

# The scientific performance of Portuguese pharmaceutical industry: A bibliometric analysis

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### **Abstract**

The premise that leads to this investigation is that Portuguese pharmaceutical industry offers new solutions and brainpower. As this sector is usually linked to innovation and scientific progress as a way to increase competitiveness we believed that Portuguese pharmaceutical industry was more than a simple production facilities.

This thesis main objective is to evaluate the scientific performance based on both qualitative and quantitative measures applying bibliometric methods. Using Scopus database, we restricted the scope of analysis to articles or reviews published in peer reviewed scientific journals in the period between 2000 and 2016. This search retrieved 435 documents, from which 94% were articles and the rest 6% reviews.

We were able to define some patterns of publication among the 10 Portuguese companies considered. As expected, Bial is, by far, the company with more published articles or reviews (243), followed by Bluepharma with about one third of the documents (69 – from which 80% were published after 2011). Most of the collaborations were with national universities and most of the authors were also Portuguese enhancing the focus on national brain-power.

In what concerns to quantity and quality, the total publication growth between 2008-2009, 2011-2012 and 2014-2015 outstands among the rest of the years and the increasing quality of the journals used by Bluepharma and Hovione and the consequent growing of their citation impact should be hilighted.

**Keywords:** Portuguese Pharmaceutical Industry; Bibliometrics; Drug Research; Scientific Publication

### Resumo

A premissa que leva a esta investigação é que a indústria farmacêutica portuguesa oferece novas soluções e capacidade intelectual. Estando este setor intimamente ligado à inovação e ao progresso científico como forma de aumentar a competitividade, acreditamos que a indústria farmacêutica portuguesa é mais do que simples instalações produtivas.

O objetivo principal desta tese é avaliar o desempenho científico com base em medidas qualitativas e quantitativas aplicando métodos bibliométricos. Usando a base de dados Scopus, restringimos o espectro de análise a artigos ou revisões publicados em revistas científicas revistas por pares, no período compreendido entre 2000 e 2016, sendo apresentados 435 documentos, dos quais 94% eram artigos e as restantes revisões de 6%.

Foi possível definir alguns padrões de publicação entre as 10 empresas portuguesas consideradas. Como esperado, a Bial é, de longe, a empresa com mais artigos ou revisões publicados (243), seguido da Bluepharma com cerca de um terço dos documentos (69 - dos quais 80% foram publicados depois de 2011). A maioria das colaborações encontradas foram com universidades nacionais e a maioria dos autores também eram portugueses realçando a aposta no capital intelectual nacional.

No que diz respeito à quantidade e à qualidade, o crescimento total do número de publicações entre 2008-2009, 2011-2012 e 2014-2015 destaca-se entre o resto dos anos e a crescente qualidade das revistas utilizadas pela Bluepharma e Hovione e o consequente crescimento do número de citações por artigo deve também ser enaltecido.

**Keywords:** Industria farmacêutica Portuguesa; Bibliometria; Inovação do medicamento; Publicações científicas

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### 1. Introduction

Annually, more than 110 billion euros are invested worldwide by the pharmaceutical industry in research and development (R&D) (European Commission, 2015). This value represents 14-17% of the annual turnover in the entire industry, making it the industry which invests the most in this area. (International Federation of Pharmaceutical Manufacturers & Associations, 2012). Progress has been achieved in several areas, including pharmacological, cell and molecular biology and molecular genetics whose advances boosted the growth of this industry. (Malerba and Adams, 2014; Gambardella, 1995). European pharma has contributed to this as European Union (EU) Industrial R&D Investment Scoreboard for 2015 shows: 316 of the top 2.500 firms (12.6%) are pharmaceutical; if we focus this analysis to the first 100 companies, the percentage rises to 24% and in TOP 10 for 40% (European Commission, 2015). These figures remind us of what has been told by Scherer (2001), there is a strong link between investment in R&D and dynamism of the pharmaceutical industry.

Although all these numbers, the common perception is that, globally, pharmaceutical industry is facing a low productivity on R&D (Rafols *et al.* 2014), lots of patents are expiring what lets the market opened to generic medicines (Ku, 2015). Yet, in spite of this perception, the Portuguese Pharmaceutical Industry's investigation is growing alongside with exports. According to Portuguese Health Cluster's *tableau de bord* the export volume grew 98% since 2008, the investment in R&D by companies doubled from 2008 to 2014 (59M€ to 120M€) and the total number of publications goes from 3.644 to 8.158.

This thesis main purpose is, at first, to question and examine the Portuguese pharmaceutical industry scientific publication numbers, evaluating their capability of producing knowledge. By looking at those numbers as an indicator of innovation activity we should see how each one of the selected companies positions itself in the market in what concerns innovation. In order to fulfill this objective, we will appeal *Scopus* database to survey the data from the last 17 years (from 2000 to 2016).

A connection between the number and impact of publications and the marketing authorization numbers is expected to be found, which means that we suppose that the more companies channel resources on research and investigation the more they publish. Bibliometric data will be compared

with the release of new drugs, stablishing a relationship between the intensity of publications and the marketing authorization.

This thesis is divided in 3 main chapters: in chapter 1 we will focus on a bibliographic review of what has been told about innovation and innovation as a competitiveness factor before relating it with the innovation dynamics in the pharmaceutical industry alongside with a brief framework of the international pharmaceutical industry and the history and origins of the Portuguese pharmaceutical industry. As this thesis focus this subgroup, it is important to know its history and background. In chapter 2, at first we will explain the bibliometric approach and the use of *Scopus* database to identify the scientific publications by the Portuguese pharmaceutical industry. Chapter 3 is dedicated to data analysis, where bibliometric data will be presented in several tables and figures, and analyzed individually, this chapter focus, mainly, on publication numbers, citations and the journals where the Portuguese pharmaceutical industry publishes.

### 2. Background

### 2.1. Introduction

This chapter's main objective is to provide the theoretical background against which the discussion and data analysis can take place. In the following pages we will present some background on Innovation, particularizing the innovation in the pharmaceutical industry. We will also provide an historical background about the pharmaceutical industry in Portugal and in the rest of the world.

### 2.2. Innovation

Schumpeter (1934) considers innovation as the main source of economic growth, defining it as the changes in the methods itself (it can be either in production, transportation or anything involved to any part of the economic chain), production of a new product, organizational change or entering a new market. Besides this theoretical definition he also believed that the process of innovation should start inside the industries and industries should be the main booster of economic revolution.

In 1942 he first referred to "creative destruction" as a theory of economic innovation and the business cycle. According to the literature, "creative destruction" was the "process of industrial mutation that incessantly revolutionizes the economic structure from within, incessantly destroying the old one, incessantly creating a new one" (Schumpeter, 1942: 82-83). Despite being published in the early 30's this is still one of the most influent works in this area.

After Schumpeter, this topic has been largely studied and mentioned as one of the most important fields of research to support management and to study social sciences.

### 2.3. Innovation as a competitiveness factor

There is a strong link between innovation and economic vitality. As Bica (2006:24) mentioned "Nowadays, the creation of knowledge and innovation are consensually accepted as determinants of economic vitality". This new paradigm comes along with the evolution of the information technologies and the consequently growth of accessible data and the need to filtrate it, making the high-tech industries the most relevant sectors to the economic growth (Bică *et al.*, 2015).

Joseph Schumpeter is claimed for many authors (Fagerberg, 2005) as one of the first economists to consider innovation as the driver of economic development. Schumpeter (1934) tells us that innovation is a entrepreneurship factor whereby new products replace old ones impacting the

market share (innovative firms gain market share on non-innovative firms). Despite not having any tangible value, innovation gives companies some competitive leverage.

The process of innovation is divided in three stages by Godinho (2013): invention, innovation and diffusion. Invention, comes first as a stage where the idea is conceived while innovation happens when the product is already ready to reach the market. The last, but not the least important stage, is diffusion, where you can evaluate how the product spread in the relevant population. Both Fagerberg (2005), supports this theory adding that, not always this stages come one, immediately, after the other because of the delay given by the productive process.

Salter and Alexy (2014), mention incremental and radical innovation. Radical innovation as something completely new comes to the market and there is nothing similar to it. Incremental innovation as an improvement of something that already existed. However, Henderson and Clark (1990) disagree with this division and divided it in: incremental, modular, architectural and radical.

As there is no consensus about a definition of innovation, after doing a survey of literature, Edison *et al.* (2013: 1041) found the following definition to be the most comprehensive.

"Production or adoption, assimilation, and exploitation of a value-added novelty in economic and social spheres; renewal and enlargement of products, services, and markets; development of new methods of production; and establishment of new management systems. It is both a process and an outcome."

### 2.4. Innovation dynamics in the pharmaceutical industry

The environment where companies are inserted is what forces them to change. If a company operates in a flat market it is less likely for it to be innovative, once it rarely happens spontaneously (Porter, 1990).

When we talk about innovation in pharmaceutical sector we can't only think about big pharma. In this sector every stakeholder is connected, so when we talk about innovation in pharmaceutical industry we should "include both large and small pharmaceutical companies, new biotechnology firms, universities, research organizations and hospitals, the medical profession, financial organizations, regulatory agencies and consumers." Malerba and Adams (2014: 193).

Both Rafols *et al.* (2014), Munos (2009) and Kaitin and DiMasi (2011), agree that the common perception is that, pharmaceutical industry is facing a low productivity on R&D because the number of new drugs by year approvals are decreasing and the fact is, when someone refers to

innovation in pharmaceutical industry, the first thing that comes to our mind is the process of creation of a new drug.

According to LaMattina (2011) pharmaceutical firms are responding to this low productivity with a series of major mergers and acquisitions involving smaller drug discovery firms, closing R&D sites, particularly in Europe and the US and placing them in emerging countries with large markets (India and China). The industry is increasingly outsourcing R&D to external research organizations, which is perceived to improve efficiency (Rafols *et al.*, 2014: 1).

### 2.5. Portuguese pharmaceutical industry: Origins and evolution

According to Apifarma (2014) most authors consider that the first steps on the development of the Portuguese pharmaceutical industry appear with the creation of the "Companhia Portuguesa de Higiene" in 1891, a little later than in some other European countries. Despite being the first in Portugal it didn't secure his commercial success due to the lack investment in biology applied to pharmaceutical solutions. Filling up this gap, late this same decade, appeared the first companies producing injectable drugs.

The beginning of the XX century is marked by the growth and the semi-industrialization of this sector and the reduction of unitary production in local pharmacies. (Sousa *et al.*, 2014) Alongside with this, Bayer stablished a productive unit in Portugal.

