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DETERMINING FACTORS FOR PHARMACEUTICAL INNOVATION AND THE HEALTH INDUSTRIAL COMPLEX IN BRAZIL AND THE BRICS

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ABSTRACT

The development of a local pharmaceutical research and development industry is essential to meet the demands of a large country with a large population such as Brazil. This work aims to explore the existing data on the ecosystem of the pharmaceutical industry in this group of countries, and through parameters based on the precursor literature, to identify the innovation factors and the position of Brazil in relation to the other representatives of the BRICS (the leading developing countries in the world). Since the mid-1940s, Brazil has received pharmaceutical multinationals and through government initiatives it has locally reproduced medicines developed abroad when the patents have ended. The BRICS represent the group of emerging countries considered "the big five", with population capacity and economic growth that tend to boost the global economy in the coming years. The comparative analysis showed that Brazil has a certain lag in fundamental parameters for the existence of a national pharmaceutical R&D industry, having placed behind Russia, India and China, even symbolically by not producing a national vaccine in response to COVID-19.

Contribution/Originality: In the midst of the recent global pandemic, this article seeks to identify the factors capable of enabling developing countries to produce vaccines and patented medicines, taking as an example the BRICS (considered leaders in global growth) Brazil, Russia, India, China and South Africa.

1. INTRODUCTION

Brazilian people are characterized by a certain irreverence when dealing with political and economic problems that directly affect their social condition, purchasing capacity and life situation (Braga, 1948). The author expresses his concern about the pharmaceutical product produced in Brazil "(...) if tomorrow I needed to buy penicillin, I would buy the North American one. (...) the pharmaceutical industry in Brazil does not deserve my trust" (Braga, 1948). According to Mota, Vigo, and Kuchenbecker (2018) only in 1999 with the creation of the Brazilian Health Regulatory Agency (*Agência Nacional de Vigilância Sanitária* - ANVISA), which oversees everything from establishments offering meals to national and international pharmaceutical industries, is a body designed to qualify the production of medicines in Brazil.

The 50-year period that comprises the interval between (Braga, 1948) and the advent of ANVISA is not exactly a regulatory gap in Brazil. Costa, Fernandes, and Pimenta (2008) indicate important actions, such as the creation of the National Health Surveillance Secretariat in 1976, which followed the creation of smaller divisions, such as the National Service of Medicine and Pharmacy, whose task was to oversee the pharmaceutical industry. The authors

comment that despite the relevance of these bodies, the rudimentary structure and low budgets limited the performance of these institutions.

The lack of consumer confidence in a generic drug produced in Brazil is still noticeable in studies such as Luppe, Rossi, Torres, and de Souza Aguiar (2020) which evidenced, in São Paulo metropolitan area, the preference of 30% of the population for medicines positioned as a reference, even when generics were available. According to the authors, the decision driver of these 30%, as they commented when answering the survey, is the perception of product quality.

The late regulatory issue and consumer confidence in the national industry (confidence which is still somewhat affected) may explain the lower representation of the Brazilian pharmaceutical industry compared to other BRICS countries (Brazil, Russia, India and China). The history of the national pharmaceutical industry dates back to the period between 1930 and 1945, in which companies such as Laboratório Paulista de Biologia and Instituto Pinheiros took great strides. These companies were created through contributions from the Brazilian government (Ribeiro, 2006).

The period in question was a milestone for the evolution of national industrialization, and Suzigan (1971) reports that until then, before the great depression of 1929, Brazilian industry was restricted to food and textile consumer goods. After the economic depression, the number of industrial workers grew by more than 50% in about 2 or 3 years. Between 1930 and 1939, with the chemical and pharmaceutical industries growing 30%, and the state of São Paulo positioning itself as a relevant industrial hub in Latin America.

This growth did not translate into good regulation, and Spiegel (1965) reports a serious problem in this regard. Even the drug-chemical packaging was confusing. Identical looking ampoules could contain novocain at concentrations of 50% or 1%. The first (50%) needed to be diluted on a large scale to sedate patients, the second (1%) could be applied at once for spinal anesthesia. In other words, a simple confusion would be fatal.

In the study by Viceconti (1977) it is clear that throughout the post-war period there was a strong advance in the chemical and pharmaceutical industry in the country, with the entry of multinationals that locally found smaller industries that were unable to face the new competition.

This view is endorsed by Cross (1988) who points out that, between 1946 and 1982, multinational pharmaceutical industries arrived in Brazil, weakened national laboratories and industries that did not have technical, productive and regulatory capacity comparable to global standards, and grew locally until make Brazil the main country in the pharmaceutical segment in Latin America and 8th in the world.

