



REVIEW

Microbial bioinputs in Brazilian agriculture

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Highlights

- Describes major categories, mechanisms of action, and global challenges of microbial bioinputs.
- Summarizes Brazil's manufacturing infrastructure for bioinput production.
- Discusses Brazilian bioinput patents and regulation in the global scenario.

Abstract

Brazil maintains a leading position in agricultural exports and stands as the world's foremost producer and user of bioinputs in agriculture. These bioinputs generate annual savings of billions of dollars that would otherwise be allocated to chemical fertilizers and pesticides. The nation's regulatory framework enables bioinput agriculture and serves as a model for countries transitioning toward regenerative agriculture. Brazilian legislation categorizes bioinputs into: 1) biofertilizers (extracts); 2) biostimulants (plant growth-promoting and biocontrol agents); and 3) inoculants (active ingredient comprises one or more living microorganisms). The inoculation of soybeans with *Bradyrhizobium* strains provides approximately 90% of the nitrogen accumulated by this crop. Brazil has registered over six hundred inoculants, with at least 60% specifically designated for soybean cultivation. The annual sales of inoculants in Brazil reach approximately 120 million doses. Although beans (*Phaseolus vulgaris* and *Vigna unguiculata*) represent an essential food crop in Brazil's staple diet and benefit from inoculation, inoculant supply remains insufficient. Regarding biocontrol, soy, corn, sugarcane, and coffee rank among the most protected crops, employing biocontrol agents against bacteria, fungi, nematodes, and insects. *Bacillus*, *Pseudomonas*, *Streptomyces*, *Rhizobium*, *Azotobacter*, and *Paenibacillus* strains were predominantly cited in the 5,000+ bioproduct patents filed between 2022 and 2024. Among fungal genera, *Trichoderma*, and *Penicillium* received the most citations. EMBRAPA's biobanks maintain over 10,000 strains of bacteria, fungi, and viruses for biocontrol, and 14,000 strains of nutrient-fixing and plant-growth promoters. Production challenges include quality control, particularly as on-farm production of inoculants becomes prevalent on larger farms, alongside product availability and supply limitations. Brazilian farmers maintain global competitiveness partly through reduced chemical fertilizer and pesticide costs enabled by bioinput usage. As components of regenerative agriculture, bioinputs enhance soil quality, decrease carbon footprints, and support Sustainable Development Goals. Brazil's leadership in microbial bioinput utilization stems from its extensive agricultural sector, rich microbial biodiversity, and progressive regulatory framework.

Keywords: bioinputs, Brazil, agriculture, regenerative agriculture, circular economy

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1. Introduction

Agriculture, which contributes to food production and other commodities, serves a vital role in socio-economic development and poverty alleviation (Nsabiyeze *et al.* 2024; Terán *et al.* 2024). Projections indicate a 70% increase in global food demand by 2050 to sustain a population of 10.1 billion and accommodate expanding middle-class consumption (Rudrakar and Rughani 2024). While global efforts aim to enhance agricultural production and ensure food security, multiple factors present significant challenges, including population growth, accelerating urbanization, unsustainable use of non-renewable resources, inadequate agricultural practices, environmental pollution, and climate change, which collectively disrupt the balance between production and consumption (Hall *et al.* 2017; Viana *et al.* 2022; Nsabiyeze *et al.* 2024).

Agricultural losses attributed to pests and diseases result in a 20–40% reduction in production, increasing control agent costs, diminishing market value, and threatening food security (FAO 2022). These challenges necessitate global regulatory measures and scientific research to prevent food shortages while promoting safe, environmentally sustainable control methods and bioinputs. Contemporary agricultural models heavily depend on synthetic fertilizers and pesticides which, despite supporting crop yields, can generate environmental concerns including soil and water contamination and health risks (Santos *et al.* 2024). Health considerations, economic costs, and ecological impacts drive increasing pressure to reduce non-biological inputs and promote biological alternatives, particularly those derived from microorganisms, which benefit both plants and soil.

As one of the world's leading grain producers, Brazil has embraced the growing trend of utilizing growth-promoting microorganisms, both domestically and internationally. In 2024, Brazil advanced its bioinput regulations, marking a significant step toward reducing dependence on national fertilizer production for internal demand (Andreati *et al.* 2024). The European Union and nations including Brazil, India, Argentina, and China have made substantial progress in biofertilizer development within the US market, although clear production and sales guidelines remain absent (Goulet *et al.* 2024; Santos *et al.* 2024; Da Silva Medina *et al.* 2024).

This review examines bioeconomy, bioinputs utilized in Brazil and globally, including their action mechanisms, legal framework, infrastructure, and production methodology, as well as patents and markets in Brazil. Additionally, it addresses the challenges and future prospects of bioinputs.

2. Bioeconomy

The bioeconomy centers on the utilization of renewable biological resources, encompassing plants, microbes, and agricultural waste, for food, materials, and energy production. This framework emphasizes biotechnology, biorefineries, and sustainable biomass production as essential components for advancing sustainable agricultural practices. The circular economy represents a broader economic model focused on efficient resource utilization through waste minimization, maximizing the utility and value of products, components, and

raw materials. This approach advocates resource efficiency, reuse, recycling, repair, remanufacturing, and closed-loop systems (Jana *et al.* 2025). The model encompasses various materials and products, including non-biological resources such as metals, plastics, and electronics. The integration of bioeconomy and circular economy concepts yields the "circular bioeconomy," encompassing activities that transform biomass into diverse product streams, including materials, chemicals, biofuels, and food (FAO 2025). Circular bioeconomy practices enhance crop yields, optimize resource utilization, and generate novel applications from waste (Nguyen *et al.* 2025). Annual global food waste amounts to approximately 1.3 billion tons, with 14 percent lost between post-harvest and retail, and 17 percent during retail and consumption phases. These statistics underscore the importance of more efficient food industry waste utilization (FAO 2022; Rashwan *et al.* 2023). Waste recycling and repurposing represent integrated practices that transform waste into alternative food products and materials, addressing growing food demand while preserving environmental resources and promoting circular economy principles.

Various applications exist for food and agricultural waste, encompassing waste from vegetables, cereals, fruits, dairy products, sugar, and meat processing (Jayathilakan *et al.* 2012; Gómez-García *et al.* 2021; Brito *et al.* 2022). These waste materials demonstrate potential utility in plant (Haefele *et al.* 2011) and animal nutrition (Jiang *et al.* 2025), novel food products such as vinegar, oils, and additives (Guiné *et al.* 2021), pharmaceutical products (Morin-Crini *et al.* 2019), bioenergy production (Keerthana Devi *et al.* 2022; Niyogi *et al.* 2024), and the biopackaging industry (Gururani *et al.* 2023). The heterogeneous biomass generated during fruit and vegetable cultivation constitutes plant waste, providing a source of bioactive compounds and antimicrobials, including polyphenols (Agourram *et al.* 2013). The citrus processing industry alone generates approximately 110 to 120 million tons of waste annually worldwide, and improper disposal can lead to land and water pollution, along with greenhouse gas emissions (Castagna *et al.* 2025). Citrus residues contain valuable compounds, such as essential oils, polyphenols, fibers, and pectins, which are extractable for use in food, cosmetic, and pharmaceutical industries (Iqbal *et al.* 2021).

Additional non-agricultural products can be converted into fertilizers. The sewage sludge obtained from the pharmaceutical manufacturing process, which undergoes standardization and control, represents one such example. This material can be safely repurposed as an organic nitrogen fertilizer (Cucina *et al.* 2021). These applications have substantially improved agricultural sector productivity and sustainability. The subsequent sections will address renewable biological resources utilized for food production in the agrarian system, particularly concerning bioinputs and bioproducts.

3. Bioinputs: A biological solution

In the international context, bioinputs encompass agricultural inputs of biological origin that enhance plant growth, soil health, and sustainable pest and disease control. While

definitions vary across countries and institutions, the concept generally includes biofertilizers, biopesticides, biocontrol agents, and biostimulants, derived from living microorganisms, plant extracts, or natural compounds. FAO provides a provisional definition: “Products of Plant, Animal or Microbial Origin Capable of Improving the Productivity, Quality and/or Health of Crops” (FAO 2025). In Brazil, law No. 15.070, of December 23, 2024 (BFG 2024), governs the production, use, and commercialization of bioinputs in agriculture. This legislation defines bioinputs as products, processes, or technologies of plant, animal, or microbial origin used in agriculture. The product or process may possess biotechnological origins or maintain structural similarity and functional identity to natural counterparts. Bioinputs serve agricultural product production, protection, storage, or processing, functioning in aquatic production systems or planted forests to influence the development of response mechanisms in animals, plants, microorganisms, soil, and derived substances (Borsari and Vieira 2022). Within this framework, the term “bioinput” specifically refers to materials employed in the agricultural sector, as examined in this review.

Bioinputs represent environmentally sustainable products derived from biological sources, including microbial cells, metabolites, plant materials, and organic or natural substances. These materials serve agricultural applications in pest and disease management, soil fertility enhancement, plant nutrient availability improvement, and growth promotion. Furthermore, agricultural products grown using bioinputs remain free from agrochemical residues, which have been associated with increased risks of neurodegenerative diseases and cancers, while also affecting soil, water, and ecosystem health (Rocha T M *et al.* 2024).

Bioinputs are experiencing global growth and increasing adoption among small- and medium-sized rural producers. In Brazil, a survey of 53 grain producers in the Cerrado region who utilized bioinputs indicated that environmental conservation commitment and development of effective production strategies were the primary motivations for adoption (Cerveira *et al.* 2025). Companies worldwide are expanding their focus on this agribusiness segment (Lee 2016; Laibach *et al.* 2019). Bioinputs are facilitating new bioeconomy-based business models in developing countries, such as Brazil and Argentina (Medina *et al.* 2023).

Understanding the plant and soil microbiome and their complex interactions is essential for bioinput application. The rhizosphere represents a dynamic zone where plant root–soil interactions influence plant health. The rhizosphere microbiome serves a vital function in promoting plant growth, resilience, and resistance to soil-borne diseases. Modern biotechnology approaches, including omics science, plant engineering, synthetic biology, sequencing, and gene-editing techniques, enable the study and identification of microorganisms and their bioproducts. These advances facilitate the development of strategies to enhance understanding and provide solutions for the agricultural sector in mitigating biotic and abiotic stresses (Afridi *et al.* 2022b; Silva *et al.* 2025). The plant microbiome components include microorganisms in the rhizosphere, seeds, endosphere

(internal plant tissues), and phyllosphere (microbial community on above-ground plant parts, primarily leaves and stems). Sustainable practices and biofertilization enhance plant microbiome interaction and functionality, contributing to increased resilience (Afridi *et al.* 2022a). The following sections discuss major categories of microbial bioinput.

