Japan was the largest patent holder with 5 patents followed by the United States with 2 patents. The other countries such as China, Russia and India each have only one patent filed (Figure 4).

Figure 4 - Distribution of patents in the EPO by country.

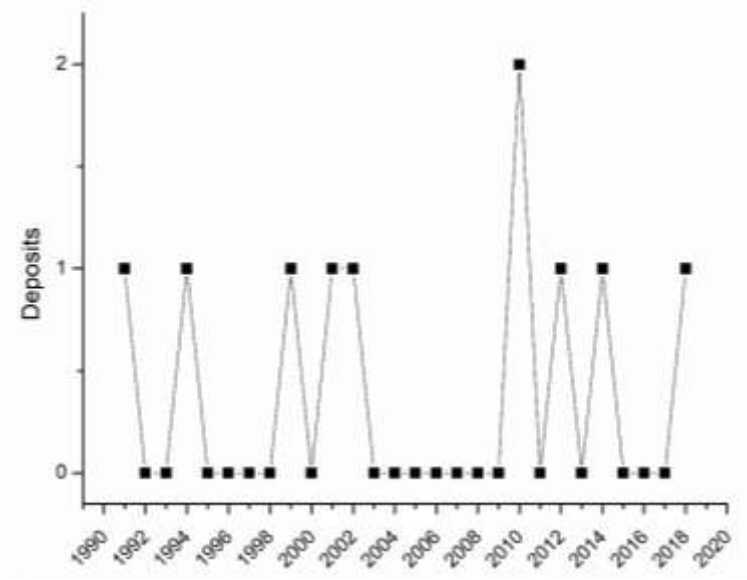


Source: Authors (2021).

The United States ranked 3rd in the 2019 Global Innovation Index rankings, excelling in the 2017 public and private R&D spending sectors with 1st place and a spending of $511 billion. Thus, the country is among the top ten economies in patent publications from 2010 to 2017, that is, it was the country that published the most patents related to biotechnology (126.581 patents) and medical technology (284.223 patents); and in the area of pharmaceuticals, it ranked 2nd, second only to China (Dutta et al., 2019).

Considering the year of patent registration found in EPO (Figure 5), patent deposits were observed between the years 1991 and 2018. The number of publications ranged between 1 and 2 patents, with the year 2010 having the highest number of patent deposits in this database.

Figure 5 - Annual evolution of patents deposited at the EPO.

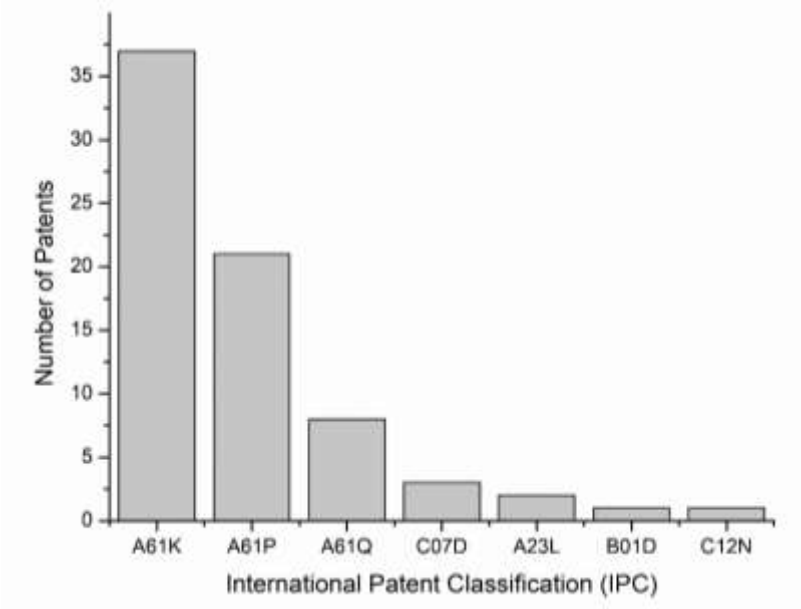


Source: Authors (2021).