The multinational pharmaceutical industry influences prescribers. Duarte (1991) reports that most physicians would like the pharmaceutical industry to increase its influence over the National List of Essential Medicines - RENAME and the Medicines Center - CEME (ministry of health guidelines that list essential medicines). These healthcare professionals used to receive direct technical sponsorship from these industries, such as congresses, symposiums and lectures often held internationally, with high-quality tickets and accommodation included. in order to avoid this misconduct, Fabbri et al. (2017) highlight the establishment of more restrictive policies, avoiding harmful influence on prescribers, especially from the 2000s onwards.

This background leads us to the current moment, in which the predominant pharmaceutical industry in Brazil continues to be the international one, the owner of reference drugs, with high added value and with a large number of patents in force in various therapies. The national pharmaceutical industry is mainly restricted to copying and execution. Brazil, after the advent of the 1999 generics law, started to create a specific industrial park for these drugs that reproduce successful synthetic drugs that lost their patents. To research and innovation, nothing or very little.

In this context, the purpose of this study is to analyze the context of the Brazilian pharmaceutical industry in comparison with the BRICS member countries. This analysis makes it possible to establish comparisons and

conjectures of the Brazilian pharmaceutical industry with other BRICS countries – Russia, India, China and South Africa.

2. LITERATURE REVIEW

This chapter addresses the main themes comprising the ecosystem of the pharmaceutical industry, as well as some fundamental factors for its existence. The theoretical background was elaborated from the context of the Brazilian pharmaceutical industry, thus positioning itself as a reference element for the comparative analysis with the other BRICS member countries.

2.1. Late Regulation and Pharmacovigilance

The history of the local pharmaceutical industry begins in the beginning of the 19th century, well before the publication of Rubem Braga's chronicle, which dates back to 1948. However, according to Helou (1986) the arrival of the first apothecary in Brazil, Diogo de Castro (who arrived in the retinue of Thomé de Souza, first general governor of the colony) dates back to 1549. This would have been the first contact on Brazilian soil with a drug obtained through chemical processing carried out by a human, at the time, the apothecaries. The official arrival of the first doctor on national territory dates back to 1645.

Centuries after these events, according to Barreira (1997) it was only in 1920 that the DNSP (national public health department) was created in the government of Epitácio Pessoa. Carlos Chagas, then discoverer of Chagas' disease and successor of Oswaldo Cruz in national research, was the first director of the DNSP between 1920 and 1934.

The DNSP had a role focused on the implementation of the first public health policies in Brazil, a country with several tropical diseases, and brought with it the need to de-urbanize the concern with health. This public department also acted on fronts for the sanitation of agriculture, which suffered sanctions caused by the autonomy of the States over rural production. Thus, from a regulatory point of view, it was a government division with very limited authority.

According to Rigo and Nishiyama (2005) throughout the 1970s, with the existence of the National Health Surveillance Secretariat, Brazil began to take some (still fruitless) efforts to establish pharmacovigilance in the national territory. This was the trigger for the idea of the need for pharmacovigilance to be disseminated in courses in the health area (medicine, nursing, pharmacy) in the 1980s and 1990s.

Brazilian literature regarding pharmacovigilance converges to the correlation between the emergence of ANVISA in 1999 and the existence of an agency with real health power and inspection equipment in the country. As commented by Oliveira and Cruz (2015), in 1988 the Brazilian National Health System (*Sistema Único de Saúde* - SUS) emerged with the proposal of being an integrating entity, and under its management and resources ANVISA is an autarchy of the Ministry of Health itself.

It is possible to understand how late the regulation and investment in drug inspection in Brazil was when putting into perspective studies such as Heath (2004) who exposes the creation of the Drug Importation Act in 1848 as the first drug regulation regime in the United States, or (Chang, Simone, & Schultheis, 2005) which presents the creation of the FDA (Food and Drug Association), an American entity equivalent to the Brazilian ANVISA, in 1906.

2.2. Innovation as an Ignition of the Pharmaceutical Industry

The national industry, as proposed by Campos and Ruiz (2009) has consolidated innovation poles in the chemical and pharmaceutical segments, and are probably the sectors of the economy that innovate the most, along with electrical and computer equipment. Although these industries are based on Research and Development(R&D), the authors reinforce the idea that national innovation is very incipient when compared to other countries.

Pharmaceutical innovation in Brazil is often based on creating a new generic and not creating a new drug. According to Yamaguishi (2014), national pharmaceutical companies such as BIOLAB have an R&D area, but its purpose is not the search for launching new molecules for new treatments and clinical research for such. The R&D area of the national industry consists of a department that assesses the next patents for foreign medicines to expire and the economic feasibility of reproducing them in Brazil.

This behavior continues to expose the country to exchange rate variations and unbalance the trade balance, according to Rodrigues, Costa, and Kiss (2018). Between 1996 and 2014, Brazil had a 43.8% shrinkage of the pharmacochemical sector (the base of the pharmaceutical industry), and the efforts of the national chemical industry were reverted to crop protection products (fertilizers, agrochemicals, etc.).

