



Journal of Technology Management & Innovation

E-ISSN: 0718-2724

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Journal of Technology Management & Innovation, vol. 4, núm. 4, 2009, pp. 32-41

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Santiago, Chile

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Technological Foresight Based on Citing and Cited Patents of Cellulose with Pharmaceutical Applications

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Abstract

The present study intends to present the relevance of cellulose by means of the technological foresight study through citing and cited documents from a patent application (WO 9745131 A1) as indicators of innovation. The European database of patents (espacenet) was used, combining keywords and IPC. The major applicants, countries of publication and uses were mapped. The patent requests collected are mainly distributed in the area of polymers to medical devices and therapeutic methods that utilize cellulose. The results obtained revealed that the US was the main country with studies directed to this technological area (18 patent applications) and the major applicant was the company Micro Therapeutics Inc. Therefore, we can understand that this is a promising technology that may reflect in an increase of R&D activities and in the patent deposits in this area.

Keywords: citing and cited documents; technological foresight; pharmaceutical patents.

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Introduction

The basic premise for any country to develop technological advance activities is having a sharp scientific and technological qualification. In this context, Brazil has gradually supported the development of scientific activities that allow technological growth in various areas, making new products like pharmaceuticals and bio pharmaceuticals to be developed, and being of fundamental importance to population.

The pharmaceutical area is a research-intensive industry, which means they are always doing research, and throughout history they have presented a fast innovation rate implemented by companies in relation to other institutions. The release of new or enhanced products represents a key element in the pattern of industry competition, particularly in the pharmaceutical industry, allowing technological innovation, demanding heavy investments in research and development and that also relies on the International Intellectual Property System and massive marketing and advertising costs.

In order to have the final price of the medicine low and that the lower purchase population's access to these medicines are made easy, a great need for the development of new technologies that require processes and raw materials that produce viable pharmaceuticals is noticeable. In this case the biopolymers are considered the great promise to supply the future perspectives of this market.

In the last decades, a large number of bio molecules naturally produced in the body, are being identified as potential substances for therapeutics use. Among them the biopolymers, which are polymeric materials classified as polysaccharide, polyester, or polyamide, due to its bio-compatibility. The main raw material for their manufacture is a renewable carbon source, generally a carbohydrate derived from large-scale commercial crops like sugar cane, corn, potato, wheat, sugar-beet; or a vegetable oil taken from soy, sunflower, palm, or any other oily plant (Pradella, 2006).

Currently, polysaccharide is considered a pharmacologically active molecule, mainly with anti-coagulating, anti-viral, anti-tumor activities (Florêncio, et. al., 1997; Sutherland, 1998) and for cancer therapy (Calazans et. al., 1997). It also prevents diseases caused by viruses (like AIDS and influenza) and bacteria (Yalpani and

Sanford, 1987). Pharmacologically, they are classified as modifiers of the biological response. In the pharmaceutical market it is already possible to find some polysaccharides to the treatment of a few diseases.

Facing the world's demands for new compounds and therapeutic methods that prevent and treat diseases whose treatments are still a challenge to scientists nowadays (like: cancer, AIDS, cardiovascular diseases, among others), together with the high cost of biopolymers to pharmaceutical use; it is necessary to develop new technologies using these biopolymers as pharmaceuticals. And, as part of the technological innovation development process, the new technologies must be protected utilizing patent rights.

Cellulose ($C_6H_{10}O_5$)_n is the most abundant biopolymer (Mutwil, 2008), of variable molecular weight, composed of only one monomer (glucose), classified as polysaccharide or carbohydrate. It is one of the main elements in the membranes of plants cells (around 33% of the plant's weight). The cellulose's structure is formed by the union of molecules of β -glucose (an hexosane) through β -1,4-glycosidic bonds (Mutwil, 2008). Cellulose is also produced by bacteria, algae, and fungi and not only by plants. It is known that few bacteria like *Acetobacter xylinum* have a cellulose producing capacity. This production happens as an outer cellular film that rapidly joins cellulose micro-fibers (Sutherland, 1990). The interest for bacterial cellulose has grown in the last years, leading to the appearing of various potential uses, like, for example, the acoustic diaphragm, sterile topical applicators, filter membranes, additive element to paper and dietetic fiber and their applications in medicine, and also in other products to substitute the skin and the temporary replacement of the tissue. (Falcão et al, 2008).

