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The Brazilian phytotherapics industry: challenges and opportunities

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Abstract *The purpose of this article is to discuss and analyze the development challenges of the medicinal plants and phytotherapics industry in Brazil. This industry represents an excellent alternative to face the paradox of abundance that exists in the health area. The methodology adopted was a field research, using semi-structured questionnaires with companies, researchers and public managers to evaluate their development between 2009 and 2015 and to point out the most serious problems faced. The results observed indicate that the main challenges found were the regulation of law on the access to the genetic patrimony in the research area, and to bring into harmony the rules in the entire chain of medicinal plants and phytotherapics production area. The slow implementation pace of public policies for the industry shows a setback regarding both productive and research activities with medicinal plants and phytotherapics in the period.*

Key words *Medicinal plants, Phytotherapics, Industry, Regulation, Access to genetic patrimony*

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Introduction

In the XXI century a paradox of abundance is faced in the health area. The knowledge acquired in science and technogy are enormous and fast, offering endless technological possibilities to deal with all forms of diseases. However, not always these possibilities have been utilized to improve the access of populations to drugs with very high prices and not consistent with the health budgets of both developed and developing countries.

The question to be asked and that was also the object of the "Sustainable Development Objectives", especially the goals to be attained before 2030[1], is how to ensure the access to safe, effective, quality drugs and compatible prices to all. The medicinal plants and phytotherapics industry may represent an excellent alternative to answer the above question. On one side, it constitutes an important source of innovation in health and can strengthen local production and innovation based on the exploitation of the rich Brazilian biodiversity. On the other side, this represents the possibility to expand the therapeutic options offered to the users of SUS – (The Public Health System), envisaging the improvement of health attention and social inclusion.

However, according to Hasenclever[2], there are challenges for its full development in Brazil. The greatest of them, on the side of offer, is the construction of a regulatory framework capable of bringing together the interests of an extensive productive chain, from the cultivation of plants, the sustainable handling, the research and development (R&D), the production, distribution and use of medicinal plants and phytotherapics. On the side of demand, the greatest challenges are: the definition of sufficient elements of products characterization (forms of presentation, dosage, etc.) published in the *National List of Medicinal Plants and Phytotherapics*; and the purchase of these drugs by the SUS system.

This article presents the partial results of an on-going research (support by CNPq - *National Council of Scientific and Tehnological Development*), which deals with an updated industry diagnosis and the examination of its evolution from 2009 to 2015, focusing upon the present challenges on the side of offer.

The phytotherapics industry is an industry undergoing full development in the world and may represent an opportunity to develop the pharmaceutical sector in Brazil. This is important not only due to our natural biodiversity wealth, but also due to the traditional and scientific knowledge acquired about the biological activity of these plants by our society and science & technogy institutions – ICTs[3]. It is expected that a contribution can be made about the critical points concerning the industry development of medicinal plants and phytotherapics in Brazil.

The article is organized in three sections, besides the introduction and final considerations. In the first section, the research methodology is presented, in the second, the main results are described and, finally, in the third section, the results are discussed in the light of the existing pertinent literature.

Methodology

This is a research of a qualitative and exploratory nature based on interviews and conducted with actors involved in companies, ICTs and in the public administration. The interviews were carried out by utilizing semistructured questionnaires between May and October of 2015, containing issues on: the characteristics and general information about companies and ICTs; R&D and biodiversity, forms and intensity of market competition among companies and the relationship ICT - company; the aspects concerning the production of items for research and production of phytotherapics; and aspects related to the institutional framework (regulation, patents and public policies). The quantitative results were tabulated on *excel* spreadsheets and the open questions were utilized to interpret the quantitative results.

The main questions to be answered are: (i) what are the main obstacles for a better adjustment effort of ICTs and companies both for production and innovation; (ii) what are the main reasons for the importation of industrial items for research and the production of phytotherapics; (iii) to what extent the present status of regulation for research and production of phytotherapics is or is not adequate; (iv) what are the problems and difficulties found by public managers for the implementation of government policies.