During the Great War, Germany, as Portugal's main medicines supplier, was not capable to maintain the supply chain, propitiating the proliferation of new Portuguese industrial pharmaceutical laboratories.

Although the governmental instability of the early twenties, great steps were taken during this period, with the creation of "Sociedade Industial Farmacêutica, S.A.R.L.", "Bial" and Bial's first registered mark "Benzo-Diacol". In parallel the firsts biology and chemotherapy laboratories started their activities. Among the stablished companies, Sanitas' Laboratory was the most relevant not only for the dimension and success on exportation but also for the well succeeded process of internationalization to Brazil. Also, the Pasteur Institute in Lisbon, which represented Lilly announced the commercialization of Lilly insulin.

In 1948 Vitoria's Laboratory, inspired by the American pharmaceutical industry, started producing the first antibiotics in Portugal. Portuguese pharmaceutical industry was growing and the first problems started to arise, as we can read in Apifarma (2014:90) "there was no regulation for competition and pricing, and the agents were little specialized". This problems were the main reason to create the Comissão Reguladora dos Produtos Farmacêuticos (CRPQF), a governmental commission responsible for the regulation of pharmaceutical products. Despite the creation of CRPQF, the amount of drugs introduced every year in the market was too high, that's why in 1957 the Comissão Técnica de Novos Medicamentos (CTNM), a commission responsible for evaluating clinical and pharmacologically new drugs marketing access applications.

The 1960s were mostly marked for the growth in exportation. In this decade the growing of the industry was evident and according to Apifarma (2014) "the registered growth rate was around 13,5%/year". Although all this numbers the market fragmentation problem was still notorious, and in 1965 a commission is created with the aim of reorganizing this industry in Portugal. Even though this reorganization never occurred, one of the main conclusions of this commission was that Portuguese pharmaceutical industry production was too dependent of foreigner patents — what means that we had production but no innovation. In 1975 "Apifarma" is created, replacing "Grémio" due to its connotation to the dictatorial regime.

Between 1980 and 1990 the Portuguese pharmaceutical industry faced several challenges, among them: the development of National Health Service, Portuguese entry in the European Economic Community and the presence of the International Monetary Fund (IMF) in Portugal.

The 1990s decade, known for the important steps given in the health sector, were marked in many aspects: In terms of regulation, the creation of the first entities focused on assuring the correct evaluation and supervision of every drug - "European Medicines Agency" (EMA) for Europe in 1990 and "Instituto Nacional da Farmácia e do Medicamento" (INFARMED) for Portugal in 1993. From this date on, CTNM went from an independent commission to an INFARMED consulting organ; On international level the mergers and acquisitions of big pharmaceutical companies; and particularly in Portugal for the emergence of the first legislation about generics (Pisano, 1991; Gambardella, 1995).

"The deepening of the European Common Market and the geographical relocation of industry, initiated globally and cross-sectorally in the 1990s, led, in this decade, to the divestment of multinationals in the production units they had established in Portugal" (Apifarma, 2014: 138) thus, several Portuguese pharmaceutical groups acquired those production units and specialized in the

production of generic medicines. The same way some companies invested in generics, others invested in the development of new drugs, and in 2014 Bial had the first Portuguese patented medicine approved by the Food & Drug Administration (FDA).

Also remarkable for the innovation process and clinical investigation, was the creation of "Comissão de Ética para a Investigação Clínica" (CEIC), the commission responsible to secure the compliance with ethical standards in clinical investigation.

### 2.6. Chapter final notes

This chapter helped us defining the framework of this thesis. The literature about innovation and its relation with the pharmaceutical industry combined with the Portuguese pharmaceutical industry history were crucial to help us defining the object of analysis and make the bridge to the methods and materials chapter.

### 3. Methods and Materials

### 3.1. Introduction

This chapter's main objective is to establish a link between the objectives presented for this thesis and the methodology that is going to be used in the further data analysis. The first part of this chapter, will describe the methodology used to collect data, both the Scientific Publication numbers and the new drugs marketing authorization for each company.

### **3.2.** Object of analysis

In order to define our object of analysis we analyzed four different groups (Apifarma, Health Cluster Portugal (HCP), Biocant Park and Portugal Biotechnology Industry Organisation (P-Bio) and APOGEN – Portuguese Generic and Biosimilar Medicines Association) known for having a strong relationship with innovation and technology in the health sector.

These four groups of companies were carefully analyzed, in order to find the companies that matched the following pre-stablished inclusion criteria:

- Portuguese share capital;
- Companies that produce medicines;
  - o Biopharmaceutical companies;
  - Biotechnological companies;
- Pharmaceutical laboratories that assume to participate in innovation activities.

All of the companies with Portuguese share capital on each one of these four groups were individually analyzed in order to validate if the rest of the inclusion criteria matched.

We collected all the companies that matched all the inclusion criteria, as described in the scheme below, and after that we selected the companies to be studied.

### APIFARMA

113 members 31 Portuguese

# Companies that respect inclusion criteria:

Bial; Bluepharma, Medinfar, Tecnimede, AtralCipan; EDOL, Azevedos; Tecnifar

### **HCP**

161 members 132 Portuguese

# Companies that respect inclusion criteria:

Bial; Bluepharma, Medinfar, Tecnimede, AtralCipan; EDOL, Azevedos; Hovione; tecnophage; Cell2b

# Biocant Park & P-Bio

60 members 48 Portuguese

# Companies that respect inclusion criteria:

Tecnophage; Cell2b; Luzitin; Blueclinical; BSIM2;

### **APOGEN**

16 members5 Portuguese

# Companies that respect inclusion criteria:

Bluepharma, Tecnimede, Generis Farmaceutica; Farmoz

After analyzing the 4 groups and checking the companies that matched the inclusion criteria we chose the following 10:

- · Bial;
- Azevedos;
- · Bluepharma;
- EDOL;
- Hovione;
- Cell2b;
- Tecnimede;
- · Medinfar;
- AtralCipan;
- Tecnifar

Figure 1 - Structure of the analized groups

Bearing in mind this inclusion criteria, the selected companies were: AtralCipan; Azevedos; Bial; Bluepharma; Cell2b; EDOL; Hovione; Medinfar; Tecnifar; Tecnimede. Although these ten companies are not the complete interception of Venn's Diagram some were chosen for its relevance.

Bluepharma data regards all the publications affiliated with Bluepharma or any of its spin-offs or companies where Bluepharma has participation – in particular: technophage, Luzitin, Blueclinical, BSIM2 and Treat-U. Which mean our, "analysis unit" are groups of companies and not only the companies by itself.

### 3.3. Scientific Publications

Scientific Publications are one of the innovation process outputs (Godinho, 2007) and will be analyzed using bibliometrics. Through publication data, such as: authors, title, citations, affiliation, date and many others – it is possible to see, if existent, the scientific publication patterns and evaluate the scientific activities. In this specific case, the publications will be filtered by affiliation restricting the search to the pre-stablished Portuguese pharmaceutical companies. Only publications classified as "articles" or "reviews" will be object of detailed analysis.

### Research papers by companies

Scientific production is the way scientific community uses to communicate results of their research (Lopes et al. 2012) and Pharmaceutical Companies are among the industries that most create scientific material. As authors use papers to build credibility around their research, companies canalize this credibility to create some leverage for commercial purposes.

Hicks (1995), Rafols et al. (2014) and Pendlebury (2008) claim that companies do publish. Yet, it is not clear why should a company bring to public their research while other companies can appropriate on it. Hicks (1995: 2) justifies this by telling us that "firms are able to publish precisely because they can choose which information to make public." and scientific publications are intimately related to unpublished knowledge.

Despite agreeing that companies do publish, many authors believe Big Pharmaceutical Companies are facing a productivity crisis. In Rafols et al. (2014: 1) paper, it is mentioned a "decline of the total number of publications by large firms and a relative increase of their external collaborations suggesting a tendency to outsource, and a diversification of the disciplinary base" alongside with this fact is the marked decrease on publications numbers by companies which R&D laboratories or headquarters are located in Europe.

Hereupon, as mentioned by Hicks et al. (1995: 3) and Rafols et al. (2014) the publications can't be assumed as the only source of data to evaluate research in the private sector, and any inferences from it have to be carefully analyzed first.

### 3.4. Citations

Citations are mentions or reference in an official, published document meant to substantiate, clarify or illustrate a point. Their purpose is to acknowledge the author of a previous idea or work, support the author investigation and allow the reader to validate the strength and veracity of the presented work.

A citation is an expression that appears in the body of a document that references the reader to an entry in the bibliographic references section, with the purpose to acknowledge other author or piece of work. Commonly, both the reference in the bibliographic section and the expression embedded in the body of the text are called citations.

Among citations is a particular type of citations, called "self-citation" – when a author cites himself in other paper. Aksnes (2003) gives us two visions of self-citation; first of all as a natural and acceptable procedure and on the other hand as a result of egotism for making their former works visible.

### 3.5. Bibliometrics

Bibliometrics is a "technique for measuring quantitative and statistical indices of production and dissemination of knowledge and monitor the development of several scientific areas and patterns of authorship, publication and use of research results" (Lopes et al., 2012: 1).

While tangible inventions outcomes can be measured in terms of sales revenues, the achievements in science research are not as easy to measure. When we talk about research evaluation, we think in evaluating its outputs – Scientific Publications – however, due to the increased amount and specificity of research it is too difficult to have each output evaluated by peers. Furthermore, there is always a certain subjectivity in peer reviewing (Pendlebury, 2008).

"Counting, measuring, comparing quantities, analyzing measurements: quantitative analysis, as Lord Kelvin's famous observation suggests, is perhaps the main tool of science. In this century, the volume of scientific research—measuring to "know something"—and recording and communicating that knowledge through publications, has itself become enormous and complex. Science research is now such a large enterprise and the substance of scientific research is so complex and specialized that personal knowledge and experience are no longer sufficient tools for understanding trends or for making decisions." (Pendlebury, 2008: 2)

Bibliometrics measures not only the number of publications but also the number of citations and, by analyzing the number of citations, we understand the trends in certain topic and the impact and influence of the researcher/research. In order to evaluate the impact of a publication we have to use relative measures, in other words, we can't compare the impact of two publications in different topics only by their absolute number of citations or even when the publications are about the same topic but have different publication dates — "should not compare absolute citation counts of an eight-year-old paper with those of a two-year-old paper, since the former has had more years to collect citations than the latter" (Pendlebury, 2008: 5).

This evaluation of scientific production serves a purpose of generating recognition of researchers and companies (Lopes et al., 2012; Hicks, 1995) and in the case of companies "credibility established through publication also serves more clearly commercial ends" (Hicks, 1995: 3).

