TRENDS OF TECHNOLOGICAL INNOVATION IN HERBAL PRODUCTS

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ABSTRACT

The therapeutic properties of plants are greatly explored by the pharmaceutical industries, they are sources of innovation for industrial property. Formulation of new products can be protected through the patent deposits, market strategy used by companies and researchers in the industry. Therefore, this research aims to conduct a survey of patents related to herbal therapeutic products to trace the technological profile and analyze trends in the use of plant genetic resources in its composition. The methodology adopted was Patent Mining in the Software Orbit Intelligence, used to filter the database and generate graphs. Trend analysis was based on patents selected by specific search script which resulted in 9,820 pharmaceutical patent deposits, 68.6% granted. As far as the origin of the publication was concerned, the United States and Japan were predominant, but for the inventors, companies and universities, the highlights were Italy and India. Species most used in the composition of the patents were of the taxonomic classification Magnoliophyta, family Fabaceae. It is concluded that patents are relevant technological indicators to trace the profile of the productive sector of herbal products, in addition to verifying trends in the use of plant genetic resources.

INTRODUCTION

The medicinal plants and herbal products are sources of innovation for industrial property in health, being its active raw material and plant derivatives, much explored by the pharmaceutical industries (Pereira et al., 2015; Saikat, Raja, 2017). The science and technology involved in its production can strengthen the proper use of genetic heritage and still favor the economic and social development of the country (Hasenclever et al., 2017). The interest in patenting therapeutic herbal products has grown significantly since the 1980s, since the use of intellectual property as a market strategy ensures the researcher and the companies the right to ownership of the product developed and a future return on investment for their research and development (R & D) (Moreira et al., 2006; Pereira, 2011). Many countries invest and encourage productivity in the area of industrial property because they perceive and believe in financial capitalization through technological innovation (Singh et al., 2009).

Patents are relevant in assessing the ability to transform scientific knowledge into products or technological innovations, and therefore are considered technological indicators (Cruz et al., 2017). In addition to reflecting the application of knowledge, it enables economic and technological development and industrial property and genetic heritage (OECD, 2004; Lopes, 2012). Furthermore, they can assist in scenario analyzes of R & D investments, monitoring of financial developments and be indicators for risk reduction among investors (Albuquerque, 2000, OECD, 2013). Therefore, the objective of the research was to conduct a survey of patents related to herbal therapeutic products to outline the technological profile and to analyze trends in the use of plant genetic resources in its composition.

MATERIALS AND METHODS

This is an exploratory research based on the mapping of national and international patents related to the technological segment of therapeutic products based on medicinal herbs. The Orbit Intelligence Software © (2018) patent search tool, which encompasses an extensive and complex database composed of
several international patent offices (over 96 countries), was used to perform simple statistical analyzes and graphing.

Two criteria were used to filter the patents of interest: The International Patent Classification (IPC) codes of the industrial sector and the taxonomic classification (group) and (subclass), both associated to the terminology "pharmaceuticals" to direct the research to the pharmaceutical branch.

The IPC includes a hierarchical system of symbols to classify patent applications, was adopted by more than 100 countries and coordinated by the World Intellectual Property Organization - WIPO (INPI, 2018, OECD, 2009). It should be noted that in the published patent letter, the main IPC code is described, and there may be up to six of these codes per patent, depending on the filing office (WIPO, 2018). IPC "A61K 36/00" refers to the group of "Medicinal, hygienic and therapeutic preparations of undetermined constitution containing material of algae, lichens, fungi or plants, or derivatives thereof, for example, traditional herbal medicinal products", according to the International Patent Classification Guide (WIPO, 2018). The patents were prospected on March 22, 2018 through the advanced search in the FullPat collection of the Orbit Intelligence, over a period of 20 years (1998 to 2018), using the IPC code classifications A61K-036, family FamPat A61K-036 and the pharmaceutical technological domain, with active legal status. Therefore, to meet these selection criteria the following search script was used: (A61K-036/00) / IPC AND (pharmaceuticals) / TECT) AND (STATE / ACT = ALIVE) AND (A61K-036) / FAN. All patents that use plant genetic resources in their composition and that met the selection criteria were considered regarding the analysis of trends in the phytotherapeutic pharmaceutical sector and the profile of its depositors.

For this, information on legal status, depositors, inventors, countries, year of publication, application, priority and concession and classification of patents were observed.