The use of the micro-biotic cellulose (like *Acetobacter xylinum*) was suggested in different areas of medicine, like: blood and lymphatic vessels substitute, hollow inner organs substitute (ureter, trachea and digestive tract), abdominal wall substitute, skin, subcutaneous tissue, articulations, cartilage, bladder suspension and hernia treatment. In human beings, it was used in wounds (burns), chronic ulcers, and leprosy, among others. (Falcão, et al, 2008).

The use of cellulose is important in the pharmaceutical industry, it is important to assess how it is implemented and how the development of research and development

(R&D) in the area was. In this context, the patent applications are among the most reliable and comprehensive sources of formal information when R&D, technology, and innovation are analyzed. Patents can be considered indicators of R&D in a particular industry and thus are directly related to the process of technological innovation, therefore, the information contained in these documents are essential for evaluating the technological overview in a particular area.

For a better analysis of patent applications, techniques applied in technological forecasting studies, such as monitoring and bibliographic studies are the most suitable, especially by the systematic use and because they have pre-established procedures worldwide, making research comparable with other studies in the area.

Technological foresight is the term applied in studies that try to anticipate and understand the potentialities, evolutions, characteristics, and effects of technological changes, particularly its invention, adoption and usage. Thus, through it, it is possible to try to anticipate the technological and scientific advances and participate in a way to influence in the guidance of technological trajectories guaranteeing competitiveness and the survival of research institutions. The main point is to identify the chances for development and the options for present action (Coelho, *et al*, 2003).

The Technological foresight was born in the U.S. in the 50's. However, in the 90's there was an increase in such methodologies in developed and developing countries, once more companies and countries made use of these studies to strengthen its competitive capacity (Coelho, *et al*, 2003).

The methods and techniques used in foreseeing are hard to categorize. One of the categories used is the monitoring & intelligence systems and the other one is the trend analysis. In a way that these categories emphasize how future conditions evaluations rely on present conditions (Coelho, *et al*, 2003).

Monitoring is the process by which pieces of information about foreseeing are monitored, identifying its sources, collecting, analyzing and structuring this information for its use. Thus, monitoring is crucial to any foresight (Coelho, *et al*, 2003).

Patent analysis comes from the thought that the increase of interest for new technologies will reflect in the growth

of Research and Development activities and this, will lead to an increase of patent deposits. Therefore, it is thought that new technologies can be identified by the analysis of patent application in some fields. The results are generally presented quantitatively, but their use in the decision-making process is based on a qualitative evaluation.

In this context, the present study intends to show the relevance of cellulose by means of the technological foresight study through citing and cited documents and a patent document that utilizes cellulose in the medicinal area. With this, it intends to analyze the uptrend of the use of this macro molecule in the pharmaceutical industry, the importance of its patenting, its main application in the pharmaceutical industry as well as the major applicant (s) and the country (ies) holding the technology in order to try to anticipate the scientific and technological advances and participate in a way to influence in the guidance of technological trajectories guaranteeing competitiveness and the survival of industries and research institutions.

Method

The methodology used in the development of this paper, was done in three stages. The first one was the selection of a patent document in the medicinal area that uses cellulose in the European Patents Database, the Espacenet. The document was obtained using the keyword, "cellulose" and the international classification "A61K31/175". The base ep.espacenet.com, also known as EPODOC, is formed by a collection of more than 60 million patent applications from almost all the countries in the world, existing since 1836 and weekly updated. It also offers an option of patent search by families. It is a database that contains biographic data, like: numbers and dates of publication, deposit and priority, International Patents Classification (IPC), inventors, applicant and title, citing and cited documents in the search. Thus, the patent document chosen was WO 97/45131, for it presented a good number of citing documents and it was cited by many other patent documents. This patent document had as its applicant the company MICRO THERAPEUTICS and describes a compound utilizing cellulose derivatives, and also the therapeutic method to treat blood vessels embolism utilizing such compound.