According to Leeuwen (2004) there are two types of bibliometric approaches: Descriptive and Evaluative, also known as top down and bottom up, respectively. Evaluative bibliometrics was first mentioned by Narin (1976) as the form of bibliometrics focused on evaluating scientific activity and performance. For Leeuwen (2000) the main differences between them remains on the level of validity of the research output. This differences come mainly from the methodology used to collect data.

While in the descriptive approach publications are filtered by general characteristics such as country or field of investigation, in the evaluative approach the publications are selected from the individual work, including a process of verification by the researcher.

### Bibliometric Indicators

In order to evaluate scientific production there are several bibliometric indicators. These indicators evaluate not only scientific activity, but also its quality, impact and research area (Amante et al., 2012).

On his research, Amante et al. (2012) describes four main indicators – Impact Factor, H-Index, Eigenfactor Metrics and SciMago Journal Rank – he describes each indicator, explaining how to use them and pointing their key gaps.

SCImago Journal Rank (SJR)

This rank measures the prestige of a journal. Subject field, quality, and reputation of the journal have a direct effect on the value of a citation. Scopus, (2017).

This score bases its quotation in the premise that not all the citations are equal, in other words, if your paper is cited in a journal with higher SJR, that citation will worth more than a citation published in a journal with lower SJR.

### CiteScore

CiteScore is a score based on metrics that calculate the citations "from all documents in year one to all documents published in the prior three years for a title." Zijlstra, (2016).

This score is calculated dividing the number of citations on year X by the number of publications in years X-1, X-2 and X-3.

### 3.6. Data collecting process

The data collecting process will be divided in two main parts: Scientific Publications and Drugs Marketing Authorization.

### 3.7. Bibliometric data

Nowadays there are three main sources of bibliometric data, Google Scholar Metrics (GSM), Web of Science (WoS) and the one to be used in this thesis, Scopus. This choice was based on several criteria, such as user interface, contents, temporal coverage and the type of access to the publications.

Comparing this three databases, Google Scholar Metrics stands out for its user interface, WoS for its temporal coverage and Scopus for the quality of data and the large amount of European contents (Moya-Anegón et al., 2015).

As we are going to analyze the Portuguese Pharmaceutical Industry's scientific production between 2000 and 2016, we choose the quality and the focus on European sources in prejudice of a bigger temporal coverage. Plus, Barros, (2016) used Scopus database as his source of data. Therefore, in order to be possible to compare the results from both documents all the bibliometric data will be

collected using Scopus and filtering search by the name of the company in the affiliation section. Scientific Publications data will be collected until 31st March 2017.

### Search details

Scopus allows users to use an advanced search engine based on queries. In this section, we will paste the query used for each one of the companies, in order to be possible to run the same exact search in further analysis. This information can be found in attachment 1.

### 3.8. Marketing Authorization

Marketing Authorization information will be collected using INFARMED's web database (http://app7.infarmed.pt/infomed) and companies' product portfolio. FDA database may also be used.

### Infomed INFARMED

Infomed is a web database, from INFARMED, with information about medicines for humans such as active substance, authorization status, authorization date, MA holder, product group, CFT among others not relevant for out research.

Search will be filtered by the MA holder (company).

### Food & Drug Administration Database

FDA is an American federal agency responsible for controlling and supervise food safety, tobacco, dietary supplements, prescription and everything related to cosmetics and medicines either for human or animal use. All the data for approved medicines can be found in an online database.

In this database, search will be filtered by the applicant (company).

### Companies Product Portfolio

Pharmaceutical companies, usually have a document with the collection of all the products they commercialize. The five companies selected for this thesis have this information with free access on their website.

### 3.9. Chapter final notes

This chapter makes an approach to the methods and materials to be used in the analysis on chapter 3. We started by defining the population to be studied and then specify the data to be collected and how we were going to do it. After clarifying the information to be collected we introduced the methods of analysis, defining bibliometrics and some bibliometric indicators.

### 4. Data Analysis

### 4.1. Introduction

This chapter pretends to summarize the data collected using *Scopus* in several analyses. In terms of Scientific Production, we will analyze, number of scientific publications by each one of the selected companies and respective number of citations, who were the authors and what are their other affiliations and the publication main subject or therapeutic area. In what concerns to drug release, we will analyze the release year and the therapeutic area associated to the drug.

While Barros, (2016) analyzed every published document, in this thesis the main analyses will be based only on publications classified as "articles" or "reviews".

### 4.2. Portuguese Pharmaceutical Industry publications

Table 1 presents the total number of publications by year for each one of the selected companies.

Company	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total
Bial	6	7	13	18	10	11	8	16	22	21	21	14	23	18	15	26	19	268
Hovione	1	0	0	3	0	1	0	1	5	4	5	4	8	11	13	13	9	78
Bluepharma	0	0	0	1	0	0	2	1	1	2	2	7	15	6	13	13	13	76
Tecnimede	0	0	1	0	3	5	3	1	5	2	3	6	1	1	1	1	0	33
AtralCipan	3	2	1	0	4	4	3	0	6	0	1	0	0	1	0	0	0	25
Medinfar	0	0	0	0	0	0	1	0	1	0	3	3	0	0	0	0	0	8
Cell2b	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	3	2	7
EDOL	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	0	4
Azevedos	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1
Tecnifar	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1
Total	10	9	15	22	17	21	17	19	40	29	36	35	49	38	44	57	43	501

Table 1 - Scientific Publications by company

### 4.2.1. Scientific publication growth

As important as providing absolute numbers is to see the growth patterns. This section focus on the number of publications by year and the evolution of each company during the time analyzed.

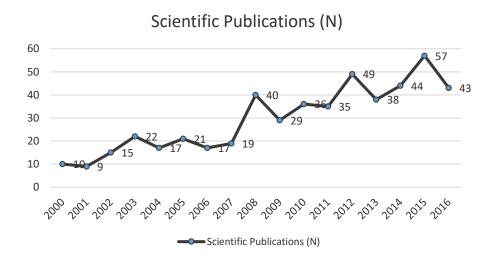


Figure 2 - Number of Scientific Publications by year

In Figure 2 we can see the evolution of the total number of scientific publications between 2000 and 2016. It is notorious the growth between 2007 and 2008 (19 to 40) as a result of the individual growth of every company in analysis except Bluepharma. This numbers come down in 2009 (39 to 29) as the individual performance of Atral Cipan passes from 6 articles to 0, Tecnimed from 5 to 2 and both Hovione and Bial with 1 less article than in the year before.

In absolute numbers, 2015 is the year with more scientific publications (57).

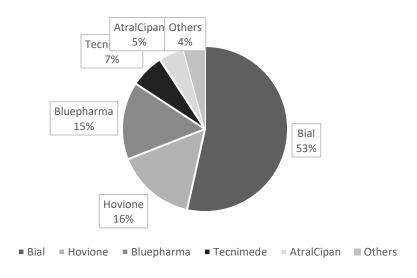


Figure 3 - Percentage of publications by each company

According to figure 3 53% of the publications from 2000 to 2016 are affiliated to Bial, Hovione have 16%, followed by Bluepharma with 15% of the total publications. Tecnimede has 7% and AtralCipan 5% and the rest of the companies have about 4%.

Analyzing these values we can see that 84% (422 out of 501) of the publications found belong to the same three companies (Bial, Hovione and Bluepharma).

When we analyze the previous figure it is notorious that Bial has the biggest number of publications but it is impossible to analyze the evolution of the publication patterns. The following three figures, present the percentage of publications stratified by years [2000-2005], [2006-2011] and [2012-2016].

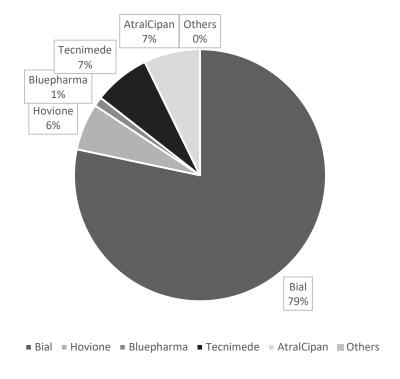


Figure 4 - Percentage of publications by company [2000-2005]

In this figure it is notorious that the publication panorama between 2000 and 2005 was completely dominated by Bial (79% of the total number of publications).

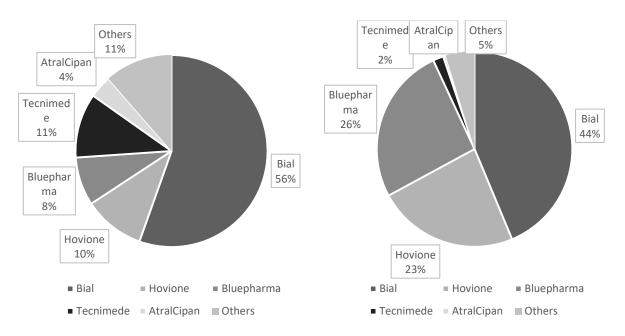


Figure 5 – Percentage of publications by company [2006-2011]

Figure 6 - Percentage of publications by company [2012-2016]

When we analyze figure 5 and 6, we notice that along the years Bial is losing some ground for Hovione and Bluepharma. While in the first 6 years of analysis Bial has 79% of the total publications, in the last 5 years this number decreases to 44%. On the other hand, Hovione and Bluepharma grow from 6% and 1% respectively to 23% and 26%.

This shows indicates a change in the publication patterns and a possible threat to Bial's hegemony in what concerns innovation.

### 4.3. Articles and reviews

The following table presents the number of publications classified as "articles" and "reviews". Further analysis will be based on this numbers.

Company	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total
Bial	5	7	12	17	10	9	8	15	22	18	20	13	20	14	13	25	15	243
Bluepharma	0	0	0	1	0	0	2	1	1	2	2	4	14	6	11	13	12	69
Hovione	1	0	0	3	0	1	0	0	4	0	3	2	7	8	6	5	9	49
Tecnimede	0	0	1	0	3	5	3	1	5	2	3	5	1	1	1	1	0	32
AtralCipan	3	2	1	0	2	3	3	0	6	0	1	0	0	1	0	0	0	22
Medinfar	0	0	0	0	0	0	1	0	1	0	3	3	0	0	0	0	0	8
Cell2b	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	3	1	6
EDOL	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	1	0	4
Azevedos	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1
Tecnifar	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1
Total	9	9	14	21	15	18	17	17	39	22	33	28	44	31	33	48	37	435

Table 2 - Articles and Reviews by company

Among the 501 publications found between 2000 and 2016, 435 (87%) are classified as "article" or "review".