3.1. Biofertilizers

Global standardization of the term “biofertilizer” remains inconsistent. While international nomenclature often uses biofertilizer and bioinoculant interchangeably, Brazilian legislation maintains distinct definitions. Biofertilizers are defined as products containing active ingredients or organic agents, free from agrotoxic substances. These products provide direct or indirect benefits to cultivated plants by enhancing productivity, excluding consideration of hormonal or stimulating effects (Decree No. 4.954/2004) (Brazil). The classification includes the following categories:

Amino acid biofertilizer Bioproducts derived through fermentation or hydrolysis of natural organic materials. Amino acid fertilizers can be produced through enzymatic and chemical hydrolysis of agro-industrial protein by-products from animal, microorganism, or plant sources. Examples include waste fermentation from animal carcasses (Liu *et al.* 2016), agricultural waste (Ghada *et al.* 2013), chicken feathers (Bhari *et al.* 2018), and microorganisms (Chen *et al.* 2023; Novaski *et al.* 2024). Amino acids contribute to stress defense, photosynthesis, nutrient uptake enhancement, pollination, and fruit formation, while functioning as hormone precursors. Additionally, these compounds serve as protein precursors and constituents, participating in metabolite synthesis that promotes plant growth and development (Shahrajabian *et al.* 2022). Amino acids provide nitrogen sources and support rhizosphere microbial growth, facilitating plant nutrient uptake from soil (Gupta *et al.* 2023).

Amino acids and peptides are components of Pilatus fertilizer, a plant extract containing fulvic acid, amino acids, and inositol. These compounds enhance crop root system growth and activity, including root length, biomass, and the absorption of water and nutrients from soil (Gupta *et al.* 2023).

Humic substance biofertilizer Humic substances (humic acids, fulvic acids, and humins) are produced through decomposition, organic material solubilization, and subsequent oxidation and polymerization. These substances comprise complex polymeric organic compounds, including polyphenols, proteins, enzymes, lipids, and polysaccharides. Additionally, non-humic substances (proteins, carbohydrates, resins, lignins, and humic) form during organic matter decomposition. Humic substances influence the environment’s physical, chemical, and microbiological structure, affecting plant metabolism and growth. Key effects include root system stimulation, physical structure enhancement, microorganism support, and nutrient availability improvement (Oliveira 2021).

In barley plants, the application of humic substances significantly enhanced yield and nutrient absorption (nitrogen, phosphorus, and potassium). Furthermore, humic acid

produced a substantial increase in grain and straw yields (El-Sheshtawy *et al.* 2019).

Foliar application of humic compounds can promote plant growth. However, soil microorganisms and humic compounds serve an essential function in soils that foliar treatment alone cannot substitute (Hafez *et al.* 2022). When absorbed by plants, humic substances accelerate nutrient turnover, stimulate gene expression, enhance respiration and photosynthesis, and regulate organic and inorganic anion ratios, as well as biosynthesis. This process includes the production of phytoncides and phytoalexins in plants. These compounds strengthen plant resistance to biotic and abiotic stress (Hafez *et al.* 2022), thereby enhancing seed germination and vigor (Hafez *et al.* 2022). However, conflicting results appear in the literature depending on the crop; Lazzarini *et al.* (2022) determined that humic substances application inhibited initial plant growth and did not enhance potato yield.

Algal extracts & processed algae These fertilizers are derived from the extraction and processing of algae (Nekvapil *et al.* 2021). Microalgae demonstrate rapid growth in challenging conditions, such as wastewater, reducing costs and improving viability. They effectively sequester CO₂ and address climate change. Additionally, utilizing microalgae as biofertilizers complements the integrated biorefinery concept, as they generate various bioproducts for industrial applications (Moreira *et al.* 2021; Braun and Colla 2023).

Microalgae extracts are extensively utilized in crop cultivation due to their growth-promoting properties and capacity to enhance crops' tolerance to abiotic stresses including extreme temperatures, drought, salinity, and mineral deficiency. The extracts contain macro- and micro-nutrients and active substances, comprising carbohydrates, proteins, lipids, vitamins, micronutrients, macronutrients, and phytohormones such as auxins, cytokinins, ethylene, abscisic acid, and gibberellin (Bello *et al.* 2021).

Blue-green algae in soil promote the formation of soil aggregates. This process minimizes soil erosion during rainy seasons and assists in regulating aeration and soil temperature. The physical and chemical properties of the soil improve, enhancing the growth environment for crops. Moreover, blue-green algae replenish soil nutrients through the secretion of exopolysaccharides and bioactive compounds (Chatterjee *et al.* 2017).

The literature documents various applications, including the use of digested *Chlorella* sp. to stimulate plant growth and increase metal content in corn. Furthermore, *Nannochloropsis oculata* has demonstrated the ability to enhance fruit quality by increasing sugar and carotenoid levels in tomato fruit (Ammar *et al.* 2022).

Plant extract biofertilizer This term refers to organic compounds extracted from uncontaminated organic materials through fermentation or alternative processing methods. Plant extracts function as growth enhancers, containing macro- and micro-nutrients, amino acids, and hormone-like substances that promote crop development (Vassilev *et al.* 2015). For example, soybean leaf and stem extracts enhance lettuce growth more effectively than urea fertilizer (Jang and Kuk 2019). Moringa leaf extract (*Moringa oleifera*)

improves seed germination and root development while delaying fruit senescence, thereby enhancing crop yield and quality. Its benefits derive from its rich content of minerals, proteins, vitamins, sugars, and phytohormones, including auxins and gibberellins (Mashamaite *et al.* 2022).

Compound biofertilizer This product results from combining multiple biofertilizers, which may include amino acids, humic substances, algae extracts, plant extracts, and other approved organic agents.

Other biofertilizers This category encompasses all biofertilizers recognized by Brazilian research and legislation.

3.2. Biostimulants

According to Brazilian legislation, biostimulants comprise microorganisms and/or metabolites that enhance plant physiological processes, preventing or responding to plant stress. These substances can regulate populations of harmful organisms, function as defoliant or desiccants, and act as growth stimulators or inhibitors. Initially introduced by horticulture specialists, biostimulants were defined in the late 1990s as substances that promote plant growth in small quantities and were classified into humic substances, hormone-containing products, and amino acid-based products. They provide multiple advantages, including resource conservation, environmental stress mitigation, and reduced production costs by enhancing natural processes in plants and soil microbiota rather than merely supplying nutrients or controlling pests (Du Jardin 2015; Meena *et al.* 2025).

Biostimulants are classified into two primary categories: non-microbial and microbial biostimulants. Non-microbial biostimulants encompass plant and seaweed extracts, humic substances, protein hydrolysates, or plant growth regulators (PGRs). These include phytohormones, hormone-like substances (e.g., melatonin), and biostimulants derived from alternative sources, such as organic materials in vermicompost. Natural polymers, including chitosan, chitin, and chitosan oligosaccharides, also serve as biostimulants. Microbial biostimulants comprise beneficial microorganisms, such as mycorrhizal fungi, which establish symbiotic relationships with plant roots to improve nutrient uptake. They also include non-mycorrhizal fungi, like *Trichoderma*, and plant growth-promoting rhizobacteria (PGPR), which enhance plant development through various mechanisms (Zulfiqar *et al.* 2024).

Main microorganisms used in biostimulants The Brazilian legislation on biostimulants remains in development, lacking a specific list of microorganisms classified for biostimulant formulation, unlike other global regions. In Europe, CMC-7 (Component Material Category 7) represents one category established under the European Fertilizing Products Regulation (EU) 2019/1009, governing biostimulants and related products within the European Union. CMC-7 specifically defines microorganisms eligible for use as components in fertilizers or biostimulants. Among bacteria, genera such as *Azospirillum* spp., *Azotobacter* spp., and *Rhizobium* spp. are included. Regarding fungi, mycorrhizal fungi are generally considered eligible. Approved

microorganisms must satisfy specific criteria, including microbiological safety, documented origin, absence of pathogenicity, and demonstrated efficacy (EPC 2019).

In the literature, other plant growth-promoting bacteria (PGPB), such as *Bacillus*, *Serratia*, *Arthrobacter*, *Pseudomonas*, *Rhodococcus*, *Enterobacter*, *Ochrobactrum*, *Acinetobacter*, *Streptomyces*, and *Stenotrophomonas*, are investigated as potential biostimulant agents (Kaushal et al. 2023).

Modes of action Microbial biostimulants, including PGPB and arbuscular mycorrhizal fungi (AMF), strengthen plant resilience to abiotic stresses such as drought, salinity, and extreme temperatures. These organisms function by activating physiological and biochemical processes, including the production of antioxidants, osmoprotectants, and stress-responsive enzymes, maintaining cellular homeostasis. Furthermore, these biostimulants address biotic stresses from pests and pathogens through induced systemic resistance, resource competition in the rhizosphere, and antimicrobial metabolite production. This promotes beneficial plant–microbe interactions, enhancing stress tolerance and improving plant growth and productivity under adverse environmental conditions while supporting sustainable agricultural practices (Kaushal et al. 2023). Drought significantly impairs plant growth and productivity through oxidative damage and disrupted physiological processes. Research demonstrates that specific *Streptomyces* strains can mitigate drought effects by enhancing stress-related transcription factor expression, such as ERF1 and WRKY70, and increasing antioxidant enzyme activity, including catalase, guaiacol peroxidase, and superoxide dismutase. These mechanisms reduce oxidative damage caused by reactive oxygen species (ROS), thereby preserving plant growth and productivity under water-deficit conditions (Abbasi et al. 2020).

Microbial metabolites significantly contribute to drought and thermotolerance by supporting plant resilience through various biochemical pathways. Compounds including phytohormones, volatile organic compounds (VOCs), exopolysaccharides, and ACC-deaminase enzymes enhance plants' capacity to withstand water scarcity and elevated temperatures, demonstrating the synergistic effects of microbial activity in improving stress tolerance (Yasmin et al. 2022).

AMF, such as *Glomus intraradices*, enhance plant tolerance to abiotic stresses, including drought and salinity. In symbiosis with *Phaseolus vulgaris*, AMF modulate aquaporin gene expression, optimizing water transport and maintaining cellular homeostasis during stress. AMF-colonized plants demonstrate higher relative leaf water content and enhanced root functionality compared to non-mycorrhizal plants, effectively mitigating water deficit impacts. Furthermore, AMF regulate stress-specific physiological responses, including transpiration rate modulation and plasma membrane integrity preservation, highlighting their essential role in strengthening plant resilience to abiotic challenges (Aroca et al. 2007).

3.3. Inoculants

According to Brazilian legislation, an inoculant is a product

containing microorganisms that promote plant growth (BFG 2004). Specifically, it is a product whose active ingredient comprises one or more beneficial living microorganisms that enhance plant development.

Research and initial implementation of inoculants in Brazil began in the 1920s and 1930s (Hungria and Nogueira 2022). However, widespread inoculant adoption commenced in the 1970s, coinciding with the country's soybean cultivation expansion. This growth was primarily attributed to soybeans' high nitrogen requirements, limited nitrogen availability in Brazil's weathered soils, and the restricted supply and high cost of nitrogen fertilizers (Telles et al. 2023).

Brazil established a legal framework in the early 1980s, providing guidelines for microorganism selection and inoculant product development and registration (Hungria and Nogueira 2022). During this period, the network of laboratories for recommendation, standardization, and dissemination of microbial inoculant technology of agricultural interest (RELARE) was established, incorporating representatives from research institutions, the inoculant industry, and the Ministry of Agriculture, Livestock, and Food Supply (MAPA). The integration of official regulations and RELARE recommendations has progressively enhanced the quality standards of market-available inoculants (Hungria and Nogueira 2022).

Currently, Brazil maintains three basic protocols for inoculant registration: one for nitrogen-fixing bacteria from the rhizobia group, another for products containing plant growth-promoting microorganisms, and a third for associative diazotrophic bacteria (MALFS 2023). However, all registered inoculants in Brazil either contain rhizobia or follow the PGPR microorganism protocol; no inoculants have been registered under the associative diazotroph protocol.

