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Profile of medicinal plants utilization through patent documents: the andiroba example

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Abstract: Today, one of the trends of the pharmaceutical, cosmetic and food market is the development of products with components of natural origin, rationally exploiting biodiversity. Brazilian population makes secular use of medicinal plants including andiroba, whose oil is used in folk medicine as febrifuge, pain-relieving, anti-parasitic, anti-allergic as well as insect repellent. The present study attempts to evaluate the profile of utilization of andiroba by analyzing the patenting trends based on information collected on the databases of the World Intellectual Property Organization, European Patent Office and Brazilian National Institute of Industrial Property in the period from 1990 to 2011. The following parameters were analyzed: chronological aspect of the applications, countries of priority, international patent classification, technologies and actors in the technological platform. The temporal analysis of the applications shows an evident increase despite a discontinuous evolution of the number of applications. Pharmaceutical, chemical and cosmetic areas were identified as the main areas for commercial application of the plant. Brazil is the country with the largest number of applications even though the majority of the patent technologies are already in public domain, indicating that the technological information contained in these documents could be used for research and investment in several areas.

Introduction

The term biodiversity, which is a shortened form of the term biological diversity, comes from the Greek *bios*, meaning life, therefore refers to the variety of life on Earth. It was first used by the U.S. Office of Technology Assessment in 1987 (U.S. Congress, 1987) and since then, both the term and the concept have been widely used.

The concept of biodiversity was discussed on the international scenario at the World Conference on Environment and Development, organized by the United Nations, in Stockholm in 1972. However, the consolidation of the term occurred only in 1992 when it was defined the concept of biological diversity in the Convention on Biological Diversity (CBD). The CBD was signed during the United Nations Conference on Environment and Development (ECO-92), held in the city of Rio de Janeiro from 5th to 14th July 1992, and brought a new approach on the issue of biodiversity as regarding access and use of genetic resources, access to technology and access to benefits from the use of biodiversity. It was the first global agreement on the conservation and sustainable use of all components of biodiversity - genetic resources, microorganisms, animal and plant species and ecosystems, being considered the first legal document that defines biodiversity in the context

of environmental, social and economic issues (Prip et al., 2010).

Brazil is the country with the largest plant diversity of the planet, considered megabiodiversity, and almost 13% of the estimated 1.9 million species of plants known today are found in Brazil. The Amazon represents 7% of the planet's surface and is home to an estimated 50% of the global biodiversity, with more than 55 000 species of plants, which are equivalent to 22% of all the species already cataloged worldwide (Prance, 1977).

Today, one of the trends of the pharmaceutical, cosmetic and food market is the development of products with the largest number of components of natural origin, especially those of plant origin, rationally exploiting Brazilian biodiversity.

Furthermore, according to the World Health Organization (WHO), approximately 80% of the world's population depends on traditional medicine to meet their needs of primary health care and much of this traditional medicine involves the use of medicinal plants, their plant extracts or their active principles (IUCN, 1993). This situation is more evident in developing countries, including Brazil, where most of the population has no access to medicines and makes secular use of plants as for example unha-de-gato, guaco, carqueja, camomila and

andiroba, all included in the National List of Medicinal Plants of Interest of the Ministry of Health.

Two species of the Meliaceae family, which is comprised of 50 genera and approximately 575 species, *Carapa guianensis* Aubl. and *Carapa procera* DC (Pennington et al., 1981) are popularly known in the Amazon under the name andiroba. Despite andiroba, this tree is also known by several other popular names, including carape, jandiroba, karapa (in South America) and crabwood (England).

Andiroba, a word from *tupi-guarani* origin which means bitter taste, is a tree that reaches up to 30 m tall, with white flowers, slightly fragrant, round fruits, large and dark leaves and seeds of brown coloring and angular side (Enriquez et al., 2003). The tree is widely distributed along the Atlantic coast of Central America; in South America from Colombia to Brazil, Ecuador and in Amazonian Peru (Pennington et al., 1981).

Aublet was the first to describe the tree in 1775, in Guyana. Its use spread to Guatemala, Peru, Colombia, Panama, Venezuela, reaching Brazil, where it was developed the first andiroba oil industry, specifically in the city of Cametá in the state of Pará (Leite, 1997). This tree has multiple uses, being the wood and the oil extracted from the seeds the most important products. The oil is one of the best selling medicinal products on Amazon, with an international demand, being exported to Europe and to the United States. However, there are no large areas for cultivation, and oil extraction is done by small groups of families who harvest the fruits.