Company	Articles	Reviews
Bial	228	15
Bluepharm a	62	7
Hovione	46	3
Tecnimede	31	2
AtralCipan	22	0
Others	19	1
Total	388	27

Table 3 - Number of Articles and Reviews by company

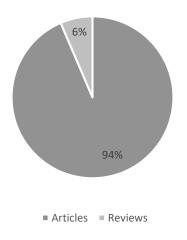


Figure 7 -Percentage of Articles and Reviews

## Citations by year by Company

Company	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total
Bial	1	7	18	66	74	93	87	129	168	271	403	454	489	566	628	664	662	4780
Bluepharma	0	0	0	0	1	0	0	10	4	7	16	26	63	66	106	173	288	760
Hovione	0	2	0	1	1	1	5	6	11	23	22	24	29	49	79	78	96	427
Tecnimede	2	0	0	1	1	3	7	9	13	14	14	15	27	39	41	33	37	256
AtralCipan	0	1	3	4	10	9	29	19	35	27	45	27	44	36	28	19	20	356
Medinfar	0	0	0	0	0	0	0	0	0	0	0	0	0	21	26	20	17	84
Cell2b	0	0	0	0	0	0	0	0	0	0	0	0	0	9	20	38	46	113
EDOL	0	0	0	0	0	0	0	0	0	0	0	0	0	3	1	5	3	12
Azevedos	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	2
Tecnifar	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	1	4
Total	3	10	21	72	87	106	128	173	231	342	500	546	652	790	932	1031	1170	6794

Table 4 - Citations by year by company

Table 5 shows us the number of citations when we exclude self-citation.

Company	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	Total
Bial	1	3	4	24	48	58	66	67	89	181	289	378	395	408	509	515	572	3.607
Bluepharma	0	0	0	0	1	0	0	4	0	2	6	8	29	47	61	101	171	430
Hovione	0	2	0	0	0	1	5	6	9	19	21	24	19	39	51	62	83	341
Tecnimede	0	0	0	1	0	3	7	9	12	12	13	14	26	39	37	34	33	240
AtralCipan	0	0	0	3	6	7	19	13	24	26	39	22	41	36	26	19	20	301
Medinfar	0	0	0	0	0	0	0	0	0	0	0	0	0	18	20	13	12	63
Cell2b	0	0	0	0	0	0	0	0	0	0	0	0	0	8	19	33	36	96
EDOL	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	3
Azevedos	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
Tecnifar	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0	1	4
Total	1	5	4	28	55	69	97	99	134	240	368	446	510	596	726	779	929	5.086

Table 5 - Citations by year by company excluding self-citations

This data shows us that among the 6.794 citations found 1.708 are self-citations. Excluding, Medinfar, Cell2b, EDOL, Azevedos and Tecnifar due to their reduced number of publications and citations, when we analyze each one of the other five companies by themselves we can see that Bluepharma is the company with the most relative frequency of self-citations (43,4% - 330 out of 760) after Bluepharma we can see Bial with 1.173 self-citations out of 3.607 (24,5%) and then Hovione (20,1%), AtralCipan (15,4%) and Tecnimede (6,3%).

### 4.4. Most cited articles or reviews by each company

In average Bial is the company with the highest citations/publications ratio (14,8 citations for each article) followed by AtralCipan (13,7). Tecnimede, Hovione and Bluepharma have 7,5, 7,0 and 6,2 respectively. In spite of being real, this numbers can't show us the real distribution of the citations.

The following tables focus on the five most cited publications for each company. The rest of the publications data will be added as attachment.

Each one of the most cited publications will be given a "Code" and in further analysis they will be identified by it.

Data in this section as already been collected and the analysis is still ongoing. We estimate to finish this analysis until the end of May.

### 4.4.1. Bial

Code	Title	Year	Source	Citations
A1	Solid dispersions as strategy to improve oral bioavailability of poor water soluble drugs (review)	2007	Drug Discovery Today	612
A2	Pharmacokinetic and safety profile of trans-resveratrol in a rising multiple-dose study in healthy volunteers	2009	Molecular Nutrition and Food Research	177
A3	Efficacy and safety of eslicarbazepine acetate as adjunctive treatment in adults with refractory partial-onset seizures: A randomized, double-blind, placebo-controlled, parallel-group phase III study	2009	Epilepsia	98
A4	Eslicarbazepine Acetate (BIA 2-093)	2007	Neurotherapeutics	79
A5	Eslicarbazepine acetate as adjunctive therapy in adult patients with partial epilepsy	2010	Epilepsy Research	70

Table 6 - Five most cited Publications (Bial)

Among this five publications, A1 stand with 612 publications over 9 years. The following graphic shows us the number of citations by year for this particular article.

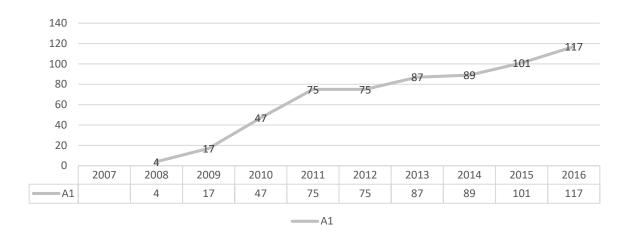


Figure 8 - Citations by year (A1)

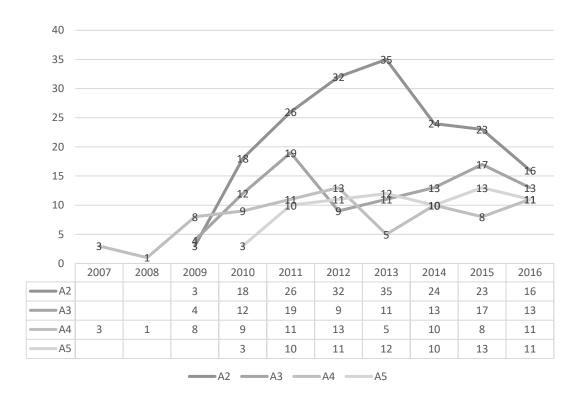


Figure 9 - Citaitons by year (A2, A3, A4, A5)

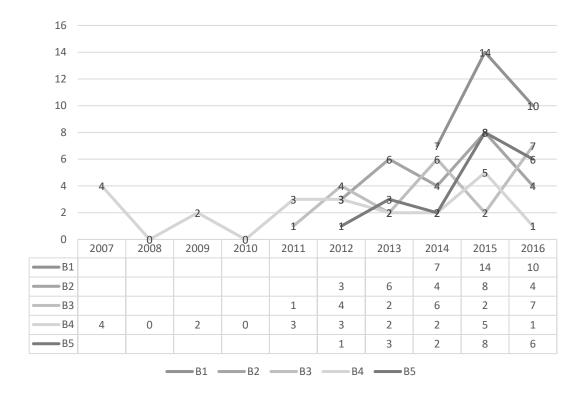
Analyzing figure 9, we can see that A2 was most cited in 2013 (35 citations), A3 was most cited in 2011 (19 citations), A4 was most cited in 2012 (13 citations) and A5 in 2013 (12 citations).

The five most cited articles from Bial were publishes between 2007 and 2010.

### 4.4.2. Bluepharma

Code	Title	Year	Source	Citations
В1	Synthesis of binaphthyl based phosphine and phosphite ligands	2013	Chemical Society Reviews	31
B2	Biodistribution and Photodynamic Efficacy of a Water-Soluble, Stable, Halogenated Bacteriochlorin against Melanoma	2011	ChemMedChem	25
В3	Synthesis and photophysical characterization of a library of photostable halogenated bacteriochlorins: An access to near infrared chemistry	2010	Tetrahedron	22
B4	Thioridazine reduces resistance of methicillin-resistant Staphylococcus aureus by inhibiting a reserpine-sensitive efflux pump	2006	In Vivo	22
В5	Combined effects of singlet oxygen and hydroxyl radical in photodynamic therapy with photostable bacteriochlorins: Evidence from intracellular fluorescence and increased photodynamic efficacy in vitro	2012	Free Radical Biology and Medicine	20

Table 7 - Five most cited Publications (Bluepharma)



Graphic 1 - Citaitons by year (Bluepharma)

The most cited publication (B1) is also the most recent of the five publications selected.

### **4.4.3.** Hovione

Code	Title	Year	Source	Citations
C1	Artery and vein size is balanced by Notch and ephrin B2/EphB4 during angiogenesis	2008	Development	65
C2	In vitro characterization of jet-milled and in-situ-micronized fluticasone-17-propionate	2003	International Journal of Pharmaceutics	51
С3	c-myc in the hematopoietic lineage is crucial for its angiogenic function in the mouse embryo	2008	Development	31
C4	Fundamental analysis of particle formation in spray drying	2013	Powder Technology	29
C5	Organic solvent nanofiltration: A platform for removal of genotoxins from active pharmaceutical ingredients	2011	Journal of Membrane Science	28

Table 8 - Five most cited Publications (Hovione)

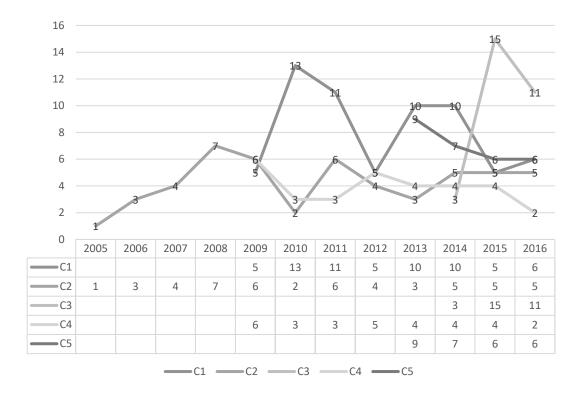


Figure 10 - Citations by year (Hovione)

### 4.4.4. Tecnimede

Code	Title	Year	Source	Citations
D1	Quinolones: Review of psychiatric and neurological adverse reactions (Review)	2011	Drug Safety	50
D2	Assessment of sex differences in pharmacokinetics and pharmacodynamics of amlodipine in a bioequivalence study	2005	Pharmacological Research	27
D3	Results of a single-center, single-dose, randomized-sequence, open-label, two-way crossover bioequivalence study of two formulations of valsartan 160-mg tablets in healthy volunteers under fasting conditions	2009	Clinical Therapeutics	11
D4	Mycophenolate mofetil 500-mg tablet under fasting conditions: Single-dose, randomized-sequence, open-label, four-way replicate crossover, bioequivalence study in healthy subjects	2010	Clinical Therapeutics	10
D5	Bioequivalence study of two formulations of enalapril, at a single oral dose of 20 mg (tablets): A randomized, two-way, open-label, crossover study in healthy volunteers	2004	Current Therapeutic Research - Clinical and Experimental	11

Table 9 - Five most cited Publications (Tecnimede)

The most cited publication from Tecnimede is a Review on Neurological and psychiatric adverse reactions. This review is also the most recent publication of the five mentioned above.