Alves (2005) takes up the issue of phytomedicines as a possibility of technological development for the local pharmaceutical industry. Phytomedicines, however, are medicines of natural/vegetable origin that involve little or no need for chemical creation for their production, consisting primarily of chemical extraction and concentration. Alves (2013) goes back to this issue, exposing the fact that since the arrival of the first Portuguese ships with the first naturalists and botanists in the 16th century, Brazil has produced herbal medicines with its local flora. It is necessary to understand if the reinforcement of herbal medicines is capable of creating a strong and innovative national pharmaceutical industry, or if the chemical technology that has already been installed in Europe and the United States is really lacking, generating the multinationals from which the Brazilian industry copies finished medicines patents.

Bastos (2005) report for the National Bank for Social Development (*Banco Nacional de Desenvolvimento Social* - BNDES) reinforces the idea that the pharmaceutical sector is based on innovations, with radical innovations being more desired, capable of generating products that change the meaning of treatments and people's perspective of life, without neglecting the importance of incremental innovations that improve existing products. BNDES, through the PROFARMA program, managed to help create a local pharmaceutical industry for generics aimed at reducing the price of treatments, but the innovation gap persists, along with the basic supply of chemical inputs.

Finally, Vargas, Gadelha, Costa, and Maldonado (2012) comments on the search for a virtuous agenda for the national innovation pharmaceutical industry. The work exposes the fact that important elements for the existence of an innovative industry already exist in Brazil: a policy for financing companies in the BNDES, public authorities with purchasing capacity and a strong regulatory agency, ANVISA. An important element that may be missing, according to Hasenclever (2015) is innovative research, often emerging in universities sponsored by multinationals that own the patents.

Previous studies on the issue of pharmaceutical innovation indicate that Brazil "imports innovations" and reproduces them in the form of a generic medicine when patents expire. This is a process that, from an innovation point of view, can be understood as copying or reverse engineering according to Eun, Lee, and Wu (2006), added to the fact that Brazil also imports a good part of the necessary inputs to produce such copies locally.

2.3. The Importance of Patents in Industry Innovation and Establishment

For patents to exist in a market, legal security in a country and the ability to ensure rights for developers and payback for investors are necessary. The study on the National Institute of Industrial Property (*Instituto Nacional de Propriedade Industrial* - INPI) by Junior and Moreira (2017) reveals that Brazil has a backlog of patents. The time required to grant a patent in Brazil has an average of 10.8 years in 2013, which goes against the speed of globalization, technology and international production capacity, leaving the country uncompetitive in this scenario.

According to the website of the United States Patent and Trademark Office USPTO, the analysis time for a new patent takes 2 years for the simplest processes, and up to 5 years for the most complex processes. In its worst-case scenario, the United States takes half of Brazil's time to review a registration application. According to Arts,

Cassiman, and Gomez (2018) there is a refined text/keyword analysis system that allows for faster patent checking, aiding the United States Patent Classification System USPCS.

This inefficiency in the process of analyzing a new patent punishes the Brazilian industry and discourages internal research, since it is much more rewarding for investors to apply for a patent in the United States, Europe, China, and obtain quick answers to start using the product resulting from their discovery and receive financial return for it.

Brazil is already behind in terms of patents and technology, according to Campos and Denig (2011). The state of São Paulo stands out as the largest applicant for patents in Brazil (more than half), largely due to the UNICAMP university and the FAPESP research development agency. However, on the international scenario, indicators such as R&D in relation to Gross Domestic Product (GDP) and patent registration in relation to GDP place Brazil in an uncomfortable situation, stagnant in both indicators.

Oliveira and Velho (2010) comment on the patenting activity in the country and the productivity of inventors from Brazilian universities. Again, it reinforces the concentration of production in the Southeast region of Brazil, with emphasis on São Paulo and FAPESP. From a regional point of view, there is no balance between production and investment in innovation in the rest of the country.

The study by Santos et al. (2014), which focuses on patent applicant and filing industries, calls attention to the fact that multinationals such as Nestlé are most responsible for patent applications from companies in the country. Of the few patents requested by companies in Brazil, most are still for multinationals installed herein. The study comments that among the more than 100 patents filed in the analyzed period, only 22% were from national companies and institutions.

And while, from the private point of view, patents do not evolve at an exciting speed and their registration process in Brazil is not effective, from the public point of view, another concern arises. According to Marques (2000), the patent law does not help to guarantee accessibility to the most innovative technologies and exposes the public system to high cost therapies.

Within the scope of the World Trade Organization (WTO) and the disputes between developed countries and their multinationals versus underdeveloped countries and their precarious local industry, Brazil is on the weaker side, according to Oliveira and Moreno (2007). Brazil is an actor making a diplomatic effort to win litigation against American and European patents, with the justification and moral appeal of accessibility to reduce the impact of its low local industrial capacity. The public policy behavior adopted by the Brazilian Ministry of Foreign Affairs chooses to affect the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).

