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REVIEW

Review of patents for agricultural use of arbuscular mycorrhizal fungi

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Abstract
Mycorrhizal biotechnology has emerged as a major component of sustainable agriculture and allied activities. Innovations related to its role in agriculture, land reclamation, forestry, and landscaping are well recognized. This review presents the evolution of innovations worldwide related to arbuscular mycorrhizal fungi (AMF) in the past two decades, from 2000 to April 2020, and maintains that such innovations must continue in the future. An analysis of 696 patents showed that AMF have been used consistently as a biofertilizer and bioremediator over that period, although an upsurge was noted in propagation technologies, next-generation production methods, and formulation technologies. This review will familiarize mycorrhizologists with novel and evolving trends and will convince them of the importance of applying for patents to safeguard their innovations and the use of those innovations by industry.

Keywords Biofertilizers · Patents landscape · Sustainable agriculture

Introduction

Among the different types of mycorrhizal associations found in ecosystems, those between arbuscular mycorrhizal fungi (AMF) and flowering plants are most exploited in agricultural biotechnology (Chen et al. 2018; Igiehon and Babalola 2017). These associations contribute to making agriculture sustainable by serving as biofertilizers and bioremediators (Adholeya 2012; Basu et al. 2018). The global demand for AMF in the mycorrhiza-based industrial market was $268.8 million in 2019 and is projected to rise to $621.6 million by 2025 at an estimated compound annual growth rate of 14.8% over the next 5 years (Mycorrhiza-based Biofertilizer Market Growth Trends and Forecast 2020–2025).

Growing interest in AMF biotechnology worldwide is evident by the scientific literature published as research and review articles, and conference proceedings that educate mycorrhizologists. For example, meta-analyses of research studies revealed the ecological and evolutionary contexts in which mycorrhizal fungi alter plant productivity (Chaudhary et al. 2016). However, to understand the translational aspect of research on AMF in agriculture and the market for AMF, a thorough analysis of patents is required.

According to the World Intellectual Property Organization (WIPO 2020), 'a patent is an exclusive right granted for an invention, which is a product or a process that provides, in general, a new way of doing something, or offers a new technical solution to a problem' (WIPO: www.wipo.int/patents/en/). Thus, patents play a key role in identifying innovations and development in any field, incentivize the inventors, and safeguard their interests and intellectual property (Chandler et al. 2016; Srivastava and Adholeya 2019). Patent landscaping is a process, whereby big data in the form of specifically selected collections of patent documents (applied or granted patents) are computationally analysed to retrieve relevant technical, legal, and business information (Chilton et al. 2016; Srivastava and Adholeya 2019). A recent landscaping of patents related to biofertilizers showed significant contributions of AMF (Srivastava and Adholeya 2019). No such patent landscaping has been attempted, specifically for AMF technologies, their patterns, geographical trends, trends with respect to inventors, investors, and associations between the two, and takeaways for the development of next-generation technologies. Therefore, this review explores the global patent landscape for AMF from 2000 to April 2020 to retrieve such information.

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Data mining and development of the patents data set

The data set for analysing the patent landscape for AMF comprised information on patent applications and granted patents collected using search engines, patent databases, and country-specific patent websites. A 'patent applied' is defined as a request (the patent specification document and the claim) submitted to a patent office for review and consideration towards granting the patent, and 'granted patents' indicate exclusive rights granted to an inventor for a designated period by the examining authority for a patented process, design, or invention. Data were mined from online searches using 'arbuscular mycorrhizal fungi' as the search term and then examining the retrieved information and links for their relevance to such aspects of AMF as biofertilizers, soil fertility, bioremediation, pest management, propagation techniques, culturing protocols and formulations, novel AMF species, and nanotechnology from 2000 to April 2020. A total of eleven online resources were explored: AUSPAT 2020 (Australia; ipaustralia.gov.au/patents), CIPO 2020 (Canada; ic.gc.ca/eic/site/cipointernet-internetopic.nsf/eng/Home), DPMA 2020 (Germany; dpma.de/english/), ESPACENET 2020 (European Patent Office; worldwide.espacenet.com), Google Patents 2020 (patents.google.com), JPO 2020 (Japan; jpo.go.jp/), PATENTSCOPE-WIPO 2020 (wipo.int/patentscope/en/), PatSeer 2020 (an international database of patents; patseer.com), ROSPATENT 2020 (Russia; /eapo.org/en/ru.html), SIPO 2020 (China; english.sipo.gov.cn/), USPTO 2020a (USA; uspto.gov/patents-application-process/search-patents)

Information about the patent (title, abstract, and claims) was manually curated and professionally annotated. The data set was organized based on whether the entries were related to AMF technology directly or indirectly, taking into account the following details: record number; record status (patent applied-for or granted); date of application, publication, or grant; priority country; title; abstract; applicants; and applicant category (university, industries, individuals, research and development (R&D) institutes, collaborations), inventor and investors, international classification, original assignee, current assignee, product/process type, and application.