By IPC, we observed a higher number of patents filed (Figure 6) in section A (Human Need), followed by section C (Chemistry and Metallurgy) and B (Processing Operations; Transportation).

According to the distribution of patents by IPC, it was possible to verify that the subclasses A61K (Preparations for medical, dental or hygienic purposes), A61P (Specific therapeutic activity of chemical compounds or medicinal preparations) and A61Q (Specific use of cosmetics or toilet preparations or similar) represented 90% of all patents filed, with emphasis on the A61K subclass that had the highest number of patents.

Figure 6 - Distribution of patents deposited at the EPO by IPC



Source: Authors (2021).

3.3 Analysis of the data referring to the INPI database

A total of 3 patent deposits were obtained in the INPI database (Table 3) after applying the inclusion criteria.

Table 3 - Results and summarized description obtained from the term *Mikania* at INPI

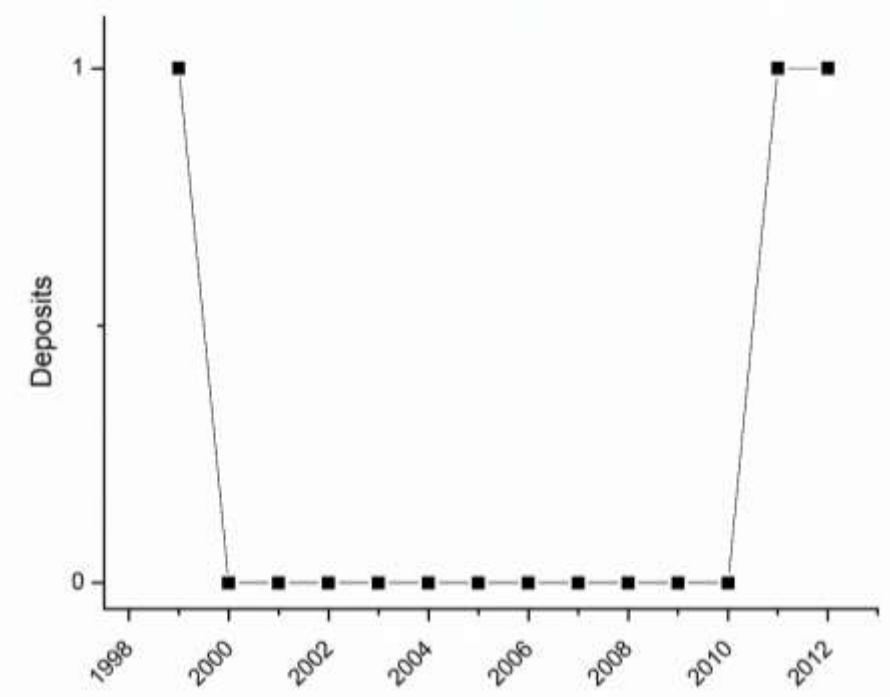
Title[a]	**Patent Description**[b]	**Species**
Formulações farmacêuticas a partir do extrato etanólico das folhas de *Mikania glomerata* Sprengel	Production of an anxiolytic agent and central nervous system depressor. Process of obtaining an agent with central action, used as an anxiolytic and central nervous system depressant obtained from the ethanolic extract of the leaves of the plant *M. glomerata* Sprengel.	*M. glomerata*
Processo de preparação de extratos secos padronizados de *Mikania* sp., Asteraceae (guaco), extratos secos padronizados assim obtidos e aplicações	Standardized dry vegetal extract in coumarin and *o*-cumaric acid, elaborated from the extraction, characterization, standardization and drying of a guaco extract. The extract was dried by nebulization (spray drying), using different adjuvants. This dry extract showed antiulcerogenic activity in the model and indomethacin induced ulcers.	*Mikania* sp.
Processo para extração de frações do extrato hidro-alcoólico da *Mikania glomerata*; fração MG1 obtida pelo processo; composição farmacêutica contendo a dita fração e uso terapêutico da composição em doenças respiratórias em geral	Obtaining fractions from the hydro-alcoholic extract of *M. glomerata* leaves with dilating activity of the respiratory smooth, anti-edema, and anti-allergic musculature. The organic fraction presented great dilating activity of the respiratory smooth muscle much more intense than the dry residue of the hydro-alcoholic extract. The inorganic fraction also presented anti-edema activity in mice and anti-allergic action in rats. From the inorganic fraction, gelatinous capsules containing this fraction were prepared and when tested in chronic asthmatic patients it showed anti-asmatic activity.	*M. glomerata*

