Pharmaceutical innovation: differences between Europe, USA and ‘pharmerging’ countries

Alessandra Cristina Santos Akkari1
Igor Polezi Munhoz2
Jorge Tomioka1
Neusa Maria Bastos Fernandes dos Santos3
Roberto Fernandes dos Santos3

Abstract: The pharmaceutical sector has been dominated by multinational companies from Europe and the USA - the so called Big Pharma. However, the importance of pharmaceutical emerging markets, especially China and Brazil, is a consensus in the literature, and these ‘pharmerging’ countries will play a vital role in the sustainable growth of the pharmaceutical industry. This study aimed to develop a technological and industrial mapping of the pharmaceutical sector based on information from international patent databases (WIPO and Derwent) between 1996 and the last year of record (2013). After that, a numerical analysis for prediction of scenarios was conducted using the Method of Least Squares and an algorithm was implemented in MATLAB. The results confirmed the leadership of Europe and the USA in the pharmaceutical sector, highlighting the innovative capacity of Hoffmann-La Roche. However, an important growth of Brazilian (41%) and Chinese (27%) patents was estimated, suggesting the beginning of technological and scientific dissemination and increased competition in the pharmaceutical segment due to the advancement of the ‘pharmerging’ countries, mainly China.

Keywords: Innovation; Patents; Pharmaceutical industry; Pharmaceutical emerging markets; Brazil; WIPO.

Resumo: Historicamente, o cenário farmacêutico mundial tem sido dominado por grandes multinacionais (Big Pharma), majoritariamente de origem europeia e norte-americana. Contudo, é consenso na literatura a importância crescente dos mercados farmacêuticos emergentes (países farmaemergentes), especialmente China e Brasil, que são vistos como os maiores responsáveis pelo crescimento sustentável do segmento farmacêutico. Esse artigo teve como objetivo realizar um mapeamento tecnológico e industrial do setor farmacêutico, a partir de informações de bancos de dados patenteários internacionais (WIPO e Derwent), entre 1996 até o último ano de registro (2013). Após isso, uma análise numérica para predizer cenários foi conduzida utilizando o Método dos Menores Quadrados e um algoritmo foi implementado no MATLAB. Os resultados confirmaram a liderança da Europa e dos EUA no setor farmacêutico, destacando a capacidade inovadora da Hoffmann-La Roche. No entanto, uma importante expansão de patentes brasileiras (41%) e chinesas (27%) foi estimada, sugerindo a comecço da disseminação tecnológica e científica e da competição no segmento farmacêutico devido ao avanço dos ‘pharmerging’ países, especialmente a China.

Palavras-chave: Inovação; Patente; Indústria farmacêutica; Mercados farmacêuticos emergentes; Brasil; WIPO.
1 Introduction

The pharmaceutical industry is characterized by intensive Research & Development (R&D) activities. The control of intangible assets linked to the innovation process, especially patents, is of extreme importance in this segment, since many resources are employed in the innovation process, resulting in a product development cost - from the discovery of the drug to the stage of launching the product into the market - of approximately US$ 1.2 billion. The high R&D costs are a reflection of the long period required for the development of a new compound, which may reach up to 13 years before the pharmaceutical formulation goes to market, associated with a very low success rate, with only one molecule of the 10,000 employed in the initial research stages reaching the commercial stage (Kaitin, 2010; Bunnage, 2011).

Furthermore, patent protection in the pharmaceutical industry is used as a defensive instrument, configuring a commonly applied anti-competitive practice. Some of strategies employed include so-called blocking (acquiring and not using new patents) and fencing (requesting patenting for any possible technology that can be used by a competitor) techniques, through which companies try to prevent the entry of new competitors into the market as well as to advance on their direct competitors (Salomão, 2006; Sternitzke, 2013).

Based on its dynamism and innovation, the pharmaceutical industry has become one of the most profitable trade sectors, in addition to actively moving the economy. The global pharmaceutical market is expected to grow from $733 billion in 2010 to US$ 981 billion in 2015, an increase of 33.8%. The increase in drug sales will be largely driven by countries with pharmaceutical emerging markets (pharmerging countries), with an expected increase in demand between 2010-2015 of 109% in China and 67% in Brazil as a result of an increasing and aging population, rising income levels and the expansion of health care systems. In contrast, the traditional USA market, which contributed to 52% of the sector’s growth, decreased its share to just 19% in 2009 as a result of the expansion of generics, the patent expiration of key blockbuster drugs, the impact of the latest global economic crisis and governmental restrictions (IMAP, 2012; PhRMA, 2012).

The report of the international consultancy IMS Health (auditing company of the global pharmaceutical market) categorized the emerging pharmaceutical markets in three levels (1, 2 and 3) according to their indicators achieved in 2009 and their estimated share in the growth of the global market for pharmaceuticals. The study revealed the outstanding potential of China (level 1), followed by Brazil (level 2), demonstrating that there is a consensus that the future growth of the pharmaceutical industry will come mainly from the pharmerging countries. The forecasts also indicate that global expenses with medication will reach US$ 1.2 trillion in 2017, corresponding to an increase of US$ 205-235 billion in relation to 2012 (IMS, 2013).

These data confirm a large market potential, placing the development of new drugs and pharmaceutical formulations at the center of the economic development, innovation and Science & Technology strategic plans in different countries. So, the pharmaceutical segment is a strategic sector that contributes to the development of a country and the generation of competitive advantages from different perspectives, especially when the pharmerging countries are concerned. This relationship, however, is dependent on the level of investment in R&D, the public innovation policies and the regulatory actions involved in the development and protection of new drugs.

From this perspective, this article aimed to perform a technological and industrial mapping of the pharmaceutical sector by evaluating patenting by country and by technology, comparing the USA and European innovation rates with those of China and Brazil; and by conducting an investigation of the pharmaceutical industries and R&D investments. This mapping will seek to outline a perspective for the sector through projections based on the development of an algorithm, highlighting the role of the pharmerging countries, which are currently considered to be mainly responsible for the potential increase in sales of medication in the world. The importance of pharmaceutical emerging markets has in fact grown, but there are still few studies based on patenting data in the literature focusing on these countries, from a historical perspective to the potential impact that their entry could have on the dynamics of the sector.