Patents in which AMF were the major reason for the claimed property, application, product, or utility model were classified as directly related, and the rest were classified as being indirectly related. Only active patent applications or granted patents were analysed. All inactive or expired documents were omitted from the collected data set as patents are territorial (country or region) rights granted for a limited period, generally 20 years (for example in the USA, Russia, China, India, Japan, and Australia) from the filing date of the application. After screening, a pre-final data set was developed and cross-checked three times (individually by each of the first two authors) to remove duplicates and develop final data set for analyses. Trends related to global and regional activity, key applicants, inventors, assignees, and innovations and technologies were identified.

To estimate the distribution pattern or trend over the past two decades with respect to applied and granted patents, the analyses were performed by calculating their percentage using MS Excel 2010. A similar procedure was followed to analyse the trends by country and by year, followed by those by applicant, assignee, and inventor. To build a list of the applicants, inventors, and investors, their contributions were counted.

To identify the AMF distribution pattern, analyses of directly related (applied and granted) patents were performed. The complete analysis was divided to answer the following four questions:

Q. 1 Was an arbuscular mycorrhizal fungus mentioned, as a single species or as part of an AMF consortium?
Q. 2 What was the pattern of distribution of single-species patents or consortia-based patents according to the nature of the invention, taking into consideration both applied and granted patents?
Q. 3 What genus of AMF was the most prevalent across the patents?
Q. 4 What species of arbuscular mycorrhizal fungus was most frequently mentioned whether as a single species or as part of a consortium?

To answer Q. 3 and Q. 4, genus- and species-specific analyses were performed which took into account the occurrence of specific genera and species as a proportion of the patents reviewed. We used with the genus and species names as presented in the patents (without correction for synonymy). Another part of the analyses identified the prevalence of bacterial partners, if any, used together with the AMF and their plant hosts.

Landscaping of patents related to arbuscular mycorrhiza fungi

Patents applied versus patents granted

Our search yielded 696 patents in all, of which 82% were related directly to AMF and 18% were related indirectly. The applications and granted patents increased over the two decades (Fig. 1), as did the proportion of patents related to AMF technologies. The number of applied patents directly related to AMF was 433 and indirectly related was 136, the corresponding numbers of granted patents being 92 and 35.