Both Chaves and Albuquerque (2006) and Januzzi and Vasconcellos (2017) place Brazil below a "threshold" of world scientific production. Developed countries have strong characteristics of investment in research, scientific production and emphasis on the health sector. Together, these three factors create a healthy situation for pharmaceutical innovation.

The need for public policy intervention is seen as a key factor to change this trend and to make the conditions for the design of patents viable, especially with regard to research, public health and encouragement to the pharmaceutical sector.

3. METHODOLOGY

For this study, an exploratory research was carried out, in which relevant articles were gathered from the existing literature on the topics of pharmaceutical industry and patents, for each of the BRICS countries, in order to enable an evolutionary construction of the history of that industry. Following the principles of Mainardes, Alves, and Raposo (2010) qualitative exploratory research brings with it the empirical knowledge existing in the people interviewed, or in the bibliographic productions that bring transcribed knowledge.

The articles in question were obtained through the platforms Web of Science, Scielo, Scholar Google, Capes and USP and chosen according to their alignment with the theme of the work, their relevance and number of citations.

Such type of research, according to Nilsen, Bowler, and Linnell (2020) allows the construction of hypotheses and inferences that help to understand the relationship between themes and causes of a given phenomenon, often resulting in confirmatory research.

Sayani et al. (2019) draw attention to the need to address socioeconomic disparities when exploratory research approaches different countries. For this purpose, parameters addressed in the international literature of the BRICS were defined in this work, which allow a comparison with the situation in Brazil, according to Table 1.

Table 1. Parameters for comparative analysis between the BRICS.

Parameter	Measures	Bibliographic Background
Regulatory Scenario	• Existence of health surveillance regulatory agencies in the country. • Time of existence. • Body's oversight capacity.	• Helou (1986) • Barreira (1997) • Chang et al. (2005) • Oliveira and Cruz (2015)
Innovation Scenario	• Existence of incentives for entrepreneurship and innovation in universities. • Innovation in the private sector. • Innovation in public sector.	• Campos and Ruiz (2009) • Yamaguishi (2014) • Rodrigues et al. (2018)
Patents and Knowledge Protection	• Existence of intellectual property protection laws. • Existence of a government agency that manages the issue. • Country efficiency in the analysis, issuance and management of patents.	• Arts et al. (2018) • Campos. and Denig (2011) • Santos et al. (2014) • Januzzi and Vasconcellos (2017)
Fostering Local Pharmaceutical Industrial Development	• Existence of government investments to promote the pharmaceutical industry. • Existence of private investments to promote the pharmaceutical industry. • Existence of public-private partnerships for the creation of medicines.	• Bastos (2005) • Vargas et al. (2012) • Hasenclever (2015)

In the comparative stage of the study, in line with Esser and Vliegenhart (2017), a comparative case study approach was adopted, and the case sample (related to articles addressing the pharmaceutical industry development in the BRICS can be considered a small-N comparative analysis given the limited number of cases. This fact, according to the authors, is not an impediment when there is a relevant amount of theoretical argument surrounding the hypotheses, as shown in Table 1.

Like Engeli and Rothmayr (2014), at the end of the data analysis, a summary table with the hypotheses and assumptions arising from the comparison of international and national parameters that determine the success of the research and development pharmaceutical industry is expected.

Finally, according to Gil (2019) the hypotheses (after an empirical verification with the analyzed data) are expected to allow the conclusion of the exploratory and comparative research, showing some relationship with the theories proposed in the precursor articles of the BRICS.

4. DATA ANALYSIS

This section presents the data obtained from the survey of other BRICS member countries. The content of the data presented herein is discussed in the next section in relation to the theoretical survey, which incorporates the Brazilian pharmaceutical industry. In this topic, Brazil's economic and structural attributes will be analyzed against

the BRICS and the performance of other countries in this group in the development of their health and innovation/patent industrial complex.

According to Vidal and Silva (2017) Brazil has a good international trade capacity, but remains vulnerable to changes in the external scenario, largely because its industry is smaller than that of Russia, India and China, which exposes Brazil in the trade balance, with Brazil being strong in commodities. According to the author, Brazil has the highest degree of industrial denationalization within the BRICS.

4.1. Russia and its Clusters

According to Austin Rating Report (2020), in 2020, Russia was ranked 11th in the ranking of the largest economies in the world, 3 positions ahead of Brazil, which fell to the 14th place.

The Russian pharmaceutical industry has grown in the same proportion as the Russian pharmaceutical market, according to a study by Rogachev (2008), a market composed of patients from the average aging of the Russian population, which starts to suffer a higher incidence of comorbidities. Between 2010 and 2018 Russian life expectancy jumped from 68 to 73 years.

Klunko and Marynia (2011) attribute this increase in life expectancy to the innovation and capacity of the Russian pharmaceutical industry, which, despite not fully satisfying the country's domestic demand, supplies a large part of it. In this segment, Russian industry is competitive and capable of providing safe service to the population, largely thanks to public investment in research and development in the sector. Innovation is still somewhat contained and prevents the maximization of the internationalization of the pharmaceutical industry.