Identification and Selection of Actors

The list of medicinal plants and phytotherapics registrations of ANVISA – *National Agency of Sanitary Surveillance* was considered as a *proxy* to outline the national market configuration for the sector. This list contained 727 registrations.

Board of Directors Resolution (RDC) number 26 of 5/14/2006[4], which permitted the registration of traditional products has added another 35 registrations to this list, totalling 762 registrations held by 166 companies. However, it has been observed that only 212 products held by 67 companies had valid registrations in 2015.

Based on the companies' websites it has been observed that 25 companies had been acquired or embodied by other 16 larger companies, between 2009 and 2015. This represented a reduction of 15% of the universe of companies acting in the medicinal plants and phytotherapics industry, leaving 41 companies out. Of these, 18 companies have been interviewed, 43% of the universe existing in 2015.

ICTs sampling was obtained from the consultation made to the *List of Research Groups* of CNPq. To this effect, the Census of 2010 and the analysis unit "company/group" were utilized, besides a filter of the company's performance. A total of 137 research groups acting with companies in the division was obtained, and 18 companies that had registrations for medicinal plants and/or phytotherapic drugs were identified. During this phase of the research, five ICTs were interviewed: *Federal University of Minas Gerais* – UFMG, *Federal University of Pará* – UFPA, *Anhanguera University of S. Paulo* – UNIAn, *Federal University of Amazonas* – UFAM, *Paulista State University "Julio de Mesquita Filho"* – UNESP Araraquara; and 14 persons responsible for the research groups, for the NITs (*Technological Innovation and Technology Transfer Nucleus)* and for the incubators (they are identified in the following as researchers).

The public administrators were identified by their importance to carry out the policies in question. A total of 10 public administrators, acting in the Ministry of Health (*Secretariat of Science, Technology and Strategic Products* – SCTIE and others), Anvisa, CNPq, CGEN (*Council of Access to Genetic Heritage*), state foundations for research support, among others.

Therefore, the results of this research are still partial and should not be taken as a representative sample of the universe of companies with active registrations at Anvisa, nor of researchers, NITs and public administrators involved. However, one believes that the disclosure of these results brings an excellent contribution to the need to improve public policies and to foster the medicinal plants and phytotherapics industry.

Results

When comparing the 2009 registration list of phytotherapic products with that of 2015, it can be observed that there are some significant differences, showing a general evolution trend of the market in Brazil. In fact, there was a drastic reduction of 72% in the number of registrations.

In 2009, the list of companies holding these registrations comprised 166 companies with a very uneven national distribution. Only in the State of S. Paulo, there was a concentration of 36% of companies and, in the Southeast region, of 60%. In 2015, the number of companies was of only 40.4% of the number of companies registered in 2009 (67 companies). Besides, the national configuration had changed, in spite of the State of S. Paulo's leading position in the number of registrations (40.6%), there was an increase in the concentration of companies in the Southern states of the country, going from 23.5 to 26.9% in total participation, while the number of registrations held by these companies increased from 33.3 to 37.7%. On the other hand, the companies located in the States of Amazonas, Ceará, Maranhão, Paraíba and Roraima no longer held registrations. This result was very unbalanced, considering the distribution of vegetal species by the Brazilian biomes. In fact, the Northern region, known by its biodiversity, in 2009, counted only with approximately 2% of companies and 1.4% of registrations, and did not participate in the list of registrations of 2015.

In 2015, the first 10 companies, among 67, concentrated 52.8% of registrations, while the first 20 companies reached a concentration of 72.6% of registrations, in accordance with Table 1. In respect of the survey carried out in 2009, the first 10 companies held only 28.2%, while the first 20 held 41.6% of registrations. These percentages indicate that there was a greater concentration in the number of registrations in a smaller number of companies, indicating that there was a consolidation of companies in the industry.

