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Brazilian scenario of inoculant production: A look at patents

Augusto Matias de Oliveira[(1)*], **Márcia Regina da Costa**[(1)], **Paulo Henrique Grazziotti**[(2)], **Caique Menezes de Abreu**[(1)], **Nicarla da Silva Bispo**[(1)], **Juan Pedro Bretas Roa**[(3)], **Diana Marques Silva**[(1)] **and Jarbas Magno Miranda**[(1)]

[(1)] Universidade Federal dos Vales do Jequitinhonha e Mucuri, Departamento de Agronomia, Produção Vegetal, Diamantina, Minas Gerais, Brasil.
[(2)] Universidade Federal dos Vales do Jequitinhonha e Mucuri, Departamento de Engenharia Florestal, Produção Vegetal, Diamantina, Minas Gerais, Brasil.
[(3)] Universidade Federal dos Vales do Jequitinhonha e Mucuri, Departamento de Ciência e Tecnologia, Biocombustíveis, Diamantina, Minas Gerais, Brasil.

ABSTRACT: Technological advances have demonstrated the need for intellectual property rights, and patent granting is one of its most widespread forms. This includes the protection of inoculant formulations for agriculture, in which Brazil is a leader. This study aimed to analyze the number of patents for formulations of biological inoculants for agriculture in Brazil and the microorganisms used. An advanced search was performed in the National Institute of Industrial Property database, using the title and abstract fields. The indexers included inoculant, bioinoculant, endophyte, endophytic, fungus, bacteria, *Rhizobium*, *Azospirillum* and *Gluconacetobacter*. The inoculant formulation patents were grouped by the number of files per decade, number of patents per holder(s), characterization of granted patents, international patent classification, and main genera of fungi and bacteria used in inoculant formulations per decade. The number of patents filed for inoculant formulations in the last four decades increased from 7 in the first decade (1981–1990) to 37 from 2011–2020. In the first decades of study, the use of *Rhizobium* in inoculants stood out, followed by other genera of fungi and bacteria. However, most inoculant patent applications are still denied, considering data from 1981 to 2020. This may be partially due to the low reproducibility of inoculant results, as microorganism activity is highly affected by climate, soil, plant cultivars and crop management. The percentage of acceptance equal to or higher than 50 % in the number of applied patents for using endophytic microorganisms may be because this group of microorganisms acts mainly inside plants and is thus more protected from the influence of climate and some soil and management factors. The growing number of patent applications in the last 40 years demonstrates the business and technological development interest in inoculants in Brazil.

Keywords: intellectual property, fungi, bacteria, endophytic, inoculant formulation.

*** Corresponding author:**
E-mail: augusto2013ufpi@gmail.com

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INTRODUCTION

Technological advancement has allowed for global development in the most diverse areas, thus giving rise to the need for intellectual property rights, whether through trade secrets or monopoly of use, i.e., patents. Patent granting allows research and development (R&D) companies to benefit from their innovations (Suzuki, 2015). Several countries had their own patent laws during the 19th century, with patents granted only to national inventors. Brazil started to grant patent protection to inventions in 1830. The International Patent System emerged at the Paris Convention for the Protection of Industrial Property in 1883 with the international development of commerce, which allowed patent protection beyond the country of origin (Macedo and Barbosa, 2000).

Microbial inoculants are within this scenario of patent protection. This biotechnology has gained importance due to its sustainability and environmental protection characteristics, allowing an increase in the yield of plants used for food production and other products. Inoculants are composed of live microorganisms capable of benefiting plants, and those most widespread are formulated with diazotrophic microorganisms (Santos and Hanna, 2017; Santos et al., 2019; Sammauria et al., 2020). Recently, microbial inoculant production, marketing and use have increased worldwide on different crops and using different microorganisms (Santos et al., 2019). Brazil is the world leader in the use of this technology (Anpii, 2017).

Microorganisms are essential in the dynamic soil system and benefit plant growth through three mechanisms: fixation, which increases N absorption through BNF and solubilizers responsible for solubilizing the unavailable P adsorbed in the available form; phytostimulation, which stimulates growth through plant phytohormone production; and biological control, protecting plants from pathogens (Sammauria et al., 2020). Initially, inoculants mainly contained *Rhizobium* due to its remarkable capacity to fix atmospheric nitrogen in symbiosis with legumes. However, studies with endophytic microorganisms began in the 1970s, and there has been increasing interest in these organisms (Colombo, 1978; Souza et al., 2004), further increasing the number of patent applications for inoculant production processes for endophytic microorganisms in the last two decades.