### 4.4.5. AtralCipan

Code	Title	Year	Source	Citations
E1	Development and validation of a method for active drug identification and content determination of ranitidine in pharmaceutical products using near-infrared reflectance spectroscopy: A parametric release approach	2008	Talanta	36
E2	Real time monitoring biomass concentration in Streptomyces clavuligerus cultivations with industrial media using a capacitance probe	2000	Journal of Biotechnology	30
ЕЗ	Evaluation of a new annular capacitance probe for biomass monitoring in industrial pilot-scale fermentations	2005	Journal of Biotechnology	27
E4	The use of NIR as a multi-parametric in situ monitoring technique in filamentous fermentation systems	2008	Talanta	22
E5	Near-infrared reflectance spectroscopy as a process analytical technology tool in Ginkgo biloba extract qualification	2008	Journal of Pharmaceutical and Biomedical Analysis	23

Table 10 - Five most cited Publications (AtralCipan)

Among the five most cited publications from AtralCipan, two of them (E1 and E4) were published in Talanta, and two (E2 and E3) in the Journal of Biotechnology.

#### 4.5. Journals

Scimago Journal Rank scores each journal for its impact in each subject area. Once every journal is classified with a score it is possible to organize them by ranking and divide them in quartiles (percentile 0-25, 26-50, 51-75 and 76-100). In this chapter we did the survey of every journal's quartile, for its' most well classified subject area, and calculated the mean publication quartile for each year per company. The most used journals by each company will be mentioned individually.

For the five selected companies, the quartile was collected for every journal where the company has published any article from 2000 to 2016, except for Bial. Due to the number of Journals where Bial published since 2000, only journals with more than one article or review were considered. All this data can be found in attachment.

### SCImago Journal Rank Quartiles

Company	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Bial	1,0	1,4	1,8	1,8	2,3	2,7	2,0	1,9	1,9	1,9	1,7	1,6	1,7	1,7	1,8	1,8	2,0
Bluepharma	-	-	-	3,0	-	-	2,0	2,0	1,0	1,5	1,5	1,0	1,4	1,2	1,6	1,3	1,6
Hovione	2,0	-	-	2,7	-	2,0	-	-	2,5	-	3,3	2,5	1,0	2,5	1,0	2,2	1,8
Tecnimede	-	-	3,0	-	2,3	2,0	2,0	2,0	2,0	1,5	1,7	1,8	2,0	2,0	1,0	1,0	-
AtralCipan	2,0	1,0	2,0	-	2,0	1,0	1,3	1	1,2	-	3,0	1	1	1,0	1	1	-

Table 11 - SJR mean quartile per year

In the first overview of the previous data, we can notice that, in mean, Portuguese Pharmaceutical Industry most publishes in 2<sup>nd</sup> quartile journals. For Bial, the mean quartile of publication is the 2<sup>nd</sup> since 2006. In this matter, Bluepharma and AtralCipan are the cases that should be highlighted for having, 5 and years publishing in 1<sup>st</sup> quartile journals (in mean) – it must be considered that for AtralCipan in 2 of this years only one article was published.

# Most used journals for each company

Data presented below allow us to make an overview of the most used journals by each company and their current SJR and CiteScore rank to give some additional information on table 11 and respective attachments.

4.5.1. Bial

Journal	Articles	SCImago Journal Rank 2015	CiteScore 2015
Journal of Investigational Allergology and Clinical Immunology	13	0.552	1.22
Epilepsia	11	2.579	4.52
Drugs in R and D	10	0.446	1.56
Epilepsy Research	9	1.026	2.29
Annals of Allergy Asthma and Immunology	7	1.268	1.94
European Journal of Clinical Pharmacology	7	1.096	2.76
Journal of clinical Pharmacology	7	0.972	2.43

Table 12 - Sources (Bial)

## 4.5.2. Bluepharma

Journal	Article s	SCImago Journal Rank 2015	CiteScor e 2015
Journal Of Porphyrins And Phthalocyanines	4	0.437	1.17
Photochemical And Photobiological Sciences	4	0.829	2.4
Chemmedchem	3	1.183	3.00
Journal Of Controlled Release	3	2.827	8.11
Tetrahedron	3	0.991	2.72

Table 13 - Sources (Bluepharma)

## **4.5.3.** Hovione

Journal	Article s	SCImago Journal Rank 2015	CiteScor e 2015
Chimica Oggi Chemistry Today	5	0.247	0.47
Organic Process Research And Development	5	1.411	2.54
Separation And Purification Technology	4	1.100	3.75
Industrial And Engineering Chemistry Research	3	0.976	2.87
Industrial Pharmacy	3	0.126	0.11

Table 14 - Sources (Hovione)

# 4.5.4. Tecnimede

Journal	Articl es	SCImago Journal Rank 2015	CiteSco re 2015
Arzneimittel Forschung Drug Research	19	0.212	N/A
Clinical Drug Investigation	2	0.620	1.79
Clinical Therapeutics	2	0.997	2.65
International Journal of Clinical Pharmacology and Therapeutics	2	0.400	1.23

Table 15 - Sources (Tecnimede)

# 4.5.5. AtralCipan

Journal	Articles	SCImago Journal Rank 2015	CiteScore 2015
Talanta	3	1.233	3.99
Bioprocess Engineering	2	N/A	N/A
Biotechnology and Bioengineering	2	1.633	4.44
Computer Aided Chemical Engineering	2	0.24	0.39
Desalination	2	1.549	4.83
Journal Of Biotechnology	2	1.064	2.87

Table 16 - Sources (AtralCipan)

## 4.6. Affiliations

The affiliations of the authors involved in each company's publication allow us to have an idea of who is collaborating with who. In this chapter, we will analyze the affiliation of the authors involved in each one of the companies' in study publications.

Only affiliations other than the company itself will be mentioned.

## 4.6.1. Bial

Affiliation	Articles or Reviews
Universidade do Porto	88
Universidade de Coimbra	69
Universidade da Beira Interior	24
Universidade de Aveiro	24

Table 17 - Authors affiliations (Bial)

## 4.6.2. Bluepharma

Affiliation	Articles or Reviews
Universidade de Coimbra	82
Uniwersytet Jagiellonski w Krakowie	16
Universidade de Lisboa	15

Table 18 - Authors affiliations (Bluepharma)

# **4.6.3.** Hovione

Affiliation	Articles or Reviews
Universidade de Lisboa	17
Instituto Superior Técnico	9
Instituto de Biotecnologia e Bioengenharia, Lisboa	7
REQUIMTE	6
Universitat Dortmund	6

Table 19 - Authors affiliations (Hovione)

# 4.6.4. Tecnimede

Affiliation	Articles or Reviews
Universitat Autònoma de Barcelona	41
Anapharm Europe S.L.	19
Anapharm, Canada	6
Anapharm	8
Hospital Clinico San Carlos de Madrid	4

Table 20 - Authors affiliations (Tecnimede)

## 4.6.5. AtralCipan

Affiliation	Articles or Reviews
Instituto Superior Técnico	21
Universidade de Lisboa	11
Instituto de Biotecnologia e Bioengenharia, Lisboa	3
Universidade de Coimbra, Faculdade de Ciências e Tecnologia	2
Instituto Nacional de Engenharia Tecnologia E Inovação	1

Table 21 - Authors affiliations (AtralCipan)

The tables presented above strong relation between Blupharma and Universidade de Coimbra and Bial and Universidade do Porto, this values are highly driven by their geographic proximity. We can also notice some collaborations with foreigner Universities and Institutes such as, Anapharm, Universitat Autònoma de Barcelona, Universitat Dortmund and Uniwersytet Jagiellonski w Krakowie. In this field, Among the five companies in this analysis, Tecnimede is the one with more foreigner collaborations.

# 4.7. Authors

# **4.7.1.** Bial

Author	Publications affiliated with the Company	First Affiliation
Soares-Da- Silva, P.	139	Bial, Department of Research and Development, Sao Mamede de Coronado, Portugal
Almeida, L.	65	Universidade do Porto, Department of Pharmacology and Therapeutics, Porto, Portugal
Falcão, A.	58	Universidade de Coimbra, Faculdade de Farmacia, Laboratory of Pharmacology, Portugal
Bonifácio, M.J.	42	Bial, Department of Research and Development, Sao Mamede de Coronado, Portugal
Nunes, T.	40	Bial, Department of Research and Development, Sao Mamede de Coronado, Portugal
Loureiro, A.I.	30	Bial, Department of Research and Development, Sao Mamede de Coronado, Portugal
Wright, L.C.	27	Bial, Department of Research and Development, Sao Mamede de Coronado, Portugal

Table 22 - Authors affiliated with Bial

# 4.7.2. Bluepharma

Author	Publications affiliated with the Company	First Affiliation
Arnaut, L.G.	23	Universidade de Coimbra, Department of Chemistry, Coimbra, Portugal
Simões, S.	22	Universidade de Coimbra, Centro De Neurociencias e Biologia Celular, Coimbra, Portugal
Pereira, M.M.	21	Universidade de Coimbra, Centro de QuImica de Coimbra, Department of Chemistry, Coimbra, Portugal
Dabrowski, J.M.	16	Uniwersytet Jagiellonski w Krakowie, Faculty of Chemistry, Krakow, Poland
Abreu, A.R.	12	Universidade de Coimbra, Centro de QuImica de Coimbra, Department of Chemistry, Coimbra, Portugal
Monteiro, C.J.P.	9	Universidade de Coimbra, Centro de QuImica de Coimbra, Department of Chemistry, Coimbra, Portugal
Cavaco-Silva, P.	8	Egas Moniz - Cooperativa de Ensino Superior, Crl, Caparica, Portugal
Stochel, G.	8	Uniwersytet Jagiellonski w Krakowie, Department of Inorganic Chemistry, Krakow, Poland