The second stage was the selection of cited and citing documents in the search for the patent document selected

and its correspondents (technological evolution), which were also obtained in the espacenet database. The choice of cited and citing documents by the espacenet database is interesting, once these documents are cited in the International Preliminary Examination Report (IPER) and thus, are documents that are similar to the chosen patent document, as for they relate to state of the art.

The third stage was the indexing and treatment of collected data and the preparation of the statistics in order to determine patenting trends in cellulose in the pharmaceutical industry. The analyzed documents were evaluated in relation to the major applications, countries of publication, and types of application.

Through the IPC analysis of documents found in the search, it is expected the possibility to observe the diversity of topics in the group of collected patents.

Results

The start document was WO 97/45131, which refers to a compound that includes cellulose derivate, as well as the

therapeutic method to administrate this compound in order to treat blood vessels embolism.

The data taken from this document were:

- ✓ Publication Date: December 4th, 1997
- ✓ Deposit Date: April 25th, 1997
- ✓ Priority (ies) Date (s): US 08/655822 – May 31st, 1996
US 08/802252 – February 19th, 1997
- ✓ Title: Compositions for use in embolizing blood vessels
- ✓ applicant (s): MICRO THERAPEUTICS
- ✓ Inventor (s): EVANS, Scott et al.
- ✓ IPC: A61K 33/04

By means of search on the website ep.espacenet.com, it was possible to obtain the family of this document (13 family documents), as well as the cited documents and documents that cited the document or any other document of the family, as it can be observed in the table below.

Family Documents	Publication Date	Category	Cited	Citing
US2003185758 A1	Feb 10 th 2003	Compound and Therapeutic method	None	None
US2003003056 A1	Feb 1 st 2003	Compound and Therapeutic method	None	None
US2002187102 A1	Dec 12 th 2002	Compound and Therapeutic method	None	WO2004080503 A1
US2002076381 A1	June 20 th 2002	Compound and Therapeutic method	None	None
US2001024637 A1	Sept 27 th 2001	Compound and Therapeutic method	None	WO2004035093 A2
US6342202 B1	Jan 29 th 2002	Compound and Therapeutic method	US4847065 A US4999188 A US5525334 A US5702361 A	None

(Continued on next page)

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WO9745131 AI	April 12 th 1997	Compound and Therapeutic method	WO8500969 AI WO9704657 AI WO9704656 AI WO9704813 AI XP002038436 A XP002038437 A XP002038215 A	USRE39456 EI AU2004201529 AI WO2004028569 AI WO02089863 AI WO0103666 A2 US6558367 B1 WO0028920 AI WO9956783 AI EP1028758 AI US6059766 A
JP2001509133T T	Oct 7 th 2001	Compound and Therapeutic method	None	None
EP0928195 AI	Jul 14 th 1999	Compound and Therapeutic method	None	None
DE69718180T T2	Aug 21 st 2003	Compound and Therapeutic method	None	None
CA2252718 AI	Apr 12 th 1997	Compound and Therapeutic method	None	None
AU2745497 A	May 5 th 1998	Compound and Therapeutic method	None	None
AT230269T T	Jan 15 th 2003	Compound and Therapeutic method	None	None

Table 1. Citing and cited documents in the WO 97/45131 family

We can observe that these documents, as well as the ones that belong to the same family are of great importance in the technological area when referring to the use of cellulose in the pharmaceutical industry, once, in spite of being a rather new document (1997), it has been cited by 12 other patent documents and cited 11 documents in its descriptive report. Making a total of 24 documents (3 being of non-patent literature). However, a more careful analysis allow to expand even more this universe of documents, once another range of documents related to the same can be obtained by means of detailed reading of

the cited documents in the patent body or by means of a search made by each examiner from each national patent office, where these applications were deposited. Together with this, relevant documents cited during opposing or invalidity procedures can also emerge.