Endophytic microorganisms, mainly fungi and bacteria, are beneficial organisms that live part or all of their life cycles inside plants without causing apparent injuries (Fedorov et al., 2013; Murphy et al., 2018). They benefit plants by producing phytohormones, facilitating nutrient absorption in the soil by promoting root growth, antagonizing plant pathogens, and inducing resistance to biotic and abiotic stressors (Jain and Kumar-Choudhary, 2014; Santos et al., 2019). Consequently, the plant provides them with protection, as well as photosynthates for their growth and propagation.

According to the National Association of Inoculant Producers and Importers (Anpii, 2019), 20.2 million inoculant doses were sold in Brazil in 2009, increasing to 73.5 million in 2018, an increase of 263 %. Therefore, Brazil's inoculant market has grown, making it an excellent investment opportunity for national and international public and private companies. The greatest use of inoculants occurs in soybean, mainly using *Bradyrhizobium japonicum* (Santos et al., 2019; Barbosa et al., 2021). Thus, Brazil is an attractive country for companies that produce inoculants, as it was the world's largest soybean producer in the 2019–2020 growing season, with 123 million tons, surpassing the United States, which had a production of 96.6 million tons (Sopa, 2021). The Brazilian soybean cultivation area inoculated in the 2017–2018 growing season was 26 million hectares, equivalent to 78 % of the total area grown with the crop (Castro, 2019). More recent data showed that 85 % of the soybean-growing area in Brazil is inoculated (Castro, 2020).

Previous studies indicated that biological nitrogen fixation (BNF) could provide 25 to 60 % of the N required by plants (Harper, 1974). With strain selection becoming more efficient and adapted, recent studies indicated that BNF provides from 50 to 60 % of the N required by soybeans (Salvagiotti et al., 2008; Mourtzinis et al., 2018). *Rhizobium* can fix 40 to 250 kg ha^{-1} yr^{-1} of N in different legume crops (Pindi and Satyanarayana, 2012), demonstrating consistency in the obtained BNF results.

Brazil has also increased inoculation of corn (*Zea mays*), cowpea (*Vigna unguiculata* (L.) Walp.), and common bean (*Phaseolus vulgaris*). Additionally, the co-inoculation of soybean and bean with *Rhizobium* and *Azospirillum* led to a 263 % increase in the number of doses marketed in recent years (Hungria et al., 2010, 2015; Anpii, 2019; Santos et al., 2019). Inoculant sales for grasses increased from 2.5 million doses in 2012 to 9.1 million in 2018, surpassing the sale of inoculants for beans, second only to inoculants for soybeans (Anpii, 2019). The use of inoculants in Brazil has resulted in an estimated savings of around five billion US dollars, which were not spent on nitrogen fertilization (Castro, 2020).

This review aimed to analyze the number of patents for biological inoculant formulations for agriculture in Brazil and the microorganisms used.

MATERIALS AND METHODS

The search for patents was carried out from November to December 2020 in the National Institute of Industrial Property database (INPI; http://www.inpi.gov.br/). An advanced search was performed in the title and abstract fields, filtering patents that dealt with agricultural inoculants and bioinoculants. The keywords used were inoculant, endophytic, microbial, bioinoculant, bacterial, fungal, fungus, bacterium, endophytic, endophyte, mycorrhizal, ectomycorrhiza, ectomycorrhizal, mycorrhiza, *Acetobacter*, *Herbaspirillum*, *Azospirillum*, *Pseudomonas*, *Bacillus*, *Lactobacillus*, *Agrobacterium*, *Azoarcus*, *Enterobacter*, *Arthrobacter*, *Aurobacterium*, *Serratia*, *Phyllobacterium*, *Flavobacterium*, *Streptomyces*, *Staphylococcus*, *Xanthobacter*, *Rhizobium*, *Bradyrhizobium* and *Frankia*.

The patents found in the search were considered when dealing with inoculants or bioinoculants for agriculture. The following data were recorded: microorganism used, year of filing, the applicant (holder), field of international patent classification, and product applications. The selected variables were the total number of applications and granted patents per decade from 1981 to 2020; among them, the number of applications and granted patents with endophytic microorganisms per decade from 1981 to 2020; numbers of patents per holder(s) from 1981 to 2000 and 2001 to 2020; code, year of filing and granting, holder, and microorganism used for patents granted from 1981 to 2000 and 2001 to 2020; international patent classification from 1981 to 2000 and 2001 to 2020; and genera of fungi and bacteria used in each decade.

