Research, Society and Development, v. 11, n. 6, e17311629022, 2022
(CC BY 4.0) | ISSN 2525-3409 | DOI: http://dx.doi.org/10.33448/rsd-v11i6.29022

Mapping of Patents Related to The Development of Products for Diabetic Neuropathy: a technological prospection from 2010 to 2022

Mapeamento de Patentes Relacionadas ao Desenvolvimento de Produtos para Neuropatia Diabética: uma prospecção tecnológica de 2010 a 2022

Mapeo de Patentes Relacionadas con ol Desarrollo de Productos para La Neuropatía Diabética: una prospección tecnológica de 2010 a 2022

Received: 04/09/2022 | Reviewed: 04/19/2022 | Accept: 04/24/2022 | Published: 04/25/2022

Giselda dos Santos Barros
ORCID: https://orcid.org/0000-0003-2980-5892
Universidade Federal de Sergipe, Brazil
E-mail: giseldaufs@gmail.com
Hilton Henrique Cruz Santos Pereira
ORCID: https://orcid.org/0000-0003-0977-155X
Universidade Federal de Sergipe, Brazil
E-mail: hilton.pereira@ifs.edu.br
Maria Suely Regis Souza
ORCID: https://orcid.org/0000-0001-6906-705X
Universidade Federal de Sergipe, Brazil
E-mail: msrsouza24@gmail.com
Maria Emília Camargo
ORCID: https://orcid.org/0000-0002-3800-2832
Universidade de Caxias do Sul, Brazil
E-mail: mariaemiliappga@gmail.com
Paula dos Passos Menezes
ORCID: https://orcid.org/0000-0002-4908-540X
Universidade Federal de Sergipe, Brazil
E-mail: paula.dp.menezes@gmail.com
Gabriel Francisco da Silva
ORCID: https://orcid.org/0000-0002-9622-2518
Universidade Federal de Sergipe, Brazil
E-mail: gabriel@ufs.br

Abstract
Diabetic neuropathy is a complication of diabetes that occurs in 40-60 million diabetics worldwide and is associated with other chronic diseases. Besides that, there are no prospective studies that present the state of the technique about technologies developed to circumvent this important public health problem. Given the above, this study aims to carry out a technological prospection about the products developed for diabetic neuropathy in the period 2010-02/02/2022. To this end, a technological prospection was carried out at the INPI and ESPACENET patent office's always making a parallel between Brazilian reality in comparison with international companies. Therefore, in this period, it was found that the countries that produced the most patents on the subject were China, the United States, and Japan, and the company that published the most patents in this period was Beijing Luyuan Qiuzheng Technology Dev. Co Ltd. Thus, the data from this study showed that Brazil did not produce patents on the subject in this period and that China, the United States, and Japan were the countries that showed the greatest interest in technological development aimed at this disease, which affects millions of people all over the world.
Keywords: Diabetes Mellitus; Diabetic neuropathies; Technology.

Resumo
A neuropatia diabética é uma complicação do diabetes que ocorre em 40-60 milhões de diabéticos em todo o mundo e está associada a outras doenças crônicas. Não há estudos prospectivos que apresentem o estado da técnica sobre as tecnologias desenvolvidas para contornar esse importante problema de saúde pública. Diante do exposto, este estudo tem como objetivo realizar uma prospecção tecnológica sobre os produtos desenvolvidos para neuropatia diabética no período 2010-02/02/2022. Para tanto, foi realizada uma prospecção tecnológica nos escritórios de patentes do INPI e ESPACENET, sempre fazendo um paralelo entre a realidade brasileira em comparação com empresas internacionais. Portanto, nesse período, verificou-se que os países que mais produziram patentes sobre o assunto foram China, Estados Unidos e Japão, e a empresa que mais publicou patentes nesse período foi a Beijing Luyuan Qiuzheng

Technology Dev. Co Ltd. Assim, os dados deste estudo mostraram que o Brasil não produziu patentes sobre o assunto nesse período e que China, Estados Unidos e Japão foram os países que demonstraram maior interesse no desenvolvimento tecnológico voltado para essa doença, o que afeta milhões de pessoas em todo o mundo.
Palavras-chave: Diabetes Mellitus; Neuropatia diabética; Tecnologia.

Resumen
La neuropatía diabética es una complicación de la diabetes que ocurre en 40-60 millones de diabéticos en todo el mundo y está asociada con otras enfermedades crónicas. Además de eso, no existen estudios prospectivos que presenten el estado de la técnica sobre tecnologías desarrolladas para sortear este importante problema de salud pública. Dado lo anterior, este estudio tiene como objetivo realizar una prospección tecnológica sobre los productos desarrollados para la neuropatía diabética en el período 2010-02/02/2022. Para ello, se realizó una prospección tecnológica en la oficina de patentes del INPI y ESPACENET, siempre haciendo un paralelismo entre la realidad brasileña en comparación con las empresas internacionales. Por lo tanto, en este período se encontró que los países que más patentes produjeron sobre el tema fueron China, Estados Unidos y Japón, y la empresa que más patentes publicó en este período fue Beijing Luyuan Qiuzheng Technology Dev. Co Ltd. Así, los datos de este estudio mostraron que Brasil no produjo patentes sobre el tema en este período y que China, Estados Unidos y Japón fueron los países que mostraron mayor interés en el desarrollo tecnológico dirigido a esta enfermedad, que afecta a millones de personas en todo el mundo.
Palabras clave: Diabetes Mellitus; Neuropatía diabética; Tecnología.

1. Introduction

Diabetes Mellitus is a chronic disease in which the body does not produce insulin or is unable to properly utilize the insulin it produces (Sarwar et al., 2010). In this context, Diabetes Mellitus is among the 10 leading causes of death in the world, especially for people under 60 years of age, and in 2021 it cost US$ 760 billion in health resources from the International Diabetes Federation (I.D. Federation, 2021).

In addition, persistently high blood glucose levels can cause several serious diseases, which affect the heart, blood vessels, eyes, kidneys, nerves, and teeth, as well as possible damage to the nerves which can be quite significant and silent, causing diabetic neuropathy. It causes impairment of nerves throughout the body and changes in sensory, motor, and autonomic functions (I. D. Federation, 2019).