2 Panorama of the pharmaceutical industry

The pharmaceutical industry is characterized as highly dynamic and globalized, with its organization being based on knowledge and high technology (Pisano, 1997). Since the 40s, multinationals (Big Pharma) have operated in the sector. These companies grew dramatically based on strong investments in R&D, which resulted in the launch of a high number of innovative medications and, consequently, extraordinary profits. As the first organizations to explore the pharmaceutical sector, which was not yet tightly structured and regulated at the start of their activities, they were privileged by a less demanding regulatory environment and a limited official control of prices and market acceptance. These
facts encouraged Big Pharma rapid and significant growth (Palmeira et al., 2012).

This scenario changed after the 90s, with questions arising about the high prices of new medication, competition from generic drugs and more demanding regulatory policies. In order to adapt themselves to the new circumstances, many pharmaceutical industries chose to dilute the R&D and to increase the size of the company; to focus on a limited number of competencies, such as certain classes of medication; and also to acquire and associate themselves with smaller biotechnology companies (Berkowitz, 2010). It should be emphasized that this work does not plan to cover the biopharmaceutical industry, which deserves a specific study.

Still in the 1990s, the TRIPS (Trade-Related Aspects of Intellectual Property Rights) agreement was signed in 1994, based on which the international standardization of Intellectual Property (IP) system was implemented, imposing the same rules for all the signatory countries. In accordance with the degree of development of each member country of the World Trade Organization (WTO), a certain transition period was granted in which the country should adapt its IP legislation to the new established provisions. The effects of the TRIPS agreement were felt differently by the signatory countries, with the growth opportunities for developing countries being indirectly diminished in the pharmaceutical industry (Orsi & Coriat, 2006).

To comply with the terms of the TRIPS agreement, Brazil passed the Industrial Property Law, also known as the Patent Law (N° 9279/1996), which started to allow the protection of pharmaceuticals products. Brazil’s adherence to TRIPS resulted in a severe restriction to increasing its national capabilities through the learning by copying mechanism, which had been an often-employed method of acquiring knowledge in such advanced countries as the USA and Japan. Now, the copying strategy remained only for the production of medication with expired patents. Another consideration concerns the institution of the pipeline, a patent application mechanism that enabled any filing party that had obtained a patent in any other country, to file for a patent in Brazil during 1996 and 1997, without the need of analyzing the patentability requirements in accordance with Brazilian legislation, with additional technical examinations only being required for national inventors. This implementation meant the granting of retroactive patents that passed only through a formal analysis, and represented a differentiation between domestic and foreign inventors (Palmeira et al., 2012).

The adherence of China to TRIPS had much more positive and harmonious effects for the country when compared to Brazil, as China had already applied changes to its IP legislation even before signing the agreement in order to attract foreign investment and encourage Chinese access to the new technologies in the developed countries. As such, the country provided for the protection of products and processes in all sectors of its economy since 1992, including the pharmaceutical industry, and an effective revision of standards occurred only in 2001 when the country joined the WTO. It was in this context, and through an attitude of the Chinese government geared toward leveraging innovation, that the country increased its level of intellectual patents differently than other developing countries, in addition to choosing not to grant retroactive patents (Zheng, 1996).

3 Pharmaceutical innovation

Innovation in medications may arise from modifications to one or more of the properties of the compound, including the chemical structure or synthesis method of the drug; the pharmaceutical form; the pharmacodynamics; the pharmacokinetics; and other therapeutic properties (Aronson, 2008). The evaluation of innovation in the pharmaceutical industry has been widely debated, involving multiple perspectives covering the patients, the industry, the government and regulatory agencies, among other actors. Furthermore, the innovative value of a drug is not simply an intrinsic property of this new compound, but also depends on the specific context in which the medication is introduced and the availability of other drugs to treat the same clinical condition (Caprino & Russo, 2006). An effort in the literature can therefore be seen to better define technological innovation in relation to pharmaceuticals in order to stimulate the innovative process, recognizing it and rewarding it properly.

Kennedy (2009) proposed that an innovative medication must offer improvements in existing therapeutic treatments and a radical change in relation to the results for the patients.

Aronson et al. (2012) adopt a broader definition of pharmaceutical innovation, incorporating clinical utility, economic elements and the type of innovation. According to the authors, first the extent to which the proposed molecule is really a novelty should be assessed, given that the characteristic of being a novelty does not simply imply being something new. If there is a new product that shares the same attributes at its predecessor, then it’s not a novelty, for example. On the other hand, new applications can be found for a product that is not new, which is a novelty. When utility is concerned, the authors recommend considering the risk-benefit balance, which means a drug may be considered innovative when it provides (1) a benefit to a condition for which
no effective treatment exists; (2) an improvement to already existing treatment; (3) a safer treatment (lower number of adverse reactions and/or drug interactions); (4) and a lower treatment cost. Finally, the authors suggest an assessment of the process by which an innovation arises, covering revolutionary (disruptive) or evolutionary (incremental) innovations, indicating that revolutionary innovations should be encouraged in order to have disruptive changes in the market.

The same group of researchers proposed mechanisms to reward pharmaceutical innovations not only to guide the patentability criteria of a new drug, but also to optimize the productivity of R&D activities by stimulating researchers. These mechanisms include tax reductions on the profits resulting from a patentable invention and the recommendation of medication for use in the National Health Service (Aronson et al., 2012). In fact, a previous work (Jayadev & Stiglitz, 2009) had already suggested policies to reward pharmaceutical innovations and to leverage the social benefits of new medications as much as possible.

The rewardable innovation concept has been applied by the Office of Fair Trading (OFT) of the United Kingdom, which, despite not creating a special definition of pharmaceutical innovation, states that innovation must be rewarded when new drugs provide or significantly improve therapeutic standards deriving from existing treatments (OFT, 2007).

Although the definition of various authors is of great value and demonstrates progress in the debates about IP (Intellectual Property) in the pharmaceutical industry, it is not something simple to be applied, requiring further studies since it involves a value judgment of the analyst and the coexistence of interests from different players involved in the process. In this sense, Canongia et al. (2004) suggest a participatory process based on the interaction of the actors in order to facilitate innovation and generate mutual gains, aiming at establishing a compromise and coordinating the national research and innovation priorities.

### 3.1 The importance of patent protection in the pharmaceutical segment

Although the IP system is not the only one to encourage innovation, the absence of such laws would significantly affect innovation in the pharmaceutical industry, unlike some other sectors, since the patent is an integral part of the company’s innovation strategy in the field of medication (Binns & Driscoll, 1998).