The andiroba oil is thick, dark yellow in color and is used for illumination and in the cosmetics industry for lotions, shampoos, creams and soaps. It is also used in folk medicine as febrifuge, pain-relieving, anti-bacterial and anti-parasitic, as well as to treat infections of the upper respiratory tract, dermatitis, abrasions (Tropical Plant Database, 2012). Its anti-allergic (Penido et al., 2006a), anti-inflammatory (Penido et al., 2006b) and antiplasmodial (Miranda Jr et al., 2012) properties have been well documented. In the homeopathic pharmaceutical industry, where it has been marketed in capsule form, the oil is used for diabetes and rheumatism, as well as in the manufacture of medicinal soaps. Moreover, according to popular markets' sellers this oil presents a supposed sunscreen activity, protecting the skin from sun damage and therefore it could be used for the prevention of skin cancer. However, a recent work showed that the andiroba oil did not present photoprotective activity (Ferrari et al., 2007). The residues left over seed oil extraction are popularly used for the manufacture of insect repellants candles, especially the *Anopheles* mosquitoes that transmit malaria and *Aedes aegypti* that transmits dengue (Mendonça et al., 2005).

As a result of the commercial and economic

importance of products originating from biodiversity, there is a growing concern of the companies and universities or research centers with protective procedures related to the technologies involved in the manufacture of these products, particularly the patenting process.

A patent is a right granted by the State to the authors of inventions that temporarily prevents others from economically exploiting an invention without permission of the owner. The system aims to reward the inventor of a new technique industrially applicable, granting him the exclusive right to the exploration of that invention for a specified period, in all countries where the patent was granted (Abrantes, 2011).

In addition to conferring legal protection against improper commercial exploitation, the published patent document provides information about new technologies, helping both directing investments within a particular technological field of interest, and determining lines of research that should be adopted to reach new market niches. The technological information disclosed in patent documents is considered a tool for prospecting and identifying new business, markets and technologies in order to identify threats and opportunities and anticipate scenarios changes.

With regard to patent protection of biodiversity assets, the CBD ensures sovereignty over genetic resources of its member countries and the ability to limit or prohibit the patenting of living organisms. Both the process of extraction/isolation of products from plants and the composition containing the extract, substance or mixture provided it does not represent a mere dilution can be patented. However, Brazilian law forbids patenting plants *per se* and products arising from the isolation and purification of natural products such as extracts of plants.

In view of the growing interest and the potential use of medicinal plants, including andiroba, along with the great number of information about new technologies that can be found in patent documents and used in the development of novel products, the present study attempts to evaluate the profile of utilization of andiroba by analyzing the patenting trends based on information collected on the databases of the World Intellectual Property Organization, European Patent Office and Brazilian National Institute of Industrial Property (INPI) in the period from 1990 to 2011.

Material and Methods

Patent search

The search of patent documents was conducted in the following databases: PATENTSCOPE (the WIPO database), Esp@cenet (the European Patent Office database) and at the database of the Brazilian National Institute of Industrial Property (INPI). The

PATENTSCOPE is a public database, available on the WIPO web portal, and gives access to patent applications filed under the Patent Cooperation Treaty (PCT) and to patent documents of participating national and regional patent offices. The basis of the European Patent Office, worldwide base of open access, periodically imports documents from more than eighty countries. The basis of the INPI is the Brazilian patent basis that contains data of patent applications filed and published in Brazil. The databases of WIPO and the EPO allow a deep research, because in most cases the documents are fully available.

The search strategy used was the "scientific name and/or common name of the plant", considering the combined fields of the abstract and/or claims. The claims define the scope of protection granted by the patent. The scientific names used in this work were *Carapa guianensis* and *Carapa procera*; the common names used were andiroba, andirobinha, andiroba-saruba, andiroba-branca, andiroba-do-igapó, andirava, aruba, saruba, carapa, andirova, cedro-macho, figueroa, tangaré, a. vermelha, angirova, comaçari, mandiroba, yandiroba, carapá, carapinha, gendiroba, jandiroba, penaiba, purga de Santo Inácio, abomidan, caraba, canapé, caoba bastarda, caoba brasileira, castanha mineira, carape, genriroba, iandirova, nhandiroba, karapa, krappa and crabwood.

The documents found were analyzed in order to remove those duplicated and the applications belonging to the same family, obtained more than once due to the independent applications at different institutions of industrial property.