Diabetic peripheral neuropathy (DPN) affects the peripheral nerves responsible for transmitting information from the brain and spinal cord to the rest of the body, occurring most often at the ends of longer nerves, such as in the legs and arms, and when it affects the nerves peripheral limbs causes several complications in the lower limbs, which are often serious and chronic and can cause loss of sensitivity, weakness and muscle atrophy, especially in the hands and legs (Altieri, 2017).

DPN is one of the most important complications of diabetes present worldwide and affects between 40 to 60 million people, causing chronic ulcers and amputations which are 10 to 20 times more common than in people without diabetes. It is estimated that every 30 seconds a lower limb, or part of it, is amputated worldwide due to diabetes, resulting in reduced quality of life and increased risk of premature death, causing a significant socioeconomic burden for public health and a huge cost to the system, as example the Unified Health System (SUS) in Brazil (Hicks & Selvin, 2019).

Even though it is such a prevalent disease in the world population, DPN continues to this day as a disease that does not have a definitive treatment, and most drugs are only to relieve the symptoms of the implications of this disease. That is, there is still no treatment to directly treat the disease. This leads us to the need to map where the companies that have been most interested in the search for new technologies with the potential to treat the disease are concentrated.

In this context, technological prospection is inserted as a type of study that makes use of a systematic approach to map scientific and technological developments, capable of significantly influencing industry, the economy, and whole society (Boeck, 2019). In view of this, this study aims to carry out a technological prospection on diabetic peripheral neuropathy in the period 2010-February 2022, as well as verify the patent deposits in the European Patent Office (ESPACENET) and National Institute of Industrial Property (INPI) patent offices, identifying the countries that produced the most patents on the theme and

determining which are the largest patent applicants, through a bibliographic, exploratory and quantitative review, to answer the following research question: Which countries developed more technologies for diabetic peripheral neuropathy in the period 2010-February 2022 and what are their main interests?

2. Literature Review

2.1 Technological development and innovation in healthcare

In general, the countries encourage scientific, technological, and innovation development, as a strategic element for the economical advance and improvement of health systems (Kruk et al., 2018). Following this incentive, in the year of the 100th anniversary of the discovery of insulin, numerous innovations occurred in glucose monitoring in patients with DM, becoming the "cornerstone of medical science" (Lee & Yoon, 2021), changing the way of treating these patients, with the advent of research and technological and innovative products, offering new solutions and benefits in the quality of life of people with diabetes.

For Galindo e Aleppo (2020) "The most recent advances are centered on continuous glucose monitoring (CGM) technologies", and further, "confers significant glycemic benefits in individuals with type 1 diabetes (DM1) and type 2 diabetes (DM2) (Galindo & Aleppo, 2020)." Innovation and technology and its advances have transformed the health of diabetics, however, not every patient with this pathology has access to essential treatment for their survival, according to a United Nations (2021): "The world has around 60 million people with type 2 diabetes who need insulin, but one in two does not have access to this essential treatment. In a new study, the World Health Organization reveals that "high price, low availability and few producers dominating this market" are the main barriers to universal access (ONU, 2021).

Another harmful factor for patients is failures in public health systems. WHO Director-General Tedros Adhanom Ghebreyesus on November 12, 2021, recalled that "the scientists who discovered insulin 100 years ago refused to profit from the feat and sold the patent for just one dollar". He explains that the WHO works with countries and manufacturers to expand access to a drug that can save lives. But only three multinationals control more than 90% of the insulin market (WHO, 2021).

The value achieved through the exchange of technology, that is, the technological innovation acquired and used by companies, generating economic and social gains, is called technological development and these innovations are consequences of the effort to produce new technologies or combinations of technologies that are indicators of the country's development (CF, 2020).

Therefore, through Brazilian Law No. 9279/1996, Industrial Property, which ensures the results acquired through the processes of technological innovations, granting investors in Research and Development - R&D a method of legal and temporary protection when requested to "Patent", allows, possession of the patent, it is possible to protect and remunerate the research, promoting technological development and thereby providing the country's socioeconomic incentive. Thus, with the speed of technological development, companies always need to be ahead of their competitors so that they must always distinguish themselves through the search for innovation and the attempt to anticipate trends and changes in the market, in which, observation of the foreign market becomes important for the dispute for leadership (Brazil, 2013a).

In this perspective, technological prospection studies, also known as prospective studies, constitute the basic tool to guide the development of technologies and must make use of at least more than one technique, method, or tool in prospecting exercises, since the joint use helps to reduce the specific difficulties of Foresight activities and the disadvantages of individual use. In this way, carrying out a prospective study can provide skillful reflections to determine the company's strategies (OECD, 2015).

Undoubtedly, studies of patent registrations have the influence of considering the existence of gaps or saturation in relation to products available on the market. And regarding the health area, it is of great importance to carry out this type of

study to assess trends in patenting on Diabetic Neuropathy, which is a highly prevalent complication of Diabetes Mellitus with no cure yet discovered. Due to constant technological changes, constant technological prospecting studies are necessary for new technological changes to occur for this disease (Amparo, 2012). So, all published patent applications are classified in the technological area to which they belong, and is named International Patent Classification (IPC), created from the Strasbourg Agreement (1971), whose technological areas are divided into classes A to H (INPI, 2021).

In the technological area, where changes occur in a very intense way, it is necessary to use alternative paths to guide the future, with technological prospection studies being one of these paths (AMPARO, 2012).