In fact, Mansfield (1986) shows that the absence of patent protection would have a small impact on the innovation efforts of most industries, but the pharmaceutical industry was an obvious exception. According to the author, this special behavior is a result of a high rate and a high cost of imitation, i.e. the discovery or the development of a new molecule requires a lot of time and investment, but once the drug is obtained, the medicinal product can be easily prepared by different laboratories with the minimal capabilities of developing chemical syntheses. As such, given that patents are seen as the main means of appropriability available to the pharmaceutical industry, delaying the development of an IP system that provides the drugs protection, in addition to maintaining an ineffective and impaired system, will have damaging consequences for the industry and also for the countries technological progress.

According to Scherer & Ross (1990), the patent is an indicator of technological progress, being one of the possible mechanisms to appropriate innovations as well as the advantages of the pioneering spirit; the benefits obtained by the inventor through the evolution of his learning curve; industrial secrets; and sales and service efforts. According to the so-called Yale Survey by Levin et al. (1987), patents are only seen as the most effective means of ensuring the returns for the release of new products and processes in the pharmaceutical and oil refining industries. In other segments, including R&D intensive sectors, industries have reported that patents are not the most important mechanism to generate profits from their innovations, which means they employ mainly other mechanisms to this purpose.

The information gathered by analyzing patents becomes especially important to guide the decision-making and the acquisition of competitive advantages by an organization, as well as the definition of public policies and strategic sectors of a country, since it enables the investigation of a global, national, regional and sectorial scenario in terms of technological innovation. According to the Frascati Manual, indicators based on patents provide a measure of a innovative production of a different countries, considering the investments and the other costs linked to the R&D activities as the inputs of the inventive activities, while patents can be considered as the output of the innovation process (OCDE, 2007).

Masiakowski & Wang (2013) state that information about patents is crucial for many aspects of a successful business, but its complexity, distribution over several different databases (in a wide variety of formats) and generation of many pure numeric values, place major challenges for their efficient and strategic use. Therefore, studies geared toward the grouping and analysis of innovation indicators (technological mappings, for example) are becoming a facilitating factor to guide organizations or countries, especially in the pharmaceutical segment.
4 Research methodology

This work can be considered an exploratory study, combining a literature study with the collection and analysis of secondary data. The article was based on the evaluation of information extracted from international patenting databases and seeks to make a projection using the least squares method, presenting agreement with other studies in the literature (Bengisu & Nekhili, 2006; Chen et al., 2011). The analysis included the time frame from 1996, the year in which the Industrial Property Law was approved in Brazil, which enabled the protection of chemical and pharmaceutical products, until the last year of record in the database. In addition, statistical reports were used in order to correlate data with the R&D investments.

The secondary data was obtained from the following information databases: (1) the Intellectual Property Statistics Data Center - maintained by the World Intellectual Property Organization (WIPO), which presents statistical data on patent applications and grants in the world as an agency of the United Nations (UN); (2) the Derwent Innovations Index – which gathers information from 42 patent issuing bodies throughout the world and is an industrial property search tool provided by Thomson Reuters Scientific (Thomson Reuters, 2015).

After the data collection, numerical analyses were carried out to predict scenarios and make comparisons through the application of the least squares method, aiming at approximating the behavior of variables with a known polynomial function; and the use of a polynomial approximation for a discrete case. In this step, an algorithm (presented in Annex A section) was implemented in MATLAB®.

In the Polynomial Approximation, a function \( y = f(x) \) is approximated by a polynomial of degree \( m \), where \( P_m(x) = F(x) \in E \). In the Discreet Case (Equations 1 to 7), the function \( F(x) \) is not known, being represented by pairs of points obtained through the collection of secondary data. Considering \( n+1 \) point pairs \( (x_0, y_0), (x_1, y_1), (x_2, y_2), \ldots, (x_n, y_n) \), where \( y_i = f(x_i), i = 0, 1, \ldots, n \), with \( n+1 \) distinct points, one gets (Franco, 2006):

\[
P_m(x) = a_0 + a_1x + \ldots + a_mx^m \tag{1}
\]

with maximum degree \( m \), with \( m < n \) and such that:

\[
Q = \| f - P_m \|^2 \tag{2}
\]

is minimal. Considering that \( m < n \), one can use the dot product:

\[
(f, g) = \sum_{k=0}^{n} f(x_k)g(x_k) \tag{3}
\]

From Equation 3, one gets:

\[
Q = \sum_{k=0}^{n} \left( y_k - (a_0 + a_1x_k + \ldots + a_mx_k^m) \right)^2 \tag{4}
\]

Equation 1 can be simplified as follows:

\[
y = Aa \tag{5}
\]

with \( A \) being the Vandermonde matrix:

\[
A = \begin{bmatrix}
1 & x_0 & x_0^2 & \ldots & x_0^m \\
1 & x_1 & x_1^2 & \ldots & x_1^m \\
\vdots & \vdots & \vdots & \ddots & \vdots \\
1 & x_n & x_n^2 & \ldots & x_n^m
\end{bmatrix} \tag{6}
\]

From Equation 5 and 6, it is possible to find the coefficients through the \( A \) inverse matrix:

\[
A^{-1}y = a \tag{7}
\]

By means of the obtained \( a \) coefficient, the polynomial described in Equation 1 can be described, enabling interpolations and extrapolations.

5 Results and discussion

In this section, the obtained data is presented as well as the respective analyses and discussions through the application of the proposed methodology.

5.1 Patent protection study by Country of origin

First, the pharmaceutical sector was evaluated according to the number of patents granted per country/region of origin. Based on a survey of the WIPO using classification 16 (Pharmaceuticals), Table 1 shows the number of patents granted in Europe, the USA, China and Brazil, between 1996-2013. It should be emphasized that the data obtained for Europe relates to the sum of protections granted in the European countries.