The search period was delimited from the WIPO database, with applications filed since 1990. The same period (*i.e.* from January 1990 to October 2011) was used for searches at the Esp@cenet and INPI basis in order to standardize them.

Analysis of the data in patent applications

In this work, the following analyses were carried out:

- Number and date of deposit;
- Number and date of priority;
- Title;
- Abstract;
- Applicant profile;
- Inventor;
- International Patent Classification (IPC);
- Object of the patent application;
- Technology focus;
- The ratio of patents granted to total number of applications.

Particularly in relation to patent documents retrieved from the INPI basis, other information was considered for an analysis of the course of the processes.

The results obtained allowed the analysis even though conclusions are limited to the period specified in the search.

Results and Discussion

The search of patent documents yielded 114 applications filed on the three databases, WIPO, Espacenet and INPI, in the period from 1st January 1990 to 31st October 2011. Table 1 shows the number of applications retrieved in each database, including applications whose purpose was the protection of the plant itself, the association of the plant with other plant species or extracts obtained from the plant. The largest number of applications was found using the term andiroba, which is the main popular name by which *Carapa* is known.

Table 1. Number of patent applications for *Carapa guianensis* retrieved in each database in the period from 1st January 1990 to 31st October 2011.

Situation / Database	WIPO	Espacenet	INPI	Total
Filed	54	24	36	114
Granted	02	05	02	09

In only 32 of the applications retrieved (28.1 %) the use of the plant is the object of protection (Figure 1). In most applications, the plant is not the essential component, but only a small part of a composition that uses several plant extracts or vegetable oils. The results shown below consider only these 32 applications.

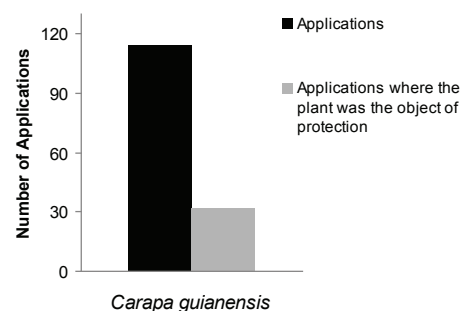


Figure 1. Total number of patent applications for *Carapa guianensis* retrieved in WIPO, Espacenet and INPI databases.

Figure 2 shows the temporal evolution of the applications, excluding those not yet published due to the statutory 18-month period for a public disclosure. One can observe a certain balance in the trend of patenting, with the years of 1998 and 2005 with the largest number of applications, with 10 and 6, respectively. Despite this

discontinuous evolution of the number of applications, there was an evident increase, which could be due to a growing consumer demand for products containing natural ingredients. Moreover these results suggest the importance of the patent system as a mechanism for the protection of research results related to the use of plants.

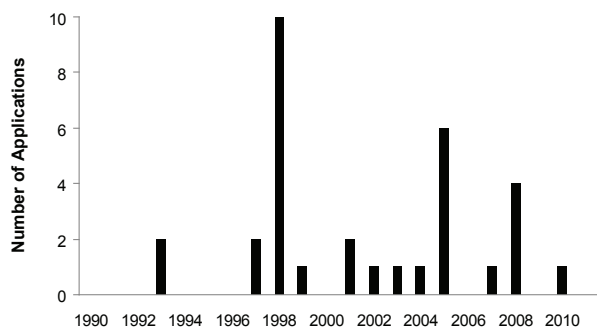


Figure 2. Temporal evolution of patent applications for *Carapa guianensis* retrieved in WIPO, *Espacenet* and INPI databases, considering the applications where the use of the plant is the object of protection.

A particular feature for a patent application is the classification according to the different areas of technology to which it relates, following the International Patent Classification (IPC), which allows the evaluation of the technological activity developed by the applicant. We then attempted to identify the subclasses of the IPC with the higher incidence of applications. As shown in Figure 3, there is a concentration in similar technological areas, as is the case of the subclasses A61K, A01N and C11B that show a higher percentage distribution of the recovered applications. One can observe that, of the total number of applications, the vast majority, 69% are in the A61K subclass - preparations for medical, dental or toilet purposes, covering both products presented as a composition (mixture) and processes of preparing the composition or processes of treating using the composition. The subclass A01N (19%) includes pest repellants and biocides, as well as compounds used in the preservation of foods or foodstuff; and the subclass C11B (6%) relates to the production of fats, fatty oils or waxes from raw materials. This study simply analyzed the main classification and secondary classifications were not considered, therefore any assumptions relating to the use and production would only be possible after analysis of secondary classifications.