Brazil has over 600 registered inoculants, with at least 60% designated exclusively for soybean cultivation, followed by maize (MALFS 2023; Telles et al. 2023). Approximately 120 million doses of inoculants are sold annually in Brazil, with over 90% intended for soybean crops, followed by maize and, to a lesser extent, other crops (ANPIIB 2024). Notably, despite beans (*Phaseolus vulgaris* and *Vigna unguiculata*) being crucial food crops that respond effectively to rhizobia inoculation, the current inoculant supply for these crops in Brazil remains minimal, limiting producer access.

In Brazil, microorganisms used in inoculants must be registered with the MAPA for specific crops, following official selection protocols. Since 2011, MAPA has classified microorganisms in inoculants as authorized and recommended. Authorized microorganisms typically include nitrogen-fixing rhizobial bacteria, for which there is extensive knowledge about their benefits to plants, suitable culture media for growth, and industrial production processes. Recommended microorganisms include lesser-known or new growth-promoting microorganisms, such as *Azospirillum* and *Bacillus* strains. This distinction is crucial, as products based on authorized strains do not require agronomic efficiency tests for registration, while recommended and new strains require field tests to validate their agronomic efficacy. In Brazil, the majority of registered inoculants are based on *Bradyrhizobium* strains for soybean cultivation,

reflecting the high demand for these products (Table 1). *Bradyrhizobium* is also recommended for cowpea, while *Rhizobium* is traditionally used for common beans. Since 2010, *Azospirillum*-based inoculants have been registered for use on various crops, including maize, wheat, sugarcane, and legumes such as soybeans and common beans. For legumes, combining *Azospirillum* with rhizobia strains enhances nodulation. Recently, inoculants based on *Bacillus* and *Priestia* have been registered to improve phosphorus utilization and mitigate drought effects. Additionally, fungal species like *Trichoderma* and AMF such as *Claroideoglomus claroideum* and *Rhizoglossus intraradices* are being registered as plant growth-promoting microorganisms (Table 1).

A fundamental mode of action is biological nitrogen fixation by rhizobia, which colonizes plants, triggers nodule formation, and contains genes encoding the nitrogenase complex, enabling the conversion of atmospheric nitrogen into a plant-usable form (Sprent et al. 2017; Camuel et al. 2023). In Brazil, research demonstrates that inoculating soybeans with

selected *Bradyrhizobium* strains accounts for approximately 90% of the nitrogen accumulated by this crop (Hungria et al. 2013). Similarly, other grain crops, such as cowpea, obtain about 50–60% of their nitrogen through symbiotic diazotrophic bacteria (Hungria et al. 2013). Another significant mode of action involves nitrogen fixation by associative diazotrophic bacteria, which fix nitrogen in the rhizosphere or during internal colonization of plant tissues without establishing true symbiosis (Bashan and de-Bashan 2010; Cassán et al. 2020). This type of plant growth promotion was extensively investigated by Dr. Johanna Döbereiner and collaborators from Embrapa, Brazil, who documented interactions between Poaceae family plants and associative bacteria, including genera such as *Azospirillum*, *Nitrospirillum*, and *Paraburkholderia* (Baldani et al. 2014; Cassán et al. 2020; Reis et al. 2020). Microorganisms such as *Bacillus*, *Azospirillum*, and *Trichoderma* serve essential functions for plants through diverse mechanisms (Harman et al. 2004; Lugtenberg and Kamilova 2009; Pérez-García et al. 2011;

Table 1 Microbial species used as inoculants in Brazil according to (MALFS 2025)

Crop	Species	Type of inoculant	Microorganism species	Number of products registered
Soybean	<i>Glycine max</i>	Nitrogen-fixing symbiotic bacteria	<i>Bradyrhizobium elkanii</i> , <i>Bradyrhizobium japonicum</i> or <i>Bradyrhizobium diazoefficiens</i>	330
			<i>Bacillus amyloliquefaciens</i> , <i>Bacillus aryabhattai</i> , <i>Bacillus licheniformis</i> , <i>Priestia megaterium</i> , <i>Bacillus simplex</i> or <i>Bacillus subtilis</i>	18
		Plant-growth-promoter	<i>Azospirillum brasilense</i>	38
			<i>Claroideoglomus claroideum</i> , <i>Rhizoglossus intraradices</i>	7
			<i>Trichoderma asperelloides</i> , <i>Trichoderma asperellum</i> , <i>Trichoderma endophyticum</i> , <i>Trichoderma harzianum</i> or <i>Trichoderma coningiosis</i>	6
			<i>Pseudomonas fluorescens</i>	7
			<i>Pantoea agglomerans</i>	1
			<i>Methylobacterium symbioticum</i>	1
			<i>B. subtilis</i> , <i>Bacillus elkanii</i> , and <i>Paraburkholderia nodosa</i>	1
			<i>P. fluorescens</i> , <i>B. amyloliquefaciens</i> and <i>P. megaterium</i>	1
			<i>A. brasilense</i>	47
			<i>B. amyloliquefaciens</i> , <i>Bacillus aryabhattai</i> , <i>B. licheniformis</i> , <i>P. megaterium</i> , <i>B. simplex</i> or <i>B. subtilis</i>	14
			<i>C. claroideum</i> or <i>R. intraradices</i>	7
			<i>P. fluorescens</i>	3
			<i>P. agglomerans</i>	1
Maize	<i>Zea mays</i>	Plant-growth-promoter	<i>M. symbioticum</i>	1
			<i>A. brasilense</i> , <i>P. fluorescens</i>	2
		Plant-growth-promoter	<i>A. brasilense</i> and <i>B. japonicum</i>	2
			<i>Bacillus megaterium</i> , <i>Lysinibacillus</i> sp.	1
			<i>Lactobacillus plantarum</i> , <i>Rhodopseudomonas palustre</i> and <i>Saccharomyces cerevisiae</i>	1
			<i>Bradyrhizobium amazonense</i> , <i>Bradyrhizobium yuanmingense</i> , <i>Bradyrhizobium viridifuturi</i> or <i>Bradyrhizobium pachyrhizi</i>	36
			<i>Rhizobium tropici</i> or <i>Rhizobium freirei</i>	73
			<i>A. brasilense</i>	7
			<i>P. megaterium</i> , <i>B. amyloliquefaciens</i> and <i>B. subtilis</i>	1
			<i>P. agglomerans</i>	1
			<i>Nitrospirillum viridazoti</i>	1
			<i>A. brasilense</i>	2
			<i>P. megaterium</i> and <i>B. subtilis</i>	1
Cowpea	<i>Vigna unguiculata</i>	Nitrogen-fixing symbiotic bacteria		
		Nitrogen-fixing symbiotic bacteria		
		Plant-growth-promoter		
Bean	<i>Phaseolus vulgaris</i>	Nitrogen-fixing symbiotic bacteria		
		Nitrogen-fixing symbiotic bacteria		
		Plant-growth-promoter		
Sugarcane	<i>Saccharum officianlis</i>	Plant-growth-promoter		

Glick 2012; Cassán and Diaz-Zorita 2016). Although reports on plant growth-promoting effects by *Bacillus*, *Trichoderma*, and *Pseudomonas* are common, products containing these microorganisms have only recently gained registration in Brazil as inoculants. Strains from these genera employ multiple mechanisms that support plant development, both directly and indirectly. In Brazil, inoculants based on *Bacillus subtilis* and *Priestia megaterium* are currently available, designed to enhance phosphorus availability and improve phosphate fertilizer efficiency (Oliveira et al. 2009; Oliveira Paiva et al. 2022). Additionally, inoculants containing *Bacillus aryabhattai* assist plants in managing drought stress, while those containing arbuscular mycorrhizal fungi, primarily from the genus *Rhizophagus*, provide other benefits (Bonatelli et al. 2021; Lacerda Júnior and Melo 2022). Moreover, inoculants with *Azospirillum* and *Nitrospirillum* are registered for various crops, with their beneficial effects attributed to multiple factors.

The growth-promoting action of these bacteria involves various biochemical and physiological mechanisms, including the solubilization of phosphorus (P) and potassium (K) elements in the soil, enhancing nutrient accessibility to plants (Glick 2012; Cassán and Diaz-Zorita 2016). These bacteria also produce siderophores, which enhance iron availability, antimicrobial compounds that protect roots from pathogens (Pérez-García et al. 2011), and compounds that simulate phytohormone effects, such as auxins and cytokinins, with indole-3-acetic acid (IAA) being a primary example. These compounds promote root development, improving the plant's ability to utilize soil resources (Harman et al. 2004).

Additional mechanisms include the secretion of exopolysaccharides, which form biofilms on roots, enhancing water retention in the soil and protecting plants against dehydration (Glick 2012), production of osmolytes that provide cellular protection under water stress, activation of antioxidant enzymes, such as catalase and superoxide dismutase, which reduce oxidative damage in plant cells (Cassán and Diaz-Zorita 2016), and modulation of aquaporin expression, proteins crucial for efficient water transport in plants. These diverse strategies establish PGPB as valuable components in sustainable agriculture, enhancing crop resilience and efficient utilization of natural resources (Harman et al. 2004).

3.4. Biocontrol agents

A more sustainable approach to controlling plant diseases has emerged through biological control, which was initially discovered through agricultural research studies (Baldani et al. 2014; Cassán et al. 2020; Reis et al. 2020). Biological control, or "biocontrol," involves the strategic use of natural antagonists, particularly microbial agents, to suppress agricultural pest populations, offering a sustainable alternative to chemical pesticides within integrated pest management frameworks. This approach proves advantageous as it not only inhibits phytopathogens but potentially enhances plant growth. Additional benefits include targeted action specificity, environmental sustainability, non-toxicity, long-term

establishment capability, cost-effectiveness, and improved plant pathogen resistance. However, this method requires strict regulatory compliance and faces challenges in scaling production (Dalitz et al. 2017).

Brazil has established itself as a global leader in biocontrol agent production and implementation, implementing stringent pesticide controls alongside government incentives, streamlined registration processes, and regulations supporting microbial biocontrol and "organic farming" practices that minimize chemical usage in soil and crops. As of 2022, biocontrol agents covered more than 70 million hectares in Brazil, primarily protecting soy, corn, sugarcane, and coffee crops, with bioproducts targeting bacteria, fungi, nematodes, and insects (Lobato et al. 2019; Bettiol and Medeiros 2023). Brazilian agricultural regulations, specifically Law No. 14.785/2023 (pesticides) and No. 15.070/2024 (bioinputs), strengthen the framework governing microbial strain usage as biocontrol agents.

The application of microorganisms as biocontrol agents presents a sustainable alternative to chemical pesticides, minimizing toxicity and environmental impact. Endophytic microorganisms, which inhabit plant tissues, demonstrate particular effectiveness due to their intimate association with host plants, strengthening disease protection (Alsubaie et al. 2024). Additional strategies and bioprospecting sources for novel microbial biocontrol agents continue to emerge, indicating significant market growth potential in coming years (Zenelt and Krawczyk 2025). Research priorities include understanding the environmental dynamics of biocontrol agents in disease management, aiming to introduce optimal and pathogen-specific biocontrol solutions (Dalitz et al. 2017).