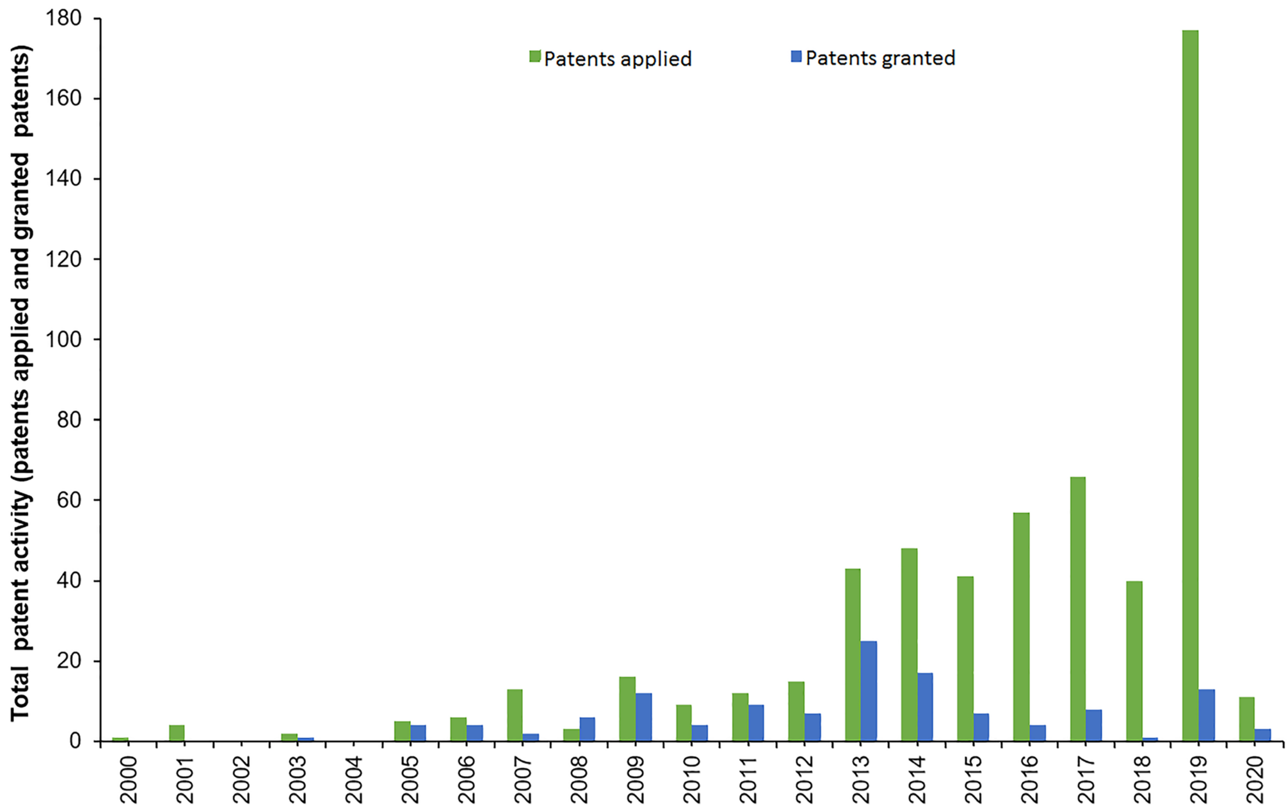

Fig. 1 Numbers of granted and applied patent from 2000 to April 2020 related to arbuscular mycorrhizal fungi

The first 5 years, 2000–2004, were relatively quiet, but the number of innovations began increasing from 2005. The most active years for patent related activity were 2019 (190), followed by 2017 (74) and 2013 (68) based on the total numbers of patents. In contrast, not a single application was filed or granted in 2002 and 2004, followed by one in 2001 and three in 2003, making them the least active years. Of the 127 granted patents, the highest number was in 2013 (25), followed by 2014 (17), and 2019 (13), while the count was zero in 2000, 2001, 2002, and 2004. The highest conversion percentage of granted patents versus number of applications filed was found for 2008 (67%), 2005 (44%), 2009, and 2011 (43%).

Geographical trend

Patent activity was observed in 27 countries during the entire period with the leading continent being Asia, followed by Europe, North America, South America, Africa, and Australia. Among those 27 countries, China (456), the USA (81), Germany (27), and Luxembourg (18) were the front runners, followed by Japan (19), France (16), India (15), and Russia (11) in terms of the total number of patents (applied and awarded) (Fig. 2). Seventeen countries had ten or fewer patents.

Patents were granted in 14 countries, the front runners being China (72 patents), the USA (16), Russia and Korea (6 each), and Luxembourg and Spain (5 each). Canada, Austria, Ukraine, Denmark, and the Netherlands awarded one patent each; Germany and France, four; and Japan, two. Countries differed in the proportion of applications for which patents were awarded; for example, Japan, Germany and China showed ratios of 1:10, 1:7, and 1:6, respectively, for granted versus total filed applications. Similarly, the USA and Canada showed a ratio of 1:5 while for Luxembourg and France it was 1:4. Countries such as Ukraine, Denmark, and the Netherlands showed 100% conversion of patent applications to granted patents.

Key players: applicants, inventors, and assignees

Applicants

The applicants fell into five major categories, namely those from industry, universities, or R&D institutes and those who were individuals or members of collaborations. Industry accounted for the largest share (45%), followed by universities (24%), R&D institutes (18%), individuals (10%), and collaborators (3%). The most productive year was 2019 (190 applicants), followed by 2017 (74) and 2013