The prominent position of the USA can be seen, with 126,747 pharmaceutical patents, corresponding to the first place among the countries with the highest number of protections in the sector. The European index exceeded North America, reaching 162,721 patents, constituting the region with the highest number of protections, with large contributions from Germany (32,534 protections), France (23,904 protections), the United Kingdom (18,915 protections) and Switzerland (17,499 protections). The expressive participation of China and Japan in the pharmaceutical industry should also be noted as they occupied the second...
(39,460 patents) and third (33,539 patents) position in the ranking of countries with most patents granted. In contrast, Brazil occupies a not very remarkable position in the global scenario (37th), since the country had only 321 protections granted in the sector between 1996-2013. The Brazilian indicator lies below that of India, which takes the 19th place with 2,988 protections.

Considering that 556,122 patents were granted worldwide, between 1996-2013, under the WIPO classification Pharmaceuticals, Figure 1 shows the global contribution of the previously cited countries in percentages.

Most patents for pharmaceutical products/processes are still concentrated in the USA (22.79%) and Europe (29.26%), with Germany, France, the United Kingdom and Switzerland being responsible for approximately 57% of the European indicator. The world ranking continues with China (7.09%) and Japan (6.03%), confirming that the pace of Chinese economic growth has allowed the country to exceed the Japanese indicator, which has always been considered a world leader in the industry next to Europe and the USA. The Indian indicator corresponded to 0.67%, while Brazil was responsible for only 0.06% of pharmaceutical patents in the world.

The obtained data indicate the low innovative power of the Brazilian pharmaceutical industry when compared to the European countries, the USA and the other pharmerging countries, such as China and

Table 1. Pharmaceutical patents granted to Europe, the USA, China and Brazil (1996-2013).

<table>
<thead>
<tr>
<th>Year</th>
<th>Europe</th>
<th>USA</th>
<th>China</th>
<th>Brazil</th>
<th>Year</th>
<th>Europe</th>
<th>USA</th>
<th>China</th>
<th>Brazil</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996</td>
<td>5,781</td>
<td>4,099</td>
<td>41</td>
<td>3</td>
<td>2005</td>
<td>9,177</td>
<td>6,477</td>
<td>2,165</td>
<td>9</td>
</tr>
<tr>
<td>1997</td>
<td>6,347</td>
<td>4,771</td>
<td>54</td>
<td>18</td>
<td>2006</td>
<td>11,109</td>
<td>9,214</td>
<td>3,304</td>
<td>32</td>
</tr>
<tr>
<td>1998</td>
<td>5,769</td>
<td>5,170</td>
<td>90</td>
<td>4</td>
<td>2007</td>
<td>10,061</td>
<td>6,599</td>
<td>3,432</td>
<td>12</td>
</tr>
<tr>
<td>1999</td>
<td>5,913</td>
<td>5,885</td>
<td>179</td>
<td>6</td>
<td>2008</td>
<td>10,500</td>
<td>6,653</td>
<td>3,287</td>
<td>19</td>
</tr>
<tr>
<td>2000</td>
<td>5,697</td>
<td>5,631</td>
<td>1,218</td>
<td>7</td>
<td>2009</td>
<td>10,670</td>
<td>6,630</td>
<td>3,869</td>
<td>19</td>
</tr>
<tr>
<td>2001</td>
<td>6,660</td>
<td>6,488</td>
<td>1,227</td>
<td>7</td>
<td>2010</td>
<td>11,063</td>
<td>7,675</td>
<td>3,089</td>
<td>26</td>
</tr>
<tr>
<td>2002</td>
<td>8,285</td>
<td>7,078</td>
<td>729</td>
<td>19</td>
<td>2011</td>
<td>11,294</td>
<td>8,400</td>
<td>4,751</td>
<td>26</td>
</tr>
<tr>
<td>2003</td>
<td>9,871</td>
<td>7,943</td>
<td>1,098</td>
<td>9</td>
<td>2012</td>
<td>12,353</td>
<td>9,826</td>
<td>4,674</td>
<td>28</td>
</tr>
<tr>
<td>2004</td>
<td>10,111</td>
<td>7,770</td>
<td>1,911</td>
<td>27</td>
<td>2013</td>
<td>12,060</td>
<td>10,438</td>
<td>4,342</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>162,721</td>
<td>126,747</td>
<td>39,460</td>
<td>321</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Criteria used: Indicator: 5-Patent grants by technology; Type: Total count by applicant’s origin; Technology: 16- Pharmaceuticals.
Source: Developed by the authors based on WIPO (2015).
India. This is a reflection of the strategy of Brazilian pharmaceutical industry to specialize mostly in the production of generic medications.

According to Frenkel (2002), the low level of technological innovation of the Brazilian pharmaceutical industry is a result of the fact that it concentrates its efforts in the value chain mainly on medication production (especially those with expired patents) and marketing activities. This means that more intensive science and technology activities that have a greater potential of providing competitive advantages, such as R&D, were not introduced and assimilated by the productive sector in Brazil, demanding capabilities that are still mostly lacking in the Brazilian medication industry. Palmeira & Capanema (2010) also suggest that political-economic circumstances favored the current Brazilian industrial scenario, with its fragile innovation system, centralization of multinational R&D activities in their headquarters and an absence of active policies for the pharmaceutical segment, which was only recognized as a strategic sector in Brazil in 2004.

In fact, at the end of 2003, the Ministry of Development, Industry and Commerce (MDIC) presented its Industrial, Technological and Foreign Trade Policies (PITCE), which included the pharmaceutical industry among its priorities (Palmeira & Capanema, 2010). In addition, the PITCE provided for the creation of the Transversal Action for Nanotechnology of the Sectorial Funds and for the launch of the National Nanotechnology Program (PNN), stimulating joint actions between companies and external researchers in order to expedite the innovation process in the country, especially in the medication sector (Alice et al., 2013).

In a way that is distinct to the Brazilian case, Big Pharma has competencies and exploits all the stages of the pharmaceutical value chain, which dictates the competitive and innovative dynamic of the sector and imposes high barriers to entry (Radaelli, 2007). Countries that have strong competitive positions in the world scenario, a high level of technological development and policies to encourage the productive sector, become attractive for the installation of large pharmaceutical laboratories, which is especially important for regions that have a relatively small local medication market (such as Switzerland, the United Kingdom and Germany), making their companies highly innovative and with a great capacity to generate profits through exports (Gassman & von Zedtwitz, 1999).