2.2 Diabetes Mellitus and Diabetic Neuropathy

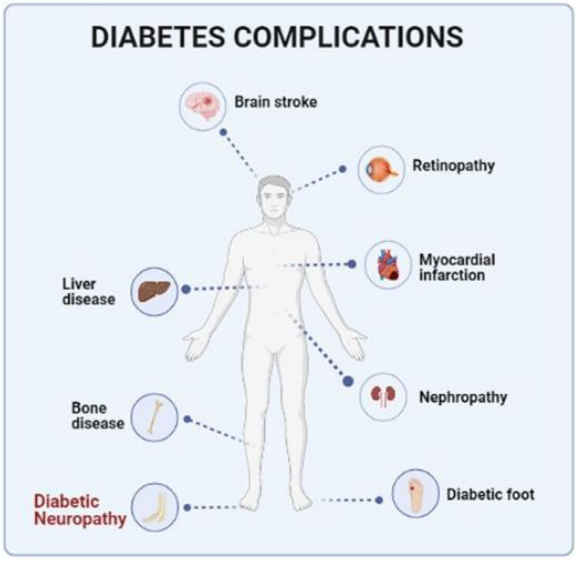
Diabetes is a disease caused by insufficient production or poor absorption of insulin, a hormone that regulates blood glucose and guarantees energy for the body. Known worldwide as Diabetes Mellitus, this can be of two types. Type 1 is a chronic, inherited disease and usually occurs in childhood and adolescence, but it can be diagnosed in adults as well, where the body uses little or none of the physiologically produced insulin. Type 2 occurs when the body does not properly use the insulin produced and is related to family history, usually occurring in adults. There is also the pre-diabetes stage, in which blood glucose levels are higher than normal, but not yet high enough to characterize type 1 or type 2 diabetes. Another type is Gestational diabetes that occurs temporarily during pregnancy (Sarwar et al., 2010).

Diabetes is considered a silent disease because while it develops in the body it does not show signs for it to be identified, so the faster it is diagnosed, the faster the treatment will be since diabetes has no cure. Signs in the body such as weight loss, weakness, mood swings, nausea, and vomiting, delayed wound healing, blurred vision, and tingling of the feet and hands are symptoms manifested when the body already has diabetes (IDF, 2021).

As mentioned above, the world has a high prevalence of diabetic diagnoses. And, although some countries such as the United States have reduced or controlled the cases of their citizens, Brazil for example, unfortunately, does not enjoy this statistic, because every year there is an increase in the number of deaths caused by this comorbidity, which has reached 65 thousand deaths in 2018, according to data from the Ministry of Health. It is estimated that 9 million Brazilians have DM and that, of these, 35% are registered in the SUS. In 2019, there were 11 million consultations for these patients and 136 thousand hospitalizations, totaling 98 million reais spent due to DM, a significant cost for the public health system (Correr et al., 2020).

According to a survey by the Surveillance of Risk and Protection Factors for Chronic Diseases by Telephone Survey (Vigitel, 2020), the percentage of people diagnosed with diabetes between the capitals of the country and the Federal District went from 6.3% in 2010 to 7, 4% in 2019. DM can harm the entire human body, leaving these organisms fragile, as illustrated in Figure 1 (Vigitel, 2020).

Figure 1 – Complications of Diabetes Mellitus in the Human Body.



Source: The authors, designed in Biorender.

The most common complication resulting from DM is Diabetic Peripheral Neuropathy, which occurs between 40 to 50% of patients with diabetes and is characterized by the progressive degeneration of the axons of the nervous system fibers and affects the lower limbs. In addition to NPD, it is important to mention that insulin resistance carries with it a series of other complications for the patient, such as retinopathy, nephropathy, amputations due to non-perceivable wounds on the skin capable of evolving into a chronic ulcer (Armstrong et al., 2017).

The pathophysiology of NPD consists of a lesion caused in the peripheral nerve, that is, axonal degeneration, causing atrophy in the muscles, decrease in size and loss of the ability to move arms or legs, and/or changes in Schwann cells. What causes demyelination that causes a decrease in conduction velocity or interruption of nerve impulse transmission. Under normal conditions, Schwann cells and oligodendrocytes are coated by the myelin sheath, which accelerates nerve impulse conduction (Baum et al., 2021).

According to the National Association for Diabetes Care, the decrease or lack of fine fibers produces a reduction in thermal and mechanical sensitivity and burning. The lack of thick fibers causes a decrease or lack of vibratory sensation, tactile and pressure discrimination, in addition to ataxia, while the lack of epidermal C-fibers and thick myelinated fibers causes paresthesia and dysesthesias (ANAD, 2020).

In this way, the absence of pain usually causes injuries, and these can consequently evolve into an ulcer which, due to Diabetes Mellitus, are difficult to heal, and may evolve to the need for amputation of the affected limb or even more serious complications (Armstrong et al., 2017). However, with tight glucose control it is possible to decrease the risk of neuropathy or improve pre-existing neuropathic symptoms if it is diagnosed early.

Therefore, it is evident the need to map the state of the technique regarding the technologies developed to circumvent this important public health problem, to contribute to the advent of new technologies.

3. Methods

This study is a technological prospection with a descriptive and quantitative approach, carried out on patent office's National Institute of Intellectual Property (INPI-Brazil) and the international European Patent Office (ESPACENET) from 2010-02/02/2022 based on published patents, and was conducted in 3 stages, as described below.

In the first stage, carried out in October 2021, the technological prospection began with consultation in the patent office's INPI-Brazil and ESPACENET, with the determination of the type of patent, advanced search and in the search field "title" in both databases, being the Boolean operators "and" and "or", were used in the searches, as well as the terms that formed the keywords, to increase the chances of finding more patent documents on the technologies of interest, also using the time frame 2010 - 02/02/2022, the keyword and IPC (International Patent Classification) with the symbols A61P25/02 and A61P3/10 were used as presented in table 1 below.

Table 1 - Analysis of the meaning of the IPC codes used in the search for patents.

Code division	Codes	Application Field
Section	A	Health needs
Class	A61	Medical or veterinary science; hygiene
Subclass	A61P	Specific therapeutic activity of chemical compounds or medicinal preparations
Complete symbol - 01	A61P 25/02	Peripheral neuropathies
Complete symbol- 02	A61P 3/10	Hyperglycemia

Source: The authors.

In the second stage, a search was carried out in the INPI database, in two ways: through the IPC and Data: (A61P25/022 AND A61P3/10) in the period from 01/01/2010 to 02/02/2022. There were 10 results found with the keyword and Date: (Neuropathy AND Peripheral) OR (Diabetic) in the period 01/01/2010 to 02/02/2022. From this search, 27 results were found. When searching the ESPACENET database, the search was performed using Keywords; IPC using in the search (ta = "diabetic" OR ta = "peripheral" AND ta = "neuropathy") AND (IPC = "A61P25/02" AND IPC = "A61P3/10") and we got 225 results.