In fact, Chart 1 shows the 16 companies that acquired another 25 companies in the industry. The capital of 10 of the 16 acquiring companies was of foreign origin, demonstrating the attraction this market represents for multinational companies. Among those of private capital of national origin, those are presenting a growth strategy in this market, both *Aché Laboratory* and *Hypermarcas,* which acquired three companies each, can be pointed out.

Table 1. The 20 main companies in the medicinal plants and phytotherapics industry by number of registrations, 2009/2015.

20 Top companies	N. registrations			
	2015		2009	
	N.	%	N.	%
Herbarium Laboratório Botânico Ltda	28	13,2	61	8,0
Ativus Farmacêutica Ltda	19	9,0	34	4,5
Bionatus Laboratório Botânico Ltda	10	4,7	16	2,1
Aché Laboratórios Farmacêuticos S.A	9	4,2	11	1,4
Laboratorio Quimico Farmaceutico Tiaraju Ltda	9	4,2	15	2,0
Mdcpharma Produtos Farmacêuticos Ltda	9	4,2	15	2,0
Laboratório Vitalab Ltda	8	3,8	17	2,2
Laboratorio Catarinense As	7	3,3	18	2,4
Pharmascience Laboratórios Ltda	7	3,3	13	1,7
Kley Hertz S/A Indústria E Comércio	6	2,8	15	2,0
Marjan Indústria E Comércio Ltda	6	2,8	12	1,6
Orient Mix Fitoterápicos Do Brasil Ltda	6	2,8	22	2,9
Farmácia E Laboratório Homeopático Almeida Prado Ltda	5	2,4	9	1,2
Luper Indústria Farmacêutica Ltda	5	2,4	19	2,5
Nycomed Pharma Ltda.	5	2,4	8	1,0
Biolab Sanus Farmacêutica Ltda	3	1,4	9	1,2
Cimed Indústria De Medicamentos Ltda	3	1,4	8	1,0
Laboratório Farmacêutico Vitamed Ltda	3	1,4	6	0,8
Laboratorio Wesp Ltda	3	1,4	3	0,4
Laboratórios Klein Ltda	3	1,4	6	0,8
Total registrations of 10 Top	**112**	52,8	**215**	28,2
Total registrations of 20 Top	**154**	72,6	**317**	41,6
Total registrations other companies (47 in 2015 and 146 in 2009)	**58**	27,4	**445**	58,4
Total registrations	**212**	100,0	**762**	100,0

Source: Prepared based on data from Anvisa.

The company with a larger number of registrations in 2015 continued to be *Herbarium Laboratório Botânico Ltda.*, with 28 registrations, representing 13.2% of the total, as per Table 1. However, even the leading company in the number of registrations has reduced the number of registrations by more than fifty percent as compared to 2009.

To sum up, it can be observed that the new configuration of the medicinal plants and phytotherapics industry is completely different from that of 2009. It shows a larger concentration in a small number of companies, but the number of registrations was reduced by two-thirds as compared to what it was before.

Profile of companies and ICTs interviewed

Almost all 18 companies interviewed hold private capital of national origin (17 companies). Most of them are medium-size companies (44%), indicated by the number of employees, and 2/3 are final products manufacturers. This is an interesting point since as they are not 'vertical' companies, most of them have reported relationship problems with their suppliers. On the other hand, this may be reflecting the difficulties of production, pointed out by the interviewees, both due to obstacles found in the bureaucratic process to access the genetic patrimony and to the absence of qualified agriculturists in the plantations capable of maintaining the quality of plants (nonuse of pesticides, correct harvesting time, etc.)

Another measure of size investigated was the annual sales revenue. Most part (69%) of companies' revenue is over 10 millions, being seven of them (44%) over 50 millions. However, it is important to point out that only in two companies the percentage represented by phytotherapics in this revenue is over 5%. That is, the major parts of the companies interviewed do not have their

Chart 1. List of acquiring and acquired companies in the period 2009-2015.