By analyzing the profile of the filed applications, we found that the technological distribution is concentrated mainly in the chemical, pharmaceutical and cosmetic areas, confirming a commercial interest in the use of this plant by these industries. These applications corroborate several publications concerning studied effects of andiroba. Vendramini et al. (2012) showed the action of andiroba oil as an alternative to control the ticks, with similar benefits

to synthetic acaricides, but less damage to nontarget organisms and to the environment. In a recent work, Prophiro et al. (2012) demonstrated the potential larvicidal activity of *C. guianensis* oil in wild populations of *A. aegypti*, which are primarily responsible for transmitting the dengue virus in the environment. In the pharmaceutical field the anti-allergic effects of TNTP, a pooled fraction of tetranortriterpenoids, isolated from *C. guianensis* have been demonstrated (Ferraris et al., 2011). Moreover, different studies show the wound healing activity of *C. guianensis* in animal models (Nayak et al., 2010; Nayak et al., 2011).

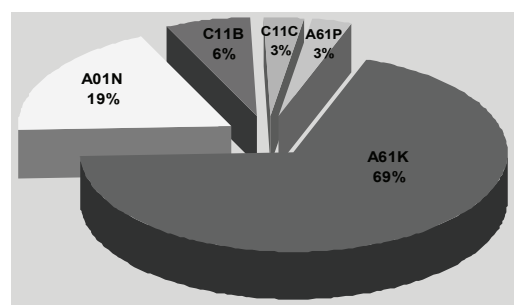


Figure 3. Percent distribution of main IPC subclasses in patent applications for *Carapa guianensis* retrieved in WIPO, *Espacenet* and INPI databases, considering the applications where the use of the plant is the object of protection. A61K: preparations for medical, dental or toilet purposes; A61P: therapeutic activity of chemical compounds or medicinal preparations; A01N includes pest repellants and biocides; C11B relates to the production of fats, fatty oils or waxes from raw materials; C11C includes oils or fatty acids by chemical modification of fats.

Figure 4 shows a percentage distribution for the technologies in the 32 selected applications. A total of eight applications claimed the use of the plant as an insect repellent and were grouped in the chemical technology. In the pharmaceutical area, for example, the applications are related to compositions for the treatment, prevention or inhibition of allergic and inflammatory conditions (BRPI0402875) and for stimulating cell regeneration and promoting angiogenesis (BRPI0501269).

Figure 5 shows the number of applicants found, distributed among companies (n=15), individuals (n=9) and universities and/or research centers (n=8). These data suggest an investment in research activities related to the use of these plants, both by companies and by universities, confirming an interest in the economic potential of the research results. We can also observe that there is a considerable volume of patent applications by individual inventors (28%), which does not necessarily indicate scientific research, but rather the interest in the protection of traditional knowledge associated with biodiversity, which could contribute to the development of researches that can result in technologies with market value.

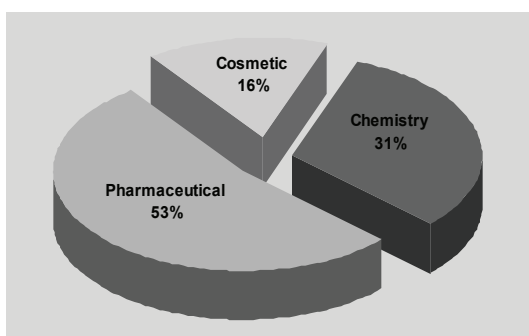


Figure 4. Percent distribution of main technologies in patent applications for *Carapa guianensis* retrieved in WIPO, Espacenet and INPI databases, considering the applications where the use of the plant is the object of protection.

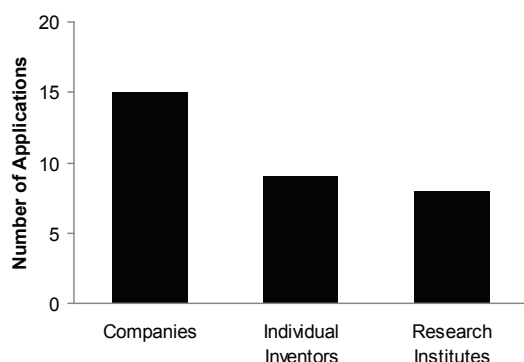


Figure 5. Distribution per main depositor of patent applications for *Carapa guianensis* retrieved in WIPO, Espacenet and INPI databases, considering the applications where the use of the plant is the object of protection.