RESULTS AND DISCUSSION

A total of 76 patents for agricultural inoculant formulations were found for 1981 to 2020 (Figure 1). Some of the purposes of these formulations were: ensilage preservation (PI 9609364-1 and PI 9608773-0); pest control (PP 1101128-9); increase in soil quality and plant yield (PI 9916134-6); seed treatment (PI 0103922-9); increase in tolerance of abiotic stress conditions and phosphate solubilization under abiotic stress conditions (PI 0205800-6); plant growth stimulation (PI 0200142-0 and BR 10 2019 008109 0); root nodule formation (PI 0312543-2); biological disease control (PI 1004530-9 and BR 10 2019 016288 0); accelerated transformation of inert organic matter (BR 10 2012 016934 7); forage grass growth promotion (BR 10 2016 025908 8); and reduction of time and increase in the multiplication of propagules by induction of cell differentiation (BR 10 2014 017389 7); among others.

Seven new patent applications were filed in the first decade (1981–1990), increasing to 37 in the last decade (2011–2020), showing a five-fold increase (Figure 1). Patent approval is not the last step for microbial inoculants' commercialization in Brazil, as national regulations require agronomic validation efficiency tests (Normative Instruction SDA No. 13, of March 24, 2011) before marketing approval (DOU, 2011).

Despite the high number of patent applications, not all are granted. Furthermore, 18 patent applications were filed from 1981 to 2000, but only six were granted (Figure 1). In contrast, 21 applications were filed in the 2001–2010 decade, demonstrating the growing technological interest, and 10 patents were granted in this period; thus, there was a 16.7 % increase in the number of applications and a 66.7 % increase in granted patents. The number of applications reached 37 in the last decade (2011–2020), a 76.2 % increase in the number of applications to protect knowledge, but no patents were granted in this period. A major concern is the time between filing and granting a patent in Brazil. The data from patent granting showed that the processes could take 15 years for analysis by the INPI (Tables 1 and 2).

The protection of knowledge in patents for inventions in the inoculant sector has a mean of 8.7 years (Tables 1 and 2) between filing and granting, considering the last 40 years, thus causing damage to the economy and innovation (Gouveia, 2007). This delay may

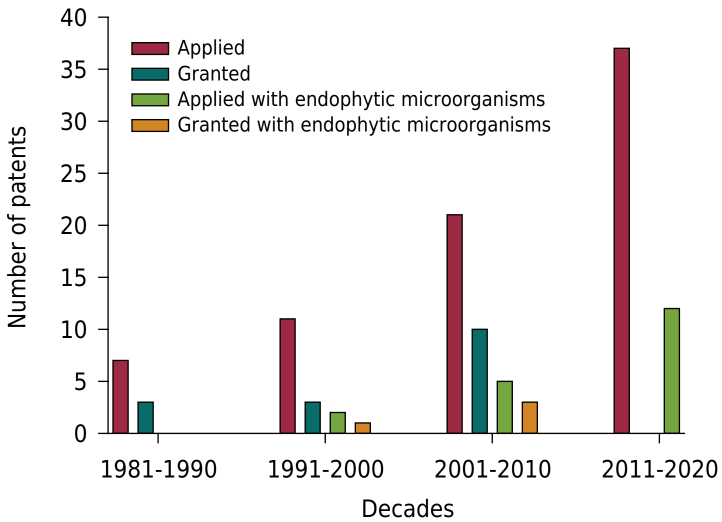

Figure 1. Total number of applied and granted patents in Brazil with rhizospheric and endophytic microorganisms for use in agriculture per decade.

Table 1. Characterization of patents granted in the period 1981–2000

Code	Filing year	Grant year	Holder	Microorganism
PI 8606028-7	1986	1996	Agracetus (US)	*Rhizobium*
PI 8708011-7	1987	1995	Nitral (BR)	*Rhizobium*
PI 8906372-4	1989	1996	Turfal (BR)	*Rhizobium*
PI 9103905-3	1991	2000	Milenia Agro Ciências S/A (BR)	*Rhizobium* spp.
C1 9103618-6	1992	2007	Hiroshi Ota (BR)	Culture of lactic acid-producing bacteria, yeasts, photosynthetic bacteria, and actinomycetes
PP 1101128-9	1997	2000	EMBRAPA (BR)	*Acetobacter diazotrophicus*, *Herbaspirillum* (*H. seropedicae* e *H. rubrisubalbicans*)

US: United States; BR: Brazil.