Table 23 - Authors affiliated with Bluepharma

# **4.7.3.** Hovione

Author	Publications affiliated with the Company	First Affiliation
Temtem, M.	11	Hovione LLC, , United States
Székely, G.	8	University of Manchester, School of Chemical Engineering and Analytical Science, Manchester, United Kingdom
Heggie, W.	7	Hovione FarmaCiencia SA, Loures, Portugal
Ferreira, F.C.	6	Instituto Superior Tecnico, Department of Bioengineering, Lisbon, Portugal
Pinto, J.F.	6	Faculdade de Farmacia, Universidade de Lisboa, iMed.ULisboa – Departamento de Farmácia Galénica e Tecnologia Farmacêutica, Lisbon, Portugal
Bandarra, J.	5	Hovione FarmaCiencia SA, Loures, Portugal
Gaspar, F.	5	Particle Design, , United States
Sellergren, B.	5	Universitat Dortmund, Faculty of Chemistry, Dortmund, Germany
Duarte, Í.	5	Faculdade de Farmácia, Universidade de Lisboa, Lisbon, Portugal
Santos, J.L.C.	5	Faculdade de Farmácia, Universidade de Lisboa, Faculty of Pharmacy, Lisbon, Portugal

Table 24 - Authors affiliated with Hovione

# 4.7.4. Tecnimede

Author	Publications affiliated with the Company	First Affiliation
Filipe, A.	31	Tecnimede Group, Department of Medicine, Prior Velho, Portugal
Almeida, S.	26	Tecnimede Group, Department of Medicine, Prior Velho, Portugal
Neves, R.	12	Sociedade Técnico-Medicinal, S.A., Department of Medicine, , Portugal
Tanguay, M.	8	inVentiv Health Clinical, Montreal, Canada
Spínola, A.C.F.	8	Tecnimede Group, Department of Medicine, Prior Velho, Portugal
Pedroso, P.	6	Tecnimede Group, Department of Medicine, Prior Velho, Portugal
Almeida, A.	5	Universidade Estácio de Sá, Centro de Ciencias da Saude, Brazil
Trabelsi, F.	5	BioPharma Services Inc., Toronto, Canada

Table 25 - Authors affiliated with Tecnimede

# 4.7.5. AtralCipan

Author	Publications affiliated with the Company	First Affiliation
Cardoso, J.P.	15	Instituto Superior Técnico, Lisbon, Portugal
Menezes, J.C.	13	Instituto Superior Técnico, Institute for Biotechnology and Bioengineering, Lisbon, Portugal
Rodrigues, L.O.	6	Universidade de Lisboa, University of Lisbon, Lisbon, Portugal
Brites Alves, A.M.	5	Instituto Superior Técnico, Department of Chemical Engineering, Lisbon, Portugal
Vieira, L.M.	4	AtralCipan, Castanheira do Ribatejo, Portugal
Barata, P.A.	3	AtralCipan, Castanheira do Ribatejo, Portugal
Martins, J.M.	3	AtralCipan, Castanheira do Ribatejo, Portugal

Table 26 - Authors affiliated with AtralCipan

## 4.8. Drug releases

As R&D is part of the innovation process we believe that there is a possible relation, to be studied, between the number of published articles and the number of released drugs. In order to stablish any relation between publication patterns and marketing authorization we collected all the drugs released by Bial with authorization dates between 01.01.2000 and 31.12.2016.

As Farmacotherapeutic Classification and Active Substance translation needs to be validated this information will be presented in the same language (Portuguese) as the source provides it (http://app7.infarmed.pt/infomed).

Product's Name	Active Substance	Authorization Status	Authorization Date (dd.mm.yyyy)	Farmacotherapeutic Classification
Uroflox	Norfloxacina	Revoked	16/06/2000	Quinolonas
Dormidina	Doxilamina	Revoked	19/09/2000	Ansiolíticos, sedativos e hipnóticos
Cardiol XL	Fluvastatina	Authorized	06/10/2000	Antidislipidémicos
Torasemida	Unat	Revoked	22/12/2000	Diuréticos da ansa
Brisomax Diskus	Fluticasona + Salmeterol	Authorized	06/06/2001	Agonistas adrenérgicos beta - Glucocorticóides
Brisomax Inalador	Fluticasona + Salmeterol	Authorized	30/08/2001	Agonistas adrenérgicos beta - Glucocorticóides
Cefixima	Cefixima Bialfar 100 mg/5 ml pó para suspensão oral	Revoked	15/11/2001	Cefalosporinas de 3ª- geração
Rinialer	Rupatadina	Authorized	08/01/2002	Anti-histamínicos H1 não sedativos
Exxiv	Etoricoxib	Authorized	08/10/2002	Inibidores selectivos da Cox 2

Product's Name	Active Substance	Authorization Status	Authorization Date (dd.mm.yyyy)	Farmacotherapeutic Classification
Tricef 400 mg Comprimido Dispersível	Cefixima	Revoked	29/12/2003	Cefalosporinas de 3ª- geração
Clavamox SR	Amoxicilina + Ácido clavulânico	Revoked	18/05/2004	Associações de penicilinas com inibidores das lactamases beta
Clavamox ES	Amoxicilina + Ácido clavulânico	Authorized	04/02/2005	Associações de penicilinas com inibidores das lactamases beta
Elontril	Bupropiom	Authorized	02/02/2007	Antidepressores
Fovital	Ácido Fólico	Authorized	03/03/2008	Medicamentos para tratamento das anemias megaloblásticas
Fefolato	Ácido fólico + Ferro	Authorized	03/03/2008	Compostos de ferro
Bialminal	Fenobarbital	Authorized	19/06/2008	Antiepilépticos e anticonvulsivantes
Zebinix	Acetato de eslicarbazepina	Authorized	21/04/2009	Antiepilépticos e anticonvulsivantes
Exalief	Acetato de eslicarbazepina	Expired	21/04/2009	Antiepilépticos e anticonvulsivantes
Folicil	Ácido fólico	Authorized	29/04/2009	Medicamentos para tratamento das anemias megaloblásticas
Diadrop	Cloro-hexidina + Benzocaína	Authorized	16/03/2010	De aplicação tópica
Dormidina	Doxilamina	Authorized	22/12/2011	Ansiolíticos, sedativos e hipnóticos

Product's Name	Active Substance	Authorization Status	Authorization Date (dd.mm.yyyy)	Farmacotherapeutic Classification
Yodafar	Iodeto de potássio	Authorized	08/11/2012	Hormonas da tiróide e antitiroideus
Veregen	Extrato seco de folhas não fermentadas de Camellia sinensis	Authorized	27/08/2015	Antivíricos
Ongentys	Opicapona	Authorized	24/06/2016	N/A

Table 27 - Drug information table (Bial)

Comparing the Marketing authorization data and the number of articles or reviews published in the year of authorization we get the following table-

	2000	2001	2002	2003	2004	2002	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Number of Drugs Released (N)	4	3	2	1	1	1	0	1	3	2	1	1	2	0	0	1	1
Number of Articles published (Nu)	5	7	12	17	10	9	8	15	22	19	20	13	19	14	13	25	15
Ratio (N/Nu)	0,8	0,4	0,2	0,1	0,1	0,1	1	0,1	0,1	0,1	0,1	0,1	0,1	-	-	0,0	0,1
Ratio (N/Nu+1)	0,6	0,3	0,1	0,1	0,1	-	0,1	0,2	0,1	0,1	0,1	0,2	-	-	0,1	0,0	-

Table 28 - Ratio between publications and drug releases

Except for 2000 and 2001 we found that, Bial releases about 10 articles or reviews for each drug released- Before this analysis, we expected to find an evident increased amount of publications the year before releasing a drug (to prepare the market) or the year the drug was released, instead of this we found a common ratio between the number of articles published and the number of the drugs released in the same year.

## 4.9. Analysis overview and chapter final notes

Raw data showed us an undoubtedly supremacy of Bial in what concerns number of publications (263 out of 501 - 53%), however, this numbers do not provide, the reader the true scenario as this overwhelming advantage is much influenced by the first years of analysis – from 2000 to 2005 79% of the publications were from Bial, from 2012 to 2016 these numbers drop to 44% as Hovione and Bluepharma, together reach 49% of the publications (23% and 26% respectively).

Despite, in a first moment, collecting every type of publication, the scope of this analysis was only articles or reviews, this way, after excluding all other types of publications, we ended up with 435 documents to be analyzed (87% of the total). At this time it was already possible to see that the bottom 5 companies were too far behind in terms of absolute numbers – only 4,5% of the publications.

In a second analysis, we focused on the impact of the publications and the number of times they were cited. We witnessed some highly-cited documents, which could, by itself, mean the impact and quality of the publication but it is also supported by the SJR mean quartile, where we were able to see that the 5 companies in analysis appear 18 times publishing (in mean) in first quartile journals.

As we believe the quality of the publications is highly influenced by the know-how, we made a short analysis on "who works with who" by making a survey of external affiliations. This data was very important not only to show some international collaborations but also to see that Portuguese pharmaceutical industry manly works with Universities. The personal experience made us raise some questions at this point, as due to regulation it is only possible for companies to fund investigators driven studies, some studies will not appear in our search as there is no affiliation with the company despite the involvement.

The authors were also analyzed in order to have an idea of whether the process of publication was divided in a large team or always centered in the same person. In this analysis we verified that despite having a large poll of authors, some of the analyzed companies have iterant authors like Soares-Da-Silva or Luís Almeida (Bial), Augusto Filipe (Tecnimede) or Luis Arnout (Bluepharma).

#### 5. Conclusions and final remarks

Portuguese pharmaceutical industry is scientifically active. As proposed in the beginning of this thesis, the analyzed data show us that, in opposition to common perception, Portuguese pharmaceutical industry is more than a few production units scattered through Portugal.

The academic output inumbers are not only high but also increasing. The scientific production is not focused only in one company anymore (Bial), and it is possible to identify emerging companies at this level – Bluepharma and Hovione increased from respectively 1% and 6% of the total articles and reviews, between 2000-2005 to 26% and 23% in the last 5 years.

The quality of the publications is growing, and this is corroborated by the increasing number of citations – Bial leads by far the number of citations by year – and the quality of the journals where the documents are published. Analyzing the journals it is also possible to identify some specialization areas for each company – two of Bial's most used journals focus on Clinical Immunology and two others on Epilepsy and Hovione focus its spectrum of publication in pure chemistry and chemistry processes journals.

Also very important is the possibility to identify the usual collaborations for each one of the companies, provided by the author analysis and their affiliation. We were able to find some international collaborations and to identify a scientific network for the Portuguese pharmaceutical industry.

Although it was not the main objective of this thesis, we tried to find some relation between scientific production and product innovation (new drugs approved). Despite not finding any obvious relation between these two scientific performance indicators we think this study should be considered for further analysis.