From figure 1 below 8 out of 22 different identified applicants to the 21 patents obtained in the search are shown. Therefore, it's observed that the major applicant is Micro Therapeutics INC with 11 patent applications, followed by Biocompatibles UK LTD with 2 patent applications.

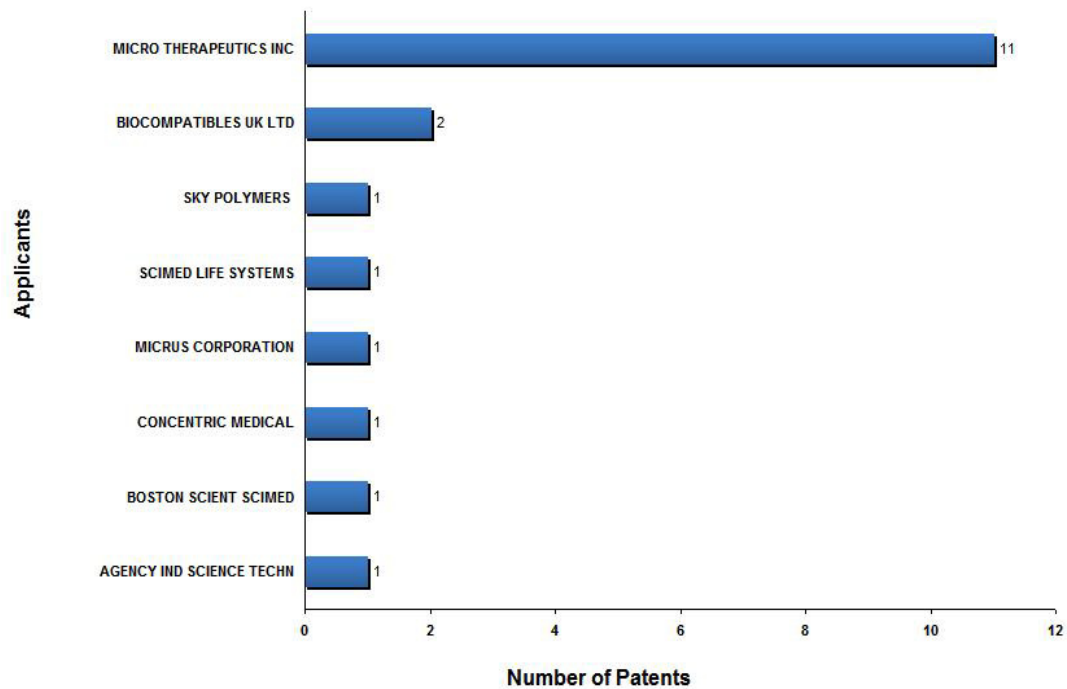


Figure 1. Main depositors by number of patent applications.

Table 2 below shows a statistic of the major assignees in this technological area and its uses. As it can be observed, the major assignee is Micro Therapeutics, whose operating

area is polymers to medical devices and therapeutic methods.

Applicant	N° of patents	Uses
AGENCY IND SCIENCE TECHN	1	Polymers to medical devices
BIOCOMPATIBLES UK LTD	2	Polymers to medical devices
BOSTON SCIENT SCIMED	1	Polymers to medical devices
CONCENTRIC MEDICAL	1	Polymers to medical devices
MICRO THERAPEUTICS INC	11	Polymers to medical devices
MICRUS CORPORATION	1	Polymers to medical devices
SCIMED LIFE SYSTEMS INC	1	Polymers to medical devices and medical instruments
SKY POLYMERS	1	Polymers to medical devices

Table 2. Key applicants and sector of activity

From figure 2 below, it is possible to understand that the main holder of technology is the U.S., once 19 of the patent applications had its origin in this country, which represents 90% of applications followed by Britain and Australia, with 5% each. Also, 13 applications were assigned directly in the World's Intellectual Property

Office (WIPO), via PCT, like WO, what represents 62% of the patent documents. This result indicates that these companies are not only thinking in the domestic market, but to ensure their protection in other countries in a globalized economy.