Table 2. Characterization of patents granted in the period 2001-2020

Code	Filing year	Grant year	Holder	Microorganism
PI 0108497-6	2001	2013	Syngenta Participations AG (CH)	*Rhizobium* spp.
PI 0103922-9	2001	2015	Sintesis Quimica S.A.L.C. (AR)	*Rhizobium* or *Bradyrhizobium*
PI 0211920-0	2002	2012	Agro.Bio Hungary Kft. (HU)	*Azospirillum brasilense* ssp., *Azotobacter vinelandii* spp., *Pseudomonas fluorescens*, *Bacillus polymyxa*, *B. megaterium*
PI 0205800-6	2002	2016	Council of Scientific and Industrial Research (IN)	*Bacillus lentimorbus*, *B. subtilis*
PI 0301447-9	2003	2016	Federico German Magri (AR)	*Rhizobium japonicum*
PI 0305600-7	2003	2014	Lallemand S.A.S (FR)	*Lactobacillus buchneri*
PI 0519258-7	2005	2017	Becker-underwood, INC. (US)	*Bradyrhizobium japonicum*, *Pseudomonas fluorescens*, *Serratia proteamaculans*
PI 0517713-8	2005	2016	Instituto Nacional de Ciências Agrícolas (CU)	*Glomus fasciculatum*, *G. clarum*, *G. spurcum*, *G. mosseae*, *G. intraradices*, *Gigaspora margarita*
PI 0709328-4	2007	2019	Adjuvants Plus Inc. (CA)	Endophyte, rosea strain Clonostachys 88-71
PI 1004530-9	2010	2018	Embrapa (BR)	*Pseudomonas chlororaphis*, *P. aureofaciens*

CH: China; AR: Argentina; HU: Hungary; IN: India; FR: France; US: United States; CU: Cuba; CA: Canada; BR: Brazil.

be due to the small number of examiners and lack of informatization. In an open letter, the Brazilian Intellectual Property Association drew attention to flaws in the information system and the need for investment in INPI infrastructure (ABPI, 2018).

Patents are rejected when they do not meet novelty, inventiveness and reproducibility requirements (McEniery, 2014). One of the factors that can affect reproducibility is the adaptability of microorganisms, as they may not have the effect(s) proposed in the patent when used under conditions other than those from which they were isolated and/or tested for patent development. Microorganisms used in inoculants undergo competition with native microorganisms, which are usually more adapted to local conditions, thus reducing the inoculant's effectiveness (Sruthilaxmi and Babu, 2017; Sun et al., 2020). The analysis of holders showed that 50 % of the applications in the first two decades (1981–2000) came from companies from the USA (Table 3), which have different edaphoclimatic conditions than Brazil.

Although US companies generated 50 % of the applications from 1981 to 2000 (Table 1), five out of six were requested by Brazilian companies and only one by an American application (Agracetus; Tables 1 and 3). Inoculant effectiveness is increased when conditions at the location of use are similar to the conditions where the strains were isolated. Increased yield due to inoculant use in different regions but with conditions similar to those in which the microorganisms were obtained for inoculant development has been reported in the literature. Examples are the inoculation of *Bradyrhizobium* isolated in Brazil (strain BR 3267) in cowpea grown in northern Mozambique and northern Ghana (Boddey et al., 2017) and inoculation of *Bradyrhizobium* (strain BR 3267) in soybean and bean grown in northern Ghana (Ulzen et al., 2016). The BR 2367 strain was isolated in the semiarid region of northeastern Brazil (Martins et al., 2003; Leite et al., 2018), and

Table 3. Number of filed patents by holders in Brazil from 1981 to 2000 and 2001 to 2020