Acquiring Company (16 companies)	Company Acquired (25 companies)
Aché (N)	Asta Médica Ltda
	Biosintética Farmacêutica Ltda
	Merck S/A
Valeant (E)	Bunker Ind Ftca Ltda
	Instituto Terapeutico Delta Ltda
Laboratório Saúde (N)	Laboratorio Quimsul Ltda
	Laboratório Sanifer Sa
Hypermarcas (N)	Barrenne Indústria Farmacêutica Ltda
	Dm Indústria Farmacêutica Ltda
	Luper Indústria Farmacêutica Ltda
Takeda Pharmaceutical (E)	Multilab Indústria E Comércio De Produtos Farmacêuticos Ltda
	Nycomed Pharma Ltda.
Pfizer (E)	Wyeth Indústria Farmacêutica Ltda
	Laboratório Teuto Brasileiro S/A
Aspen Pharma (E)	Infabra Industria Farmaceutica Brasileira Ltda
	Cellofarm Ltda
Avert Laboratórios (E)	Zurita Laboratorio Farmacêutico Limitada
Franchel Cosméticos (N)	Sauad Indústria Farmacêutica Ltda
Nikkho (E)	Ativus Farmacêutica Ltda
Natura (N)	Flora Medicinal J Monteiro Da Silva Ltda
Johnson & Johnson (E)	Janssen-Cilag Farmacêutica Ltda
Abott (E)	Knoll Prods Quims Farmaceuticos Ltda.
Sanofi Aventis (E)	Medley S/A Indústria Farmacêutica
Servier Laboratories (E)	Perflora Industria Farmaceutica Ltda
Novartis (E)	Sandoz Do Brasil Indústria Farmacêutica Ltda

Source: Research on companies' websites.

core business based on phytotherapics, which seems to be the rule in this market.

Since the prices in this sector are not regulated by Anvisa, most companies (five) regulate their prices at the level of the IPCA (*Index of Prices to the Consumer)* or above (four companies). However, one company tries to follow the official índex of readjustment for allopathic products.

Most companies do not export (10) and those that do it, export a percentage (1 company) or less (3 companies) equal to 20% of the total production. The internal market consists in the main destination of phytotherapics production, especially the private market. In fact, none of the companies interviewed stated to be a supplier of the SUS system, even if there is a National Policy to encourage the use of phytotherapics in the System[5,6].

Among the ICTs interviewed, there are four public, being three of them federal and one state, and one private, only this last one lacks a structured NIT. The four public ICTs have very differentiated NITs, as legal entities or not, with the objective of managing the institutional innovation policy based on the creation of the Innovation Law. The competences and responsibilities of these structures are basically to oversee and to follow up on the institutional policy of encouragement to the protection of creation, licensing, innovation and other forms of technology transfer.

As to the researcheres's area, out of a total of 11 respondents, over 70% were involved in Ethnobotany and/or Phytochemistry, and the others in Pharmacology and/or Synthetic Chemistry. The main activity conducted by the researchers was applied research. Other less relevant activities are basic research, development and consultation.

Biodiversity is utilized by most interviewees but in different forms: examination of the plant's activity for a specific disease and its toxicity; the analysis of the knowledge of people about plants and related diseases; prospection of amylase and expression of target molecules; survey and char-

acterization on medicinal plants, and artisanal drugs; analysis, physical or chemical and forms of use of plants, vegetal material, vegetal drug, and substances in general; detection of the biological activity of extracts of plants and fungi; recuperation of traditional information on plants.

Characteristics of research, production and competition

Among the companies interviewed, most of them (94.4%) conduct R&D activities and a little over half of them (54%) utilize Brazilian biodiversity. For this, five companies use the biodiversity genetic patrimony, three companies only have access to it and two companies collect it. Most companies interviewed (10) use intellectual protection of new processes and products. Nine companies have filed at least one patent request between 2003 and 2013, most of them under their own title. Several problems with Anvisa, CGEN and the INPI (*National Institute of Industrial Property*) have been mentioned in the conduction of R&D activities.