In China’s case, since its IP legislation provides for the protection of pharmaceutical products and processes since 1992, the pharmaceutical industrial development in the country was fostered, which also was a consequence of the acknowledgment by the government during the opening of the Chinese economy that the medication sector is strategic. As such, the Chinese pharmaceutical industry received strong government support through public policies between 1996 and 2005 (two 5 year plans, 1996-2000 and 2001-2005), culminating in the construction of various research centers and the attraction of large industries to the country, in order to force an optimization of the activities of the domestic companies. As a result, a jump in the number of Chinese protections granted between 1996 (41 patents) and 2000 (1218 patents) can be seen, as well as between 2001 (1227 patents) and 2005 (2165 patents), with the biopharmaceutical sector being identified as China’s first priority in the medium and long-term plan for the development of Science and Technology (2006-2020) (Wang et al., 2009).

Figure 2 presents the forecast for the next 5 years (2014-2018) in order to estimate the behavior of the countries regarding the innovation in their respective pharmaceutical sectors. Table 2, in turn, presents the relative variation between the data, considering a period of 5 years.

The leadership of the USA and Europe in the industry is confirmed, with a similar number of patents granted and with both regions leading in the production of new medication since the beginning of the period under study (Figure 2). In the USA a faster growth can be seen than in Europe, with a leap from 6,630 (2009) to 10,438 (2013) patents. Brazil was the country that presented the highest relative variation (Table 2), i.e. the difference between the number of patents granted to Brazilian filers between 2009 and 2013 was 163% greater than the index reached by the country in 2009. When the absolute values are compared, China has always been significantly in front of Brazil in terms of protections, even with a lower relative growth (12%).

Studies in the literature have used the least squares method to develop estimates of scenarios based on historical information, providing useful data for decision-making (Batista et al., 2011; Yang et al., 2014). In this article, the expected scenario (Table 2) pointed to a significant increase in the number of Brazilian protections, with a drop occurring in 2014, followed by a recovery so as to reach 568 patents until 2018. In the same period, China is expected to obtain approximately 69 thousand pharmaceutical patents, corresponding to a relative increase of 27% between 2014-2018. Although the absolute values are significant, a more discreet growth (less than 10%) in the number of European and North American protections is expected, reaching 227,170 and 176,089 pharmaceutical patents, respectively, since 1996 until the last year under study.

The most outstanding forecast refers to the estimate of the Chinese figure reaching those of the world...
leaders (USA and Europe), even in the medium term. In fact, between 1996-2005, the number of Chinese patents corresponded to only 11.8% of total European pharmaceutical protections and 14.3% of the American indicator. In the 1996-2010 period, the relative increase of Chinese protections was not accompanied by an elevation in the number of patents of the world leaders, with the total number of Chinese patents corresponding to 20.2% of those obtained by Europe and to 26.2% of those obtained by the USA. Between 1996-2013, the number of Chinese patents in the pharmaceutical segment was equivalent to 31.1% of the American total, and the forecasts indicate that, by 2018, the Chinese numbers will correspond to 30.4% of the European and 39.2% of the American figures.

![Figure 2. Comparison of the number of patents granted in the USA, Europe, China and Brazil, considering a forecast of 5 years (2014-2018). Developed by the authors based on WIPO (2015).](image)

**Table 2.** Forecast total of pharmaceutical patents granted to Europe, the USA, China and Brazil, between 2014-2018; and relative variation in the number of patents, considering two moments in time stretching 5 years (2009-2013 and 2014-2018).

<table>
<thead>
<tr>
<th>Period</th>
<th>Europe</th>
<th>USA</th>
<th>China</th>
<th>Brazil</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014e</td>
<td>12,456</td>
<td>9,425</td>
<td>5,189</td>
<td>41</td>
</tr>
<tr>
<td>2015e</td>
<td>12,692</td>
<td>9,651</td>
<td>5,529</td>
<td>45</td>
</tr>
<tr>
<td>2016e</td>
<td>12,908</td>
<td>9,872</td>
<td>5,872</td>
<td>49</td>
</tr>
<tr>
<td>2017e</td>
<td>13,107</td>
<td>10,090</td>
<td>6,220</td>
<td>54</td>
</tr>
<tr>
<td>2018e</td>
<td>13,286</td>
<td>10,304</td>
<td>6,571</td>
<td>58</td>
</tr>
</tbody>
</table>

\[
VR_y = \frac{y_{t+5} - y_t}{y_t}
\]

<table>
<thead>
<tr>
<th>Relative Variation</th>
<th>09-2013</th>
<th>2014-2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>13%</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>57%</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>12%</td>
<td>27%</td>
<td></td>
</tr>
<tr>
<td>163%</td>
<td>41%</td>
<td></td>
</tr>
</tbody>
</table>
From this perspective, the number of patents granted annually to China in 2036 (13,524 patents) is expected to exceed the protections granted to the USA (13,499 patents) and Europe (13,333 patents). China, therefore, is currently already challenging American and European supremacy in the pharmaceutical segment, suggesting that, in up to 20 years, this pharmerging country will be the innovation leader of the sector.

These data indicate that, historically, China has been growing at a much faster rate than Europe or the USA, and the forecasts confirm the continuation of this trend. One can therefore see that the expansion of innovation in the pharmaceutical industry through the entry of pharmerging countries, especially China, is increasing the hope that technology will spread and competition will increase for the Big Pharma.

5.2 Patent protection study by office

Factors such as the degree of technological capabilities, the qualification of labor, the infrastructure of the productive sector, the direction of public policies, regulatory aspects and political and economic stability influence how attractive a country is for the filing of patent applications in a given sector (Sanyal, 2004). Table 3 shows the number of pharmaceutical patents granted by offices in Europe, the USA, China and Brazil, between 1996-2013, based on the WIPO records.

The USA granted the most pharmaceutical patents between 1996-2013, corresponding to a total of 74,761 protections. Europe and China come in second and third place, with 75,651 and 65,785 patents granted, respectively. The high number of patents granted in Europe and in the USA was expected, since the large pharmaceutical companies have their headquarters in these regions with intense R&D activities. In addition, these are highly globalized locations, with expressive economic indicators, a productive sector with state-of-the-art technological capabilities, well-established IP systems, among other factors that attract people or companies of other countries to protect their products/processes in strategic locations.