1981-2000	2001-2020
Nitral (BR) (5)	Novozymes Bioag A/S (DK) (10)
Agracetus (US) (3)	Novozymes Bioag A/S (DK) / Monsanto Technology Llc (US) (3)
Pioneer Hi-Bred International, INC (US) (3)	EMBRAPA / UFRJ (BR) (3)
Turfal Ind. e Com. de Prods. Biols. e Agrons Ltda (BR) (1)	Universidade Estadual de Londrina (BR) (3)
Milenia Agro Ciê (BR) (1)	Azotic Technologies Ltd (GB) (2)
Hiroshi Ota (BR) (1)	Becker-Underwood, Inc. (US) (2)
EMBRAPA (BR) (1)	EMBRAPA (BR) (2)
Wisconsin Alumni Research Foundation (US) (1)	Bioarts Indústria e Comércio de Biotecnologia Ltda (BR) (2)
Tatko Biotech, Inc. (US)(1)	Universidade Federal Rural de Pernambuco (BR) (2)
W. R. Grace & Co. (US) (1)	Nitral Urbana Laboratórios Ltda. (BR) (1)
	UENF Darcy Ribeiro / Luciano Pasqualato Canellas (BR) (1)
	Ibra Agrisciences Ltda (BR) (1)
	Velmir Machado da Silva / Cicero Augusto Celestino (BR) (1)
	UFRGS / Tecnano Pesquisas e Serviços / FAPERGS (BR) (1)
	UFAL (BR) (1)
	Biocampo Nut. An. Importacao e Exportacao Limitada (BR)
	Universidade Federal Rural do Rio de Janeiro (BR) (1)
	EMBRAPA / Universidade Federal do Recôncavo da Bahia (BR) (1)
	Sintesis Quimica S.A.L.C. (AR) (1)
	Federico German Magri (AR) (1)
	YPF Tecnología S.A. (AR) (1)
	Monsanto Technology LLC (US) (1)
	Advanced Biological Marketing (US) (1)
	Agbiome, INC. (US) (1)
	Bayclassic Pty Ltd (AU) (1)
	The Flinders University of South Australia (AU) (1)
	Sustainable Organic Solutions Pty LTD (AU) (1)
	Agro Innovation International (FR) (1)
	Lallemand S.A.S (FR) (1)
	Adjuvants Plus Inc. (CA) (1)
	Agro.Bio Hungary Kft. (HU) (1)
	Council of Scientific and Industrial Research (IN) (1)
	Instituto Nacional de Ciencias Agrícolas (CU) (1)
	Chr. Hansen A/S (DK) (1)
	Wim de Laat Consultancy B.V. (PB) (1)
	Bayer Intellectual Property GMBH (DE) (1)
	Pontificia Universidad Javeriana (CO) (1)
	Syngenta Participations AG (CH) (1)

BR: Brazil; US: United States; DK: Denmark; GB: United Kingdom; AR: Argentina; AU: Australia; FR: France; CA: Canada; HU: Hungary; IN: India; CU: Cuba; PB: Netherlands; DE: Germany; CO: Colombia; CH: China.

the climate and humidity conditions in Mozambique and northern Ghana are similar to those in northeastern Brazil (Santos et al., 2019).

Biotic and abiotic factors can affect inoculant effectiveness, making it inefficient in conditions with nutrient-poor or unbalanced soils, inappropriate salinity or temperature, water stress, or the occurrence of pests and diseases (Bashan et al., 2014; Khan et al., 2017; Thilakarathna and Raizada, 2017; Samago et al., 2018). Another important factor for good inoculant performance is the use of adequate carriers. The inoculation of bacterial suspensions with no extra components that improve survival and/or aid in the initial population growth usually leads to a rapid reduction in the population of most species of plant growth-promoting bacteria (Bashan et al., 2014).

Inoculant formulations must provide an adequate environment, associated with physical protection for a sufficient period to avoid a rapid decrease in the microorganisms used for inoculation (Bashan et al., 2014). Moreover, the success of inoculants depends on the formulation and application method, and the literature cites many potential strains, but they are not commercially available, possibly due to inadequate formulations. Thus, inoculants need an adequate composition to enable the contact and establishment of interaction between microorganisms and the host plant.

Brazilian public and private institutions obtained 21 of the 58 patent applications in Brazil in the last two decades (2001–2020), representing 32.2 % of the applications (Table 3). Brazilian research for inoculant production and marketing is advanced, having one of the most complete legislations in the area (Santos et al., 2019). Three of 10 patents were granted in this period for individuals and companies in South American countries (two in Argentina and one in Brazil) and one for each of the following countries: Switzerland, Hungary, India, France, the United States, Cuba and Canada (Table 2).