As to the R&D activities carried out by the ICTs, 63% of them were involved in biodiversity collection and/or access to the biodiversity genetic patrimony, while 45%, even if not involved in the collection of genetic material, have also declared its use. Surprisingly, 27% had no interaction with the CGEN. In spite of most groups being devoted to applied research, only two researchers mentioned specific therapeutic classes in the execution of their work, i.e. leishmania, malaria (neglected diseases) and cancer.

The main source of raw material to carry out R&D activities at the ICTs is preponderantly of national origin. The national vegetal drug is utilized by 45.5% of the interviewees, while only 9.1% import it. As to the national vegetal derivative, it is utilized by 36.4% of researchers, while none of them utilizes that of foreign origin. Based on these results, it is possible to draw a parallel about companies mostly utilizing foreign raw material, which may indicate a lack of concern on the part of researchers with the regulatory standards required for the development of products or an obstacle to a greater use of Brazilian biodiversity.

The main activity segment in which the responder companies are involved is the production of phytotherapics (11 companies), three of them only manufactured materials and two produced both the materials and the final product. The most frequent therapeutic classes are laxatives and digestives. In average, each company is specialized in one or two thereapeutic classes. Only four companies have more than one productive unit, being 1.4 the average of productive units among the 18 companies analyzed.

According to the inteviewees, the relationship with suppliers can be different in several ways, which permits to obtain an absolute number of replies above the total number of companies interviewed. The results demonstrate that the relationship beween suppliers and phytotherapic manufacturers is predominantly made through purchase and sale (14 companies), confirming the absence of companies' verticalization, already observed before, and the predominance of nonlasting contract relations. Secondly, joint development partnerships with the suppliers are pointed out (seven companies) and, finally, purchase and sale partnerships established in long duration contracts (two companies).

ICT's production activities are different in nature: 36% refer to researches made with the phytotherapic traditional product and 27% with the phytotherapic drug. This shows that applied research activities aim mostly at identifying the activity of plants and not their use as development models of synthetic products, production of extracts or phythotherapic drugs. This point immediately indicates that there is a huge distance beween research developed at ICTs and companies.

When asked about their perception on the relative size of their companies as compared to their competitors, eight companies considered themselves smaller, five of them of equal size, and five of them larger. In what respects the prices differential in relation to their competitors, the answers were distributed differently as to the relative size of their competitors. Eight companies considered their prices above those practiced by their competitors, seven of them equal and two companies considered their prices smaller than those of their competitors. These results can indicate an inverse relation between the company size and the prices practiced. This aspect would evidence that the use of scale economy is a necessary condition for average unitary costs reduction and lower prices of phytotherapic drugs.

The types of adjustments that exist between companies and ICTs have been separated by universities and research centers. The most frequent relations encountered with the universities concern the rendering of services (75%) and joint research projects (53.8%). In third place, one can mention the presence of research activities made

Ciência & Saúde Coletiva, 22(8):2559-2569, 2017

by order (23.1%). As to the adjustments between companies and research centers, once again activities of research (55.6%) and joint research projects (44.4%) stand out. As for research work orders and technology transfer, each one was pointed out by 22.2% of the interviewees.

The NITs represent the most important means of relationahip of ICTs with the companies. During the interview with their managers several tpes of difficulties concerning interaction have been reported. One of the NITs mentioned that this is a timid and slow process and that its activity is being carried out by specific research groups and postgraduation programs, besides the participation of companies in institutional events. Another NIT pointed out that in spite of receiving several proposals from the companies, the problems related to its own institutional model do not permit the fostering of operations defined in the Innovation Law, thus making it difficult the interaction with companies.