China’s third position proves to be quite relevant, since is very close to the USA and European number. This fact can be explained by the fast growth and great importance that the country has been acquiring over the years, associated with the fact that it has a qualified workforce, significant economic growth trends, commercial expansion strategies, and policies to attract foreign laboratories and to encourage the pharmaceutical and other national industries. As has been stated previously, it is also a country with a growing pharmaceutical market, so as to attract a high and increasing number of patent guarantees as a result of the interest of companies in ensuring exclusive commercial rights in the country.

In the global scenario, Brazil holds the 34th place, corresponding to a total of 461 protections. The first patent in Brazil was granted only in the year 2000 because the Brazilian Industrial Property Law only provided for the protection of chemical and pharmaceutical products in 1996, with some time being required to structure the system, in addition to a certain slowness of Brazilian agencies, especially the National Institute of Industrial Property (INPI). An increase in the number of grants can be seen after 2008 due to the public policies of 2004, which identified the pharmaceutical industry as a strategic sector.

Comparing the number of patents granted by country of origin and by office reveals that China and Brazil have granted approximately 67 and 44% more patents than the number of protections that were granted to them, reflecting the foreign interest in these pharmerging countries (Sun, 2003). In contrast, Europe and the USA had more pharmaceutical patents granted, demonstrating the high level of innovation

Table 3. Pharmaceutical patents granted in offices in Europe, the USA, China and Brazil (1996-2013).

<table>
<thead>
<tr>
<th>Year</th>
<th>Europe</th>
<th>USA</th>
<th>China</th>
<th>Brazil</th>
<th>Year</th>
<th>Europe</th>
<th>USA</th>
<th>China</th>
<th>Brazil</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>3,952</td>
<td>3,357</td>
<td>156</td>
<td>0</td>
<td>2006</td>
<td>4,078</td>
<td>3,804</td>
<td>4,187</td>
<td>4</td>
</tr>
<tr>
<td>1998</td>
<td>3,560</td>
<td>3,885</td>
<td>213</td>
<td>0</td>
<td>2007</td>
<td>4,415</td>
<td>3,411</td>
<td>4,361</td>
<td>1</td>
</tr>
<tr>
<td>1999</td>
<td>3,657</td>
<td>4,230</td>
<td>342</td>
<td>0</td>
<td>2008</td>
<td>4,765</td>
<td>3,390</td>
<td>4,195</td>
<td>16</td>
</tr>
<tr>
<td>2000</td>
<td>3,431</td>
<td>3,998</td>
<td>1,506</td>
<td>6</td>
<td>2009</td>
<td>4,901</td>
<td>3,652</td>
<td>4,836</td>
<td>81</td>
</tr>
<tr>
<td>2001</td>
<td>3,343</td>
<td>4,421</td>
<td>1,531</td>
<td>5</td>
<td>2010</td>
<td>4,592</td>
<td>5,133</td>
<td>5,820</td>
<td>114</td>
</tr>
<tr>
<td>2002</td>
<td>3,937</td>
<td>4,581</td>
<td>1,118</td>
<td>2</td>
<td>2011</td>
<td>4,890</td>
<td>5,088</td>
<td>9,010</td>
<td>82</td>
</tr>
<tr>
<td>2003</td>
<td>4,236</td>
<td>4,247</td>
<td>1,752</td>
<td>3</td>
<td>2012</td>
<td>4,849</td>
<td>6,034</td>
<td>9,900</td>
<td>39</td>
</tr>
<tr>
<td>2004</td>
<td>3,917</td>
<td>3,167</td>
<td>3,071</td>
<td>4</td>
<td>2013</td>
<td>4,875</td>
<td>6,980</td>
<td>10,372</td>
<td>101</td>
</tr>
<tr>
<td>Total</td>
<td>74,651</td>
<td>74,761</td>
<td>65,785</td>
<td>461</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Criteria used: Indicator: 5- Patent grants by technology; Type: Total count by filing office; Technology: 16 – Pharmaceuticals. Source: Developed by the authors based on WIPO (2015).
in these regions. The interest of European and North American companies to continuously globalize their activities can also be inferred through their patent applications in other countries, such as in pharmaceutical emerging markets. In fact, recent data suggest that large multinationals have resorted to acquiring companies in key countries of the pharmaceutical industry. The acquisition of Medley, in Campinas (Brazil), by Sanofi could be mentioned, for example, in addition to the participation of Pfizer in Indian and Brazilian companies and the purchase of the Chinese company Nanjing MeiRui by GlaxoSmithKline (Kessel, 2011).

Figure 3 is presented in order to estimate the behavior of the number of protection grants for the next 5 years based on the WIPO record. Once again, quite similar trajectories can be seen for Europe and the USA, while China showed a different behavior and always ahead of Brazil, reaching the position of the country that most grants pharmaceutical patents in the world after 2010.

Between 2009 and 2013, China and the USA were the regions that had the fastest relative growth (Table 4), showing a jump in the number of grants during the period under consideration. Europe, on the other hand, had a negative variation, reflecting a slight decrease in the number of protections granted because of the growing interest in different countries with a high potential for medication sale.

The forecasts (Table 4) showed a rising trend in the number of patents, especially in Brazil, which is expected to have a relative increase of 66% between 2014-2018, corresponding to 1,221 pharmaceutical patents until 2018. There is also an expectation of considerable growth in China (137,320 protections until 2018), outperforming USA (112,541 protections until 2018) and European (102,669 protections until 2018) numbers, illustrating the greater attractiveness of pharmaceutical emerging markets.

5.3 Analysis of pharmerging Countries – China and Brazil

A specific evaluation was developed in order to better understand the profile of pharmerging countries. Considering China and Brazil, the percentage of patents granted to residents and non-residents (foreigners)

Figure 3. Comparison of the number of patents (classification 16 of the WIPO - Pharmaceuticals) granted in the US, Europe, China and Brazil, considering a forecast of 5 years (2014-2018). Developed by the authors based on WIPO (2015).
was evaluated. Of the 65,785 pharmaceutical patents granted in China, about 58% belonged to residents, corresponding to a total of 37,967 protections, compared to 27,818 patents granted to non-residents. In contrast, 91.5% of patents in Brazil in the same period were granted to non-residents, which means a total of 422 protections in the medication sector, as opposed to only 39 patents granted to Brazilian filers.