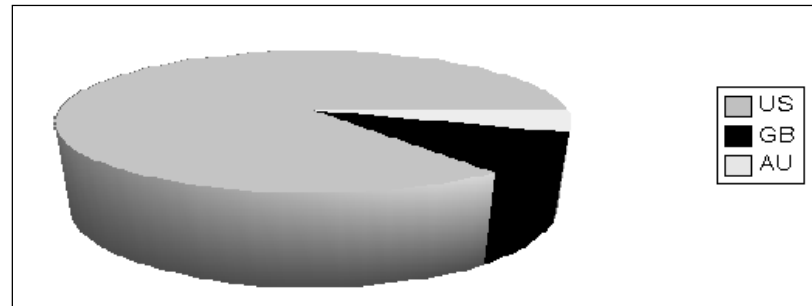


Figure 2. Graphic of origin of patent application - distribution by country.

Figure 3 below shows the major inventors out of the 64 identified. It is noticeable that the major inventor is Greff Richard J. that appears in 9 patent documents followed by Evans Scott, with 5 patent documents. Therefore, it can be

stated that the researcher Greff R. J., together with Evans S., based on this case study, come to be two of the experts who have shown a high degree of development in the area. It is noticeable that the two act in Micro Therapeutics.

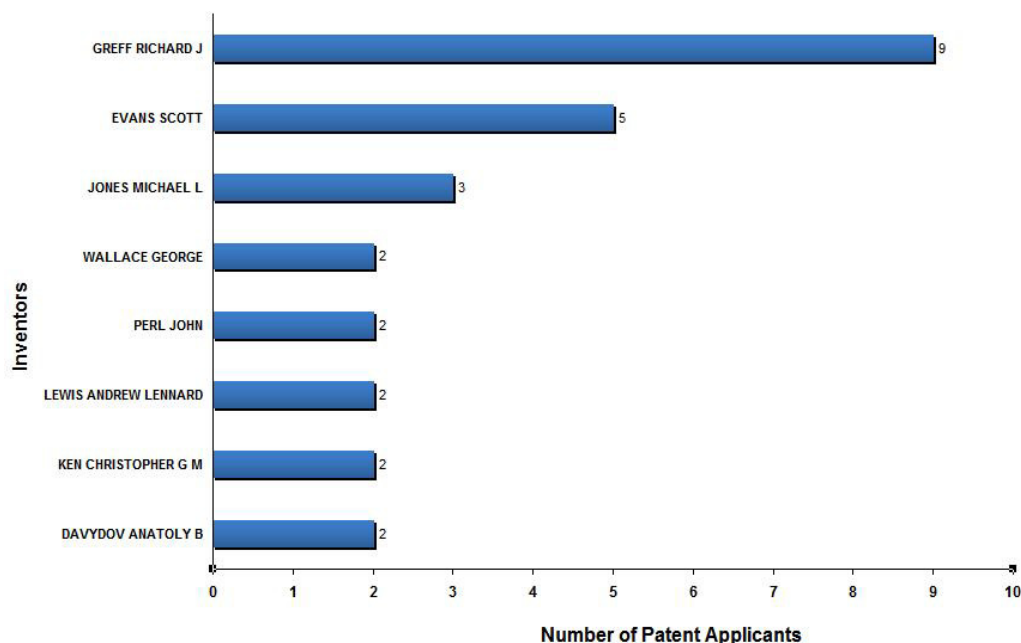


Figure 3. Graphic of major inventors by number of patents.

Also, an invention is usually classified according to its nature or intrinsic function, except when its application alone determines its technical features. Thus, we can make an evaluation of the technological areas involved in the use of cellulose using IPC as a reference.