Main microorganisms used as pest and disease control agents According to the Brazilian Agricultural Research Corporation (EMBRAPA), *Bacillus* spp., *Pseudomonas* spp., and *Streptomyces* spp. are the genera most frequently found in patent requests in Brazil. *Bacillus* spp. accounts for more than 60% of the total deposits. Other bacterial genera include *Rhizobium* spp., *Azotobacter* spp., and *Paenibacillus* spp. Among fungal genera, *Trichoderma* spp. and *Penicillium* spp. are the most requested in patent deposits inside the country. These microorganisms are utilized to promote plant growth or act as biocontrol agents (Bettiol and Medeiros 2023). Still, Brazilian agriculture has a vast catalog of microorganisms that can still be explored in this scenario. Recent findings of these microbial genera will be briefly discussed in this section.

The bacterial genus *Bacillus* is renowned globally in biotechnology and various industrial sectors, and has been extensively studied as a biocontrol agent for preventing multiple plant diseases. These bacteria, isolated from soil and plants, produce metabolites that prevent phytopathogen infections. A comprehensive review recently highlighted the crucial role and biocontrol attributes of *Bacillus* sp. strains in controlling numerous plant diseases (Etesami et al. 2023). Notable research includes several *Bacillus* sp. strains isolated from oyamel-fir forest soil affected by fire, which prevented systemic infection and reduced mycelial growth of *Fusarium* sp., a known maize pathogen (Chávez-Díaz et al. 2024). Another study demonstrated the antagonistic activity

of *B. siamensis* against *Fusarium* sp. strains, achieving up to 80% reduction in disease index in tomato plants (Zhang et al. 2024). Additionally, a Brazilian research group reported a strain of *Bacillus velezensis* that inhibited mycelial growth and sporulation of *C. musae* (anthracnose in postharvest bananas) (Damasceno et al. 2019). Another Brazilian team isolated a *Bacillus* sp. strain (B157), showing promising results as a biocontrol agent against rust, a prevalent coffee disease in Brazil (Haddad et al. 2009). As Brazil maintains its position as the world's largest coffee producer, with annual production exceeding 50 million bags, additional research on biocontrol in Brazilian coffee plantations could strengthen its global leadership in coffee production and export (Oliveira Silva et al. 2025; Sousa et al. 2025). *Bacillus velezensis* has also demonstrated effectiveness in controlling nematodes of the genus *Meloidogyne* spp. (Keshmirshakan et al. 2024). Notably, all mentioned strains exhibited plant growth-promoting capabilities, further emphasizing their agricultural potential.

The *Streptomyces* genus, the most prominent member of the Actinobacteria phylum, is distinguished for its production of bioactive metabolites and proteins across various biotechnological applications (Sharma et al. 2020). Despite limited reports of *Streptomyces* as a plant pathogen, this genus has attracted significant attention for its potential application as a biocontrol agent in agriculture (Nazari et al. 2023). Through an observational literature review, Law et al. (2017) documented numerous studies where metabolites produced by *Streptomyces* spp. strains demonstrated antifungal activity against *Magnaporthe oryzae*, a significant fungal pathogen causing rice blast disease (Law et al. 2017). Research has shown that *Streptomyces* sp. can be effectively applied through cell-free culture filtrate, owing to its secretion of various hydrolases and secondary metabolites, which inhibit *B. sorokiniana* infection in wheat seedlings (Cai et al. 2024). Furthermore, several bioactive compounds produced by *Streptomyces* spp. strains, including blasticidin-S, kasugamycin, and other bioformulations, are commercially utilized for crop and rice cultivation protection (Minuto et al. 2006; Copping and Duke 2007; Tapadar and Jha 2013; Law et al. 2017).

Regarding bacterial representatives in biocontrol, *Pseudomonas* spp. has been extensively studied for controlling phytopathogen growth due to its production of VOCs and its documented role as a PGPB in plants, either independently or in combination with other bacteria (Georgieva et al. 2023; Papade et al. 2024; Tienda et al. 2024; Wang et al. 2024). Bacterial suspensions of *P. mediterranea* PVCT 3C demonstrated effectiveness against mal secco disease (fungus *Plenodomus tracheiphilus*) and reduced disease severity in citrus plants (Dimaria et al. 2024). In the same study, culture filtrates containing VOCs produced by *P. mediterranea* PVCT 3C also inhibited mycelial growth of the phytopathogen. Recent studies have further demonstrated the potential of *Pseudomonas* spp. strains as both plant growth promoters and phytopathogen inhibitors (Chetan et al. 2024).

Fungal strains have also demonstrated efficacy in managing and preventing phytopathogen diseases, expanding

the range of genera available for biotechnology applications. The entomopathogenic fungus *Beauveria bassiana* represents the most widely utilized microorganism for biological control in Brazil, with 39 registered commercial products based exclusively on this fungus. Current research explores novel techniques involving microorganism encapsulation with nanoparticles to enhance the stability and effectiveness of biocontrol agents under adverse environmental conditions, such as solar radiation, as documented by Sousa et al. (2025) in a biocontrol study for coffee plantations.

Trichoderma spp. has emerged as one of the most promising biocontrol agents due to its disease-preventing metabolites (Asad 2022). A strain of endophytic fungus *Diaporthe caatingaensis* demonstrated effective antagonistic activity against *Fusarium* spp. strains associated with coffee plantations in Saudi Arabia (Alsubaie et al. 2024). Another study examining endophytic fungi found that isolates of *Colletotrichum* sp., *Aspergillus* sp., and *Annulohyphoxylon* sp. effectively reduced disease severity caused by *Rhizoctonia solani* in rice seedlings (Muthu Narayanan et al. 2024).

Notable attention should be given to the ascomycete *Clonostachys rosea*, which exhibits multiple modes of action as a biocontrol agent in plants against *Fusarium* spp., *Ganoderma* spp., *Moniliophthora* spp., and numerous others, employing strategies such as enzyme secretion and antibiotic compound production, which will be examined later in this section. These characteristics have led to the commercialization of *Clonostachys rosea* formulations as biocontrol agents in the U.S., EU, and Brazil (Nagaraj and Kolanthasamy 2025).

Microorganisms play a crucial role in contemporary agricultural technology, and their utilization is expected to increase given their advantages over chemical control products. In Brazil specifically, investment in microbial agents and their application for plant disease control is projected to expand. Future research priorities include developing new bioherbicides, exploring combinations of biological agents, and identifying strains adaptable to changing climatic conditions (Bettiol and Medeiros 2023).

Modes of action Agricultural applications favor microorganisms due to their diverse metabolic pathways, which enhance plant growth or inhibit pathogen infection. These modes of action encompass both direct and indirect strategies, utilizing various gene clusters, biochemical pathways, and secondary metabolites that affect either the plant or the phytopathogen. Understanding these mechanisms is fundamental for implementing both established and newly identified microorganisms across Brazilian cultivars. The following discussion will briefly examine the mechanisms of the most commonly used microbial agents in Brazilian agriculture.

1) Antibiosis. Biocontrol agents that secrete secondary metabolites with antimicrobial properties play a crucial role in controlling plant diseases. *Bacillus velezensis*, one of the primary species utilized in Brazil for this purpose, serves as an effective biocontrol agent due to its numerous gene clusters that produce antimicrobial metabolites targeting a broad spectrum of phytopathogens (Keshmirshakan et al. 2024). This species possesses gene clusters responsible for generating antibacterial polyketides (macrolactin, bacilaene,

difficidin), dipeptides (bacilysin), lipopeptides (surfactin, iturin), and additional secondary metabolites with potent antagonistic effects against phytopathogenic agents (Keshmirshekan et al. 2024; Wang et al. 2024). These molecules disrupt cell membranes, causing cellular component leakage and altering vital metabolic pathways (Wang et al. 2024). Researchers have also explored combining antimicrobial compounds produced by *Bacillus* species with chemical compounds to control plant diseases (Kim et al. 2024).

Among other significant bacterial genera, multiple strains of *Streptomyces* spp. and *Pseudomonas* spp. demonstrate various disease control mechanisms. The genus *Streptomyces* is renowned for producing diverse metabolites, including antibacterial, antifungal, and antiviral compounds, as well as insecticides, pesticides, herbicides, and hydrolytic enzymes, which find extensive applications in biotechnology (Nazari et al. 2023; Kim et al. 2024). For instance, research identified specific antimicrobial metabolites (gougerotin, natamycin, nystatin, and anisomycin) and VOCs (alkenes, alcohols, esters, and alkanes) produced by *Streptomyces noursei* C27 in fermentation broth that effectively controlled *Botrytis cinerea* infection in grape leaves and fruit (Lu et al. 2024).

Recent research has described a strain of *Pseudomonas atacamensis* (GZ-3) that produces VOCs, primarily 3-methyl-1-butanol and 2-heptanone, which inhibit mycelial growth and conidial germination of the phytopathogen *Colletotrichum gloeosporioides* (Ge et al. 2025).

Additional research investigating *Pseudomonas* spp. strains has demonstrated that the biosynthesis of antimicrobial peptides including phenazines, pyrrolnitrin, 2,4-diacetyl phloroglucinol, and pyoluteorin by *Pseudomonas chlororaphis* subsp. *aurantiaca* (SRP19) effectively suppresses *Fusarium sacchari* growth (Chetan et al. 2024).

Trichoderma produces volatile antibiotics, VOCs, and peptaibols when inhibiting pathogens through antibiosis (Asad 2022). Research has shown that four endophytic strains of *Trichoderma* exhibited antagonistic activity against three phytopathogens (genera *Sclerotinia*, *Sclerotium*, and *Fusarium*) (Rajani et al. 2021). In this latter work, the *Trichoderma longibrachiatum* strain 2 generated different volatile organic compounds when cultivated in pure culture and mixed culture with double plates (biocontrol agent and phytopathogens). *Trichoderma* spp. also demonstrated antagonistic effects against pathogens through the secretion of hydrolytic enzymes, such as chitinase and glucanase (Da Silva et al. 2016).

2) Mycoparasitism. A significant mechanism for plant disease control occurs when biocontrol agents infect phytopathogens and destroy their cells. For instance, *Trichoderma* exhibits mycoparasitism, demonstrating the capacity to parasitize and suppress other fungi. This characteristic was documented for all four *Trichoderma* species in research examining these strains for biocontrol of various phytopathogens (Da Silva et al. 2016). *Trichoderma* strains develop alongside and coil, advancing to the mycelia of the pathogen-host. During this interaction, *Trichoderma* identifies the antagonistic fungus, attaches, and attacks by secreting lytic enzymes (glucanase, chitinase, N-acetyl-

glucosaminidase) to degrade the host cell wall, ultimately causing the host's death (Rajani et al. 2021; Asad 2022).

Additionally, regarding this agent, research investigating the deletion of the *hex1* gene in *T. simmonsii* as a biocontrol agent revealed that it impacted fungal growth, resulting in a substantial reduction of antagonistic properties against target phytopathogens of the wheat plant, affecting the processes of mycoparasitism, antibiosis, and competition exhibited by this biocontrol agent (Pedrero-Méndez et al. 2025). Beyond this genus, other microorganisms have been investigated and characterized with mycoparasitic activity against phytopathogenic fungi. In this context, a *Diaporthe caatingaensis* strain demonstrated antagonistic activity against *F. proliferatum* and *F. oxysporum* OP969874 strains through mycoparasitic modes of action (coiling and appressorium formation), showing potential as a biocontrol agent for sustainable coffee cultivation (Alsubaie et al. 2024).