The countries of priority for the patent applications and the number of applications by each country are shown in Figure 6. The priority country is the country where a patent application was first filed, even though the applicant may request the priority of the application in a country other than the country where he lives. Brazil is the country with the largest number of applications, with nineteen, followed by France, with nine published applications. These data indicate that the technologies are being developed, probably in the listed countries, since, in general, applicants request the priority of the application from their countries of residence; or indicate the interest of the first deposit to be in the markets of these countries. If the application is filed and the privilege is required only in one country, Brazil for example, any institution in the world can replicate the research and commercialize the resulting product, except in the Brazilian territory.

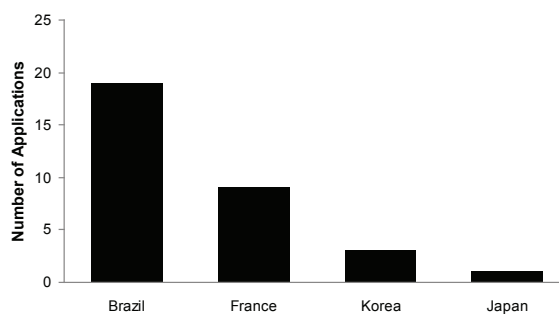


Figure 6. Countries of origin of the depositors of patent applications for *Carapa guianensis* retrieved in WIPO, Espacenet and INPI databases, considering the applications where the use of the plant is the object of protection

Considering the applications by domestic applicants, it is important to have a more detailed analysis regarding the Brazilian regions and the information in these documents. Most Brazilians are individual applicants, which contrasts with the known data from developed countries, such as the U.S., where the main applicants are private companies. Among universities and/or research centers the highlights are the Oswaldo Cruz Foundation (Fiocruz) and Universidade Estadual de Campinas (Unicamp), confirming that research and development of new technologies are still carried out by universities and public research centers.

The applications filed by Brazilians were distributed among regions, according to the applicant statement. It can be seen by analyzing Table 2 that the largest number of applications is concentrated in the regions of major research centers, universities and companies, such as the Southeast, while other regions still show little research on this plant. The North region in particular, although having the largest Brazilian biodiversity, has a small number of applications, suggesting the need for a better interaction among academia, industry and the government to facilitate actions enabling research results to be protected and to reach the market.

Table 2. Geographical distribution of Brazilian depositors of patent applications for *Carapa guianensis* retrieved in WIPO, Espacenet and INPI databases, considering the applications where the use of the plant is the object of protection.

States	Applications
Rio de Janeiro	10
São Paulo	03
Minas Gerais	02
Paraná	01
Santa Catarina	01
Mato Grosso	01
Unidentified	01
Total	19

Table 3 presents some information regarding the progress of the applications made by Brazilians, which suggests the freedom to operate within these technologies. Most applications are already in the public domain, either because they have been rejected or were shelved. This data indicates that the technological information in these documents can be a starting point for universities and research institutes, especially in the Amazon region, to determine, for example, new research lines that should be adopted for the development of new technologies from the Brazilian flora, thus achieving new market niches. As for the patents already granted in Brazil the number is yet negligible - only two - with two other applications still being examined.

Table 3. Situation of patent applications for *Carapa guianensis*, considering the applications where the use of the plant is the object of protection, filed by Brazilians.

Database	Granted	Technical examination	Rejected	Shelved
INPI	2	2	1	6
Espacenet	-	7	-	-
WIPO	1	-	-	-

Conclusion

The interest on traditional uses of plants and their products in Brazil has been gradually increasing during the last few years resulting in a significant body of publications in this area. Nevertheless, there is little incentive by institutions to encourage the conversion of research results into patents and to use all the information about new technologies that can be found in patent documents, which can lead to a loss of opportunities for the commercial and economic exploitation of biodiversity.

The relevance of this study is based on the small amount of statistical and qualitative data about protecting the use of Brazilian plants through the patent system. The analysis of the patent documents allows prospects evaluation, the development of technological skills and opportunities to work and commercially explore the area.

Authors' contributions

IMF contributed to the conception and design of the study, acquisition of data, analysis and interpretation of data, drafting and revising the manuscript critically for important intellectual content. LFGA contributed with the analysis and interpretation of data and critical reading of the manuscript. Both authors have read the final manuscript and approved the submission.

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