Legend: a. The titles are presented in the language in which they were published; b. The descriptions were translated into English.
Source: Authors (2021).

The INPI is responsible for the filing and publication of patents in the Brazilian territory. Thus, the three patents found originated in Brazil, with two of these publications using *M. glomerata*.

Figure 7 shows the annual evolution of patent deposits in the INPI database, in which the three publications occurred in the years 1999, 2011 and 2012.

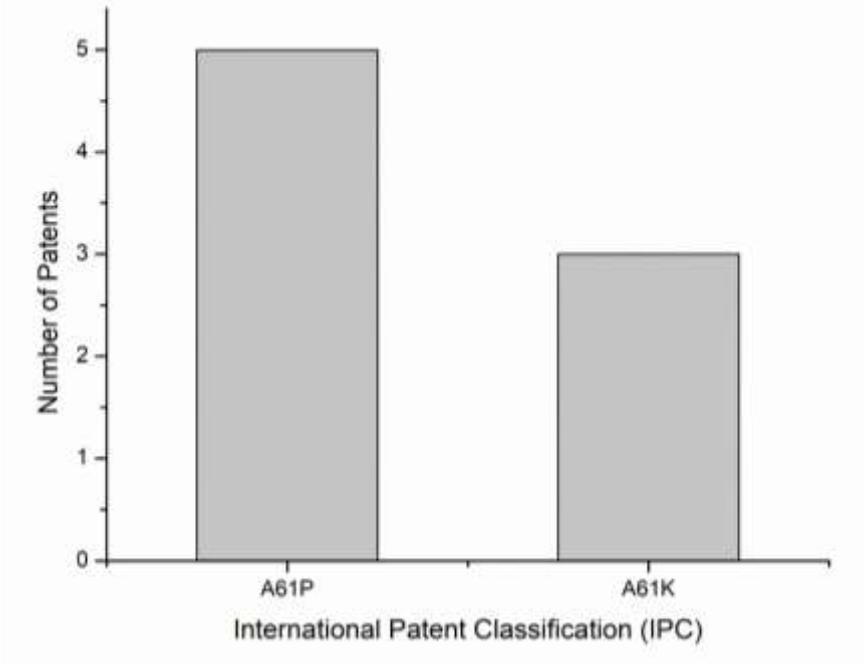
Figure 7 - Annual evolution of patent deposits at the INPI



Source: Authors (2021).

Regarding IPC, it can be seen in Figure 8 that the only subclasses present were A61K and A61P, and these may have more than one group to characterize. In Table 4 you can see all the meanings of the IPCs highlighted in Figure 8.

Figure 8 - Distribution of patents filed at INPI by IPC



Source: Authors (2021).

Table 4 - International Patent Classifications found at INPI

Classification Code	Meaning of classifications
A61K 31/37	Coumarins
A61K 36/28	Asteraceae or Compositae
A61P 1/04	For ulcers, gastritis, or reflux esophagitis
A61P 11/00	Drugs for respiratory system disorders
A61P 11/08	Bronchodilators
A61P 25/22	Anxiolytics
A61P 31/04	Antibacterial agents

Source: Authors (2021).