3) Competition. This mode of action involves interaction between different organisms competing for the same space, nutrients, water, and light. This mechanism was documented in research where a *B. velezensis* strain reduced the infection of *Burkholderia glumae* in rice plants after both microorganisms competed for identical root exudate compounds and colonized the same ecological niches in the plants (Perea-Molina et al. 2022). In a separate study, *B. subtilis* HJ4 demonstrated significant antagonistic effects against *A. versicolor* growth in wheat, both *in vitro* and *in vivo*, mediated by various mechanisms, including competition for nutrients and space (Huang et al. 2025).

Trichoderma spp. also utilize various strategies to enhance their efficiency in occupying these spaces, such as overexpressing ABC transporters to reduce toxic metabolites within their cells and secreting siderophores under iron-deficient conditions to facilitate the acquisition of the limited mineral (Asad 2022). Previously, for other genera, competition for infection sites was identified as one of the mechanisms of action of *Glomus clarum*, an AMF, against *R. solani* under greenhouse conditions.

4) Induction of resistance in plants represents an indirect biocontrol mechanism that operates through modifications in plant metabolic pathways and immune responses when exposed to biocontrol agents or their biocompounds. This resistance induction typically manifests in plant hosts by preventing infections from multiple phytopathogen classes, regardless of the biocontrol agent's genus. A notable example emerges from a recent study examining a *Pseudomonas rhizophila* strain as a biocontrol agent against *P. syringae* pv. *actinidiae*, a significant kiwifruit pathogen (Tian et al. 2025). Through qRT-PCR assays monitoring immune-related gene expression in kiwifruit, the researchers observed that Z98 treatment induced up to 15.7-fold upregulation in resistance genes. Mannaa et al. (2024) demonstrated that *B. subtilis* JCK-1398 upregulated resistance genes and enhanced pinoselin production, a compound associated with nematode resistance in *Pinus densiflora*, leading to over 70% reduction in plant disease incidence. Soybean cyst nematode (SCN), *Heterodera glycines*, a microscopic roundworm, ranks among the most destructive soybean crop pests globally (Bent 2022). It represents the most significant yield-reducing

pathogen affecting soybean crops in the US and maintains major pathogen status in Brazil and China (Bandara *et al.* 2020; Peng *et al.* 2021; Rocha M R D *et al.* 2024). *Pochonia chlamydosporia* PC10 (Rizotec), *Bacillus methylotrophicus* UFPEDA 20 (Onix), and *Trichoderma koningiopsis* GF 362, applied *via* seed inoculation or in-furrow treatment at planting, decreased the nematode population, with *Trichoderma koningiopsis* showing particular effectiveness. Root-associated microorganism analysis revealed a 50% increase in *Mortierella* spp. and approximately 30% decrease in *Fusarium* spp. following treatment with *T. koningiopsis* and *B. methylotrophicus*. The microbial community exhibited increased complexity and cohesion after the second year of biocontrol product application (Siddique Afridi *et al.* 2024). The nematode *Meloidogyne exigua*, which causes damage in *Coffea arabica* plantations, represents another significant pathogen. Afridi *et al.* (2024) examined biological control agents' effects on root-knot nematode control and coffee plant rhizomicrobiome. The evaluated bioproducts included *Trichoderma asperellum* URM 5911 (Quality), *Bacillus subtilis* UFPEDA 764 (Rizos), and *Bacillus methylotrophicus* UFPEDA 20 (Onix). Cadusafos (Rugby), a chemical nematicide, was tested independently and in combination with *T. asperellum*, *B. subtilis*, and *B. methylotrophicus*. The research revealed no significant differences between biological and chemical agents or between treated groups and controls. Furthermore, neither nematicides nor biocontrol agents substantially altered the existing microbiome diversity.

Among fungi with potential application as biocontrol agents, research has shown that treatment of citrus fruit peel with *Cluyveromyces marxianus* activated the expression of 90 biological pathways and significantly expressed more than 1,000 genes (Isaac Delali *et al.* 2022). These genes encoded the production of phenolic compounds, flavonoids, and lignin, among others, resulting in enhanced antifungal activity and defense responses compared to untreated peels. *Trichoderma* spp. has also been identified as an inducer of pathogen resistance in certain plants (Yang *et al.* 2024). Research utilizing marked gene detection in onion plants demonstrated that the *T. asperellum* BCC1 strain induced systemic defenses against the *Stromatinia cepivorum* pathogen (Rivera-Méndez *et al.* 2020). Additional fungal genera have been documented to induce immune systems in plant hosts (Daroodi *et al.* 2021).

4. Legal framework for bioinputs in Brazil

4.1. Brazilian regulation

Following the description of primary biostimulants, commonly utilized microorganisms, and their mechanisms in supporting plants and agriculture, it is crucial to outline the relevant norms and regulations governing this domain in Brazilian territory. Prior to the enactment of the Bioinputs Law, No. 15.070, on December 23, 2024 (BFG 2024), bioinputs were regulated under provisions designed for chemical, synthetic, or mineral products, including the Agrochemicals Law (Law No. 14.785/2023) (BFG 2023) and the Fertilizers Law (Law No. 6.894/1980) (BFG 1980).

Before the implementation of Law No. 15.070/2024, Brazil's regulation of bioinputs lacked cohesion, with existing legislation not specifically adapted to their distinct characteristics. This fragmentation created inconsistencies and legal uncertainties, impeding industry development and access to specialized credit lines (Borsari and Vieira 2022). The new legislation addresses these challenges by establishing a comprehensive framework for bioinput production, registration, and commercialization, promoting sustainability and innovation in Brazilian agriculture. The upcoming regulations, planned for 2025, are expected to align with international safety standards recognized by organizations such as the Food and Agriculture Organization (FAO) and the Organization for Economic Cooperation and Development (OECD) (Croplife Brasil 2024).

The pending regulation aims to establish specific criteria for ensuring the safety and efficacy of advanced bioinputs, including those based on genetic and molecular techniques, alongside traditional natural-based inputs such as insects and biofertilizers. This initiative is projected to foster innovation, attract investment, and strengthen Brazil's position in sustainable agricultural practices. Industry stakeholders anticipate an effective and transparent regulatory process that ensures the selection of innovative, efficient, and consumer-safe products (Borsari and Vieira 2022; Faria and Wander 2024).

The new law regulates 18 items: production, importation, exportation, registration, marketing use, inspection, supervision, research and experimentation, packaging, labeling, advertising, transportation, storage, fees, provision of services, disposal of waste, and incentives for producing bioinputs.

Brazil's Law No. 15.070/2024 establishes a comprehensive framework for bioinputs in agriculture, encompassing production, import, export, registration, commercialization, use, inspection, and supervision. It applies to all conventional, organic, and agroecological cultivation systems, as well as all bioinputs used in agricultural activities. The law incentivizes bioinput production through financial mechanisms, including fiscal and tax incentives, to promote research, development, production, use, and commercialization of bioinputs for agricultural, livestock, aquaculture, and forestry purposes. Priority is given to micro-enterprises producing bioinputs for commercial purposes, and to agricultural cooperatives and family farmers producing bioinputs for their use. Federal, state, district, and municipal authorities may create policies and develop fiscal and tax mechanisms to stimulate and facilitate the production and use of bioinputs. The National Rural Credit System may apply differentiated interest rates to rural producers and their cooperatives that utilize bioinputs in their production systems.

Brazil's regulatory framework for microbial bioinputs has undergone significant modernization with the enactment of Federal Law No. 15.070/2024, positioning the country as a global leader in this area, however, the ongoing regulation of this law should define requirements to address IP and biosafety concerns. Here's a breakdown of its strengths and a comparison with the U.S., EU, and India (Table 2).

Brazil's framework stands out for its progressive stance

Table 2 International comparison of regulation in Bioinputs¹⁾

Country ²⁾	On-Farm production	Registration	Scope	Innovation Support	Regulatory Agencies
Brazil	Allowed (personal use only)	Required for commercial use; simplified for some	Broad: microbial, plant, animal, biotech	High: flexible definitions, intellectual property focus	MAPA, ANVISA, IBAMA
U.S. (EPA/USDA)	Not regulated federally	Required via EPA (biopesticides) or USDA (biofertilizers)	Focus on biopesticides and biofertilizers	Moderate: slow approval process Moderate	EPA, USDA
EU (EFSA/EC)	Not permitted	Required via EFSA; strict data requirements	Focus on biopesticides; biostimulants under REACH	Moderate: harmonized but slow	EFSA, EC
India (FCO/RCF)	Not formally regulated	Required under FCO	Focus on biofertilizers and biopesticides	Low: outdated definitions, slow updates	FCO, RCF, State Departments

¹⁾ REACH, Registration, Evaluation, Authorisation and Restriction of Chemicals; MAPA, Ministry of Agriculture and Livestock; ANVISA, National Health Surveillance Agency; IBAMA, Brazilian Institute of Environment and Renewable Natural Resources.

²⁾ EPA, Environmental Protection Agency; USDA, United States Department of Agriculture; EFSA, European Food Safety Authority; EC, European Commission; FCO, Fertilizer Control Order; RCF, Rashtriya Chemicals and Fertilizers Limited.

on on-farm production, broad scope, and innovation-friendly definitions. While the U.S. and EU have more established systems, they are often slower and more rigid, especially for novel microbial products. India's system is less harmonized and slower to adapt to new technologies.

4.2 Brazil's regulatory strengths

Comprehensive scope The law covers the entire lifecycle of bioinputs: production, import/export, commercialization, research, and use. It encompasses inputs of microbial, plant, and animal origin, as well as products derived from biotechnology or with similar structural properties.

On-farm production legalization Brazil uniquely permits on-farm production of microbial bioinputs for personal use, exempting these products from complete registration requirements. This policy facilitates smallholder innovation and reduces costs, though it raises concerns regarding intellectual property and biosafety.

Simplified registration While commercial products require registration, simplified procedures exist for specific categories. "Inoculants" and end-use products must maintain registration to ensure quality control.

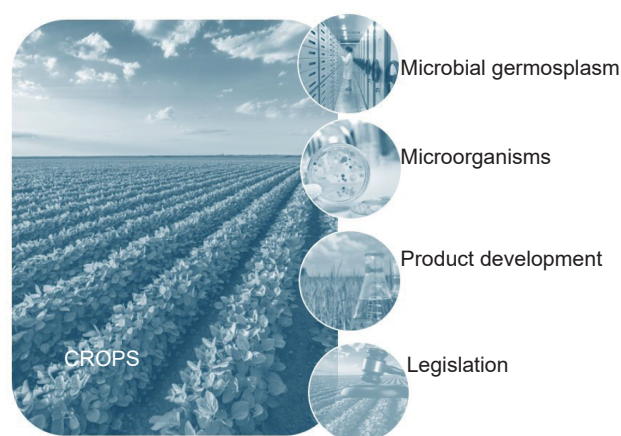
Multi-agency oversight MAPA leads regulatory efforts, with ANVISA and IBAMA overseeing human health and environmental safety aspects.

Innovation-friendly definitions The legislation provides flexible definitions for biostimulants, biofertilizers, and biological control agents, fostering research and development, and market expansion.

4.3. Key factors for the development of agriculture

Microbial germplasm encompasses the genetic material of microorganisms — such as bacteria, fungi, and other microbes — that can be utilized to enhance crop productivity and sustainability (Fig. 1). These genetic resources are vital for developing bioinputs in agriculture, promoting sustainable practices, and improving plant health.