Applications with endophytic microorganisms are another important factor shown in figure 1, as they have increased in recent decades. One of the pioneering studies with endophytic microorganisms was carried out by Colombo (1978). Eighteen patent applications for inoculants were submitted from that time until 2000, which is a span of more than 20 years, but only two of them used endophytic bacteria (11 %), one in 1997 (PP 1101128-9), requested by Embrapa (BR/DF) with *Acetobacter diazotrophicus*, *Herbaspirillum seropedicae*, and *H. rubrisubalbicans*, and another in 1999 (PI 9916134-6), requested by the American company Tatko Biotech, with *Azospirillum brasilense*. However, 17 of 58 applications in the last two decades (2001–2020) involved endophytic microorganisms (29.3 %). Their discovery partially explains this difference between the number of inoculants based on endophytic and rhizosphere microorganisms. The first references in Brazil studying the symbiosis between *Rhizobium* and legumes date back to 1930, in reports from the Agronomic Institute of Campinas on the performance of inoculation experiments and the distribution of bacterial cultures (Freire and Vernetti, 1999). One of the pioneering studies with endophytic bacteria was developed by Colombo in 1978, after observing the occurrence of endophytic bacteria in the stalks of algae between siphons and coenocytic filaments. Thus, research with endophytic microorganisms became more frequent only after the 1980s.

Two patent applications with endophytic microorganisms were submitted in the 1991–2000 decade, and one of them was granted (PP 1101128-9). The number of applications with endophytic microorganisms increased to five in the 2001–2010 decade, with three patents granted (PI 0211920-0, PI 0205800-6 and PI 0709328-4; Figure 1 and Tables 1 and 2). It represents an acceptance rate equal to or higher than 50 % of patents with endophytic microorganisms. The replicability of results of endophytic microorganisms is even clearer when analyzing the three patents with endophytic microorganisms granted in the decade from 2001 to 2010 (PI 0211920-0, PI 0205800-6 and PI 0709328-4; Table 2), as they are from holders belonging to Hungary, India and Canada. Endophytic microorganisms live inside plant tissues, receiving nutrients and shelter (Farrar et al., 2014) and being protected from adverse environmental conditions, thus increasing their chances of success compared to rhizosphere microorganisms; in some cases, this negates that the conditions of the place of use are similar to those of the place of isolation.

The most prominent field of patent filing in the international patent classification from 1981 to 2000 was C12N (25.8 %; C—Chemistry, metallurgy; 12—Biochemistry, beer, alcohol, wine, vinegar, microbiology, enzymology, genetic or mutation engineering; N—Microorganisms or enzymes, their compositions), followed by A01N (22.6 %; A—Human needs, 01—Agriculture, N—Conservation of human or animal bodies or plants parts, their parts; Figure 2a). However, there was an inversion of these two fields in the last two decades, in which 23.3 % of the patents were classified in the A01N field and 20.7 % in the C12N field (Figure 2b). This demonstrates that initial studies were directed towards knowledge of microorganisms (microorganisms or enzymes, their compositions) and were later directed towards applications in agriculture after discovering their potential.

Inoculant production processes in the first decade (1981–1990) used only *Rhizobium* (Table 4), but applications that used bacteria from the genera *Enterococci*, *Bradyrhizobium*, *Acetobacter*, *Sinorhizobium*, *Azospirillum*, *Lactobacilli*, *Enterococcus* and *Pediococcus* occurred in the 1990s. Applications with 17 genera of bacteria and fungi were recorded in the last two decades. Patent applications with *Rhizobium* have already been well consolidated since 2011, which makes the novelty factor difficult, with only three applications for this genus, following those from the genera *Penicillium* (9), *Bacillus* (8) and *Bradyrhizobium* (6).

Rhizobia were classified into *Rhizobium* and *Bradyrhizobium* until 1984 (Jordan, 1984). However, the advancement of molecular and chemotaxonomic techniques allowed their later division into *Rhizobium*, *Bradyrhizobium*, *Sinorhizobium*, *Azorhizobium*, *Mesorhizobium* and *Allorhizobium* (Chueire et al., 2003). Bacteria classified as *Rhizobium* in the first decade could now belong to another genus. However, the genus described in the patent was considered for discussion purposes.

Fungi and bacteria used in inoculant formulations have shown positive results in several studies. Endophytic species of *Penicillium* (e.g., *P. funiculosum* and *P. chrysogenum*) have been characterized as phytoremediators, biocatalysts, plant-growth promoters, and antibacterial agents, among others, and can protect plants against stress (Devi et al.,