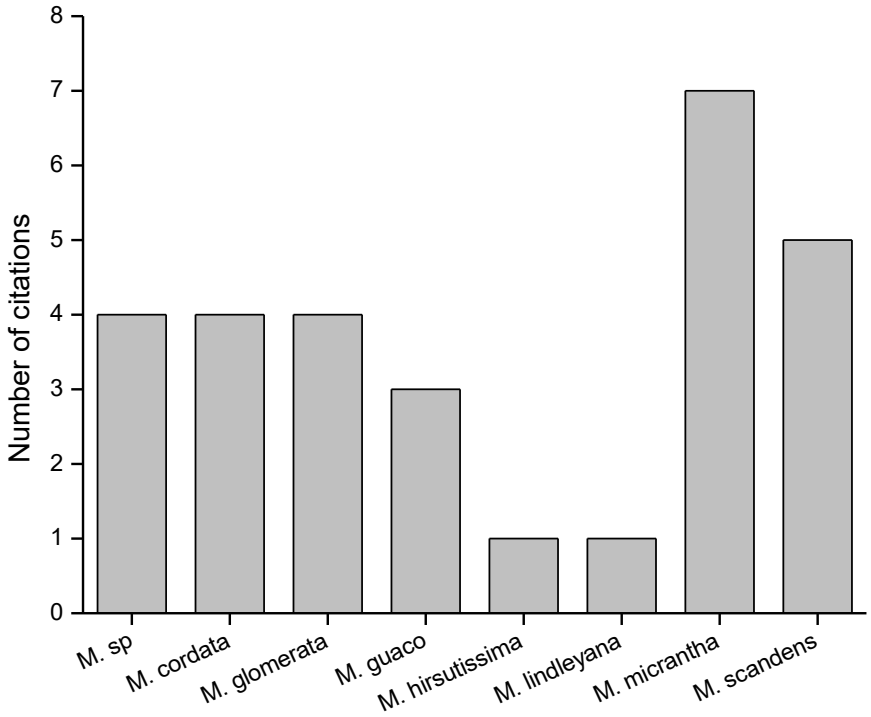
From the analysis of the deposits in the INPI database it was possible to observe low expressiveness, which can be justified by the lack of incentive and practice of patenting among Brazilian researchers (Sampaio et al., 2018). In developing countries, as is the case of Brazil, educational institutions, especially universities, are responsible for scientific and technological knowledge (Perucchi & Mueller, 2014).

Patenting research conducted at universities or that had public funding is seen as controversial, since the role of universities is to create and disseminate knowledge and not charge for it, however, the junction between scientific knowledge, generated by universities, and applied knowledge, provided by companies, is important for technological and scientific advancement and allows them to offer a return to society in the form of an innovative product (Pojo, 2014; Póvoa, 2010).

3.4 Analysis of the Mikania species cited in the patents

From the analysis of the patents accepted in the investigated databases, a compilation of the most cited species was made (Figura 9).

Figure 9 - Number of citations of species in technological prospecting.



Source: Authors (2021).

When analyzing the species of *Mikania* cited in the selected patents, during this review, it was observed the occurrence of 7 species of this genus, as well as in some cases there was no specification of the species used (*Mikania sp.*). Also, in some patents, more than one species was cited.

The two most cited species were *M. micrantha* and *M. scandens*, with 7 and 5 citations, respectively. *M. micrantha* Kunth, is an invasive vine that causes economic losses related to sunlight blockage (Liu et al., 2020). However, *M. micrantha* also has several studies proving its medicinal use for its antibacterial, antitumor, antimicrobial, cytotoxic, and phytotoxic activities (Dou, Zhang, Sun, Wu, & Li, 2014). According to the study by Dong et al. (2017) (Dong et al., 2017) it was also proven that *M. micrantha* has phenolic compounds with antioxidant activity.

M. scandens (L.) Willd. is characterized as a fast-growing invasive weed. However, aqueous extracts of the leaves are used for medicinal purposes in the Indian subcontinent to treat stomach ulcers, gastric problems, and a variety of other ailments. The species has several constituents, including mykanolide and dihydromikanolide. The species has analgesic and antioxidant activity and preliminary studies have proven antinociceptive effects and central nervous system depressant action (Dey, Chandra, Chatterjee, & Bhattacharya, 2011; Piyasena & Dharmaratne, 2013; Siddiqui et al., 2017).