According to the information above, it seems that the use of the IPC as a source of information is extremely necessary when evaluating this technological area, since it may have different applications for cellulose in different areas.

From the documents collected various different classifications were taken, where the main one was the A61K, this classification toward to preparation for medical, dental or toilet purposes (International Patent Classification), which refers to the medicinal preparations, which appears 40 times in the analyzed patent documents, as it can be observed in picture 4 below.

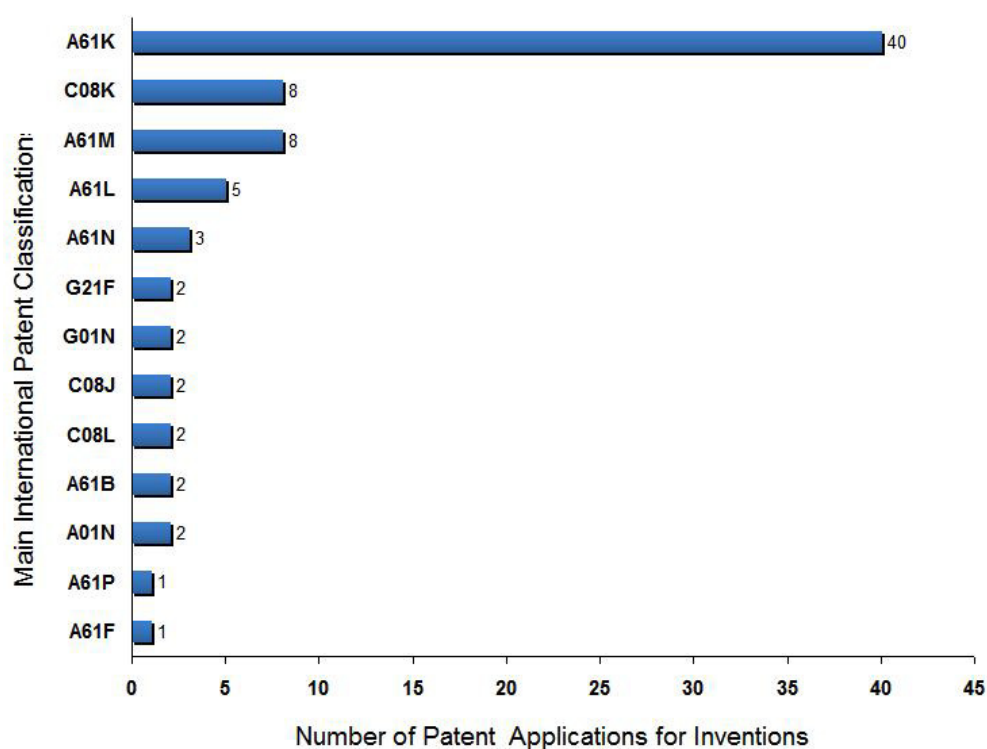


Figure 4. Main international patent classifications obtained in the query - by number of patent applications

The expansion of the subclass A61K in the groups can be observed in picture 5 below, where it's evident that the A61K 31 group (Medicinal preparations containing organic active ingredients) is the most relevant one, followed by the A61K 49 group (Preparations for testing *in vivo*), A61K 47 group (Medicinal preparations characterized by the non-active ingredients used, e.g. carriers, inert additives) and A61K 33 group Medicinal preparations containing inorganic active ingredients. It is valid to stress that this

analysis considers all the subgroups appearing in the analyzed patent documents, once each patent can have more than one international classification to refer to all protection categories claimed.

This result shows the wide range for the use of cellulose in the medicinal, applied in compounds with an organic or inorganic active ingredient and even applied to preparations for *in vivo* tests, which can be explained by the greater availability of this polymer.

