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Short communication

Promotion of technological development and determination of biotechnology trends in five selected Latin American countries: An analysis based on PCT patent applications

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ABSTRACT

Background: Science and technology are two desirable elements for the economic and social development of a country. Biotechnology has a particularly important potential for economic development. Nevertheless, patent production in Latin America remains underdeveloped, which creates the need to analyze its trend and the efforts made to promote patent production. Therefore, the purpose of this study was, on the one hand, to determine trends in biotechnology-related PCT (Patent Cooperation Treaty) applications in Chile, Mexico, Argentina, Brazil, and Cuba from 1999 to 2015, and, on the other hand, to determine whether there is a relationship between the gross domestic expenditure on research and experimental development as a percentage of gross domestic product (GERD/GDP) and PCT applications for biotechnological inventions from 2007 to 2015 (in this case, the period under study was limited from 2007 to 2015, due to data availability for GERD/GDP in the five selected countries).
Results: The first part of this study shows that the growth in biotechnology PCT applications has been moderate and gradual and the trend was fitted to a linear model. The second set of results shows that GERD/GDP is associated with biotechnology-related PCT applications issued during the study period with a significance level of $\alpha = 0.01$.
Conclusions: Even though results indicate a gradual and modest progress, it is necessary that these five representative Latin American nations continue acting toward the protection of intellectual property in the area of biotechnology, especially by configuring strategies for further progress based on investments on research and development.
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1. Introduction

The growing interest and depth of biotechnological studies throughout the world, including Latin America, is reflected by a significant increase in the amount of scientific production in the area [1]. Publications describe numerous applications in agriculture and medicine and resources for energy production, among others, which can be used as viable solutions for global problems, especially in developing countries, although there is a still controversy around some of these applications, for example, in agriculture, that must continue being addressed to guarantee biosafety for the population and to prevent the loss of biodiversity [2,3,4,5,6].

The production sector in Latin America is based on intensive low-tech industries or on integration to larger processes as part of the production chain. The phenomenon is complex and comparative advantages are static; while some countries in the region specialize in raw material processing, others focus on manufacturing. As a result, endogenous technological capabilities are limited with regard to countries in Asia, where, for instance, gradual yet strategic import substitution programs have been established. Concerning intellectual property, data show that Latin America has remained within traditional industrial sectors and has yet to move on to high-demand technological paradigms such as biotechnology, genetics, and other fields [7].

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In view of the progress and commercialization of biotechnological developments, Latin America has come to the necessity of addressing intrinsic issues by pursuing relevant development, as well as associated aspects such as public perception, intellectual property protection mechanisms, the construction of regulatory framework, and the various aspects derived from these activities [8]. Latin America intends to engage emerging scientific areas related to biotechnology, such as nanotechnology, but the significance of associated research and commercialization in the region is meager [9].

Therefore, these countries have certain elements relevant for their development that can be nurtured by strengthening innovation in the form of strategies aimed at protecting intellectual property and fostering research and development (R&D) within companies [10]. It is thus important to study the dynamics of national innovation systems, their actors, relationships, and constituent processes, as well as to analyze how biotechnology can converge with other knowledge areas to contribute to the progress and consolidation of these systems [11].

Patents are one of the mechanisms to protect inventions, and there are global efforts seeking to establish an adequate legal framework to achieve consensus on the standard process to obtain them. Even though patenting regulation is currently more suitable for developed countries given their own progress in the area, developing countries can take advantage of these mechanisms to protect and disseminate local inventions [12].

The relationship between the capacity to patent inventions and a country's economic development can be established; however, as in the case of the most developed economies, the goal is to protect inventions in differentiated knowledge areas [13]. In the specific case of Latin America, patent development is unfortunately limited in comparison with other groups of countries presenting more significant innovation dynamics [14].

Given that the cheaper part of the production chain in Asia is labor, whereas in Latin America, it is the natural resources, the potential in the latter creates the need for strategies that allow for the positioning of the region in technological areas that will bring important changes in the future, both in biotechnology and in nanotechnology, as well as in interdisciplinary areas such as bioelectronics and new material creation [15].

It should be mentioned that the United States leads patent production worldwide; this evolution has been based on risk capital investment, but the derived benefits have resulted in considerable market share [16]. Different cases have demonstrated that studying patents filed under the PCT is useful for technology analyses, although there are, as expected, certain inconveniences that make this work more difficult due to the existence of heterogeneous criteria [17].