Institutional Framework

The activity conducted by companies and ICTs with the organizations involved in the regulation of research and production in the medicinal plants and phytotherapics area is very distinct. The companies have been unanimous in confirming that they knew and maintained activities with Anvisa. Besides, about 70% of them already knew and had worked with both INPI and CNPq. On the other hand, the institutions that some companies did not know were: *National Defense Council* – CDN (43%), *Chico Mendes Institute for Biodiversity Conservation* – ICMBio (14%) and *Research Ethics Committee/National Research Ethics Commission* – CEP/CONEP (7%). Approximately 20% to 40% of the companies stated that they knew but never had interaction activities with the following institutions: *Brazilian Environment Institute and Renewable Natural Resources* – Ibama, *National Indian Foundation* – Funai, *Navy, CGEN and National Historic and Artistic Patrimony Institute* – IPHAN.

In the case of ICTs, in general, the NITs are the agents responsible for operations with the competent institutions to support researchers in the R&D process involving biodiversity. CBN and Navy are known but not much utilized. The following institutions have stronger operation links: ICMBIO, IPHAN and CEP/CONEP. The four NITs interviewed do not carry out activities with CNTBio and Anvisa. As to CNTBio, the process held with the Commission is conducted by the researcher, what can explain NITs' absence. In respect of Anvisa, this can be explained by the fact that ICTs do not act in the production but in R&D activities.

The NITs totally act in conjunction with Funai, Ibama, CGEN and INPI. The activity with Funai resulted from specific and particular cases. CNPq's platform was praised by everyone. Also, the difficulties found by researchers have been reported, especially the oldtimers, to understand the legislation to access biodiversity, mainly concerning CGEN and Ibama, that were fined for not complying with the legislation.

There is no specific guideline in the NITs to act with the indians and traditional societies, even when these are located in the Amazon region. This point shows how neglected is the opportunity to insert biological diversity of fauna and flora in the traditional scientific research knowledge.

As to the regulation issue, the lack of standard practices in the concentration degree of extracts and the absence of a clear and specific norm for control and supervision of vegetal species utilized in the manufacture of phytotherapics were pointed out. This is the main difficulty encountered in the relationship maintained with the suppliers. As a result, the companies have to perform two analyses in each purchase, initially in the sampling and then in the delivery of product. The norm of Anvisa focuses on the quality of final products and not on that of suppliers, what makes final products manufacturers responsible for this control due to the low quality of products and the sector's nonregulation.

Besides, there is an uncertainty as to the existing norms that are frequently changed and are not considered with the same severity by the whole of responsible analysts who lack the necessary technical qualification for this fuction. Thus, regulation is considered as one of the main obstacles in this sector. For example, one of the companies mentioned that the creation of the *National Fund of Biodiversity* causes an enormous concern due to the possibility of resources curtailment. Another company stated that there is no knowledge of all norms and procedures to comply with regulatory requirements, even concerning medium size and high income companies.

In what respects regulation and the NITs, the problems pointed out refer to the lack of clarity found in the legislation and in the administrative formalities of CGEN. As a result, one of the interviewees mentions that, in general, research starts before autorization is granted. Besides, of

course, the total absence of motivation found on the part of researchers, who are permanently struggling to find out how to fit into the confused legislation. Such problems confirm a fragile institutional condition and legal insecurity in R&D involving biodiversity.

As to the contribution of the NITs in the preparation of Law number 13.213[7], approved in May of 2015, dealing with the access and use of biodiversity and associated traditional knowledge, this was created by the *National Forum of Innovation and Transfer of Technology Managers.* However, it was considered that the final legislation did not contemplate in special the questions involving the traditional communities. Besides, another point raised was the importance of withdrawing from ICTs some of the obligations that are not their responsibility, such as the partition of benefits, releasing the institutions from a heavy bureaucratic burden.

On the other hand, questions that may hinder or harm the advancement of legislation have been reported: conflicting problems due to the indefinition of biological and legal concepts, questions related to the indians and to the associated traditional knowledge, besides some legal foresights that are far from the practical reality of institutions and traditional communities.

The use of intellectual protection in the development of new products and processes is practiced by 53% of the companies interviewed, while 50% of the companies use patents database or another database for research or identification of the technology sought. In the period of 2003 to 2013, 56% of the companies have filed some patent requests, totalling 26 requests. Among those, 82% owned the patent title and 54% were not involved with any type of partner in the patent development. Only two companies interviewed (13%) have pending patent filings since they did not have previous approval from CGEN.