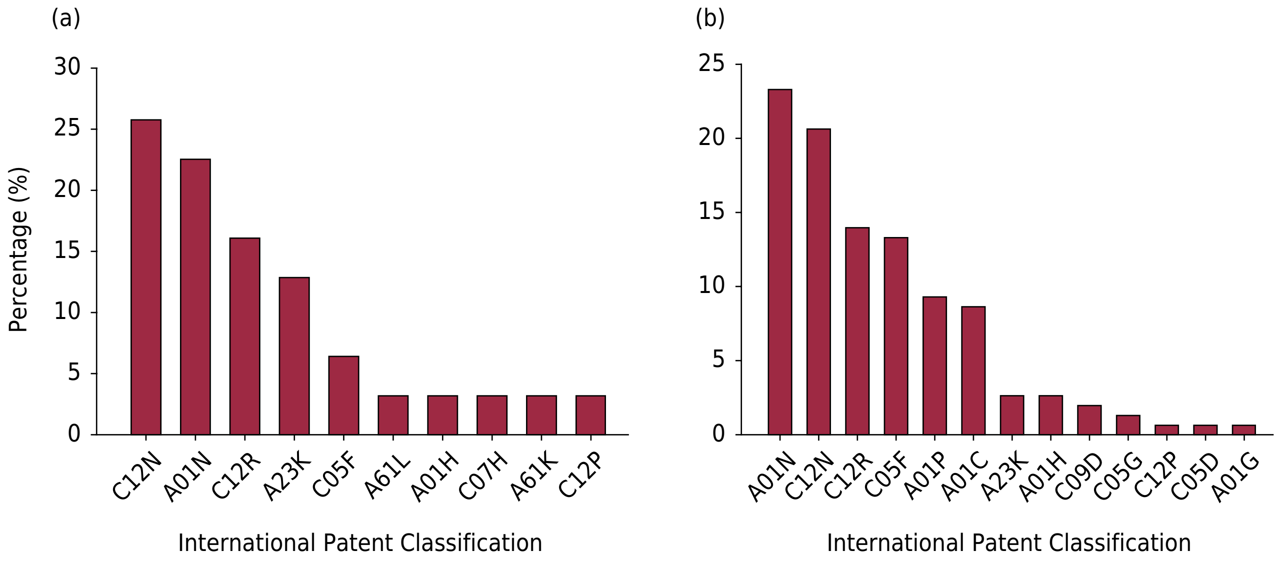

Figure 2. International classification (WIPO, 2021) of all patents found from 1981 to 2000 (a) and from 2001 to 2020 (b).

Table 4. Genera of microorganisms used in the production of inoculants for agriculture from 1981 to 2020

1981-1990	1991-2000	2001-2010	2011-2020
Rhizobium (7)	*Enterococcus* (3)	*Rhizobium* (8)	*Penicillium* (9)
	Rhizobium (3)	*Pseudomonas* (4)	*Bacillus* (8)
	Bradyrhizobium (1)	*Lactobacillus* (3)	*Bradyrhizobium* (6)
	Acetobacter (1)	*Bradyrhizobium* (2)	*Rhizobium* (3)
	Sinorhizobium (1)	*Azospirillum* (2)	*Gluconacetobacter* (2)
	Azospirillum (1)	*Glomus* (2)	*Azotobacter* (2)
	Lactobacillus (1)	*Enterococcus* (1)	*Pseudomonas* (1)
	Enterococcus (1)	*Pediococcus* (1)	*Saccharomyces* (1)
	Pediococcus (1)	*Herbaspirillum* (1)	*Beijerinckia* (1)
		Gluconacetobacter (1)	*Glomus* (1)
		Burkholderia (1)	*Clostridium* (1)
		Bacillus (1)	*Streptomyces* (1)
		Azotobacter (1)	*Burkholderia* (1)
		Entrophospora (1)	*Lactobacillus* (1)
		Mesorhizobium (1)	*Yersinia* (1)
		Serratia (1)	*Lysinibacillus* (1)
		Gigaspora (1)	*Rhizophagus* (1)

2012; Khan and Lee, 2013; Toghueo and Boyom, 2020). Strains of *Bacillus* spp. have been characterized as biocontrol agents and/or plant-growth promoters (Krebs et al., 1998). *Bradyrhizobium* is one among several genera that contain nitrogen-fixing bacteria that form symbiotic nodules in legumes (Ormeño-Orrillo and Martínez-Romero, 2019).

Gluconacetobacter are diazotrophic endophytic bacteria associated with sugarcane plants, assisting in plant growth and promoting activities, such as an increase in the solubility of phosphate and zinc under *in vitro* conditions (Saravanan et al., 2007); antagonism against *Xanthomonas albilineans*, a sugarcane pathogen (Blanco et al., 2005); and antifungal activity against *Helminthosporium carbonum*, *Fusarium* spp., and *Pythium* spp. (Mehnaz and Lazarovits, 2006). *Pseudomonas* is present in the rhizosphere and also in plant tissues, being used in agriculture to promote plant growth and disease control (Kumar et al., 2017).