The WIPO data reveals that 75 different countries applied for medication or pharmaceutical process patents in China, while only 30 countries showed interest in protecting their products in Brazil. The patents field by Chinese residents stand out in the country, followed by European, North American and Japanese applicants, who represent approximately 10.0, 9.0 and 4.0%, respectively, of total grants in the region. Other pharmerging countries, especially India (149 protections; 0.02%), have shown enthusiasm in protecting their pharmaceutical products in China.

Europe and the United States also were the greatest patent filers in Brazil, answering for 48.4 and 26.2% of protections granted in the country, respectively. Among the European countries, Germany (66 patents; 14.3%), France (39 patents; 8.4%) and the United Kingdom (28 patents; 6.07%) again stand out. The protections granted to Brazilian residents occupy the third place, with 39 patents, as mentioned above. Applications from India and China correspond to 1.08 and 0.02% of the total. The temporal evaluation revealed that the number of grants in Brazil to foreigners is traditionally much higher than the protections granted to residents, mainly due to the low innovative power of the Brazilian pharmaceutical industry. In 2010, for example, 78 of the 81 patents in Brazil were granted to non-residents; in 2013, only 3 patents were granted to Brazilian holders, of a total of 101 protections.

The ratio between patents granted to residents and non-residents expresses a link between the countries technological capabilities (reflected by the total patents to residents) and the attractiveness of its national market (expressed by the number of patents to non-residents). As such, the pharmaceutical emerging markets of both countries have a strong attraction, but at the same time the fragility of Brazil is clear, since the temporary monopoly of pharmaceutical products implies a considerable barrier to entry for the domestic industries (Brentani et al., 2011).

The high percentage of patents to non-residents also leads to questions as to why Brazilians inventors show so little interest in protecting pharmaceutical products in their own country of origin. Of the total of 321 patents of Brazilian origin, only 39 were granted in Brazil, i.e., approximately 87.5% of the Brazilian pharmaceutical patents were granted in offices abroad, mainly in the USA, Europe and China. In China, on the other hand, approximately 97% of the 39,460 Chinese patents were granted within its own territory, indicating the effectiveness of exploiting the potential of the Chinese pharmaceutical market by national companies.

Although it is known that domestic companies need to venture into the international market in order to sustain their activities, it is clear that national companies are not fully exploiting the emerging Brazilian pharmaceutical market, leaving space for massive operations by multinationals. Recent data from the National Bank for Economic and Social Development (BNDES) may point to a growth in the share of national capital in the Brazilian pharmaceutical market, but they also suggest that the Brazilian industry has not been able to meet the domestic demand for pharmaceuticals, which can be demonstrated by the growing negative trade balance, which reached US$ 8 billion in 2013. As a result, there has been an increase in the import of pharmaceutical products in Brazil, exceeding the value of US$ 10 billion in 2013. In the 90s, the import of the active principle corresponded to approximately 70% of the deficit, while today finished products answer for a similar share, especially those obtained through biotechnology.

<table>
<thead>
<tr>
<th>Period</th>
<th>Europe</th>
<th>USA</th>
<th>China</th>
<th>Brazil</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014e</td>
<td>5,257</td>
<td>6,506</td>
<td>11,529</td>
<td>115</td>
</tr>
<tr>
<td>2015e</td>
<td>5,423</td>
<td>6,995</td>
<td>12,845</td>
<td>133</td>
</tr>
<tr>
<td>2016e</td>
<td>5,596</td>
<td>7,520</td>
<td>14,234</td>
<td>151</td>
</tr>
<tr>
<td>2017e</td>
<td>5,777</td>
<td>8,081</td>
<td>15,696</td>
<td>170</td>
</tr>
<tr>
<td>2018e</td>
<td>5,965</td>
<td>8,678</td>
<td>17,231</td>
<td>191</td>
</tr>
</tbody>
</table>

Relative Variation

\[
VR_x = \frac{y_{x+5} - y_x}{y_x}
\]

Period | 09-2013 | 2014-2018 |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>-5%</td>
<td>13%</td>
</tr>
<tr>
<td>China</td>
<td>91%</td>
<td>33%</td>
</tr>
<tr>
<td>Brazil</td>
<td>114%</td>
<td>49%</td>
</tr>
<tr>
<td>Brazil</td>
<td>25%</td>
<td>66%</td>
</tr>
</tbody>
</table>
techniques, proving the lack of know how in the national industries (Pimentel et al., 2014).

5.4 Study of patent protection in companies of the pharmaceutical segment

Using the Derwent database (Thomson Reuters, 2015), the 15 companies of the pharmaceutical segment with the largest number of IP instruments, particularly patents, in the search area Pharmacology & Pharmacy, were investigated between 1996-2014 (Figure 4). First, the importance of industries of European origin should be noted, with emphasis on Hoffmann La Roche, which occupies 1st place with 1,032 protections; Novartis, which occupies 2nd placing with 671 patents; AstraZeneca; and Boehringer Ingelheim, totaling 2,540 patents. The American companies were represented by Merck Sharp & Dohme, with 584 patents and the 3rd position in the global ranking; Mondobiotec Lab.; Schering; BASF and Bristol-Myers; reaching 1,668 protections. A total of 4 Japanese companies (Kao Group, Daiichi Sankyo, Takeda Pharma and Kowa Co.) appear among the 15 largest holders of pharmaceutical patents, with 858 protections. A Chinese research institute (Beijing Guanwuzhou Biological Sci.) also shows up, taking the sixth position (367 protections), with China being the only representative of the pharmerging markets.

As can be seen, the data from Derwent corroborate and complement the survey conducted in this article on the WIPO database, showing that the pharmaceutical sector is still dominated by industries from Europe, the USA and also from Japan, which hold a large part of the patents in the industry, enabling the maintenance of their competitive advantages, exclusive exploitation of different markets, price-fixing of medication and the achievement of exceptional profits (Das, 2011). The presence of a Chinese research center among the 15 largest holders of protections in the medication industry, however, reiterates that scientific and technological knowledge is beginning to spread in the pharmaceutical field.

It should be emphasized that according to Bartlett & Ghoshal (2000), a high innovation rate is a necessary, but not a sufficient factor for an industry to keep ahead in the pharmaceutical market. As such, other elements present in these large organizations in Europe and the USA make them achieve these expressive performances, including a positive organizational image, well defined objectives, a capacity for constant learning, leadership and creativity in marketing and sales initiatives. These elements should be used as guidelines for industries in the pharmerging countries.