This internationalization is addressed by Filippov (2011), who explains the strong growth of the Russian technology industry (especially software) in the international scenario and reinforces the thesis that the other segments, such as pharmaceuticals, are not bigger only due to the aversion to Russian businessman to risks. Economic and political uncertainties experienced in the past affect the appetite of the private sector to invest in R&D and wait for distant results.

As in other developing countries, Russia demands access to treatments. Klunko (2013) indicates that 30% of the Russian drug market is focused on high-cost and innovative drugs, and this has made the government look for alternatives as well as investing in the future of local industries to eventually meet part of this demand locally. There is a relevant pharmaceutical cluster in St. Petersburg that conducts most of the research in the country by allocating resources to research institutions, medical centers and public incentives for the productive sphere. Clusters like this one, according to Sapir, Andreeva, Karachev, and Zherenkov (2016) has been gaining strength in the export scenario and in the birth of Russian multinationals. The study reveals that to achieve sustainable export growth, Russian industries should increase their attention to organizational innovations and strengthen supply chains for such clusters (Belgrade, Kaluga, etc.).

The study by Ashmarina, Streltsov, Dorozhkin, Vochozka, and Izmailov (2016) argues that strengthening the Russian pharmaceutical industry is strategic to ensure local health and accessibility. For the authors, Russian pharmaceutical clusters need to strengthen competitiveness in the local and international scenario by focusing on their best attributes: productive capacity, portfolio scope, innovations. Russia follows regulatory principles from the EMA (European Medicines Agency).

The results of Russian government efforts have already been gathered and felt by the population in recent years. According to Lichtenberg (2018), Russia launched 14 drugs to treat cancer between 1995 and 2004 and after this period there was a significant improvement in death indicators between 65 and 75 years of age. There is statistical evidence of the proportional relationship in the investment and launch of new drugs to fight cancer and the drop in indicators related to this comorbidity during the period. Such drugs are estimated to have increased a cancer patient's life expectancy by 7 years.

More recent studies such as Sowmya et al. (2019) reveal a positive path for the Russian pharmaceutical industry, with government programs and investment in digital patient access channels, which are facilitating direct industry/patient communication. Mingazov, Tufetulov, and Khadiullina (2019) also comment on the public policy to encourage innovation and investment in R&D in Russian industry, which tends to strengthen in the coming years and consolidate a position with multinational industry and exports. According to Balakrishna (2021), this advance is noticeable in the advent of the Sputnik V vaccine for COVID-19, created by the Gamaleya Institute in Moscow.

4.2. India – From Generics to Innovation (the Power of Patents)

India, according to Austin Rating Report (2020), ranked 7th largest economy in the world in 2020, 7 positions ahead of Brazil. Mueller (2006) brings the tumultuous shift in patent law in India as a driver for the birth and strengthening of the innovative pharmaceutical industry. "*O Tigre Acorda*" comments on the dramatic growth of patent applications in India after 18 months of the law change. The focus shifted from the strong Indian generics industry to the new industry as they called it. All of this grew out of India's exclusion from the list of patent protectors in 1972.

Feinberg and Majumdar (2001) analyze the impact of the weak policy of intellectual property protection in India between 1980 and 1994. Their results show that in this interval multinationals gained market, productive capacity in India, and national industries did not develop. An unsupportive political environment and weak legal certainty affected the local industry at that time.

Throughout early 2000s, according to Mani (2006) three pillars were crucial for the change of direction of the Indian national industry: proactive policies for the intellectual property protection (patents), strengthening of research institutes with government funding and entry of private capital in the sector in search of innovation.

Pradhan (2008) reinforces the possibility of a developing country that until the mid-1990s did not have a local productive basis in relation to the modern pharmaceutical industry, to change course and meet its local needs. The government's strategic short-lived patent policies, investment in local production, and strong monitoring of foreign companies encouraged the growth of local investment. The author cites the pharmaceutical market as one of the most dynamic in mergers and acquisitions, which is an obstacle for Indian companies, even small, which do not have the capacity to acquire other business units and are often acquired for this reason. However, even though it is a minor industry, it already exports medicines to all continents.

These mergers and acquisitions, according to Mishra and Chandra (2010) brought scale gains that in the short term improve the financial performance of companies in the sector. The size of the pharmaceutical industry is a variable with a strong influence on profitability, but in the long term, innovation prevails as a factor of greater value generation in the pharmaceutical segment.

There is a need to focus on the ability to convert an industry that was purely focused on generics and imitations into a beginning of innovation and R&D, according to Kale and Little (2007). For the authors, in the late 1990s, India was already relevant from the point of view of production and supply, including for developed countries. It is worth noting the Indian government's ability to shift its patent policies to something more dynamic and supportive by leveraging the foundation created by the generic and imitation industry to bring R&D and innovative products. Additionally, the authors claim that this strategy could be adopted by other developing countries.