Microorganisms, such as *Rhizobium*, *Bradyrhizobium*, *Sinorhizobium*, *Azospirillum*, *Bacillus*, and *Mesorhizobium*, used in the formulations of inoculants in patent applications are included in the list of microorganisms authorized for use by the Ministry of Agriculture, Livestock, and Supply of Brazil, in accordance with SDA Normative Instruction No. 13 of March 24, 2011 (DOU, 2011). However, the list needs to be updated, as currently, microorganisms that make up the majority of new patents, such as *Pseudomonas*, *Penicillium*, *Azotobacter*, *Herbaspirillum*, *Gluconacetobacter*, *Glomus*, and *Acetobacter*, are not on that list.

Scientific advances in inoculants of rhizospheric and endophytic fungi and bacteria might be even higher because patents are an imperfect form of protection, as the entire process of innovation technology development has to be described in detail at the time of patent application (Suzuki, 2015). Competitors obtain information that helps them follow and further innovate the technology with partial information disclosure, leading many companies to opt for trade secrets (Suzuki, 2015). The guarantee of knowledge protection in patents for inventions is associated with the impediment of third parties. The holder has the power to decide to exploit the technology as a monopoly and is also entitled not to allow third parties to produce, market, use or import their protected technologies without express consent. It is a strategic decision for companies, and it is also possible to opt for other means of protecting knowledge, such as protection in the form of an industrial secret.

In biotechnology, fungi, bacteria and viruses represent the main groups of interest for companies (Nair and Ramachandranna, 2010). However, currently, Brazilian legislation does not allow the patenting of part or all microorganisms, except when they are genetically modified, as long as they meet the requirements of novelty, inventive activity and industrial application (LPI 9,279/96, art. 18), allowing only the patenting of inoculant production processes. This understanding is different from that set out in Sections 5 and 6, Article 27 on Patentable Subject Matter of Uruguay Round Agreement organized by the World Trade Organization in 2010 (WTO, 2010). In that agreement, microorganisms are recognized as patentable material, and some countries, such as India and the United States, already grant this type of protection (Nair and Ramachandranna, 2010; WTO, 2010). Brazil has a territory that stands out for its diversity and quantity of biomes. A possible change in Brazilian legislation, allowing this type of protection, may attract new companies, national and foreign, and enhance the development of technologies in the sector.

Development in biotechnology must be accompanied by efficient mechanisms regulating access to genetic resources and, especially, the fair and equitable sharing of benefits obtained from the economic exploitation of associated traditional knowledge or reproductive material derived from access to genetic heritage (Law No. 13,123 of May 20, 2015, Article 1, Section V). In addition to this regulation, effective inspection is necessary to prevent the expatriation of this genetic heritage without generating value. Thus, biotechnologies can generate benefits for the development, production, and use and for the populations that will benefit from the increase in the production of food, medicines, and environmental conservation.

CONCLUSION

Patent applications for inoculant formulations have grown significantly in Brazil in the last four decades. However, not all patent applications are granted despite significant technological advances. The reproducibility of applications may be a factor for not granting patents because the microorganisms are used under conditions different from those in which they were isolated. A proposal to solve this type of challenge is the use of endophytic microorganisms from plant tissues, which are more protected from adverse environmental conditions, allowing for a greater chance of success compared to rhizosphere microorganisms.

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AUTHOR CONTRIBUTIONS

Conceptualization: Juan Pedro Bretas Roa (lead).

Data curation: Augusto Matias de Oliveira (equal), Caique Menezes de Abreu (equal), Juan Pedro Bretas Roa (equal), Nicarla da Silva Bispo (equal) and Paulo Henrique Grazziotti (equal).

Formal analysis: Márcia Regina da Costa (lead).

Investigation: Diana Marques Silva (equal), Jarbas Magno Miranda (equal) and Nicarla da Silva Bispo (equal).

Methodology: Caique Menezes de Abreu (lead).

Software: Augusto Matias de Oliveira (equal) and Jarbas Magno Miranda (equal).

Supervision: Paulo Henrique Grazziotti (lead).

Visualization: Diana Marques Silva (lead).

Writing – original draft: Augusto Matias de Oliveira (lead).

Writing – review & editing: Augusto Matias de Oliveira (equal), Juan Pedro Bretas Roa (equal), Márcia Regina da Costa (equal) and Paulo Henrique Grazziotti (equal).

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