In the third stage, data analysis was performed using Microsoft Excel software, where the following were collected: Order No.; Request Date; Patent Title; Publication No.; Publication Date; Summary; IPC – International Patent Classification; PCT – Patent Cooperation Treaty; W.O. – World Intellectual Property Organization - technology protection in several countries; Name of the depositor; inventors; countries.

4. Results and Discussion

The searches carried out in the INPI and ESPACENET patent offices retrieved 262 documents published in the period of 2010 – 02/02/2022. Table 2 shows the number of documents retrieved using the keywords and their combinations in the selected patent offices.

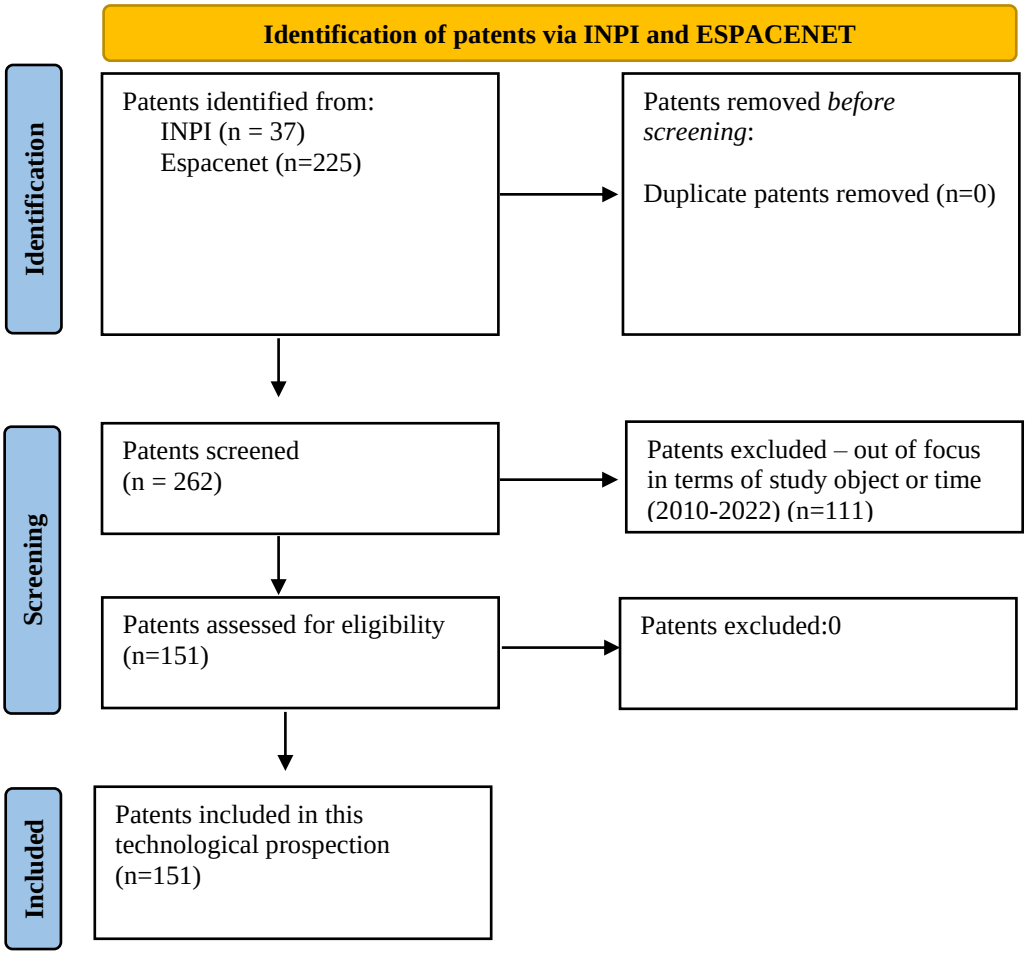
Table 2 - Total mapped patentes.

	Advanced Search	***INPI***	***ESPACENET***
IPC and Date	(A61P25/02 AND A61P3/10) AND 01/01/2010 - 02/02/2022	10	---
Keywords and Date	(Neuropathy AND Peripheral) OR (Diabetic) and 01/01/2010 - 02/02/2022	27	---
Keywords; IPC	(ta = "diabetic" AND ta = "peripheral" AND ta = "neuropathy") AND (ipc = "A61P25/02" AND ipc = "A61P3/10")	----	225
	SubTotal	37	225
	Total of Patents		**262**

Source: Authors.

After the survey carried out in the patent documents found in the INPI and ESPACENET patent offices, using the Diabetic Peripheral Neuropathy filter in the title and abstract, it was possible to retrieve 151 documents (Figure 2 and Table 3), with 19.2% from the INPI and 80.8% from the ESPACENET. Here we can make a parallel about the Brazilian's companies interests in develop new products for NPD in comparison with other countries.

Figure 2 – Total patents recovered from the patent offices.



Source: Authors.

Table 3 - Total patents recovered according to the object of study and research period.

Advanced Search		*INPI*	*ESPACENET*
IPC and date	(A61P25/02 AND A61P3/10) and 01/01/2010 - 02/02/2022	7	---
Keywords and date	(Neuropathy AND Peripheral) OR (Diabetic) and 01/01/2010 - 02/02/2022	22	---
Keywords; IPC and date	(ta = "diabetic" AND ta = "peripheral" AND ta = "neuropathy") AND (ipc = "A61P25/02" AND ipc = "A61P3/10")	----	122
	SubTotal	29	122
Total of Patents			**151**

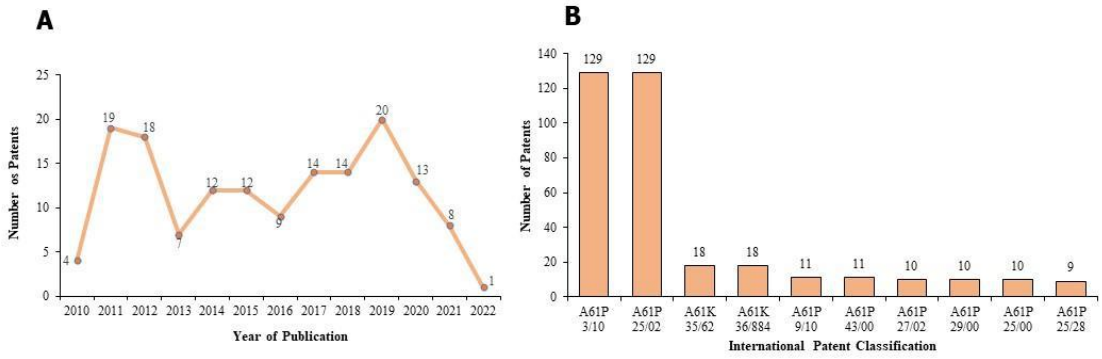
Source: Authors.