In accordance with the companies and ICTs interviewed, among the main reasons for the low number of existing Brazilian patents of products obtained with native plants are: the inadequate regulation and methodology of Anvisa and the inefficiency of CGEN and INPI. In a general manner, there is a lack of strategic view, with the absence of investment and financing on the part of the government and an insufficient joint effort among universities, companies and development and regulation organs. One of the companies stated that the main obstacle encountered for the development of phytogherapics based on Brazilian biodiversity is the bureaucracy for the creation of partner agreements with public institutions. On the other hand, ICTs main complaint refers to the functioning of NITs that are not prepared to meet the requirements involved in the writing of patents and their appropriate trading.

However, all the NITs suggest the use of intellectual property in the R&D strategies of ICTs to which they are connected. They also use patents database or another database for research or identification of technology of their interest. To this effect, they utilize predominantly a free of charge database, such as USPTO, Spacenet, Derwent, with the exception of a NIT with Thomson Innovation access.

As to the filing of patents, all the interviewees state that they have filed at least one patent request based on biodiversity between 2003 and 2013. Two NITs had two patent filings turned down for not presenting the required previous authorization from CGEN. The difficulties pointed out have discouraged the researchers to file patent requests, even if these aspects, in the interviewees' opinion, had no negative influence on the research activity of the ICTs.

Among the companies (14) that have evaluated the new Anvisa regulation on phytotherapics, especially RDC number 26/2014[4], there was a positive perspective in 72% of the cases, 29% have evaluated negatively the change in regulation, and the others declared it was not possible to evaluate it yet.

Concerning Law number 13.123/2015[7], all the companies that use biodiversity in their R&D activites or as a source of raw material have positive perspectives as to its functioning after regulation, but one of the companies fears a greater facility of foreign access to the national genetic patrimony. The regulation of Law was enacted on May 11 of 2016 by Decree number 8.772[8].

The companies interviewed understand that public policies for the phytotherapics segment are inadequate, because they are unable to correct the regulatory problems involved in the sector. As mentioned by one of the companies, the problems are of a structural nature and their solution would require an integrated action on the part of companies, universities, development and regulatory organs. An agile, flexible and long term government strategy is most needed. However, no change in this situation is expected in Brazil.

As far as support actions from municipal or state governments to R&D involving the phytotherapics sector are concerned, all the interviewees both in the companies and ICTs stated they had no knowledge of specific official notices

issued for the area, especially municipal notices. However, state support to initiatives in the pharmaceutical area are reported, in a broad form, through the proposition of local productive arrangements or postgraduation programs of a regional scope. There are also support actions devised to structure the NITs, on the part of state foundations for research support, either with activity-based costing or professional scholarships.

Discussion of results

Between 2009 and 2015, a new and more concentrated design of the medicinal plants and phytotherapics industry has been observed, with a smaller number of companies and a reduction of two-thirds in the number of registrations. Most companies interviewed are not 'vertical' companies and have to purchase products for their manufacturing operations. This production with the necessary quality for research and manufacture of drugs in the country is practically non-existent. These results have been evidenced by previous studies conducted by Rodrigues and Nogueira[9] and Hasenclever[2], and also by a more recent study by Alves[3].

The role played by Anvisa in 2004 was a little drastic as regards the adaptation of companies and, afterwards, it proved to be too slow to correct the balance needed between quality in health and local industry development. This can be demonstrated by the elapsed period of ten years between RDC publication number 48/2004[10], that levelled phytotherapics and drugs, requiring clinical tests for their registration, and RDC number 26/2014[4], that broadened industry definition to include traditional products that are confirmed by usage. Besides, there are still flaws in the regulation about compliance issues with the regulatory standards to be adopted concerning raw material. The solution adopted has been the importation of products, both transformed and *in natura,* as evidenced in this recent research conducted in the companies and previously pointed out by Hasenclever[2].