The main participation for biotechnology PCT applications worldwide is carried out by transnational corporations. Table 1 shows the five companies with more PCT biotechnology applications in medicine, plant breeding, genetic modification, and water treatment areas, during 2008–2018. It is clear that the main dominance comes from transnational private companies, while the academy and related institutions have a smaller participation, and for the same period of study, there are several Latin American academic institutions, which stand out:

Argentina: 1. National Scientific and Technical Research Council (Consejo Nacional de Investigaciones Científicas y Técnicas – CONICET) and 2. National Institute of Agricultural Technology (Instituto Nacional de Tecnología Agropecuaria – INTA).
Brazil: 1. Federal University of Rio de Janeiro (Universidade Federal do Rio de Janeiro – UFRJ); 2. University of Sao Paulo (Universidade de São Paulo-USP); 3. Campinas State University (Universidade Estadual de Campinas – UNICAMP); and 4. Federal University of Minas Gerais (Universidade Federal de Minas Gerais – UFMG).
Colombia: 1. University of Antioquia (Universidad de Antioquia – UdeA); 2. Valley University (Universidad del Valle); and 3. Pontifical Xavierian University (Pontificia Universidad Javeriana).
Cuba: 1. Center for Genetic Engineering and Biotechnology (Centro de Ingeniería Genética y Biotecnología – CIGB); 2. Center of Molecular Immunology (Centro de Inmunología Molecular – CIM).
México: 1. National Autonomous University of Mexico (Universidad Nacional Autónoma de México – UNAM); 2. Autonomous Morelos State University (Universidad Autónoma del Estado de Morelos – UAEM); 3. Center for Research and Advanced Studies of the National Polytechnic Institute (Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional – CINVESTAV); 4. Mexican Social Security Institute (Instituto Mexicano del Seguro Social – IMSS); and 5. Technological Institute of Superior Studies of Monterrey (Instituto Tecnológico y de Estudios Superiores de Monterrey-ITESM) [18].

Table 1
PCT patents applications in biotechnology by fields of knowledge (five main organizations during 2008–2018).
Source: Authors' elaboration based on WIPO [19].

PCT patents apply

Processes for modifying genotypes			Plant reproduction by tissue culture techniques			Medicinal preparations containing peptides		
No.	Company	Total	No.	Company	Total	No.	Company	Total
1	Pioneer Hi-Bred International, Inc.	3698	**1**	Monsanto Technology LLC	762	**1**	Genentech, Inc.	4810
2	Monsanto Technology LLC	3412	**2**	Pioneer Hi-Bred International, Inc.	741	**2**	The Regents of the University of California	2907
3	Syngenta Participations AG	920	**3**	Stine Seed Farm, Inc.	213	**3**	Human Genome Sciences, Inc.	2427
4	Stine Seed Farm, Inc.	580	**4**	Seminis Vegetable Seeds, Inc.	180	**4**	Eli Lilly And Company	2289
5	Seminis Vegetable Seeds, Inc.	351	**5**	Syngenta Participations AG	155	**5**	Novartis AG	1712

Medicinal preparations containing antigens or antibodies			Medicinal preparations containing genetic material, which is inserted into cells of the living body to treat genetic diseases; Gene therapy			Biological treatment of water, wastewater, or sewage		
No.	Company	Total	No.	Company	Total	No.	Company	Total
1	Genentech, Inc.	5421	**1**	Human Genome Sciences, Inc.	1549	**1**	Kurita Water Industries Ltd	199
2	Novartis AG	3145	**2**	The Regents of the University of California	917	**2**	Mitsubishi Heavy Industries, Ltd	116
3	The Regents Of The University Of California	1699	**3**	The Trustees of the University of Pennsylvania	608	**3**	Kubota Corp.	99
4	GlaxoSmithKline Biologicals S.A.	1217	**4**	Isis Pharmaceuticals, Inc.	385	**4**	Ebara Corp.	97
5	Pasteur Institute	821	**5**	SmithKline Beecham Corp.	383	**5**	Hitachi Plant Engineering & Construction Co. Ltd	95

Table 2
PCT and direct patent applications for biotechnology according to the international classification in five selected Latin American countries.
Source: Authors' elaboration based on WIPO [19].