From the analysis of data on the annual evolution of published patents on diabetic peripheral neuropathy over time (Figure 3A), it appears that only four patents were published in 2010. While in 2011 there was a peak of 19 publications and in 2012 reached 18 publications, which may have happened due to the revision of the Brazilian Patent Law nº 9.279/1996 launched in 2010, "Revision of the Patent Law: innovation in favor of national competitiveness" submitted to the Council for High Studies and Technological Assessment, of the Chamber dos Deputies, in Brasília and was unanimously approved by the councilors on March 2, 2011, according to (Brazil, 2013b) with the presence of INPI representatives. Regarding the international reality, Boehm and coworkers published a review where they showed the interest of large pharmaceutical companies (including Merck, Eli Lilly, Boehringer Ingelheim, and Novo Nordisk) of discovery and consequently protect new targets for treatment of diabetes in the period of 2011-2016 (Boehm et al., 2018).

In 2019 there was another peak, this time it could be explained by the implementation of Brazilian Resolutions Nos. INPI/PR 240/2019 and INPI/PR 241/2019, on July 9, 2019, instituted new procedures to reduce the backlog of patent applications pending decision (backlog) and achieved significant effects with the INPI. Still following up with the release of Resolution No. INPI/PR 21/2021 that "Disciplines the preliminary requirement of the application for patents for inventions filed in 2017 and pending examination, using the results of searches carried out in Patent Offices of other countries, of International or Regional Organizations" (Brazil, 2021). In the same period Zhu and coworkers highlighted the big interest of Chinese companies in develop oral antihyperglycemic drugs based on their antihyperglycemic mechanisms (Zhu et al., 2019). Here again we can observe the companies interests in treat the disease instead to search by curative alternatives.

Therefore, it can be seen in Figure 3 that these peaks occurred at a time when there was a change in the patent bases, allowing for a greater number of patent grants to occur. In the years 2020 to 2022, there was a decrease in patents on the subject, due to the challenges of the global economy arising from the COVID-19 pandemic. Although according to the United Nations Brazil news of 11/10/2021, according to the World Intellectual Property Organization (WIPO) annual balance sheet, it was highlighted that patent registrations rose 1.6% and industrial design increased 2% in 2020, with new products and services being created in response to the pandemic.

Figure 3 – A) Number of patents granted in the INPI and ESPACENET offices in the period 2010 – 02/02/2022. B) IPC framework of mapped patents.



Source: Authors.

When analyzing the 151 patents recovered in the research, it was found that they had more than one technology and by grouping these technologies in the international classification of patents (IPC), a total of 830 technologies were found that,

grouped by session, show that in session A - Human Needs having 89.5%, session C - Chemistry; Metallurgy 10% and G – Physics got 0.5% as shown. The two subclasses A61K and A61P together account for approximately 87.8% of the grand total.

Table 4 – Total IPC included in the 151 mapped patents.

Technological areas	Subtotal of technologies	Description	Subtotal by session
Session A - HUMAN NEEDS			
A01N	1	A01N - CONSERVATION OF BODIES OF HUMAN BEINGS OR ANIMALS OR PLANTS OR PARTS THEREOF.	743
A23L	12	FOODS, FOOD PRODUCTS, OR NON-ALCOHOLIC BEVERAGES NOT COVERED BY SUBCLASSES A21D OR A23B - A23J.	
A61B	1	DIAGNOSIS; SURGERY; IDENTIFICATION	
A61K	326	PREPARATIONS FOR MEDICAL, DENTAL, OR HYGIENIC PURPOSES.	
A61P	403	SPECIFIC THERAPEUTIC ACTIVITY OF CHEMICAL COMPOUNDS OR MEDICINAL PREPARATIONS	
Session C - CHEMISTRY; METALLURGY;			
C07C	12	ACYCLIC OR CARBOCYCLIC COMPOUNDS.	83
C07D	54	HETEROCYCLIC COMPOUNDS.	
CO7H	11	SUGARS; THEIR DERIVATIVES; NUCLEOSIDES; NUCLEOTIDES; NUCLEIC ACIDS.	
CO7K	3	PEPTIDES	
C12N	3	MICROORGANISMS OR ENZYMES; ITS COMPOSITIONS; PROPAGATION, CONSERVATION, OR MAINTENANCE OF MICRO-ORGANISMS; GENETIC OR MUTATION ENGINEERING; CULTURE MEDIUMS.	
Session G - PHYSICS			
G01N	3	RESEARCH OR ANALYSIS OF MATERIALS BY DETERMINING THEIR CHEMICAL OR PHYSICAL PROPERTIES.	4
G06T	1	IMAGE OR GENERATION DATA PROCESSING IN GENERAL	
Total	830	---------	------

Source: Authors.

By evaluating the technologies found in the prospective research in the period 2010 - 02/02/2022, it was found that, despite technological innovations having been developed, the understanding of the effects of the pathological processes of diabetic neuropathy on normal physiological activities remains unclear, because of the 830 technologies observed in this research, most of the technologies consist of treatments focused on relieving symptoms and reducing adverse effects, as shown by the result of this research where 729 are A61K technologies that are preparations for medical, dental or hygienic purposes and A61P which are specific therapeutic activities of chemical compounds or medicinal preparations. Thus, we infer that the development of these therapeutic alternatives is still focused on relieving the symptoms caused by the complication of diabetes and not on its cure since it is known that Diabetic Peripheral Neuropathy is the most common complication of diabetes capable of compromising all tissues of the body and be a cause of significant morbidity and mortality (Singh et al., 2014). This is a trend already observed in previous patent reviews (Boehm et al., 2018; Zhu et al., 2019).