Microbial germplasm banks exclusively preserve and characterize microorganisms, biological pest control agents, and plant growth promoters. Brazil maintains a collection exceeding 10,000 strains of bacteria, fungi, and viruses that assist in controlling pests and plant diseases. Additionally,

**Fig. 1 Critical components in agricultural development.**

Germplasm banks housing well-characterized microorganisms, maintained under proper preservation conditions and demonstrating economic viability, are essential. Product development requires investment in innovative formulations, despite associated risks. Furthermore, market expansion into underexplored production chains facilitates comprehensive agricultural advancement.

more than 14,000 strains of nutrient-fixing microorganisms and plant growth promoters exist. This extensive collection is distributed across at least seven separate research units of EMBRAPA.

These biobanks or microbial resource centers are located in several countries, including the National Agriculturally Important Microbial Culture Collection (NAIMCC) in India, among others (Sharma *et al.* 2019).

Investment in innovation by governments and private entities represents another crucial factor. Research and development of new bioproducts requires substantial financial resources to advance technological growth and innovation. The integration of classical biotechnology with modern smart agriculture techniques promotes high-quality agricultural and rural development (Mileva and Georgieva 2022; Li and Nanseki 2023). This consideration holds particular significance in nations where agriculture serves as a primary driver of economic growth (Yogi *et al.* 2025).

Bioinputs represent a green and sustainable technology, essential for developing countries facing climate change

vulnerabilities, capital shortages, and heightened investment risks (Li and Wu 2025).

Additionally, expanding and strengthening underexplored production chains remains crucial. Each country's legislation functions as a regulatory framework and facilitating agent. The legal organization, production, commercialization, and inspection of these novel bioproducts constitute sensitive aspects. Bioinputs encompass products with considerable biological diversity and applications, necessitating well-structured legal support to address this complexity. This situation presents challenges in establishing an adequately flexible framework to address all requirements.

5. Bioinputs market in Brazil and growth potential

The agribusiness sector in organic agriculture has grown significantly in recent years. Brazil is considered a global leader in the use and production of bioinputs, including inoculants, biofertilizers, and biological products for pest control. The increasing use of bioinputs reflects the country's commitment to sustainable agricultural practices and acknowledges the economic and environmental benefits that this approach offers. Nearly 50% of producers in Brazil utilize these bioproducts. According to CropLife, the Brazilian bioinputs market has grown at an average annual rate of 21% over the past three years, a growth rate four times higher than the global average. Among the main crops, the total use of bioinputs in Brazil is distributed as follows: 55% for soybeans, 27% for corn, 12% for sugarcane, and 6% for cotton, coffee, citrus, fruit, and vegetables (Croplife Brasil 2024). Fig. 2 represents the sales in the Brazilian market.

Recent data from the Center for Agribusiness Studies at Fundação Getulio Vargas (FGVAgro) indicate a 50% increase in agricultural land in Brazil cultivated with bioinputs between the 2021/22 and 2023/24 crop seasons. According to EMBRAPA, 55% of the country's cultivated land now utilizes some form of biological input, demonstrating the nation's substantial potential in this sector (Morrison 2024).

The bioinputs market in Brazil has experienced significant growth, with retail sales reaching 5 billion reais (\$924 million) in the 2023/2024 season. This represents an average annual increase of 21% over the past three years, quadrupling the global average. Projections indicate that the worldwide bioinputs market could expand to \$45 billion by 2032, with Brazil positioned to contribute significantly. The application of bioinputs in Brazil is particularly prevalent in key crops such as soybeans, corn, and sugarcane, with additional usage in cotton and coffee farming. Regarding the biofertilizers market, ANPIL Bio (National Association for the Promotion and Innovation of the Biological Industry) reports 141.1 million doses sold in 2023, generating approximately R\$441.8 million (~US\$73.8 million), representing an 18% increase in doses compared to 2022 (Faverin 2024).

The adoption of inoculants in Brazil's leading crops has shown consistent annual growth, according to research institute data presented below. In soybean crops, inoculants currently cover 85% of the planted area in the 2022/2023 harvest, and co-inoculation (joint use of *Bradyrhizobium* and *Azospirillum*) has reached 35% of the crop area in the country, demonstrating significant advancement in this management practice. In corn cultivation, inoculants extend to more than 22% of the planted area, showing steady progress across harvests (Alves et al. 2003)

Brazil ranks among the world's largest grain producers, and the utilization of growth-promoting microorganisms has become prevalent both nationally and globally. In 2024, Brazil advanced its bioinput regulations, marking a crucial step toward reducing dependence on converting national fertilizer production to meet internal demand (Andreata et al. 2024). The European Union, along with Brazil, India, Argentina, and China, has made substantial progress in biofertilizers in the US market. However, clear guidelines for biofertilizer production and sales remain absent (Goulet et al. 2024; Santos et al. 2024).

In summary, Brazil's substantial increase in bioinput cultivation, combined with its significant market growth and

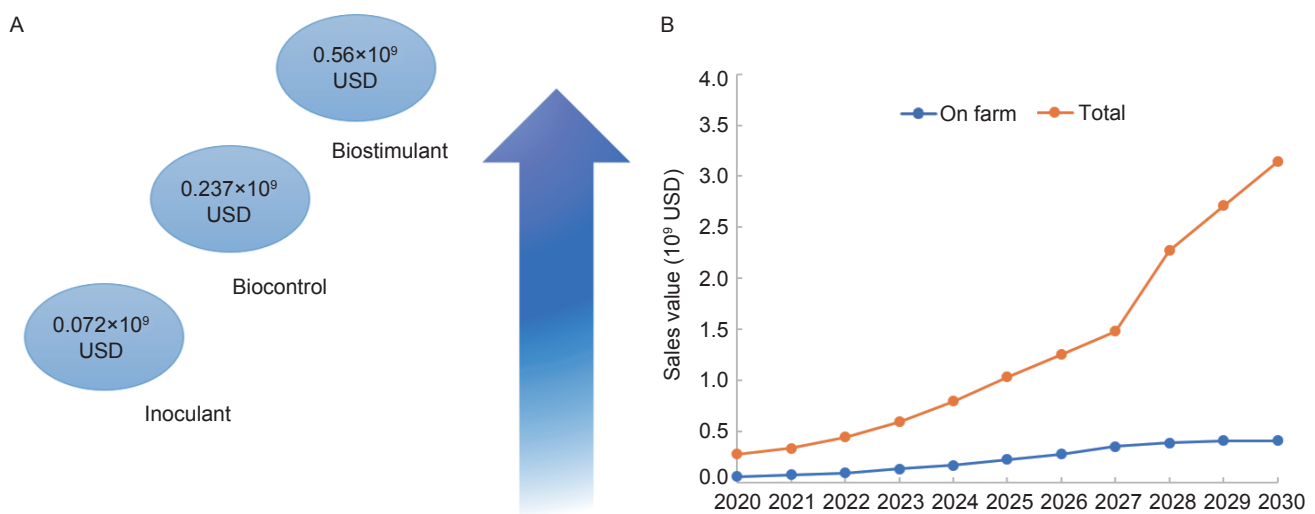


Fig. 2 Bioinputs market. A, market values for 2022 (sales value in billions). B, historical development and projected growth of Brazilian biocontrol agents (sales value in billions)

high adoption rates across various crops, reinforces its leading position and extensive potential in the global bioinputs sector (Camargo *et al.* 2024).

6. Manufacturing infrastructure and bioinputs production in Brazil

6.1. Quality control in the production of bioinputs based on isolated microorganisms

Implementing stringent quality control in microbiological product manufacturing ensures compliance with legal standards while maintaining high quality. This process requires thorough testing of raw materials, equipment, and final products to prevent contamination and ensure safety. Strict adherence to these procedures minimizes defects, maintains consistency, and upholds product guarantees, supporting sustainable production practices.

6.2. Laboratories

The equipment utilized in industrial laboratories, including exhaust fans, laminar flow hoods, autoclaves, and bioreactors, is designed to maintain sterile environments and serves a crucial role in contamination control (Lordelo *et al.* 2010).

Laboratory equipment such as exhaust fans, laminar flow hoods, autoclaves, and bioreactors ensures sterile environments and effective contamination control. Exhaust Fans or HVAC Filtration systems with HEPA filters remove particles and gases, while laminar flow hoods maintain aseptic conditions. Autoclaves sterilize materials using steam, and bioreactors provide controlled, sterile environments for microbial cultivation. These systems prevent cross-contamination, ensuring optimal conditions for each production cycle. These systems and sterilization procedures establish a physical barrier against cross-contamination, maintaining optimal conditions for each production cycle.

Laboratories also employ disposable and pre-sterilized materials to prevent cross-contamination, particularly in shared environments and equipment:

- 1) Disposable materials. Items such as vials, syringes, and tubes are used once and discarded immediately to eliminate reuse and contamination risks.

- 2) Factory-sterilized materials. Products that arrive pre-sterilized ensure no contaminants are introduced into the environment.

- 3) Sterilizable materials. Equipment, such as pipette tips, glass pipettes, and beakers, is sterilized within the laboratory as needed.

- 4) Packaging of microorganisms. The packaging of microorganisms follows strict protocols designed to prevent contamination. Access to storage areas is restricted and controlled by the curator, permitting entry only to trained and authorized personnel. For enhanced protection, microorganisms are contained within primary and secondary packaging systems in environments tailored to their specific requirements. Organizations periodically obtain strains from germplasm banks, adhering to recommended activation and preparation protocols (Oliveira *et al.* 2016). Comprehensive

records of microorganisms and storage conditions are maintained throughout the process to ensure complete traceability.

6.3. Production, weighing, packaging, and storage

The methods for microbial multiplication in industrial biological product manufacturing differ according to the microorganism and process requirements. Bacterial cultivation typically occurs in liquid medium using bioreactors, while fungal production often employs semi-solid or biphasic processes on substrates such as cooked grains. Although production methods vary, shared facilities for bacteria and fungi remain viable when implementing rigorous quality control measures to ensure safe and effective fermentation processes (Morandi *et al.* 2011).

The diversity of production methods and unique characteristics of each microorganism notwithstanding, production facilities can accommodate different bacteria and fungi when maintaining strict quality control throughout the process. This approach ensures safe and effective fermentation while preserving biological product integrity. Quality control in the bioinput industry ensures the effectiveness, safety, and consistency of market-ready products. Given their direct agricultural application, meticulous monitoring of composition, purity, and stability remains essential for regulatory compliance and maintaining biological integrity (Daniel *et al.* 2022).

Furthermore, quality control reduces cross-contamination risks, prevents field efficacy issues, and builds trust among rural producers, essential for sustainable management programs utilizing biological products.

The following elements are essential for ensuring quality control and production safety in industrial processes. These protocols facilitate the safe sharing of infrastructure, equipment, and raw materials/components while maintaining production integrity.

Rigorous product quality control Product quality control maintains safety and integrity through strict standard operating procedures (SOPs), systematic testing, and comprehensive documentation. Any deviations undergo investigation, sterilization and equipment calibration receive regular maintenance, and contaminated batches face disposal or re-sterilization to ensure quality and compliance (ANVIS 2022).

Equipment and cleaning procedures in the production area Industrial-scale bioreactors serve as critical manufacturing components, ensuring sterile environments during biological fermentation and playing a vital role in contamination control. Clean-in-Place (CIP) systems provide essential automated internal cleaning of equipment and pipelines (Chisti and Moo-Young 1994).