International classification of patents for biotechnology	Mexico	PCT	Total	Argentina	Brazil	Colombia	PCT	Total	Cuba	PCT	Total
A01H1/00	329	190	519	557	329	36	26	62	4	0	4
A01H4/00	66	23	89	80	134	8	6	14	8	0	8
A61K38/00	4581	2283	6864	2640	4816	645	358	1003	43	6	49
A61K39/00	4291	2994	7285	2814	3233	1073	465	1538	102	10	112
A61K48/00	731	310	1041	308	959	61	24	85	1	0	1
C02F3/34	36	25	61	24	149	11	4	15	2	0	2
C07G(11/00,13/00,15/00)	30	6	36	74	42	0	0	0	2	0	2
C07K(4/00,14/00,16/00,17/00,19/00)	7381	4740	12,121	4722	6386	962	351	1313	83	15	98
C12M	370	286	656	182	696	39	22	61	8	1	9
C12N	8796	4193	12,989	6125	8321	892	493	1385	108	8	116
C12P	2248	1342	3590	1862	3837	293	236	529	30	3	33
C12Q	2259	1125	3384	1134	2360	168	73	241	20	1	21
C12S	37	7	44	88	194	9	2	11	1	0	1
G01N27/327	34	17	51	10	41	0	0	0	0	0	0
G01N33/(53*,54*,55*,57*,68,74,76,78,88,92)	2221	1144	3365	1035	2418	209	53	262	14	2	16

Regarding the analysis of biotechnology patent applications by direct presentation and PCT from 2008 to 2018 in countries such as Mexico, Brazil, Argentina, Colombia, and Cuba, they are mainly concentrated, for example, in certain knowledge areas such as compound preparations for medical, dental, and toilet purposes; synthesis of compounds through fermentation processes; devices used in enzymology or microbiology; compounds whose composition is unknown; and material analysis among others (see Table 2, in the Argentina and Brazil cases, more detailed statistics for PCT applications are not available in Patentscope).

According to the WIPO [19], the main classifications refer to the following technical sections, which may include these subsections:

1. A01H: "new plants or processes for obtaining them; plant reproduction by tissue culture techniques";
2. A61K: "preparations for medical, dental, or toilet purposes";
3. C02F: "treatment of water, waste water, sewage, or sludge";
4. C07G: "compounds of unknown constitution (sulfonated fats, oils, or waxes of undetermined constitution)";
5. C12M: "apparatus for enzymology or microbiology";
6. C12N: "microorganisms or enzymes; compositions thereof for propagating, preserving, or maintaining microorganisms; mutation or genetic engineering; culture media";
7. C12P: "fermentation or enzyme-using processes to synthesize a desired chemical compound or composition or to separate optical isomers from a racemic mixture";
8. C12Q: "measuring or testing processes involving enzymes, nucleic acids or microorganisms; compositions or test papers therefore; processes of preparing such compositions; condition-responsive control in microbiological or enzymological processes";
9. G01N: "investigating or analyzing materials by determining their chemical or physical properties".

With the aim of carrying out a more detailed analysis, the present study uses biotechnology-related PCT applications as an axis to establish, first, the trends that can be observed in a group of Latin American countries from 1999 to 2015 and, second, the existence or absence of a relationship between GERD/GDP and biotechnology-related PCT applications from 2007 to 2015.

These selected indicators are relevant because the first reflects the applicants' intentions to protect their inventions by patenting in different geographical regions, which will drive innovation dynamics, as the invention is eventually commercialized, and in the second case, the proportion between GERD and GDP represents the starting point for the development of many inventions.

It is clear that, for transnational corporations, the patent applications through the PCT framework allow them to use their inventions in other countries or territories. For developing countries, with regard to the applications of academic researchers (or independent inventors), the situation is different because their intentions do not always respond to commercial purposes. Instead, they prefer to prioritize aspects related to their productivity and academic evaluation.

2. Methods

The first step consisted in selecting five of the most important economies in Latin America to analyze the growth and trends associated with biotechnology-related PCT applications during 1999–2015. The selected countries are Chile, Mexico, Argentina, Brazil, and Cuba, and the criterion for choosing them was on the basis of key factors such as the size of their economies, their performance, and availability of data for PCT applications by applicant's place of residence and application date (within the biotechnology-related PCT application variable, several Latin American countries reported a large number of years in zero. According to OECD [20], indicators by country and year use fractional counting.) With the purpose of outlining the trend of PCT applications in this group of countries, the annual average presented by the five countries from 1999 to 2015 was fitted to a linear function (Fig. 1a) [20,21], (for Argentina, PCT applications are possible because of the ninth article of PCT, see Patent Cooperation Treaty [22]), which resulted in the following values for a and b calculated according to the following formula:

$$a = \overline{y}_{t'} - b\overline{t'} = 0.4$$

$$b = \frac{S_{yt'}}{S_{t'}^2} = 1.1$$

Trend was defined as $y_t^* = a + bt'$, where $t' = t - 1$, and the result as:

$$y_{t'}^* = 0.4 + 1.1\ t'$$

This analysis produced a linear trend (Fig. 1b), where the R^2 value was determined as follows:

$$R^2 = r_{yt'}^2 = \frac{S_{yt'}^2}{S_{t'}^2 S_{yt'}^2} = \frac{(47.4)^2}{(2326.32)} = 0.966$$