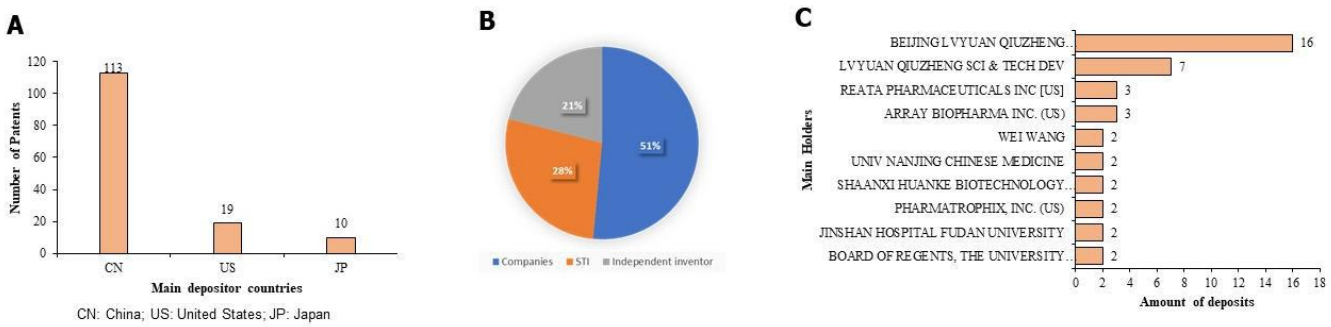
More specifically about IPC, Figure 3B presents the analysis of the first 10 technologies used, where it was found that the first two IPC symbols were part of the research searches. From the IPC symbols we can see that most belong to Section A (Human Needs), and subclass A61P (Specific therapeutic activity of chemical compounds or medicinal preparations). Being

specifically from Group and subgroup A61P25/02 (drugs for the treatment of diseases of the nervous system, for peripheral neuropathies) and A61P3/10 (Drugs for the treatment of metabolism disorders, for hyperglycemia). The data above corroborate with the study conducted by Acioli & Oliveira Júnior (2014) carried out in the EPO and WIPO patent offices, which showed in their studies that the subclasses A61K and A61P of the International Patent Classification were also the first in the patent framework in both technological offices (Acioli, 2014).

However, from the analysis of Figure 4A, it was possible to observe that 151 of the listed patents originated in 10 countries. Brazil does not have a patent in the offices selected for the object of study of this review demonstrating that are the large companies who has more interest in this subject. Six countries obtained one patent each, totaling 4%, Switzerland obtained 3 patents with 2% and only three countries stood out, China – CN with 74.8%, followed by the United States – the US with 12.6% and Japan – JP with 6.6%.

It is worth noting that China's leading role in the production of patents on the subject in question is due to the government's position of investing massively in human resources to train individual inventors, in addition to constant incentives for the Research and Development (R&D) sector of companies, as well as support from the China Patent Office (CNIPA).

Figure 4 – A) Main depositor countries. B) Types of depositors. C) Main holders.



Source: Authors.

All these efforts culminated in the result released by the WIPO in 2019 in the Global Innovation Index Report (GII) which showed that China moved to the 14th position, climbing three positions to join the top 15 innovative economies. Thus, the data of the present study corroborate with previous work conducted by Acioli and Oliveira Júnior (2014) which showed that China is the country that holds the highest number of patents involving Diabetes, followed by the Republic of Korea and Japan, and that China also leads the world ranking of people with diabetes, which can explain the major interest of this country in develop new therapeutic strategies (Acioli, 2014; Zhu et al., 2019).

Regarding the distribution of the number of patent documents identified by the type of depositors, the main depositors, in their majority, 51% of the patent documents are from companies, 28% are from Science and Technology Institutions (STIs - Figure 4B) and 21% are distributed among independent inventors. From this analysis, it was observed that of the 151 patents, there were a total of 167 applicants, of which 86 were companies, 46 were STIs, and 33 were independent inventors.

The main patent holders in the period 2010 – 02/02/2022 on Diabetic Peripheral Neuropathy were respectively Beijing Lvyuan Qiuzheng Technology Dev Co Ltd, Lvyuan Qiuzheng Sci & Tech Dev and Reata Pharmaceuticals Inc [US] as well as Array Biopharma Inc. (US) which together own 18% of the 167 patent applicants, as shown in figure 4C.

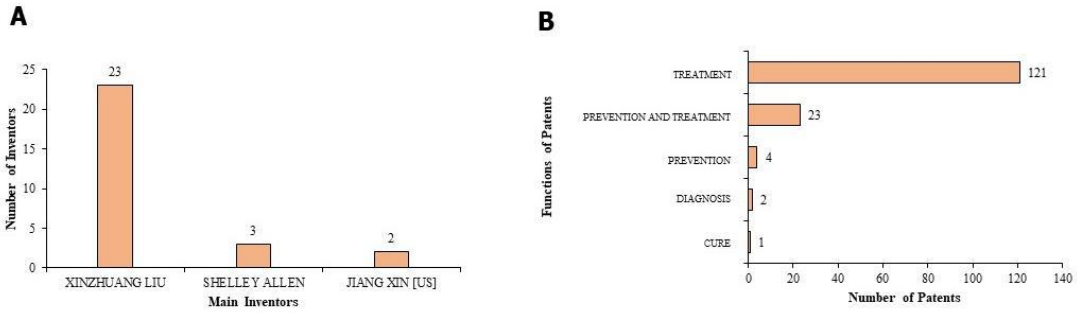
The company Beijing Lvyuan Qiuzheng Technology Dev Co Ltd obtained 9% of the patents deposited in the period 2010 – 02/02/2022 on the subject addressed in Espacenet. It is a company that is in the 5th position in the Ranking of the ten

largest Patent Holders in China, according to "The top ten granted invention applicants in biology industry in 2011" published by the magazine China Report Intellectual Property 13/06/12.

Also, there is an ever-increasing interest in therapies for diabetes and its complications, as DPN. This interest is explained by the gap in the pharmaceutical market options as the currently available drugs are limited to treating the main symptoms of the diseases. This gap highlights the need to seek new technological alternatives to cure this important and worldwide health problem.