Industrial-scale bioreactors cultivate microorganisms with advanced controls for parameters such as temperature and agitation, utilizing high-efficiency filters to ensure sterility.

- 1) Clean-in-place (CIP) systems. Clean equipment automatically with hot water or solutions, ensuring safety and quality and reducing downtime in industries requiring aseptic conditions, like food and pharmaceuticals.

Proper cleaning of equipment and environments is essential to prevent contamination between different production batches. Ensuring that there are no residues or microorganisms between production cycles involves:

Preliminary cleaning. Removes residues using suitable agents, followed by sterilization through steam, dry heat, or chemicals. Sterility and efficacy tests ensure no contamination, confirming the environment's readiness for microorganism cultivation. Periodic validation (Efficacy testing), including surface swabs and environmental plates, confirms effective cleaning procedures before production.

Team training. The competence of the production and quality control team represents a primary factor in preventing cross-contamination. The following practices support this objective:

Regular training. Personnel undergo periodic training on cleaning protocols, sanitization, sterilization, equipment handling, and quality control to maintain high standards.

Personal hygiene procedures. Staff adhere to strict hygiene standards, including wearing clean clothing, gloves, and masks, and following disinfection procedures before entering production areas.

Technical responsibility. Professionals with technical training and proven experience supervise critical processes, ensuring that quality control and safety practices are rigorously followed.

These measures are essential for maintaining a sterile environment and ensuring the integrity of laboratory experiments.

2) Containment of cross-contamination. The risk of accidental cross-contamination arises from the release of dust, gases, vapors, organisms, and residues, alongside potential contamination from pests and operators' clothing. Detailed procedures document any irregularities before initiating new processes (Coyle 2023). Cross-contamination presents significant financial and operational risks, compromising product quality and safety. This can necessitate batch disposal, rework requirements, operational disruptions, and regulatory penalties. Therefore, maintaining contamination-free production remains crucial, particularly for industries governed by Brazil's Law 14.515 of 2022 (Self-Control Law). Organizations implement strict quality control and sterilization protocols to mitigate these risks, continuously monitoring production integrity to maintain safety and efficiency standards while protecting commercial performance and reputation. A systematic approach remains essential for preventing contamination from raw materials and ingredients, particularly in fermentation and biotechnological processes.

Forms of production in liquid fermentation In liquid fermentation processes, various strategies are implemented to cultivate microorganisms effectively:

1) Multiple use. Encompasses sequential cultivation of different microorganisms in the same fermenter. Following each microorganism's fermentation cycle, the equipment undergoes sanitization and sterilization before introducing the subsequent microorganism. Rigorous quality control and sterilization between cycles are essential to prevent contamination.

2) Co-cultivation. Involves the simultaneous fermentation

of different microorganisms in the same fermenter. This approach requires precise planning to ensure each microorganism's fermentation occurs at the appropriate time and complies with the product's registered specifications. Both methods require careful management to maintain product quality and prevent contamination.

3) Formulation of the blend after fermentation. In this approach, microorganisms undergo separate fermentation under optimal conditions for each strain. Following fermentation, they are combined in a mixing tank to form a blend. This procedure enables precise control, and ensures optimal performance in the final product.

Methods such as exposing Petri dishes, and using swabs help verify the cleanliness and sterility of production areas. Environmental monitoring is essential for controlling contamination, facilitating early risk detection through continuous assessment of air quality, surface cleanliness, and water systems (Sandle 2020). According to the Code of Federal Regulations Title 21, manufacturers must maintain properly identified reserve samples from each lot in every shipment of active ingredients.

Weighing. The handling of raw materials in the weighing room demands meticulous care. Systematic cleaning and disinfection of surfaces and equipment help control contaminant spread. Separate weighing for different materials reduces cross-contamination risk.

Filling. Product filling in the same facilities is feasible when strict decontamination measures are implemented after each cycle. Appropriate cleaning, and sanitization prevent cross-contamination between products.

Packaging/Boxing. Ensuring primary packaging integrity minimizes contamination risks. Implementing cleaning protocols maintains environmental safety. Prior to packaging, verify box integrity and ensure proper labeling, and weight distribution to prevent damage, and facilitate transport.

Storage and shipping. Raw materials, components, and finished products are stored in sealed containers to minimize contamination. Each pallet bears labels with information about the microorganism, filling date, production order, and quarantine status. This labeling adheres to regulations ensuring quality and process integrity. Product labeling follows the provisions of Normative Instruction No. 13 of March 24, 2011. These practices ensure that, even when raw materials, components, and finished products are similar, contamination risk in production is minimized, thereby protecting process and final product integrity (MALFS 2011).

6.4. Biotic and abiotic factors affecting bioinput performance

The performance of bioinputs in the field, including microbial inoculants, biofertilizers, and biopesticides, depends on complex interactions between biotic and abiotic factors that can limit or enhance their effectiveness. Understanding these variables is essential for optimizing product use and achieving consistent results.

Among biotic factors, competition with native soil microorganisms plays a critical role. Introduced strains, such as *Rhizobium* spp. in association with legumes, face

resistance from established microbial communities, which compete for nutrients and colonization sites (Bashan *et al.* 2014).

Furthermore, the presence of pathogens or antagonistic microorganisms can inhibit the activity of PGPR, such as *Pseudomonas* and *Bacillus*, thereby reducing their efficiency (Mendes *et al.* 2013).

The specificity between the bioinput and the host plant is also decisive, since low affinity can compromise processes such as biological nitrogen fixation or the formation of mycorrhizae (Smith 2009).

Abiotic factors include soil and climate conditions, and management practices that directly influence the survival and activity of the applied microorganisms. Soil pH, for example, affects the stability of bacterial inoculants, with extreme values (very acidic or alkaline) harming strains such as *Bradyrhizobium* and *Azospirillum* (Basu *et al.* 2021).

Furthermore, when the soil has high availability of mineral N (in the form of nitrate or ammonium), there is a metabolic repression of nitrogenase, the enzyme responsible for Biological nitrogen fixation (BNF). This occurs because the assimilation of inorganic N requires less energy than the fixation of atmospheric nitrogen leading plants and bacteria to prioritize the direct absorption of the nutrient (Richardson *et al.* 2009). Studies show that concentrations greater than 50 kg ha⁻¹ of mineral N can reduce nitrogenase activity by up to 70% in *Azospirillum brasilense* crops, such as corn and wheat (Fukami *et al.* 2018).

Furthermore, an imbalance in the N:P ratio in the soil significantly affects symbiosis. Although phosphorus is essential for ATP synthesis and nitrogenase activity, excessive inorganic P (above 80 mg dm⁻³) can inhibit root colonization by *Azospirillum*, likely due to alterations in root organic compound exudation. This effect is particularly significant in tropical soils, where intensive phosphate fertilization is commonly practiced.

Humidity and temperature are critical determining factors, as drought or flooding conditions restrict microbial activity, while temperatures outside the optimal range can render root colonization ineffective (Nannipieri *et al.* 2017).

The application of agrochemicals, including fungicides and herbicides, presents an additional challenge, as numerous compounds are toxic to beneficial microorganisms, thereby reducing nodulation in legumes and biopesticide efficacy (Zobiolo *et al.* 2010). Moreover, exposure to UV radiation during foliar application can degrade bacterial or fungal spores, such as those of *Bacillus thuringiensis* and *Trichoderma* spp., necessitating protective formulations for enhanced persistence.

To address these challenges, viable approaches include selecting strains adapted to local conditions, developing encapsulated formulations, and incorporating them with conservation management practices.

The implementation of protective vehicles, such as polymers and clays, can enhance resistance to environmental stresses, while combination with organic matter promotes microbial colonization (Bashan *et al.* 2014). Furthermore, monitoring soil characteristics and implementing crop rotation can establish a more favorable environment for bioinput

effectiveness. Future research should prioritize developing technologies that enhance product resilience under field conditions, ensuring greater predictability and facilitating widespread adoption.

7. Brazilian patents in bioinputs

Patent databases serve as crucial repositories of publicly available technological information, comprising up to 70% of global data in specific fields. Inventors must disclose their technologies during patent application, often years before commercial release. This presents a valuable opportunity to inform R&D initiatives and monitor global innovation trends. As sustainable development policies advance globally, Brazil, with its extensive biodiversity, can utilize patent information to assess innovation and assist stakeholders in understanding developments and challenges in agriculture and bioinputs.

The agricultural bioinput sector patent landscape underwent recent analysis in a report by the Brazilian Patent and Trademark Office (INPI *et al.* 2023b). The sector has recorded over 44,000 patent families (inventions) in the past two decades. China leads the global landscape for agricultural bioinput inventions, representing 80% of worldwide inventions during this period. This pattern mirrors the dominance observed in traditional NPK fertilizers (INPI *et al.* 2023a). China's proportion of bioinput inventions globally has increased substantially, rising from 30% between 2000 and 2009 to 80–90% post-2010. However, these technological developments, primarily from Chinese applicants, seek patent protection exclusively within China, indicating domestic market focus.

Beyond China, the leading countries in bioinput inventions include South Korea, the United States, Russia, Japan, India, Germany, Indonesia, Ukraine, and Brazil. This demonstrates the significance of bioinput technology in agriculture. Although not major technology producers, developing nations like India, Indonesia, Ukraine, and Brazil actively pursue bio-based innovations for sustainable agricultural advancement.

The United States, followed by China and Japan, dominates international patent applications for valuable inventions under the Patent Cooperation Treaty (PCT) and the Paris Convention. Agricultural bioinput technologies primarily encompass biofertilizers (86%) and biocontrol (42%). Bacteria and fungi constitute the primary microorganisms utilized, with viruses, algae, and protozoa generating less interest. *Bacillus* predominates in biofertilizer inventions. Other significant microorganisms include *Rhizobium*, *Azotobacter*, *Azospirillum*, *Bradyrhizobium*, *Methylobacterium*, *Glucanacetobacter*, *Nitrospirillum*, and *Glomus* for biofertilizers, while genera like *Streptomyces*, *Penicillium*, and *Pantoea* are recognized for their biocontrol functions as fungicides.

Agricultural technology represents a domain of substantial inventive activity globally, with two primary research focuses identified: non-pesticide pest and disease management and soil and fertilizer management. The application of microorganisms has emerged as a crucial trend in non-pesticide pest and disease management, particularly in fertilizer formulation and as pesticide alternatives.

In Brazil, 954 patent applications for bioinputs (Figs. 3 and 4) have been submitted (INPI *et al.* 2023b). The country serves as a significant market for global companies seeking patent protection for their technologies. Brazilian applicants constitute 18% of these filings, while 82% originate from foreign entities, predominantly from the United States (40%).

Despite the significant presence of foreign technologies related to bioinputs seeking patent protection in Brazil, the proportion of patent applications from Brazilian entities in this field is notable compared to other advanced technology

categories protected by Brazilians. For example, in gene editing, the corresponding percentage is minimal, not exceeding 1% (INPI *et al.* 2024). Thus, the patent landscape in Brazil demonstrates that the country serves both as a substantial market and a significant generator of bioinput technologies.