The next step consisted in a test of independence contrast between GERD/GDP and biotechnology-related PCT applications from 2007 to 2015 [20,21,23]. Accordingly, the following test of hypothesis was established:

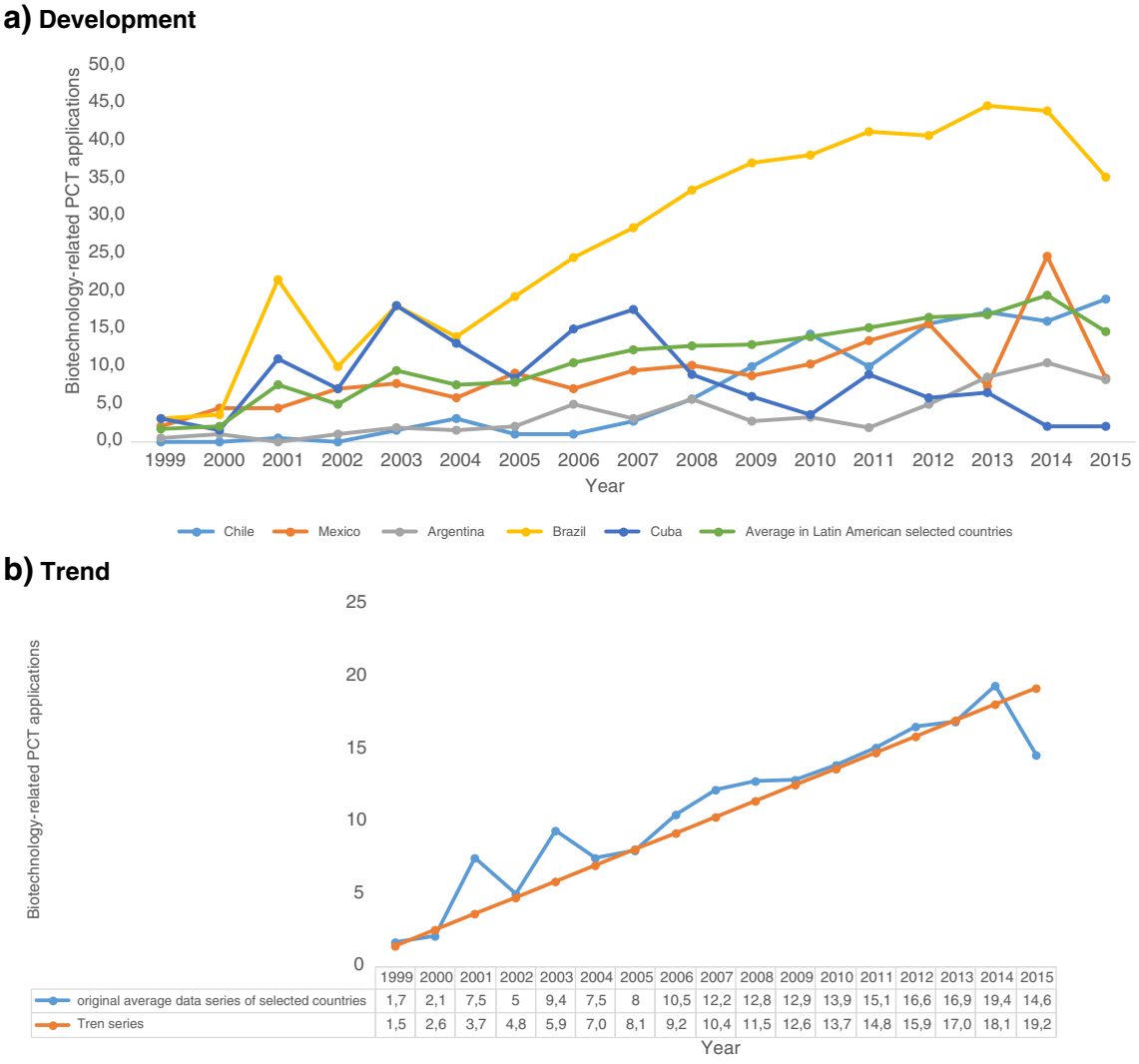

Fig. 1. Growth and trend of biotechnology-related PCT applications by applicant's place of residence.
Source: Authors' elaboration based on OECD [21].