According to data presented in figure 5 of this study, the inventor who is more worried about this topic and consequently who filed the most patents on this topic was "Xinzhuang Liu", who resides in Shenzhen, attended high school at Shenzhen College of International Education, and higher education at Imperial College London. Of the 519 inventors, this inventor alone owns 4.4% of the patents studied.

Figure 5 – A) Main inventors. Ranking of the Top Ten Patent Holders in China. B) Main functions of mapped patents.



Source: Authors.

To know in greater depth the intellectual property history of this inventor, a survey was carried out on ESPACENET during the same period of the present research (2010 – 02/02/2022) and 1070 inventions were found in total, which gives an average of 89 inventions per year. Of these, the inventor has kept 177 patents under wraps as he has only issued 893.

"Xinzhuang Liu" is one of the five key people in the management and development of machine technology – he is the CEO of Machinery Technology Development CO LTD. – BAT The profile of "Xinzhuang Liu" is: researcher, research supervisor, having received a special subsidy from the State Council, awarded twice as outstanding Young Specialist of Zhengzhou City, Academic Trans-century Pacesetter of Zhengzhou City and he was the 1st Labor Medalist of the city of Zhengzhou in May 1999 and in April 2000. This shows that he is an inventor of excellence and therefore deserves to be highlighted.

The data presented in Figure 5B corroborate the information in Table 04 and Figure 3B, that among the 151 patents, 99.3% are preparations for medical, dental, hygienic purposes and specific therapeutic activity of chemical compounds or medicinal preparations, for diagnoses, prevention, and treatment and only 0.7% for cure as stated in abstracts or patent publications.

Although 151 patents containing 830 technologies were mapped, only one patent referred to the cure of DPN, a patent retrieved from the ESPACENET database, published under number CN102389503, entitled TRADITIONAL CHINESE MEDICINE FOR CURING DIABETIC PERIPHERAL NEUROPATHY, with Beijing Luyuanqiuzheng Technology Dev Co Ltd as depositor and inventor Xinzhuang Liu and used only three technologies A61K36/8884; A61P25/02; A61P3/10 (LIU, 2012). Which explains that the main country worried about this topic is China and they started to seek by curative approaches instead to only treatments.

The aforementioned patent is a product from traditional Chinese medicine for the cure of diabetic peripheral neuropathy and aims at a quick effect, the technology refers to capsules or tablets containing common andrographis herb, radix paeoniae alba, white caltrop, lucid ganoderma, pseudo-ginseng, salvia miltiorrhiza, rhizome alismatis and other raw materials, with the functions of strengthening the healthy energy, reinforcing the vital energy, tonifying qi, nourishing the blood, promoting the blood circulation, removing the blood stasis and eliminating dampness and heat, and has the advantages of obvious effect, precise efficacy and faster effect.

According to the clinical information provided in the patent document, 22 patients with DPN were followed, 12 men and 10 women without other serious diseases, whose ages ranged from 45 to 79 years with an average of 60.7 years, having as a pattern Patients diabetic with weak constitution and fatigue, dry skin, numbness and pain in hands and feet, abnormal limb sensation, tingling, an ant walking and burning sensation.

During clinical trials, other drugs and health supplements were suspended and patients took only the Chinese medicine capsule of the present invention (2 capsules 4 times a day, each capsule contains fine powder of Chinese medicine and extract 0.3g, take it with warm water after a meal), patients were followed for three months. After one month, relief of symptoms was observed, and after 3 months symptoms improved significantly. To measure efficacy, of the 22 participants in the clinical trial, 13 people had markedly effective effects from the product; in 7 participants the product was effective and ineffective in only 2 participants. Thus, the total effective rate was 90.9%.

To judge the efficacy was considered: a) Significant effect: physical enhancement, strong limbs; numbness of hands and feet, pain relief; abnormal tingling, an ant walking, burning sensation of limbs disappeared or significantly relieved; b) Effective: The body is vigorous, and the numbness, pain and abnormal feeling of the limbs have been relieved; c) Invalid: No change in illness.

The other patents recovered in the present study referred just to the treatment of symptoms (figure 9). Given this, it is suggested that efforts be dedicated to developing new technologies such as this one that was published in China in 2012 (CN102389503), focusing on curing the disease and not just treating the symptoms. Only in this way will we be able to restore the quality of life of patients who suffer from DPN and reduce public health expenditures that are earmarked for this important health problem.

5. Conclusion

Given the above, it was possible to infer that the greater incentive provided by the government, both for the patent bases and the development of research, the greater the proportionately greater is the patent publications, having occurred outstandingly in the years after investments.

Another interesting finding observed through the analysis was that China obtained an impressive profile since it is the country that most deposited patents within the theme of this study and has the main depositor and the largest inventor of patents also is the only one that protect a curative technology. It is worth mentioning that, unlike other studies in which the public sector has been prominent in this area, the type of applicants that most had patents published were private companies, and of these, the one that stood out the most for having the largest number of patents is the one company that is in the 5th position in the Ranking of the ten largest patent holders in China. Noting that in IPC the most mentioned area was Section A of Human Needs.

Therefore, it was observed that the countries with the most developed technologies were China, the United States, and Japan, which together reached 93% of the patents studied. Unfortunately, for many government officials, politicians, and entrepreneurs (as Brazil as example), Research and Development (R&D) are still considered expenses and not investments, even though innovation can bring a certain and guaranteed return.

Thus, given the research carried out, it is understood that greater investment is necessary for studies related to DPN, changing focus from just treating the symptoms to the search for a cure and greater study of patent number CN102389503, aiming at greater growth of technological innovations and, above all, improvement in the well-being of the population. So, we suggested more efforts in future studies to develop new curative alternatives for the disease and its comorbidities and not just for the symptoms.

Acknowledgments

We thank CAPES-Brazil for the grant to PPM "Bolsista CAPES/BRASIL" under process number 88887.625437/2021-00 through CAPES PREMIO - Programa Prêmio Capes de Teses.