However, by adding the innovation aspect, the Indian pharmaceutical industry has not lost an attribute that has made it globally competitive: operational efficiency. For Saranga and Phani (2009), this know-how was acquired mainly over the years 1992 - 2000 when the Indian industry was mostly focused on generics and needed to be efficient to compete with multinationals. The ICDSCO (India Central Drug Standard Control Organization) is equivalent to the FDA in the country and governs all the pharmaceutical regulatory sector.

Although public policies are very relevant to provide a fertile scenario for the existence of innovation and industrial research, Lenka and Gupta (2019) rescue the relevance of entrepreneurship by local agents, and the so-called "human capital". For the authors, a proactive personality, emotional intelligence and learning ability of industry members were crucial to the success of the Indian pharmaceutical model, which offers Covaxin as its main vaccination alternative for COVID-19.

4.3. China and the Ambition for Innovation Leadership

In 2020, China was the 2nd largest economy on the planet according to Austin Rating Report (2020), accounting for about 17% of the world GDP (6% less than the United States, which accounted for 23% of the international GDP). Brazil, in turn, in the 14th position has 1.5% of world production. China's GDP is today in current values approximately 10 times greater than the Brazilian GDP. It is worth remembering that in 1980 Brazil's GDP (US$ 280 billion) was 50% greater than that of China (US$ 190 billion).

According to Grace (2004) together with the economic prosperity experienced by China after its opening to world trade, came fundamental public policies to regulate this growth. Examples within the Chinese pharmaceutical sector, which experienced a strong evolution in 1990 and was consolidated in the early 2000s, include a sophisticated system of price adjustments, strong intellectual property and patent laws and large investment in public-private partnerships, especially involving local universities.

Such a large involvement of research incentive policies, according to Wang, Hong, Marinova, and Zhu (2009) strengthened the Chinese biotechnology segment in terms of R&D beyond commercial development in the same sector. The research overlapped trade and profit at that first moment.

Another aspect that influenced the success of the Chinese pharmaceutical industry, according to Kumar, Dileep, Ravindra, and Suthakaran (2014) was the establishment of a regulatory system. China's National Medical Products Administration (NMPA) was created based on standards from the European Union, Japan and the United States, and follows similar processes for evaluating clinical research.

This scenario provided by public policies then began to attract venture capital and private investments in R&D, according to Qiu, Chen, Lu, Hu, and Wang (2014), most often involving intellectual capital generated by Chinese universities, along with investor resources. With the achievement of this confidence of businessmen, public resources could be reserved for the poorest regions of China that lack basic attention, sanitation, health and education. Eun et al. (2006) had brought this concept of reducing public investment in technology development, as the private sector saw less risk. This combination reached such success that many Chinese public universities also stopped depending on transfers of funds and were able to finance themselves with the financial results generated by their start-ups, not only pharmaceuticals, but in various industrial segments.

The study by Ni et al. (2017) lists as main strengths of China in the pharmaceutical segment and future potential its growing pharmaceutical market (proportionate to the largest population in the world, it is the largest pharmaceutical market), in addition to the research capacity related to the supply of academic and industrial professionals.

Zhihua (2021) claims that China is rapidly climbing the world's pharmaceutical innovation ladder. There are reports of interest from global industries such as Pfizer in Chinese biotechs that have patents on products for cancer and degenerative diseases, and that only need the ignition of investment for such products to have a chance to become blockbusters. Today's largest Chinese pharmaceutical company is the Shanghai Pharmaceutical Group, with annual revenues of approximately US$30 billion in 2020, ahead of traditional American pharmacists such as Eli Lilly and Gilead.

Finally, Zhang and Zhou (2017) in a work carried out for McKinsey consultancy, comment that the Chinese pharmaceutical industry is not yet the world's leader in innovation but is working to achieve for this position in the future, with improvements in its clinical development processes, along with its technical capacity in R&D and with

the Chinese entrepreneurial capacity. Such a capacity is seen in the development of vaccines such as Coronavac and Sinopharm, and other vaccine alternatives that are being investigated for COVID-19.

4.4. South Africa and the Unstable Institutional Environment

Within the African continent, South Africa is the most important country in market strategies for pharmaceutical industries, which, according to Fatti (2013), is an industry represented by strong competitive intelligence in the country. The South African government has been implementing measures since 2010 to make the health system more equitable and inclusive for the population.

At the regulatory level, according to a study by Narsai, Williams, and Mantel-Teeuwisse (2012), South Africa is part of the AMRHI (African Medicines Registration Harmonization Initiative), which aims to uniform quality requirements for drug registration across the continent. Despite having the American FDA as a benchmark, most African countries have strong budget restrictions in these regulatory bodies, which makes the inspection of industries unfeasible and makes it difficult to make them meet international requirements. The SAHPRA (South African Health Products Regulatory Authority) is equivalent to the FDA in the country.