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Zijlstra, H. et al. 2016. *CiteScore: a new metric to help you choose the right journal.* Available at: <a href="https://www.elsevier.com/authors-update/story/impact-metrics/citescore-a-new-metric-to-help-you-choose-the-right-journal">https://www.elsevier.com/authors-update/story/impact-metrics/citescore-a-new-metric-to-help-you-choose-the-right-journal</a> Accessed: 1st May 2017

#### **Attachments**

### 1. Search Details (Queries)

## **1.1. Bial**

AF-ID ("Bial" 60029357) OR AF-ID ("Bial-Aristegui" 100335431) OR AF-ID ("Laboratory Bial Arístegui" 112571309) OR AF-ID ("Bial Industrial Farmacéutica S-A-" 115058781) OR AF-ID ("Bial-Aristegui" 101236433) OR AF-ID ("Bial-Aristegui Laboratorios" 112699442) OR AF-ID ("Bial-ARISTEGUI- R and D Department" 113076630) OR (---) OR AF-ID ("Bial Laboratory" 101167165) AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "re")) AND (EXCLUDE (PUBYEAR, 1999) OR EXCLUDE (PUBYEAR, 1998) OR EXCLUDE (PUBYEAR, 1997)) AND (EXCLUDE (PUBYEAR, 2017))

#### 1.2. Hovione

AFFIL (hovione ) AND (EXCLUDE (PUBYEAR, 2017) OR EXCLUDE (PUBYEAR, 1999) OR EXCLUDE (PUBYEAR, 1998) OR EXCLUDE (PUBYEAR, 1996) OR EXCLUDE (PUBYEAR, 1994) OR EXCLUDE (PUBYEAR, 1992) OR EXCLUDE (PUBYEAR, 1991) OR EXCLUDE (PUBYEAR, 1988)) AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "re"))

## 1.3. Bluepharma

(AFFIL (bluepharma)) OR (AFFIL (luzitin)) OR (AFFIL (blueclinical)) OR (AFFIL (bsim2)) OR (AFFIL (treat-u)) OR (AFFIL (technophage)) AND (EXCLUDE (PUBYEAR, 2017)) AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "re"))

#### 1.4. Tecnimede

AF-ID ("Tecnimede Group" 60046666) AND (EXCLUDE (PUBYEAR, 2017)) OR EXCLUDE (PUBYEAR, 1998) AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "re"))

## 1.5. AtralCipan

AF-ID ("AtralCipan" 60094265) AND (EXCLUDE (PUBYEAR, 1999) OR EXCLUDE (PUBYEAR, 1997) OR EXCLUDE (PUBYEAR, 1996) OR EXCLUDE (PUBYEAR, 1995) OR EXCLUDE (PUBYEAR, 1983)) AND (LIMIT-TO (DOCTYPE, "ar")) OR LIMIT-TO (DOCTYPE, "re"))

### 1.6. Medinfar

AFFIL ( "medinfar" ) AND ( LIMIT-TO ( DOCTYPE , "ar" ) ) OR LIMIT-TO ( DOCTYPE , "re" ) )

### 1.7. **EDOL**

AFFIL ("EDOL") AND (LIMIT-TO (DOCTYPE, "ar")) OR LIMIT-TO (DOCTYPE, "re"))

## 1.8. Tecnifar

AFFIL ("Tecnifar") AND (LIMIT-TO (DOCTYPE, "ar")) OR LIMIT-TO (DOCTYPE, "re"))

## 1.9. Cell2b

AFFIL ("Cell2b") AND (LIMIT-TO (DOCTYPE, "ar")) OR LIMIT-TO (DOCTYPE, "re"))

### 1.10. Azevedos

AFFIL ("Azevedos") AND (LIMIT-TO (DOCTYPE, "ar")) OR LIMIT-TO (DOCTYPE, "re")

# 2. SJR quartiles

**2.1. Bial** 

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Journal of Investigational	Q	4	3	4	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Allergology and clinical Immunology	N	0	0	0	0	2	0	2	0	1	2	0	2	2	0	1	0	0
Epilepsia	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	N	0	1	0	0	1	0	0	1	0	1	1	0	2	3	0	1	0
Drugs in R and D	Q	4	3	3	4	3	3	3	3	3	3	2	2	3	3	3	3	3
	N	0	0	0	2	0	2	0	0	2	0	1	1	1	1	0	0	0
Epilepsy Research	Q	1	1	1	1	1	1	1	2	2	2	2	1	1	2	2	2	2
	N	0	1	0	0	0	0	0	0	0	0	1	1	0	4	2	0	0
Annals of Allergy, Asthma and	Q	1	1	1	1	1	1	1	1	1	1	1	1	2	1	2	1	1_
Immunology	N	0	0	2	1	0	0	0	1	1	0	1	0	0	0	0	0	1
European Journal of	Q	1	1	2	2	2	1	2	2	1	2	1	1	1	2	1	1	1_
Clinical Pharmacology	N	0	0	0	1	0	0	0	1	3	0	0	0	0	0	1	0	0
Journal of Clinical	Q	1	1	1	1	2	1	1	1	1	1	1	1	1	1	2	2	2
Pharmacology	N	0	0	0	1	1	1	0	0	1	1	0	0	2	0	0	0	0
Allergy: European Journal of allergy and	Q	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1
clinical Immunology	N	0	1	2	0	0	0	0	1	0	0	0	0	0	0	0	1	1_
European Journal of	Q	1	1	1	1	1	1	1	1	2	2	2	1	2	1	2	2	2
Pharmacology	N	1	1	0	1	0	0	0	0	0	0	0	0	0	0	1	2	0
International Journal of Clinical	Q	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3
Pharmacology and Therapeutics	N	0	0	0	0	0	0	0	0	5	1	0	0	0	0	0	0	0

# The scientific performance of the Portuguese pharmaceutical industry

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Journal of Medicinal	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Chemistry	N	0	0	1	0	1	1	1	0	0	0	1	0	0	0	1	0	0
Allergologia et	Q	3	3	4	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Immunopathologia	N	0	0	0	0	0	0	1	2	1	0	1	0	0	0	0	0	0
Biomedical	Q	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3
Chromatography	N	0	0	0	0	0	0	0	1	0	0	1	0	1	0	0	0	1
Clinical Drug	Q	2	2	2	2	3	3	3	3	2	2	2	2	2	2	2	2	2
Investigation	N	0	1	1	1	0	1	0	0	0	0	0	0	0	1	0	0	0
	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2	1
Clinical Therapeutics	N	0	0	0	0	0	0	0	0	0	1	1	1	0	1	0	0	0
	Q	0	0	0	0	0	0	0	0	0	0	3	2	2	2	2	3	2
Immunotherapy	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	2
	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Neuropharmacology	N	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0
A -4- NI1	Q	2	2		2	2	2	2			1		2					
Acta Neurologica Scandinavica	N			2					1	2	1	2		2	2	2	2	2
av : 151	Q	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	1
Clinical Pharmacology in Drug Development	N	0	0	0	0	0	0	0	0	0	0	0	0	0	3	2	3	3
	Q	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2
Drug Metabolism and Disposition	N	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
	Q	0	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0	0
Journal of Separation Science	N	0	3	3	1	1	1	1	1	1	1	1	1	1	1	2	2	2
		0	0	0	0	0	0	0	0	0	0	0	1	0	1	1	0	0
Xenobiotica	Q	2	2	2	1	2	3	3	2	2	2	2	2	2	2	2	2	3

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
	N	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	2	0
Alergologia e	Q	4	4	4	4	4	4	4	4	4	0	0	0	0	0	0	0	0
Inmunologia Clinica	N	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
Bioconjugate	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Chemistry	N	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Biopharmaceutics and	Q	2	2	2	1	1	2	2	2	2	2	2	1	1	1	1	1	2
Drug Dispositon	N	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0
Clinical and	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Experimental Allergy	N	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Clinical	Q	1	1	1	1	1	2	2	1	1	2	2	2	2	2	2	2	2
Neuropharmacology	N	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0
Current Organic	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	3	2
Chemistry	N	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0
	Q	0	3	2	2	2	2	1	1	2	2	2	2	2	2	2	2	1
Epilepsy and Behavior	N	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0
Experimental	Q	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Gerontology	N	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0
Fundamental and	Q	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Clinical Pharmacology	N	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0
	Q	2	2	1	2	1	1	1	1	1	1	2	2	1	1	1	1	1
Hypertension Research	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0
International Archives	Q	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
of Allergy and Immunology	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0

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		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Journal of	Q	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Biotechnology	N	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0
Journal of Chromatography B:	Q	1	1	1	1	1	1	1	1	2	1	1	1	2	2	2	2	2
Analytical Technologies in the Biomedical and Life Sciences	N	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0
Molecular	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1_
Pharmacology	N	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Organic Process Research &	Q	3	2	3	3	2	2	2	2	2	2	2	1	1	1	1	1	1
development	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1
Pharmaceutical	Q	3	3	3	2	3	4	4	3	3	3	3	4	3	3	3	3	3
Medicine	N	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0
Pharmacology and	Q	2	3	3	2	2	2	2	2	2	2	2	2	2	2	2	3	3
Toxicology	N	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Synthetic	Q	2	2	2	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Communication	N	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Total Articles and Reviews		3	5	10	11	6	7	6	8	17	9	12	8	15	12	8	15	9
Mean Quartile by year		1	1	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2

Table 29 - Quartile by journal per year (Bial)

# 2.2. Bluepharma

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Journal Of Porphyrins	Q	1	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2
And Phthalocyanines	N	0	0	0	0	0	0	0	0	0	1	0	0	2	0	0	1	0
Photochemical And	Q	0	0	0	3	2	2	2	2	2	2	2	2	2	2	2	2	2
Photobiological Sciences	N	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	1
Chemmedchem -	Q	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
Chemmedenem	N	0	0	0	0	0	0	0	0	0	0	0	2	0	0	1	0	0
Journal Of Controlled	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Release	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0
Tetrahedron -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2
retraneuron	N	0	0	0	0	0	0	0	0	1	0	1	0	1	0	0	0	0
Biotechnology And	Q	2	1	2	1	2	1	2	2	2	2	2	2	2	2	2	2	3
Applied Biochemistry	N	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0
Cancer Chemotherapy	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
And Pharmacology	N	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0
Free Radical Biology And	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Medicine	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0
International Journal Of	Q	0	3	3	3	2	2	3	3	3	3	2	2	2	2	1	1	1
Molecular Sciences	N	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0
Microbial Drug	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Resistance	N	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0
Plos One -	Q	0	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1
rios One	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
AIDS -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
AlD3	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Advanced Synthesis And	Q	4	4	3	2	1	1	1	1	1	1	1	1	1	1	1	1	1
Catalysis	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Applied Microbiology	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
And Biotechnology	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
BMC Microbiology	Q	0	0	1	2	2	2	1	1	1	1	1	1	1	1	1	1	2