References

Acioli, G. D. R., & Oliveira Júnior, A. M. (2014). *Prospecção tecnológica sobre a cura do Diabetes Mellitus.*

Altiere, C. E. (2017). Neuropatia periférica causa perda da sensibilidade e formigamento. Retrieved from https://www.hospitalsiriolibanes.org.br/sua-saude/Paginas/neuropatia-periferica-causa-perda-sensibilidade-formigamento

Amparo, K. K. D. S., Ribeiro, M. D. C. O., & Guarieiro, L. L. N. (2012). Case study using mapping technology foresight as the main tool of scientific research. *Perspectivas em Ciencia da Informacao*, 17, 195-209.

Anad. (2020). O que saber sobre neuropatia por pequenas fibras. Retrieved from https://www.anad.org.br/o-que-saber-sobre-neuropatia-por-pequenas-fibras/

Armstrong, D. G, Boulton, A. J, & Bus, S. A (2017).Úlceras do pé diabético e sua recorrência.*New England Journal of Medicine*,*376* (24), 2367-2375.

Baum, P., Toyka, K. V, Blüher, M., Kosacka, J., & Nowicki, M. (2021). Mecanismos Inflamatórios na Fisiopatologia da Neuropatia Periférica Diabética (ND)—Novos Aspectos. *International Journal of Molecular Sciences*, 22 (19), 10835.

Boeck J. A. (2019). A Prospecção Tecnologica como Estratégia Competitiva para inovarmos Retrieved from https://neitzkeconsultoria.com/prospeccao-tecnologica/

Boehm, M., Crawford, M., Moscovitz, JE, & Carpino, PA (2018). Análise de participação de patentes na área de diabetes – parte II: anos 2011-2016. *Opinião de Especialista em Patentes Terapêuticas*, 28 (2), 111-122.

Brazil. (2013a). Brazil'S Patent Reform: INNOVATION TOWARDS NATIONAL COMPETITIVENESS. https://www2.camara.leg.br/a-camara/estruturaadm/altosestudos/pdf/brazils_patent_reform_eng.pdf

Brazil. (2013b). Lei de patentes 9279/1996. A revisão da Lei de patentes: inovação em prol da competitividade nacional.

Brazil (2019) Resolução INPI PR nº 240, de 03 de julho de 2019

Brazil (2019) Resolução INPI PR nº 241, de 03 de julho de 2019

Brazil (2021) Portaria INPI PR nº 21, de 26 de março de 2021, (2021).

CF, M. R. D. M. (2020). Competitive intelligence, innovation and performance: theoretical model proposal. *Braz. J. of Develop*, 6(1), 657-678.

Correr, C. J., Coura-Vital, W., Frade, J. C. Q. P., Nascimento, R. C. R. M., Nascimento, L. G., Pinheiro, E. B., João, W. S. J. (2020). Prevalence of people at risk of developing type 2 diabetes mellitus and the involvement of community pharmacies in a national screening campaign: a pioneer action in Brazil. *Diabetology & Metabolic Syndrome*, 12(1), 89. 10.1186/s13098-020-00593-5

Federation, I.-I. D. (2021). The Diabetes Atlas. https://www.idf.org/news/240:diabetes-now-affects-one-in-10-adults-worldwide.html

Galindo, R. J., & Aleppo, G. (2020). Continuous glucose monitoring: The achievement of 100 years of innovation in diabetes technology. Diabetes Res Clin Pract, 170, 108502. 10.1016/j.diabres.2020.108502

Hicks, C. W., & Selvin, E. (2019). Epidemiology of Peripheral Neuropathy and Lower Extremity Disease in Diabetes. *Curr Diab Rep*, 19(10), 86. 10.1007/s11892-019-1212-8

IDF. (2021). Diabetes now affects one in 10 adults worldwide. https://www.idf.org/news/240:diabetes-now-affects-one-in-10-adults-worldwide.

INPI. (2021). Classificação Patentes. Retrieved from https://www.gov.br/inpi/pt-br

Kruk, M. E., Gage, A. D., Arsenault, C., Jordan, K., Leslie, H. H., Roder-DeWan, S., & Pate, M. (2018). High-quality health systems in the Sustainable Development Goals era: time for a revolution. *The Lancet Global Health*, 6(11), e1196-e1252. 10.1016/S2214-109X(18)30386-3

Lee, S. H., & Yoon, K. H. (2021). A Century of Progress in Diabetes Care with Insulin: A History of Innovations and Foundation for the Future. Diabetes Metab J, 45(5), 629-640. 10.4093/dmj.2021.0163

Liu, X. (2012). *Traditional chinese medicine for curing diabetic peripheral neuropathy*, number CN102389503, 2012-jun-07.

MINAYO, M. C. S. (1994) (org.) Pesquisa social: teoria, método e criatividade. Petrópolis – Rio de Janeiro, Vozes.

Ministério da Saúde. (2020). Vigitel 2020: vigilância de fatores de risco e proteção para doenças crônicas por inquérito telefônico. Transinf, 102-104.

OECD. (2015). Education at a Glance 2015.

ONU. (2021). 100 anos depois, 50% dos diabéticos ainda enfrentam barreiras no acesso à insulina. Retrieved from https://news.un.org/pt/story/2021/11/1770212

Sarwar, N., Gao, P., Seshasai, S. R., Gobin, R., Kaptoge, S., Di Angelantonio, E., & Danesh, J. (2010). Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet, 375(9733), 2215-2222. 10.1016/s0140-6736(10)60484-9

Singh, VP, Bali, A., Singh, N., & Jaggi, AS (2014). Produtos finais de glicação avançada e complicações diabéticas.*O jornal coreano de fisiologia e farmacologia18* (1), 1-14

Who. (2021). 100 years after its discovery, insulin still out of reach for many living with diabetes. Retrieved from https://www.who.int/news/item/12-11-2021-new-who-report-maps-barriers-to-insulin-availability-and-suggests-actions-to-promote-universal-access

Zhu, W., Huang, W., Xu, Z., Cao, M., Hu, Q., Pan, C., & Yuan, H. (2019). Analysis of Patents Issued in China for Antihyperglycemic Therapies for Type 2 Diabetes Mellitus. Frontiers in Pharmacology, 10. 10.3389/fphar.2019.00586