Regarding foreign technologies, prominent countries filing inventions in Brazil include Germany, France, Denmark, Japan, Spain, Switzerland, and Australia. Major global agricultural and biotechnology companies, such as Bayer/

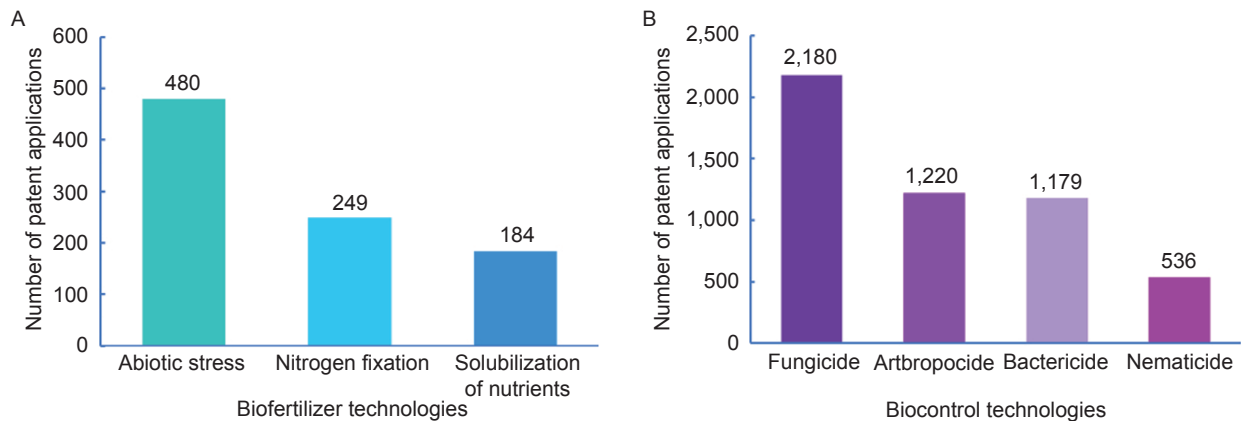


Fig. 3 Number of patent applications for biological inputs filed in Brazil between 2000–2022, categorized by biofertilizer technologies (A) and biocontrol technologies (B).

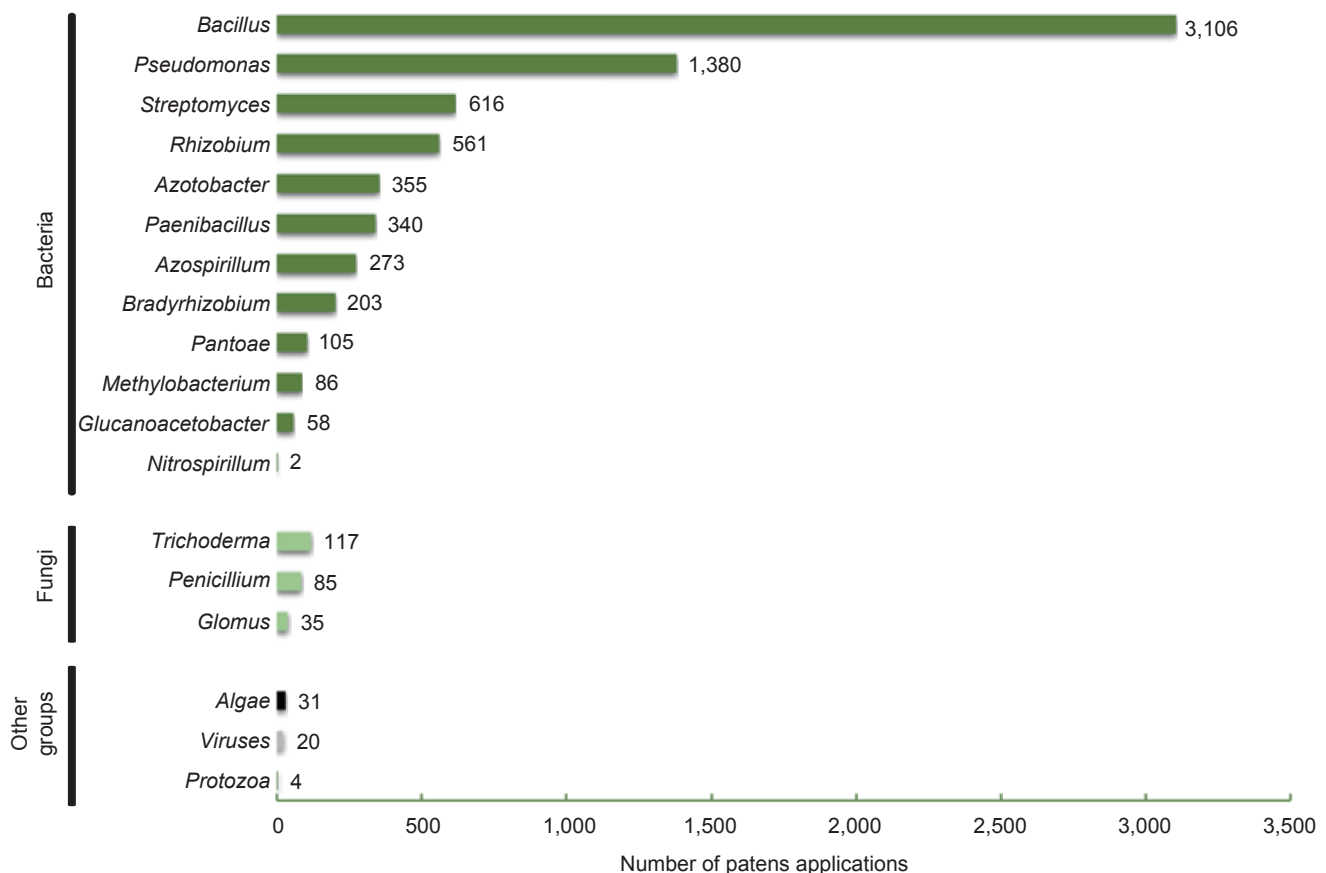


Fig. 4 Distribution of bioinput patent applications filed in Brazil (2000–2022), categorized by primary bacterial and fungal genera and other microbial groups.

Monsanto, BASF, and Novozymes, are among the principal applicants. Several American firms specializing in agricultural bio solutions, including Locus Agriculture, New Leaf Symbiotics, Pivot Bio, Indigo Agriculture, Spogen Biotech, and Marrone Bio Innovation, are also significant applicants. EMBRAPA emerges as the sole Brazilian entity among the top ten applicants, demonstrating Brazil's capability in generating bioinput inventions through local companies, research institutions, and universities.

8. Global challenges of microbial bioinputs, perspectives for Brazil and conclusions

Microbial bioinputs — including biofertilizers, biopesticides, biostimulants, and inoculants — represent sustainable alternatives to synthetic agrochemicals and constitute a foundation for climate-resilient agriculture. These inputs utilize beneficial microorganisms' capabilities to enhance nutrient availability, promote plant growth, control pests and diseases, and improve crop tolerance to abiotic stresses. Despite their increasing importance and environmental benefits, the widespread adoption and technological development of microbial bioinputs encounter several global challenges.

A significant obstacle exists in the inconsistency of field performance. While microbial products frequently show promising results in controlled environments, their effectiveness under real-world conditions can be limited by factors including native soil microbiota, local edaphoclimatic conditions, plant genotype interactions, and application mode and timing (Harman 2019). This variability reduces farmer confidence and limits adoption, particularly among smallholder producers. Standardized field-testing protocols and enhanced understanding of plant–microbe–environment interactions are essential to improve consistency and predictability.

Another constraint relates to formulation technology. Maintaining microbial viability and activity throughout production, transport, and field application remains challenging, especially for mixed consortia and metabolite-based products. Challenges regarding shelf life, stability, and delivery mechanisms are intensified by insufficient investment in strain improvement, large-scale production systems, and long-term ecological assessments (Villavicencio-Vásquez et al. 2025).

Regulatory fragmentation impedes innovation. Complex and extended registration processes — particularly for products involving multiple strains or genetically modified microorganisms — create commercialization delays and discourage private investment. Moreover, intellectual property protection for microbial strains remains inadequately defined globally. The lack of harmonized international standards for microbial patents inhibits innovation and limits equitable access to genetic resources (Trujillo-Roldán et al. 2013).

Climate change introduces additional uncertainty. The rising frequency of extreme weather events and alterations in temperature and precipitation patterns affect soil microbiomes and the stability of introduced microorganisms. Bioinputs

that prove effective under current conditions may perform differently in future scenarios, emphasizing the need for climate-resilient strains and systems-based approaches to microbial product development (Hu et al. 2015; Kaushal et al. 2023).

Lastly, knowledge gaps and limited technical capacity — particularly among small and medium producers — restrict adoption. Training programs on bioinput application, compatibility with agroecosystems, and post-application monitoring are critically needed to build trust and ensure proper usage.

Despite global challenges, Brazil emerges as a global leader in microbial bioinputs, supported by an extensive agricultural sector, rich microbial biodiversity, and recent regulatory advances. Law No. 15,070/2024 requires regulation to establish a comprehensive legal framework for the production, registration, and commercialization of bioinputs, harmonizing and strengthening governance in this sector.

Brazil currently maintains over 600 registered microbial inoculants and approximately 600 products for biological control. However, focus has primarily centered on *Bradyrhizobium*, *Azospirillum*, *Bacillus*, *Trichoderma*, *Metarhizium*, and *Beauveria* species for major crops such as soybean and maize.

Infrastructure for production and quality control has developed considerably, emphasizing good manufacturing practices, fermentation technologies, clean-in-place systems, and microbial germplasm banks — essential elements for ensuring viability, efficacy, and traceability of microbial strains.

Brazil's bioinputs market demonstrates remarkable expansion, growing at an annual rate of 21%, which is four times the global average. The year 2023 witnessed sales exceeding 141 million doses of biofertilizers, while biocontrol agents were implemented across more than 70 million hectares. National policies actively promote bioinput adoption among family farmers and cooperatives, with public and private institutions, including EMBRAPA, serving essential functions in research, development, patenting, and training initiatives.

The convergence of bioeconomy and smart agriculture presents emerging opportunities. Developments in synthetic biology, genomics, nanotechnology, and AI-driven precision agriculture facilitate the development of more resilient microbial consortia adapted to climate challenges. Strategic investments in regional microbial libraries, application technologies, and specialized formulations are crucial for extending adoption beyond primary crop systems.

In conclusion, microbial bioinputs demonstrate significant potential for advancing sustainable and regenerative agriculture, decreasing dependence on agrochemicals, and enhancing crop system adaptability to climate variations. However, global adoption faces constraints related to field efficacy, formulation, regulation, intellectual property protection, and climate resilience. Brazil's experience illustrates how progressive legislation, scientific investment, and market incentives can effectively promote bioinput adoption at a national level. Through improved accessibility, innovation promotion, and integration of traditional and

digital farming approaches, Brazil provides a viable model for nations pursuing sustainable agricultural solutions.

To achieve this potential, systematic interventions are required, encompassing regulatory framework enhancement and international standard harmonization, reinforcement of microbial germplasm banks, establishment of public-private R&D collaborations, development of scalable and adaptable formulations, enhancement of technical training and farmer support systems, and emphasis on microbial solutions that demonstrate compatibility with diverse agroecosystems and resilience to climate change.

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Declaration of competing interest

The authors declare that they have no conflict of interest.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this manuscript, the authors used generative AI tools to assist in improving the clarity and readability of the language. All content generated was carefully reviewed and revised by the authors as necessary, and the authors take full responsibility for the final content of the article.

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