- H_0: There is no relationship between GERD/GDP and biotechnology-related PCT applications.
- H_1: There is a relationship between GERD/GDP and biotechnology-related PCT applications.

For that purpose, average values for GERD/GDP and the number of biotechnology-related PCT applications (including the five countries) were calculated. The following scenarios were established using such average values:

1. GERD/GDP and PCT applications ≥ average;
2. GERD/GDP ≥ average and PCT applications < average;
3. GERD/GDP < average and PCT applications ≥ average;
4. GERD/GDP and PCT applications < average.

This resulted in 45 observations, whose frequencies were arranged as shown in Table 3a. The data obtained were used to construct a contingency table (Table 3b).

Using the contingency table, an independence test was applied based on the Q statistic for a distribution x^2 with (2–1) (2–1) degrees of freedom, which rejected H_0 if the value of $Q > x_{1,\ \alpha}^{\ 2}$ for an α significance level equal to 0.01, according the following:

$$Q = \sum_{i=1}^{2} \sum_{j=1}^{2} \frac{\left(n_{ij} - \frac{n_i \cdot n_j}{n}\right)^2}{\frac{n_i \cdot n_j}{n}}$$

3. Results

The first part of the present study shows that the trend of biotechnology-related PCT applications with time is linear for the group of countries selected for the study, at least for the period between 1999 and 2015. This was confirmed by the method of fitting to a linear function, which produced an R^2 value of 0.966, quite close to 1.

On the other hand, the results of the test of independence demonstrated that the null hypothesis is rejected for the period between 2007 and 2015 for a significance level of $\alpha = 0.01$, given that $Q = 7.3 > x_{1,\ \alpha}^{\ 2}$. These values confirm the association between the

Table 3
Relationship between GERD/GDP and biotechnology-related PCT applications.
Source: Authors' elaboration based on OECD [19] and RICYT [20].

a)

	2007	2008	2009	2010	2011	2012	2013	2014	2015
Chile	4	4	4	4	4	3	3	3	3
Mexico	4	4	4	4	4	3	4	3	4
Argentina	4	4	4	4	4	2	2	4	2
Brazil	1	1	1	1	1	1	1	1	1
Cuba	3	4	2	2	4	4	4	4	4

	1: GERD/GDP and PCT applications ≥ average.
	2: GERD/GDP ≥ average and PCT applications < average.
	3: GERD/GDP < average and PCT applications ≥ average.
	4: GERD/GDP and PCT applications < average.

b)

	Biotechnology-related PCT applications by applicant's place of residence ≥ average of selected countries.	Biotechnology-related PCT applications by applicant's place of residence < average of selected countries.	
GERD/GDP ≥ average of selected countries.	9	5	14
GERD/GDP < average of selected countries.	7	24	31
	16	29	45

GERD/GDP spent by these countries during the study period and the average number of biotechnology-related PCT applications.

4. Conclusions

The present study shows that the number of patent applications through PCT in the area of biotechnology has seen both periods of progress and periods of setback. However, in general, a gradual and modest increase in that number can be observed, and the trend for the average shared by the selected countries is linear. In this context, all stakeholders must carry out certain actions aimed not only at promoting patent production at the local level but also at the international level for their future commercialization.

On the other hand, the relationship between GERD/GDP and biotechnology-related PCT applications points out the importance of investing in research and development activities, especially for those conveying high rates of return, which are typically associated with emerging disciplines such as biotechnology and nanotechnology, among others. However, it should be highlighted that such investments should be underpinned by actions in support of the development of endogenous technology, including the protection of intellectual rights for commercialization in different countries.

Nomenclature

y_t^* Trend of the annual average presented by the five countries (1999–2015).

R^2 Square of the linear correlation coefficient of the average biotechnology-related PCT applications by applicant's place of residence (application date) and the time (1999–2015).

Q Measurement of differences between the observed and expected frequencies in four possible scenarios with regard to the values for GERD/GDP and the number of biotechnology-related PCT applications by applicant's place of residence (application date) based on the average of the five countries.

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Conflict of interest

The authors declare that there is no conflict of interest.

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