RESULTS AND DISCUSSION

Area of technological domain, Pharmaceutical, presented in 9,820 deposits, with legal status corresponding to 68.6% (6,736) of patents granted and 31.4% (3,084) pending. Other technological areas also fit the study of this IPC group, such as food chemistry (2,457), basic materials chemistry (671), chemical engineering (334) and medical technology (292) (Figure 1). Regarding the number of patent publications, there was gradual linear growth between 1998 and 2007 and between 2008 and 2014 (Figure 2). The occurrence of a peak in the number of patents published in 2014 could indicate a maturity in the sector, but the drop-in deposits from the year 2015 contradicts this deduction and shows a decrease in the patent publications of this area (Figure 2). However, trade estimates are growing at a rate of 15 to 25% a year, and according to estimates the World Health Organization – WHO, demand will reach $ 5 trillion per year by 2050 (Booker; Johnston; Heinrich, 2012). It is worth mentioning that the decrease in the number of patent publications after 2015 (Figure 2) may be related to the 18-month delay between requesting and publishing, but also to changes in legislation, access to genetic heritage and associated traditional communities, such as target 16 of the Nagoya Protocol, one of the Aichi Targets, which establishes this year as the deadline for countries to meet this requirement (Weigand JR et al., 2011). In this same period, the regulatory requirements of these norms are set out in intellectual property laws, such as research registries and technological development with access to genetic patrimony, agreement of traditional communities,
fair and equitable sharing of the benefits derived from their use, among others. In 2014, more patents in this area were granted and, consequently, more published (Figure 3). The evolution of patents granted over time may indicate the inventive dynamics of phytotherapics in the pharmaceutical field, involving the discovery of new plants, as well as their ability to obtain effective protection. While the evolution of the applications over time makes possible the evaluation of this portfolio in order to analyze if these patents have become obsolete or if they are being squeezed in the industrial development, in the case of phytotherapics there is a stable trend line. It is possible to infer strategic countries for patent deposits related to herbal therapeutics through the number of patents deposited per country priority, so in this research, the analysis of the data indicated the United States (2761), Japan (1389), India (1064) and Canada (845), respectively, as the main strategic countries for phytotherapics (Figure 4).

When examining the same criterion by international offices, the World Intellectual Property Organization - WIPO, the base that registers patents of most of the countries, was highlighted, but the Espacenet main patent office in Europe, did not present the same performance. Brazil ranks 14th place (133 patents) in terms of number of publications and 17th place (52 patents) in relation to the priority index. It is considered an important placement, due to the fact that it is among the strategic countries for legal protection of herbal patents, since being among the countries selected by priority, means opportunities to attract investors from the sector to the country. The economic importance and interest in patent deposits in Brazil may be related to the country being considered as one of the world powers of the pharmaceutical market, since 40% of Brazilian drug market revenues come from innovative medicines, according to CMED/Anvisa report (BRASIL, 2017).
Regarding the analysis of the individual performance of Brazil in relation to its publication indexes and priority, the most evident difference is the index of publications, mainly when compared to the number of deposits of the offices of the United States (US) and Japan (JP), Brazil has an equidistant index, and compared to the Espacenet and WIPO offices the country also has a trend line below the level of publication in the world (Figure 5). The main depositors in the field of herbal patents are Industria Derivati Naturali - Indena and Council of Scientific & Industrial Search, followed by GW Pharmaceuticals and Nestlé / Nestec (Figure 6).

Indena is a company whose research and development center is based in Italy, and its production units in France, India and Italy. With expertise in the identification, development and production of high quality active ingredients derived from plants for use in the pharmaceutical, health food and personal care industries, it has 150 major patents and 700 published scientific studies (https://pt.linkedin.com/company/indena). In the ranking presented only two institutions of education and research stand out, they are the CSIR and the University of Missouri, the others represent large companies or multinationals in the pharmaceutical and food industry. The Council of Scientific and Industrial Research (CSIR), second place in the ranking (Figure 6) is a Scientific and Industrial Research Council of the Ministry of Science and Technology, pioneer in intellectual property of India, its R&D development policy is differentiated, therefore, receive 90% of the US patents granted, a process allowed by the government to any publicly funded R&D organization (http://www.csir.res.in).

CSIR is an international highlight in the production of anticancer patents (Dara and Sangmwar, 2014). It is believed that India has become a promising country in the discovery of new drugs perhaps due to the fact of possessing a large collection of medicinal plants, a cultural system of traditional medicine, and also a database on its medicinal plants, formulations and therapeutic use, known as the "Traditional Knowledge Digital Library" (TKDL) (Saikat and Raja, 2017). This basis is maintained, developed and protected by the government through national and international laws of Intellectual Property Rights, a fact that may be influencing the decision-making of international companies in patenting their products in the country's national patent office (Booker, Johnston (1988). In recent years, herbal products from India have been showing annual growth rates, and the main exporting countries of herbs are the United States, Pakistan, Germany, Japan, the United Kingdom, Spain, China, France, Vietnam and Mexico (Booker et al., 2012). As for the inventors, we highlight Ezio Bombardelli and Paolo Morazzoni, who together are co-inventors of 38 patents granted, both of which are of Italian origin and work for the Indenacompany (Figure 7). The most outstanding inventors work in a network of collaborating inventors. The inventor, Ezio Bombardelli, first place with 91 patents, owns 38 of these in common with second place Paolo Morazzoni (79), and this also shares deposits with the fourth place Marcello Duranti (35), research professor at the Università degli Studi di Milano (UNIMI), proving an interaction between university and company for the development of technological research in a
collaborative network. The third in this ranking was Zhengliang Ye, with 41 patents, which is not part of this network, and belongs to a Chinese company, Tasly Pride Pharmaceutical, sixth place ranking (Figure 6). Among the deposits contained in the portfolio of patents studied (IPC A61K-36/00) the main code of greatest occurrence was IPC A61K 36/18, which represents the taxonomic classification of plants Magnoliophytes (Angiosperms), followed by reference A61K-036/48 to the taxonomic family of Fabaceae or Leguminosae and A61K-036/185 referring to Magnoliopsides or Dicotyledons (Figure 8) (WIPO, 2018).