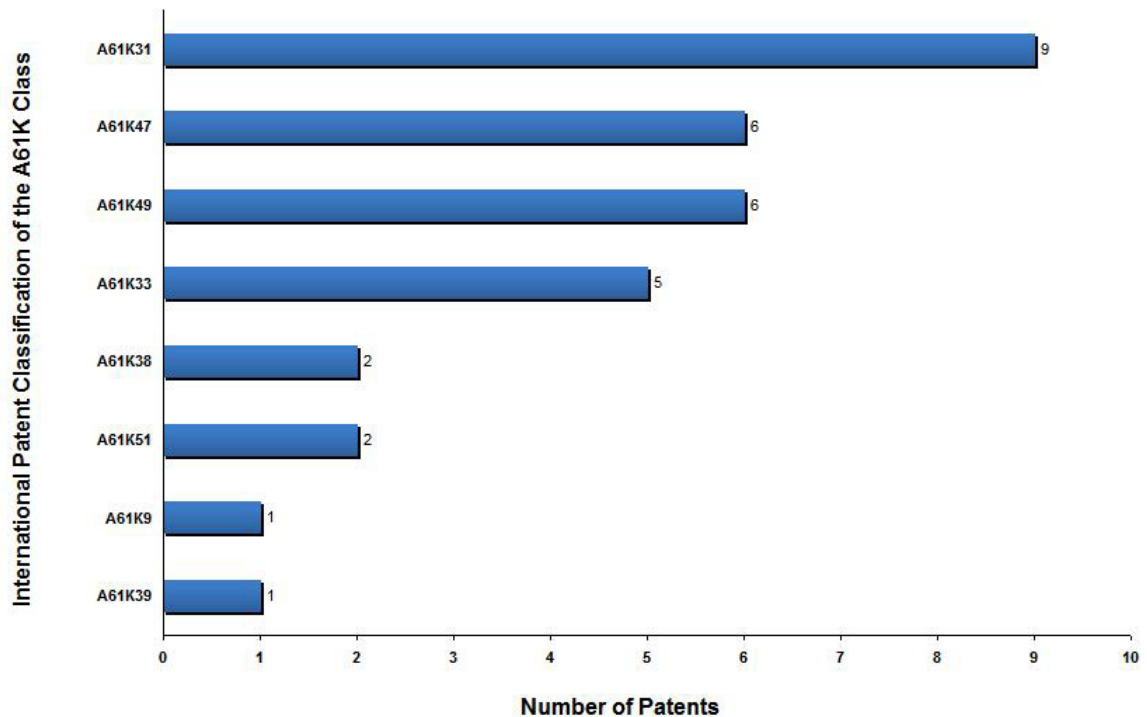


Figure 5. Patent application obtained in the query using the International patent classification (A61K class)

Discussion

The present study represented an analysis of the technological evolution related to the bio polymer cellulose in the pharmaceutical industry utilizing citing and cited patent applicants from a patent application (WO 97/45131 A1) as innovation indicators.

Accordingly, 21 documents for patent application were obtained and 3 of non-patent literature. In which the major applicant of patent application about the use of cellulose in the pharmaceutical industry was the company Micro Therapeutics Inc. that works in the area of polymers to medical devices, but other companies also appear in the study, showing a diversity of actors involved in the sector.

The patent application found are mainly distributed in the area of polymers to medical devices followed by a therapeutic method that utilizes cellulose.

By analyzing the countries where the patent application originated from, as well as countries where they were requested, it was observed that they mainly originated from the U.S. (18 requests) But other and the vasmajority of applications were filed via the PCT (13 requests),

indicating the demand for protection of various countries, a result that reflects the current globalization experienced by technology and most of the applications were filed via PCT (13 applications), indicating that many countries rely on protection, and this result reflects the current globalization experienced by technology.

Also, by means of IPC, it is verified that cellulose has acquired many uses, like organic or inorganic active ingredients and even in preparations for *in vivo* determinations, indicating the possibilities of its use.

From the patent application analyzed, it was also observed that there isn't a concentration of patent applications in only one company, depicting that many companies look for patent protection when it comes to the use of cellulose in the pharmaceutical industry.

From the exposed above, it can be understood that the application of cellulose in the pharmaceutical industry is a promising technology that has as its major technology holder the U.S.

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