Based on the Derwent data, a qualitative correlation between the innovation rate of the pharmaceutical industry and its investment in R&D was sought. According to the 2014 EU Industrial R&D Investment
**Scoreboard** (Hernandez et al., 2015), a report of the European Union on investments in R&D based on projects financed by the company itself, 22 of the 100 companies that invested most in R&D in 2014 were pharmaceutical industries, regardless of the technological field. Hoffmann La Roche (1st among the pharmaceutical companies and 6th in the general ranking), Novartis (2nd among the pharmaceutical companies and 7th in the general ranking) and Merck (3rd among the pharmaceutical companies and 8th in the general ranking) stand out.

One can therefore see that the industries that invested most in R&D in the year 2014, 15 also appear among the largest holders of protections, from which one can infer the importance of well-developed R&D activities and a qualified staff for the generation of innovation in the pharmaceutical segment. The case of Hoffmann La Roche highlights this observation, as it’s the company with the largest number of protections of pharmaceutical products/process and also the 6th company that most invests in R&D in the world since 2012, with its investments increasing 169% between 2005 and 2012. However, it also fair to say that companies like Pfizer (5th among the pharmaceutical companies and 10th in the general ranking) and Sanofi-Aventis (6th among the pharmaceutical companies and 15th in the general ranking) invest massively in R&D, but nevertheless don’t appear among the 15 pharmaceutical companies with the highest number of patents, revealing that their R&D activities should be optimized.

These data point to a serious problem in Brazil in all fields of technology, given that only 1% of the Brazilian GDP was invested in R&D since 2012. The Brazilian pharmaceutical sector invests more in R&D (4.8% of its revenues) than the average Brazilian industry, but the allocation of resources for this type of activity is still well below the level in the rest of the world (more than 17% of total sales) (Gomes et al., 2012; Pimentel et al., 2014). These low investments may be reflected in the fact that only 169% between 2005 and 2012. However, it also fair to say that companies like Pfizer (5th among the pharmaceutical companies and 10th in the general ranking) and Sanofi-Aventis (6th among the pharmaceutical companies and 15th in the general ranking) invest massively in R&D, but nevertheless don’t appear among the 15 pharmaceutical companies with the highest number of patents, revealing that their R&D activities should be optimized.

6 Conclusions

In the current scenario, the USA and Europe emerge as the regions with the largest number of pharmaceutical patents, demonstrating their great capacity to generate innovation in the sector and to dictate the competitive dynamics. Derwent data corroborate these results, with the performance of Hoffmann-La Roche standing out, which holds the largest number of pharmaceutical patents and is the 6th company that has invested most in R&D in the world, reflecting the importance of these activities to optimize the innovation rate.

An expressive involvement of China could be seen in the global context. The country took over the second position among the countries with the greatest number of pharmaceutical patents, while Brazil still has a very unremarkable position in the ranking. The low innovative power of the Brazilian pharmaceutical industry is a reflection of the fact that national businesses concentrate mostly on medication production (especially those with expired patents) and marketing activities in the value chain, illustrating that more intensive science and technology activities with a greater potential of providing competitive advantages were not introduced and assimilated in the pharmaceutical industry in Brazil. This weakness prevents the leveraging of the Brazilian pharmaceutical industry, since the temporary monopoly hinders the entry of national companies in the sector in an effective way.

However, the developed forecasts showed a positive trend for the pharmerging countries, with an expressive increase in the number of grants by country of origin and office being expected when China and Brazil are considered. The estimates for the USA and Europe, on the other hand, were not so optimistic, demonstrating a slower pace in the generation and granting of protections. It could be said, therefore, that China is already challenging the supremacy of the USA and Europe in the pharmaceutical segment, suggesting that in the coming 20 years, this pharmerging country will take the lead in pharmaceutical innovation. This confirms that technological and scientific knowledge is starting to spread and that the competition with the Big Pharma is increasing, interfering directly in the dynamics of the sector.

These data indicate that the large multinational pharmaceutical companies will have to revise their organizational strategies in order to seek a greater penetration in pharmaceutical emerging markets. Additionally, the entry of the Chinese pharmaceutical industries based on their elevated innovation rates will tend to force multinationals to optimize the productivity of their R&D activities, if they want to recover their dominant position in the segment. One can also infer that if other pharmerging countries, such as Brazil, were to take the Chinese case as example, then they should review their public policies for science, technology and innovation in order to prioritize this strategic sector and to strengthen the capacity and the gains of national pharmaceutical industries in order to exploit their emerging markets and take competitive positions in the global scenario. The development of more daring industrial and technological policies are therefore recommended in the Brazilian case, in addition to the formation of...
public-private partnerships, the decentralization of R&D activities and the acquiring of technological skills and knowledge that are already consolidated in leading countries.

A fair suggestion for future work would be an evaluation of other pharmerging countries, such as India and Russia, in addition to an expansion of the study so as to encompass biopharmaceutical technologies.

References


Annex A. Algorithm implemented in MATLAB®.

% Algoritmo Método dos Mínimos Quadrados - Desenvolvido em MATLAB
% Aproximação polinomial de funções
% Caso Discreto

clc
format long g
x = input('Entre com os valores de x como um vetor: ');
y = input('Entre com os valores de y como um vetor: ');
z = input('Entre com o valor a ser determinado (x): ');
OrdemMaxima = input('Entre com a ordem do polinômio: ');

teta = zeros(OrdemMaxima+1,OrdemMaxima);
error = zeros (OrdemMaxima,1);

for norder=1:OrdemMaxima,
d = norder+1;
vandermonde = zeros(length(x),d);
Y = zeros(length(x),1);
for i=1:length(x),
phi = zeros(d,1);
for dd=1:d,
    phi(dd) = x(i)^(dd-1); % Matriz de Vandermonde
end
vandermonde(i,:) = phi';
Y(i) = y(i);
end
teta(1:d,norder) = inv(vandermonde'*vandermonde)*vandermonde'*Y;
error(norder) = sum((Y - vandermonde*teta(1:d,norder)).^2);
end

for i = 0:OrdemMaxima
    x_achar(i+1) = z^i;
end

% Calculo
coefficientes = teta(:,OrdemMaxima);
y_achar = x_achar*coefficientes;

% Saída de informações
disp(' ')
disp(['O valor aproximado para x = ',num2str(z), ' é ', {y_achar}])