Following the number of citations in the selected patents, it was observed that the species *M. cordata* and *M. glomerata* had three citations each. *M. cordata* (Burma f.) B. L. Robins is used therapeutically against coughs, gastrointestinal disorders, and eye sores (Siddiqui et al., 2019) some of the proven properties of the species are psychopharmacological activities, neuropharmacological, antibacterial, and therapeutic properties against pain and inflammation (Siddiqui et al., 2018).

In contrast *M. glomerata* Spreng has several pharmacological properties, in particular antiallergic, antimicrobial, analgesic, anti-inflammatory, anti-hemorrhagic, anxiolytic, antioxidant, and antidiarrheal activities (Moreira et al., 2016; Moreti et al., 2017). It was also observed that *M. glomerata* was the predominant species in Brazilian patents, being cited in

two of the three deposits found. The species *M. glomerata* is present in the National List of Medicinal Plants of Interest to SUS (2018) (Brazil. Ministry of Health. Secretariat of Science, 2018) and in the National List of Essential Medicines 2020 (RENAME) (Brazil. Ministry of Health. Secretariat for Science, Technology, 2020) as a phytotherapic of the basic component of pharmaceutical assistance, justifying the incentive in studies and patents on the species in Brazil (Brazil. Ministry of Health. Secretariat for Science, Technology, 2020).

The species *M. guaco* Humb. et Bonpl. has been cited 3 times and is noted for its anti-inflammatory activity in traditional Central American medicine (Rüngeler, Brecht, Tamayo-Castillo, & Merfort, 2001). The species is also indicated for snake bites, cholera and respiratory diseases described in the "Medical Form and Guide" published in 1874 (Ricardo, Paula-Souza, Andrade, & Brandão, 2017).

Such pharmacological properties described for these species related to the number of patents found, demonstrate the potential of plants of the genus *Mikania* in innovative pharmacological development.

4. Conclusion

The publication of patents is a resource that aims to register the innovation and protection of an invention with the purpose of producing it commercially. Thus, the study of technological prospection carried out in this work from the research in WIPO, EPO and INPI, ratified the therapeutic potential the species of the genus *Mikania*.

Furthermore, it was possible to evidence that although Brazil has a great diversity of flora, it is still necessary that research be encouraged. Another relevant point is the innovation of patenting natural products, since the use of technological prospecting as a tool for strategic planning provides a forecast of scientific advances and thus the direction of new technologies.

Therefore, due to the relevance of technology prospecting for the development of new research projects and the potential of the genus *Mikania* in medicinal properties, this technology mapping assisted in understanding the state of the art of *Mikania*-related inventions and the results presented can assist researchers in finding collaborators for new technologies.

The data presented reinforce the importance of Brazilian companies investing in the production of scientific studies involving natural products, by applying financial resources to strengthen and boost the research, technology, and innovation sector.

Acknowledgments

This study was supported by financial contributions from the Brazilian Ministry of Health, the Brazilian agencies National Council for Scientific and Technological Development (CNPq) [405778/2018-0] and Coordination for the Improvement of Higher Education Personnel (CAPES).

References

Bittencourt, C. B., Nascimento, M. G. P., Araújo, J. C. M., Costa, D. N., Santos, J. O., & Andrade, I. M. (2020). Scientic and Technological Prospection of the Pilocarpus Vahl Genus. *Cadernos de Prospecção*, *13*(4), 1205–1219.

Brazil. Ministry of Health. Secretariat for Science, Technology, I. and S. H. I. D. of P. A. and S. I. (2020). *National List of Essential Medicines 2020*.

Brazil. Ministry of Health. Secretariat of Science, T. and S. I. D. of P. A. and S. I. (2018). *Medicinal Plants of interest to SUS: Mikania glomerata Spreng., Asteraceae - Guaco*.