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Biomaterials -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Diomaterials	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Chembiochem -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Chemolochem	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Chemical Society	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Reviews	N	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Chemistry A European	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Journal	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Chinese Journal Of	Q	0	0	0	3	3	3	4	4	4	4	0	0	0	0	0	0	0
Clinical Rehabilitation	N	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Comparative Medicine -	Q	2	2	2	2	2	2	2	2	2	2	2	1	2	1	2	1	2
Comparative Medicine	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Computer Aided	Q	4	3	2	2	2	2	3	2	3	3	3	3	3	3	3	3	3
Chemical Engineering	N	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Current Bioinformatics -	Q	0	0	0	0	0	0	0	0	2	2	3	3	4	3	3	3	4
Current Bioinformatics	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Current Organic Synthesis -	Q	0	0	0	0	0	0	1	1	1	1	1	1	1	2	3	3	3
Current Organic Synthesis -	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Enfermedades Infecciosas	Q	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Y Microbiologia Clinica	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
European Journal Of	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Cancer	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Expert Opinion On Drug	Q	0	0	0	0	0	2	1	1	1	1	1	1	1	1	1	1	1
Delivery	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Green Chemistry -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Green Chemistry	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
In Vivo	Q	1	1	1	1	2	1	1	2	2	2	2	2	2	2	2	2	2
III VIVO	N	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
International Journal Of Pharmaceutics	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Journal Of Biomedical	Q	1	1	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1
Science	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Journal Of Chemical	Q	0	0	0	0	0	0	1	1	1	1	1	1	1	1	1	1	1
Theory And Computation	N	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Journal Of Coordination	Q	2	2	3	3	2	2	2	2	2	3	2	2	2	2	2	2	2
Chemistry	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Journal Of Fluorine	Q	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Chemistry	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Journal Of Generic	Q	0	0	0	0	2	3	3	3	3	3	3	3	3	3	3	3	3
Medicines	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Journal Of Medical	Q	1	1	1	1	1	1	2	1	2	2	1	2	2	2	2	2	2
Microbiology	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Journal Of Molecular	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Catalysis A Chemical	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Journal Of Nanoscience	Q	0	0	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2
And Nanotechnology	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Journal Of Organometallic	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	1	1
Chemistry	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Madahamaan	Q	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1
Medchemcomm -	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Malasslau Mianakialaass	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Molecular Microbiology -	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Nuclear Medicine And	Q	2	1	1	1	1	1	1	1	1	2	1	1	1	1	1	2	2
Biology	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Dhammaaasti aal Dagaarah	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Pharmaceutical Research -	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Progress In Polymer	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Science	N	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Prostate	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

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		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
	N	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Pure And Applied	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Chemistry	N	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Radiation Physics And	Q	3	2	2	2	3	2	2	2	2	2	2	2	2	2	2	2	2
Chemistry	N	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
Revista Portuguesa De	Q	0	0	4	3	3	3	3	4	4	3	3	3	3	3	3	3	3
Pneumologia	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Rsc Advances	Q	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1
RSC Advances	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Trends In Biotechnology	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Trends in Biotechnology	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Wound Repair And	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Regeneration	N	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Total Articles and Reviews		0	0	0	1	0	0	2	1	1	2	2	4	14	6	11	13	12
Mean Quartile by year					3			2	2	1	2	2	1	1	1	2	1	2

Table 30 - Quartile by journal per year (Bluepharma)

# 2.3. Hovione

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Chimica Oggi	Q	3	3	3	3	3	3	3	3	3	3	3	3	3	3	4	3	3
Chemistry Today	N	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	1	1
Organic Process Research And	Q	3	2	3	3	2	2	2	2	2	2	2	1	1	1	1	1	1
Development Development	N	0	0	0	0	0	1	0	0	0	0	0	0	2	1	1	0	0
Separation And Purification	Q	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	2
Technology	N	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1	0	1
Industrial And Engineering Chemistry -	Q	2	2	2	2	1	1	2	1	1	1	1	1	1	1	1	1	1
Research	N	0	0	0	0	0	0	0	0	1	0	0	0	0	0	2	0	0
Industrial Pharmacy -	Q	0	0	0	0	0	0	0	0	0	0	0	4	4	4	4	4	4
industrial i narmacy	N	0	0	0	0	0	0	0	0	0	0	0	1	0	2	0	0	0
Development -	Q	3	3	2	3	2	2	2	2	3	2	2	2	3	2	3	3	3
Development	N	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0
International Journal	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Of Pharmaceutics	N	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
Journal Of Membrane	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Science	N	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0
Powder Technology -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Towder Technology	N	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
ACS Macro Letters -	Q	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1
ACS Macio Letters	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
American Pharmaceutical -	Q	0	0	0	3	3	2	3	2	3	3	2	2	3	2	3	3	3
Review	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Arkivoc -	Q	0	4	4	4	4	4	3	4	3	3	3	3	3	3	4	4	4
Aikivoc	N	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Chemical Reviews -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Chemical Reviews	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Chemical Week -	Q	4	3	3	4	3	3	4	3	4	4	4	4	4	4	4	4	4
Chemical Week	N	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Chimica Oggi	Q	3	3	3	3	3	3	3	3	3	3	3	3	3	3	4	3	3

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
	N	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Cleanroom	Q	3	0	3	4	4	4	4	4	4	4	4	4	4	4	4	4	4
Technology	N	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Computer Aided	Q	4	3	2	2	2	2	3	2	3	3	3	3	3	3	3	3	3
Chemical Engineering	N	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
Data In Brief -	Q	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	2
	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Drug Development And Industrial -	Q	2	2	2	2	2	2	3	2	2	3	2	2	2	2	2	2	2
Pharmacy	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Drug Testing And	Q	0	0	0	0	0	0	0	0	0	0	2	1	1	1	1	1	1
Analysis	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
European Journal Of Pharmaceutical -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Sciences	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Green Chemistry -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Green Chemistry	N	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Journal Of	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Chromatography A	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Journal Of Pharmaceutical And	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Biomedical Analysis	N	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Journal Of	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Supercritical Fluids	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Pharmaceutical	Q	3	4	3	3	2	2	3	3	3	3	3	3	3	3	3	3	4
Engineering	N	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Pharmaceutical Manufacturing And -	Q	0	0	0	0	0	0	0	0	0	0	4	4	4	4	4	4	4
Packing Sourcer	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Pharmaceutical	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Research	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Pharmaceutical	Q	2	2	2	2	2	2	2	2	3	2	2	2	2	2	2	3	3
Technology	N	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Pharmacopeial Forum	Q	1	2	2	1	2	2	2	2	2	1	1	1	1	3	3	2	2

# The scientific performance of the Portuguese pharmaceutical industry

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Total Articles and			0	0	2	0		0	0		0	2	2	7	0	í		0
Reviews  Mean Quartile by		1	0	0	3	0	1	0	0	4	0	3	2	/	8	6	5	9
year		2			3		2			3		3	3	1	3	1	2	2

Table 31 - Quartile by journal per year (Hovione)

# 2.4. Tecnimede

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Arzneimittel Forschung	Q	1	1	1	1	2	2	2	2	2	2	2	2	2	2	2	3	2
Drug Research	N	0	0	0	0	2	4	3	1	4	0	2	2	1	0	0	0	0
Clinical Drug	Q	2	2	2	2	3	3	3	3	2	2	2	2	2	2	2	2	2
Investigation	N	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0
Clinical Therapeutics -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	2	2	2	1
Chinical Therapeutics -	N	0	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0
International Journal Of Clinical Pharmacology	Q	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	3
And Therapeutics	N	0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0
Current Therapeutic Research Clinical And	Q	2	3	2	2	3	3	3	3	3	3	3	3	3	3	3	2	2
Experimental	N	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
D D	Q	1	1	1	1	2	2	2	2	2	2	2	2	2	2	2	3	2
Drug Research	N	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Down Cafeton	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Drug Safety -	N	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
European Journal Of Drug Metabolism And	Q	3	3	3	3	3	3	3	3	3	3	3	3	3	2	3	3	3
Pharmacokinetics	N	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Journal Of Biotechnology -	Q	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Journal Of Biotechnology	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Journal Of Inclusion Phenomena And	Q	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	3	2
Macrocyclic Chemistry	N	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Journal Of	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Psychopharmacology	N	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Dharmanalagiaal Dasaarah	Q	2	2	2	2	2	2	1	2	1	1	1	1	1	1	1	1	1
Pharmacological Research -	N	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Total Articles and Reviews		0	0	1	0	3	5	3	1	5	2	3	6	1	1	1	1	0
Mean Quartile by year				3		2	2	2	2	2	2	2	2	2	2	1	1	

Table 32 - Quartile by journal per year (Tecnimede)

# 2.5. AtralCipan

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Talanta -	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
тапапта -	N	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0
Diammanaga Empiroprima	Q	2	3	2	3	2	3	3	2	2	2	2	2	2	2	2	2	2
Bioprocess Engineering -	N	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Biotechnology And	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Bioengineering	N	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Computer Aided	Q	4	3	2	2	2	2	3	2	3	3	3	3	3	3	3	3	3
Chemical Engineering	N	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0
Desalination -	Q	1	1	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Desamation	N	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Journal Of	Q	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Biotechnology	N	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
Arkivoc -	Q	0	4	4	4	4	4	3	4	3	3	3	3	3	3	4	4	4
AIRIVOC	N	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
Dietachmala ay Dua anasa	Q	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Biotechnology Progress -	N	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
Chemical Engineering	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Science	N	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Chemometrics And Intelligent Laboratory	Q	1	1	1	1	1	1	1	1	1	1	2	2	1	1	1	2	2
Systems	N	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
T.i	Q	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Idrugs -	N	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
Industrial And Engineering Chemistry -	Q	2	2	2	2	1	1	2	1	1	1	1	1	1	1	1	1	1
Research	N	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Journal Of Pharmaceutical And	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Biomedical Analysis	N	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
Journal Of Supercritical	Q	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Fluids	N	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
	Q	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	2

Separation And Purification Technology	N	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total Articles and																		
Reviews		4	1	1	0	2	3	3	0	6	0	1	0	0	1	0	0	0
Mean Quartile by year		2	1	2		2	1	1		1		3			1			

Table 33 - Quartile by journal per year (AtralCipan)