Some obstacles have been found in the bureaucratic process involving access to the genetic patrimony that disencourages biodiversity research. This problem jams the patent analysis process because, as mentioned, the researchers start their research work without the proper authorization and the request remains pending at INPI. However, both companies and ICTs interviewed reported that there was a great interest in the use of intellectual property as a strategy of R&D investments appropriation. These were also the findings of Vasconcellos et al.[11], demonstrating that patent interest in the phytodrugs area has grown in the 1990's as a result of the increasing requirements imposed by Anvisa which made the market more selective and competitive. However, it draws one's attention to observe the lack of information on the part of the traditional communities about the patents system and a possible need to recognize some sort of *sui generis* mechanism of partition of benefits for patents substitution. However, Moreira et al.[12], when studying 278 native plants, demonstrated the enormous technological potential of these plants, since more than 65% patent requests had been filed but, when the origin of these processes was investigated, it was found out that 35% of them were filed by foreigners.

There is also an absence of qualified agriculturists for the proper choice of plants *in natura* to ensure the quality of final materials (adequate soil handling and non-use of pesticides, proper harvesting time, etc.) These questions were also evidenced by Souza et al.[13] and by Castro and Albiero[14] in their respective studies, about the trading of medicinal plants and the raw materials market for the phytotherapics industry. At this point, there is a problem resulting from the lack of existing standards between the several stages of the productive chain of medicinal plants and phytotherapics industry which is very relevant for the assessment of policies involving this industry: the absence of an adequate coordination among the organs that act in the regulation of the several phases of the productive chain.

As to the specific market to which phytotherapic products are destined, few companies export them and none of the companies interviewed reported the condition of being a SUS[15] supplier, even if there is a National Policy to stimulate the use of phytotherapics in the System[5]. This result indicates government's action fragility, because the public health system should make itself visible for the phytotherapics incentive program. Among the reasons pointed out by the companies for this situation, the absence of a particular indication of SUS demand in terms of presentations and dosage of products can be mentioned.

Final considerations

The objective of this article was to update the diagnosis on the medicinal plants and phytothera-

pics industry, conducted in 2009, and to observe the existing challenges regarding its development. The results suggest that there was an industry regressive development, both in the production of these drugs in Brazil, and in the progress of applied research aiming at the achievement of a greater number of innovations and a better use of biodiversity. The industry that could represent an alternative to reach the goals and objectives of sustainable developement up to 2030 is below the perspectives envisaged.

The main impediment encountered for a better adjustment of ICTs and companies for the production of innovation still seems to be the poor role performed by the NITs due to the inexperience of ICTs in this regard. The discussion with companies and ICTs about the main reasons for the importation of industrial products for research and phytotherapics production has demonstrated that the importance of this for the companies is due to the requirements imposed by Anvisa on the regulatory standards. This point indicates that the adjustment of the present regulation situation for research and production of phytotherapics along the entire productive chain involved in this industry is an urgent matter and the only one capable of preventing market invasion with the importation of phytotherapics and raw material. The problems and difficulties found by public managers for the execution of government policies seem to be the lack of agility and governmental strategy, and the difficulty in the coordination of so many bureaucratic stages interfering in the phytotherapics productive chain.

In spite of all the problems identified, both companies and ICTs interviewed seem very optimistic as to the potential of the improved use of biodiversity as an alternative to a sustainable development to reach the goals to be attained before 2030. In fact, 59% of companies and all ICTs interviewed have positive expectations for the phytotherapics segment based on the Brazilian biodiversity, even if this depends on a greater coordination between the regulatory aspects and the reduction of legal and administrative obstacles mentioned above.

Collaborations

L Hasenclever worked on designing, analyzing, discussing the results, writing the article and approving the version to be published. J Paranhos worked on the critical review of the article. CR Costa worked in field research on the science and technology institutions and article writing. G Cunha worked on tabulating the results of field research on business, article analysis and writing. D Vieira worked in the field research on the companies and writing their results in the article.

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