Brazil, & Environment, M. of. (2021). Fauna e Flora.

Correia, R., Júnior, R. A., Spósito, R., & Pungartnik, C. (2020). Technological Prospection of the Species Cyperus esculentus L.: a panorama about the

scientific and technological production. *Cadernos de Prospecção*, *13*(3), 721–732. Retrieved from http://dx.doi.org/10.9771/cp.v13i3.30769

Coutinho, L. A., Gonçalves, C. P., & Marcucci, M. C. (2020). Chemical composition, biological activity and safety of use of plants from genus Mikania. *Revista Fitos*, *14*(01), 118–144. https://doi.org/10.32712/2446-4775.2020.822

Dey, P., Chandra, S., Chatterjee, P., & Bhattacharya, S. (2011). Neuropharmacological properties of Mikania scandens (L.) Willd. (Asteraceae). *Journal of Advanced Pharmaceutical Technology and Research*, *2*(4), 255–259. https://doi.org/10.4103/2231-4040.90883

Dong, L. M., Jia, X. C., Luo, Q. W., Zhang, Q., Luo, B., Liu, W. Bin, & Tan, J. W. (2017). Phenolics from Mikania micrantha and Their Antioxidant Activity. *Molecules (Basel, Switzerland)*, *22*(7), 1–10. https://doi.org/10.3390/molecules22071140

Dou, X., Zhang, Y., Sun, N., Wu, Y., & Li, L. (2014). The anti-tumor activity of Mikania micrantha aqueous extract in vitro and in vivo. *Cytotechnology*, *66*(1), 107–117. https://doi.org/10.1007/s10616-013-9543-9

Dutta, S., Lanvin, B., & Wunsch-Vincent, S. (2019). *Global Innovation Index 2019: Creating Healthy Lives - The Future of Medical Innovation*. Retrieved from https://www.wipo.int/edocs/pubdocs/pt/wipo_pub_gii_2019.pdf

Honório, A. C., Quaresma, A. S., Oliveira, C. T., & Loiola, M. I. B. (2019). Flora of Ceará, Brazil: Mikania (Asteraceae: Eupatorieae). *Rodriguesia*, *70*, 1–15. https://doi.org/10.1590/2175-7860201970003

Liu, B., Yan, J., Li, W., Yin, L., Li, P., Yu, H., & Wan, F. (2020). Mikania micrantha genome provides insights into the molecular mechanism of rapid growth. *Nature Communications*, *11*(1), 1–13. https://doi.org/10.1038/s41467-019-13926-4

Moreira, M. R., Souza, A. B., Soares, S., Bianchi, T. C., De Souza Eugênio, D., Lemes, D. C., & Veneziani, R. C. S. (2016). Ent-Kaurenoic acid-rich extract from Mikania glomerata: In vitro activity against bacteria responsible for dental caries. *Fitoterapia*, *112*, 211–216. https://doi.org/10.1016/j.fitote.2016.06.007

Moreti, D. L. C., Leandro, L. F., da Silva Moraes, T., Moreira, M. R., Sola Veneziani, R. C., Ambrosio, S. R., & Martins, C. H. G. (2017). Mikania glomerata Sprengel extract and its major compound ent-kaurenoic acid display activity against bacteria present in endodontic infections. *Anaerobe*, *47*, 201–208. https://doi.org/10.1016/j.anaerobe.2017.06.008

Perucchi, V., & Mueller, S. P. M. (2014). Study about the produced patents and the profile of the inventors of the federal institutions of education, science and technology. *RDBCI: Revista Digital de Biblioteconomia e Ciência Da Informação*, *12*(1), 191–213. https://doi.org/10.20396/rdbci.v12i1.1624

Pires, E. A., Ribeiro, N. M., & Quintella, C. M. (2020). Patent Search Systems: Comparative Analysis Between Espacenet, Patentscope, Google Patents, Lens, Derwent Innovation Index and Orbit Intelligence. *Cadernos de Prospecção*, *13*(1), 13–29. Retrieved from http://dx.doi.org/10.9771/cp.v13i1.35147

Piyasena, K. G. N. P., & Dharmaratne, H. R. W. (2013). Allelopathic activity studies of Mikania scandens. *Natural Product Research*, *27*(1), 76–79. https://doi.org/10.1080/14786419.2012.656110

Pojo, S. da R. (2014). *Proteção e licenciamento de patentes da universidade: a experiência da UFRGS*.