Possibly, the Angiosperms have this prominence because they are plants that produce more biological and chemical resources (flowers and fruits) for industrial production. Among the patents analyzed in this research are 162 deposits that are composed of fungi, even if they are not considered Kingdom Plantae species, the Fungi Kingdom fits into the IPC studied through the code A61K-036/06 and was not excluded from the analyzes because it was considered the potential of biodiversity to be important (Figure 8) (WIPO, 2018). In relation to the classification of patents by biological family or taxonomic classification by family, the most cited subclasses

![Figure 7. Ranking of Inventors who have patent deposits related to therapeutic products derived from plants](image)

![Figure 8. Number of published patents classified by IPC / subclass related to patents for therapeutic products derived from plants](image)

![Figure 9. Distribution of the frequency of the number of patents classified by IPC and Family taxonomic group of plant species](image)
refer to patent deposits composed of Fabaceae (878), Asteraceae (685), Lamiaceae (484), Poaceae (464). Both belong to the division of angiosperms, present great species richness and great agricultural and economic importance (Bruneau et al., 2000).

![Figure 10. Frequency distribution of the number of patents related to herbal therapeutics classified by IPC referring to the genus of plant species](image)

However, the Asteraceae and Fabaceae families are among the most frequent in research on medicinal plants (Rodrigues & Carvalho, 2008; Pereira et al., 2009). The Fabaceae, or leguminous plants, represent one of the largest botanical families in existence and have as biological characteristic the ability to fix atmospheric nitrogen in the soil through symbiosis (Moura, Karam, Silva, 2011). Their species have varied habitats and sizes, which adapt well to different environmental conditions justifying their importance and use in several industrial sectors, such as food, timber, fertilizers, chemicals and medicinal herbs (Bratti et al., 2013; However, Asteraceae is the largest family of angiosperms and accounts for about 10% of the world's total flora, mostly small plants, but may be shrubs, vines or aquatic plants. Its main feature is the presence of numerous flowers in one chapter (Araújo et al., 2008). The Lamiaceae family has proven therapeutic properties and appears in several works on the use of medicinal species, such as Moreira et al. (2002), Mosca & Loiola (2009) and Neto et al. (2014).

Among the IPC codes related to the genus of plants, the most frequent were Panax (277), Mentha (191), Citrus (151), Salvia (149), Allium (148) and Prunus (144) (Figure 10). The genus Panax, from the family Araliaceae, is the only one containing ginsenosides, a substance that is responsible for its therapeutic action. It is therefore widely used for the treatment and control of several pathological conditions (diabetes, hypertension, erectile dysfunction, anxiety and cancer), its species are popularly known by the name Ginseng (Kuntze, 2012). It is composed of 11 species from the Northern Hemisphere and is widely used in Eastern countries (Korea, China and Japan) where they are known for anti-inflammatory and antioxidant action (Fernandes Braga et al., 2011). Mentha is among the main genera of the Lamiaceae family, composed of 61 species, is commonly used in the Mediterranean diet as herbal and spice teas, but also in different traditional medical systems like herbal remedies (Brahmi et al., 2017). The botanical orders or families in the patents are linked to the specific IPC codes, so the analysis of their frequency of citation allowed inferences regarding the use of biodiversity in the technological production. Therefore, the categorization of patents by IPC code as well as assisting in the profile analysis of the productive sector also allows to visualize possibilities of new applications and also the phylogeny of the species mentioned in the patents.

Conclusion

Research on the technological development of medicinal herbal products through the mapping of patents allowed to verify their geographical and strategic distribution, the profile of the depositors, and the tendency of the use of plants of greater interest for the sector of the pharmaceutical industry. The patenting of medicinal, hygienic and therapeutic herbal products demonstrated the potential use of plant biodiversity in technological production and made visible a market interest in phytotherapeutic products. New technologies associated with the therapeutic power of herbal medicines can expand the supply of affordable medicines to the population, increase the quality and safety of medicinal plants, contribute to public health systems and boost the industrial and economic development of resource rich countries genetic plant.

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