As for patents, according to Azam (2014), South Africa imports around 70% of the medicines used, and 80% of this imported portion are destined to the treatment of patients with HIV/AIDS. With a patent law of 1978, South Africa adhered to the PCT (Patent Cooperation Treaty) of 1999, thus drugs with a critical public impact are now considered as "public goods", and consequently local industries can produce generics of these drugs. It is noteworthy that South Africa displeased the United States when they entered the PCT and started to reproduce drugs that still have an international patent.

The debate on access to medicines is critical in the country, and although the early breaking of patents brings commercial tension to the country at the WTO, it did not guarantee the expectation of treatment for all patients with HIV/AIDS, i.e., access to medicines is a serious public health problem in Africa. The local generics industry meets 30% of the country's demand and is still not able to produce enough for the necessary coverage.

In addition to institutional disputes in defense of knowledge property, according to Shah (2003), South Africa is now facing problems in clinical research, including lawsuits filed by local entities against multinational pharmaceutical industries, aiming at breaking the confidentiality of ongoing research , to obtain knowledge in advance.

For Khoele and Daya (2014) South Africa's institutional instability also influences the continuity of executives who work in the country's pharmaceutical segment. The average annual turnover in the pharmaceutical industry is 22% of employees. The main factors identified in interviews with people who left the companies were related to the economic situation of the sector, insecurity about the future and the search for migration to other countries.

The development of innovative chemical drugs via R&D is low in South Africa compared to other BRICS members, and the country is a strong producer of herbal treatments and medicinal plants. There is no vaccine created or developed by South Africa for COVID-19, and according to data from the South African Government for COVID-19 website, the country acquired immunization agents from foreign companies such as Pfizer, Johnson & Johnson and AstraZeneca.

5. DISCUSSION

In this section, observing the purpose of consolidating the information on the BRICS, in relation to the Brazilian pharmaceutical industry (prepared in the exploratory phase and presented in the theoretical framework), the study presents a comparison between the BRICS member countries.

The differences in the maturity of the national pharmaceutical industry compared to the other countries that make up the study are shown in Table 2.

Table 2. BRICS (Brazil, Russia, India, China and South Africa) pharmaceutical industrial ecosystem.

National Pharmaceutical Industry in BRICS	Brazil	Russia	India	China	South Africa
Regulatory Scenario	• ANVISA • Since 1999 • High inspection capacity, follows FDA standards	• ROSDRAVNADZOR • Since 2004 • High inspection capacity, follows EMA standards[1]	• ICDSCO • Since 1940 • Medium inspection capacity, but follows FDA	• NMPA • 1950 (updated in 2018) • High inspection capacity, follows FDA and EMA	• SAHPRA • 1965 (updated in 2018) • Low inspection capacity, but follows FDA
Innovation Scenario	• Low incentive to pharmaceutical innovation in universities. • Low private investment in pharmaceutical innovation, limited to generic processes. • Medium public investment in pharmaceutical innovation, Fiocruz, Bio-Manguinhos, Butantã.	• Medium incentive to pharmaceutical innovation in universities • Medium private investment in pharmaceutical innovation, but there are already local patents. • High public investment in pharmaceutical innovation, creation of St. Petersburg cluster.	• Medium incentive to pharmaceutical innovation in universities • High private investment in pharmaceutical innovation, and there are already local patents. • High public investment in pharmaceutical innovation, PLI 2020 (production linked initiative).	• High incentive to pharmaceutical innovation in universities • High private investment in pharmaceutical innovation, and there are already local patents. • High public investment in pharmaceutical innovation, US$ 8.5bi per year according to CSYST[2].	• Low incentive to pharmaceutical innovation in universities • Low private investment in pharmaceutical innovation, high institutional risk. • Low public investment in innovation, greater investment in generics.
Patents and Knowledge Protection	• There is intellectual property law, law 9.279/1996 • INPI - national institute of intellectual property governs the subject in the country • Low efficiency in the analysis and issuance of patents, deadlines reach 10 years.	• There is intellectual property law, law 3.517/1992 • SPARF – state patent agency of Russia Federation governs the subject in the country • High efficiency in the analysis and issuance of patents, average term of 1.5 to 2 years.	• There is IPA (India Patent Act) of 1970 for intellectual property • IPO (India Patent Office) of the Department of Industrial Policy governs patents • Medium efficiency in the analysis and issuance of patents, average term of 4 to 6 years.	• There is the PLRC (Patent Law of Republic of China) of 1984 • CNIPA (China National Intellectual Property Administration) governs patents. • High efficiency in the analysis and issuance of patents, average term of 3 to 5 years.	• There is the SAPA (South Africa Patent Act) of 1978 • O CIPC (Companies and Intellectual Property Commission) governs patents • High efficiency in the analysis (about 1 year), but few patents filed.
Fostering Local Pharmaceutical Industrial Development	• High government investment in fostering generic industries/BNDES. • High private investment in the generics industry. • Low existence of PPP's such as FURP, which burdened the state	• High government investment in fostering innovation industries. • Medium private investment in the innovation industry. • High existence of PPP's since 2005, St. Petersburg, IFRF	• High government investment in fostering innovation industries. • Medium private investment in the innovation industry. • High existence of PPP's (over 1000 initiatives launched)	• High government investment in fostering innovation industries. • High private investment in the innovation industry. • High existence of PPP's, ACT[3] Malaria em 1999	• Low government investment in fostering innovation industries. • Low private investment in the innovation industry. • Low existence of PPP's, evident institutional risks.