Póvoa, L. M. C. (2010). Should Universities Patent their Inventions? *Revista Brasileira de Inovação*, *9*(2), 231–256. https://doi.org/10.20396/rbi.v9i2.8649001

Ricardo, L. M., Paula-Souza, J., Andrade, A., & Brandão, M. G. L. (2017). Plants from the Brazilian traditional medicine: Species from the books of the Polish physician piotr czerniewicz (Pedro Luiz Napoleão Chernoviz, 1812–1881). *Revista Brasileira de Farmacognosia*, *27*(3), 388–400. https://doi.org/10.1016/j.bjp.2017.01.002

Ritter, M. R., Gandara, A., Simão-Bianchini, R., Souza-Buturi, F. O., & Abreu, V. H. R. (2020). Mikania Willd.

Rufatto, L. C., Gower, A., Schwambach, J., & Moura, S. (2012). Genus Mikania: Chemical composition and phytotherapeutical activity. *Revista Brasileira de Farmacognosia*, *22*(6), 1384–1403. https://doi.org/10.1590/S0102-695X2012005000099

Rüngeler, P., Brecht, V., Tamayo-Castillo, G., & Merfort, I. (2001). Germacranolides from Mikania guaco. *Phytochemistry*, *56*(5), 475–489. https://doi.org/10.1016/S0031-9422(00)00394-0

Sampaio, P. A., Filho, J. M. T. A., Souza, N. A. C., Teixeira, H. A. P., Araújo, T. C. L., Neto, P. J. R., & Rolim, L. A. (2018). Technological prospection of Morus nigra L. *Revista GEINTEC*, *8*(2), 4381–4391.

Siddiqui, S. A., Islam, R., Islam, R., Jamal, A. H. M., Parvin, T., & Rahman, A. (2017). Chemical composition and antifungal properties of the essential oil and various extracts of Mikania scandens (L.) Willd. *Arabian Journal of Chemistry*, *10*, S2170–S2174. https://doi.org/10.1016/j.arabjc.2013.07.050

Siddiqui, S. A., Rahman, A., Oliur Rahman, M., Akbar, M. A., Shamsur Rouf, A. S., Ali, M. A., & Farah, M. A. (2018). Evaluation of anti-nociceptive, anti-inflammatory and antipyretic potential of Mikania cordata (Burm. f.) Robinson in experimental animal model. *Saudi Journal of Biological Sciences*, *25*, 1049–1055. https://doi.org/10.1016/j.sjbs.2018.01.009

Siddiqui, S. A., Rahman, A., Rahman, M. O., Akbar, M. A., Ali, M. A., Al-Hemaid, F. M. A., & Farah, M. A. (2019). A novel triterpenoid 16-hydroxy betulinic acid isolated from Mikania cordata attributes multi-faced pharmacological activities. *Saudi Journal of Biological Sciences*, *26*, 554–562. https://doi.org/10.1016/j.sjbs.2018.03.002

Silva, A. S. B., Owiti, A. O., & Barbosa, W. L. R. (2018). Pharmacology of Mikania genus: A systematic review. *Pharmacognosy Reviews*, *12*(24), 230–237. https://doi.org/10.4103/phrev.phrev

Silva, J. C., Oliveira-Júnior, R. G., Ribeiro, F. P. R. A., Santos, M. R. M. C., Quintans-Júnior, L. J., & Almeida, J. R. G. S. P. (2015). Technological prospection of alkaloids used in the treatment of pain. *Revista GEINTEC*, *5*(3), 2284-2295.