Notes: [1]EMA – European Medicines Association; [2]CSYST – China Statistical Yearbook of Science and Technology; [3]ACT – Artemisinin Combination Therapy, malaria treatment created by Chinese researchers in partnership with Novartis; PPP – Private Public Partnership; FURP – *Fundação para o Remédio Popular* (Foundation for Popular Medicine).

According to the data presented, Brazil is at an intermediate stage among the BRICS in its local pharmaceutical industry ecosystem. It is possible to highlight positive and developing attributes as follows:

Positive aspects: Regulatory environment - ANVISA's high inspection capacity, submitted to the Ministry of Health and the SUS, has, over the last 20 years, built an international reputation in the analysis and approval of drug marketing in the national territory.

Aspects to be developed: i) Innovation environment: compared to countries like China and India, there is little connection between universities and private investors, capable of enabling the cost of costly clinical research, necessary for the approval of a new drug. Public investment is more focused on creating vaccines and drugs to treat typical local/tropical diseases, rather than on frontier research on more advanced chronic comorbidities that could even be exported; ii) Patents and Knowledge Protection – despite having a current patent law, in effect since 1996, Brazil recurrently faces the removal of intellectual property of the pharmaceutical industry for local reproduction of generic drugs. As did South Africa, which with these measures caused a recognized institutional instability in the country's pharmaceutical system, driving away private investors. Another point that directs international private investors to countries such as China, India and Russia is the analysis time required for a new patent to be granted, which in Brazil takes a 10-year wait (compared to 2 to 6 years in other countries); iii) Fostering Local Pharmaceutical Industrial Development – Since the enactment of law 9787/1999 on generics, Brazil has established a relevant industrial park for the production of generic and similar drugs, financed by BNDES and the private sector in the country. This is a less complex industry that consists of repeating chemical processes and formulations developed abroad and that even so, according to the ICTQ (2020) Brazil imports 90% of API's (Active Pharmaceutical Ingredients) used in local production. However, investment in the local drug research and development (R&D) sector did not occur in the same proportion. As for pharmaceutical PPPs, there are no records of projects that have had positive effects, and the partnership between the pharmaceutical companies EMS and FURP in São Paulo generated losses to the public budget that led to the search for an early termination of this PPP.

In line with the data presented in the comparative analysis, it can be seen that China is currently the country, among the BRICS, with the best ecosystem for the development of the local innovative pharmaceutical industry. Russia and India occupy important intermediary positions and already register patents, while South Africa is going through a troubled time due to patent breaches, which even generate international processes, and which did not result in full access to treatment for the South African people.

6. CONCLUSION

The study, restricted to data published by government entities of the BRICS and by precursor academic works, on the pharmaceutical market, innovation and patents in the countries, allowed for an important comparative analysis, established on the most relevant attributes of the existing literature.

Through the comparative analysis of the cases, it was possible to understand the context of the pharmaceutical industry scenario in these countries, their similarities, differences and stages in which they are in relation to the parameters established as foundations of R&D in the local pharmaceutical industry.

The conjecture that Brazil lags behind the BRICS in aspects inherent to the success of the national conception and perpetuation of this industry was confirmed against 3 countries (China, Russia and India), especially in the trigger of innovation caused by the connection between academics and investors from the private sector, in the speed and efficiency in the management of patent applications received and in promoting the development of a local industrial park, not only for mass production of generics. There is a low rate of research, tests and the search for the advent of cutting-edge treatments for chronic and more complex diseases, advents that could possibly be exported as, done by Russia, India and especially China. South Africa, in turn, has the worst situation in the group, due to the hostile environment between the government and the pharmaceutical industry, generated after patent breaches and clinical research secrecy.

In addition to being necessary to boost the search for local research and technology (since the other BRICS countries, with the exception of Russia, have a history of temporal industrialization similar to that of Brazil), it is also necessary to recognize that the country currently has an industrial park of generics that did not exist before Law 9787/1999.

The COVID-19 pandemic has once again raised the question of the importance of a country's capacity to react, in the proposal of technologies to fight a new disease, and also in its local capacity to produce API (Active Pharmaceutical Ingredients), intended for the production of medicines, in both cases Brazil is dependent on the foreign market to meet local demands.

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