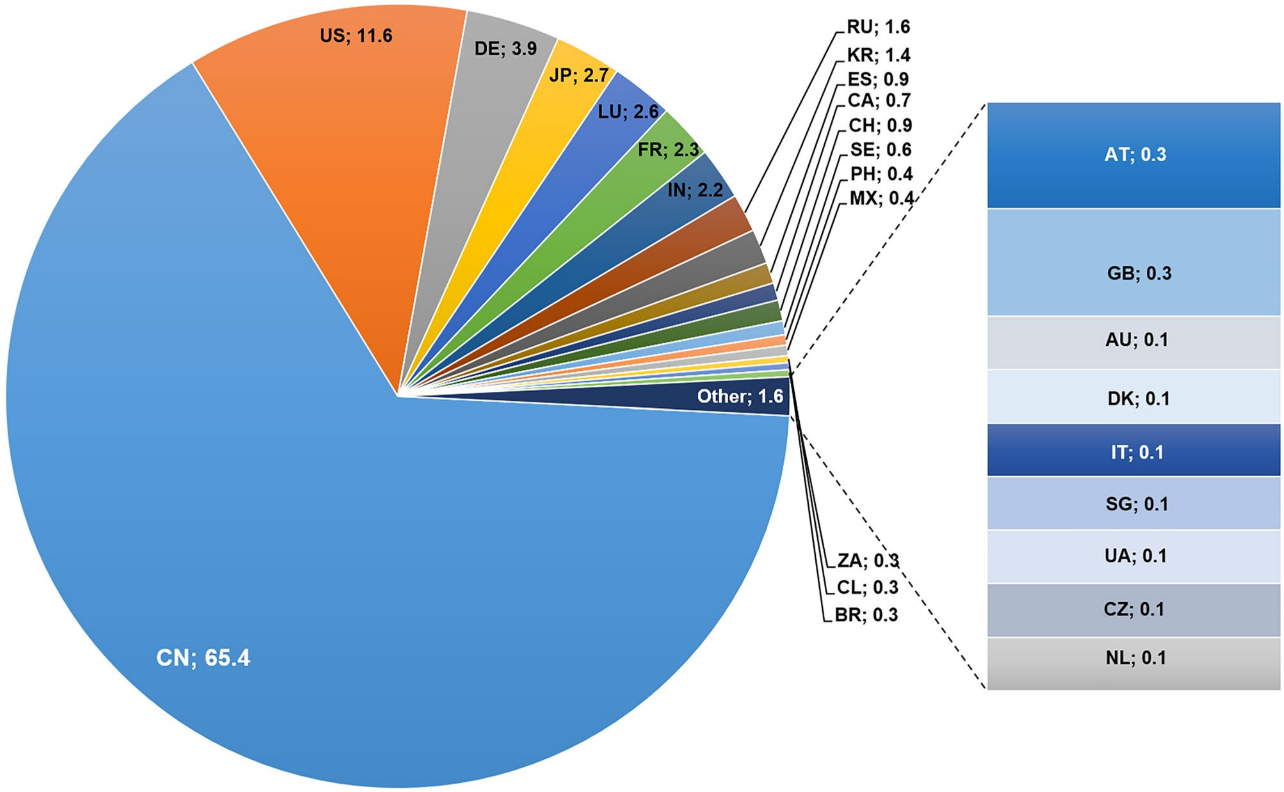

Fig. 2 Country-specific percentage of total patent activity related to arbuscular mycorrhizal fungi from 2000 to April 2020

(55) (Fig. S1). In each of these years, the rank order of categories was the same (industry, 45%, 38%, and 55%, respectively) followed by universities (28%, 28%, and 29%) and then by R&D institutes (15%, 27%, and 11%). These numbers point to a growing industrial interest in AMF.

The top five applicants were Nanjing Agricultural University in China (9), Symplanta GmbH & Co. KG in Germany (16), and Consejo Superior de Investigaciones Científicas (the Spanish National Research Council) (5). For more details, see Supplementary Table 1.

Inventors

We confined our attention to those inventors who had applied or were granted at least three patents. The inventors were either individuals or groups with the same set of inventors (Supplementary Table 2). Arthur Schuessler, from Symplanta GmbH Co. KG, topped the list, with 16 patents, followed by Wang Sheng, from Weifang Yourong Industry Co., Ltd (10 patents), and Kristi Woods and Erin Divers, from Novozymes, with 9 patents. Inventors from industry were the major players.

Assignees

Patent laws of the USA define the 'assignee of a patent' as 'a person who holds, by a valid assignment in writing, the whole interest of a patent or any undivided part of such whole interest' (USPTO 2020b: www.uspto.gov/web/offices/pac/mpep/s301.html). For assignees, we tabulated the same five categories (Fig. 3) as those used earlier for applicants. Industry led with nearly half (47%) of the total registrations, followed by universities (21%), R&D institutions (14%), individuals, and collaborations (9% each). Those with at least three patents numbered 23, with a total of 112 patents among them. Symplanta GmbH & Co. KG was the leading assignee, with 18 patents to its credit focused mostly on methods of propagation and mass multiplication of AMF; Weifang Yourong Industry Co., Ltd., with 10 patents focused on organic fertilizers, followed by BASF, with 9 patents mostly related to promoting plant growth. Industry was the top category, followed by universities.

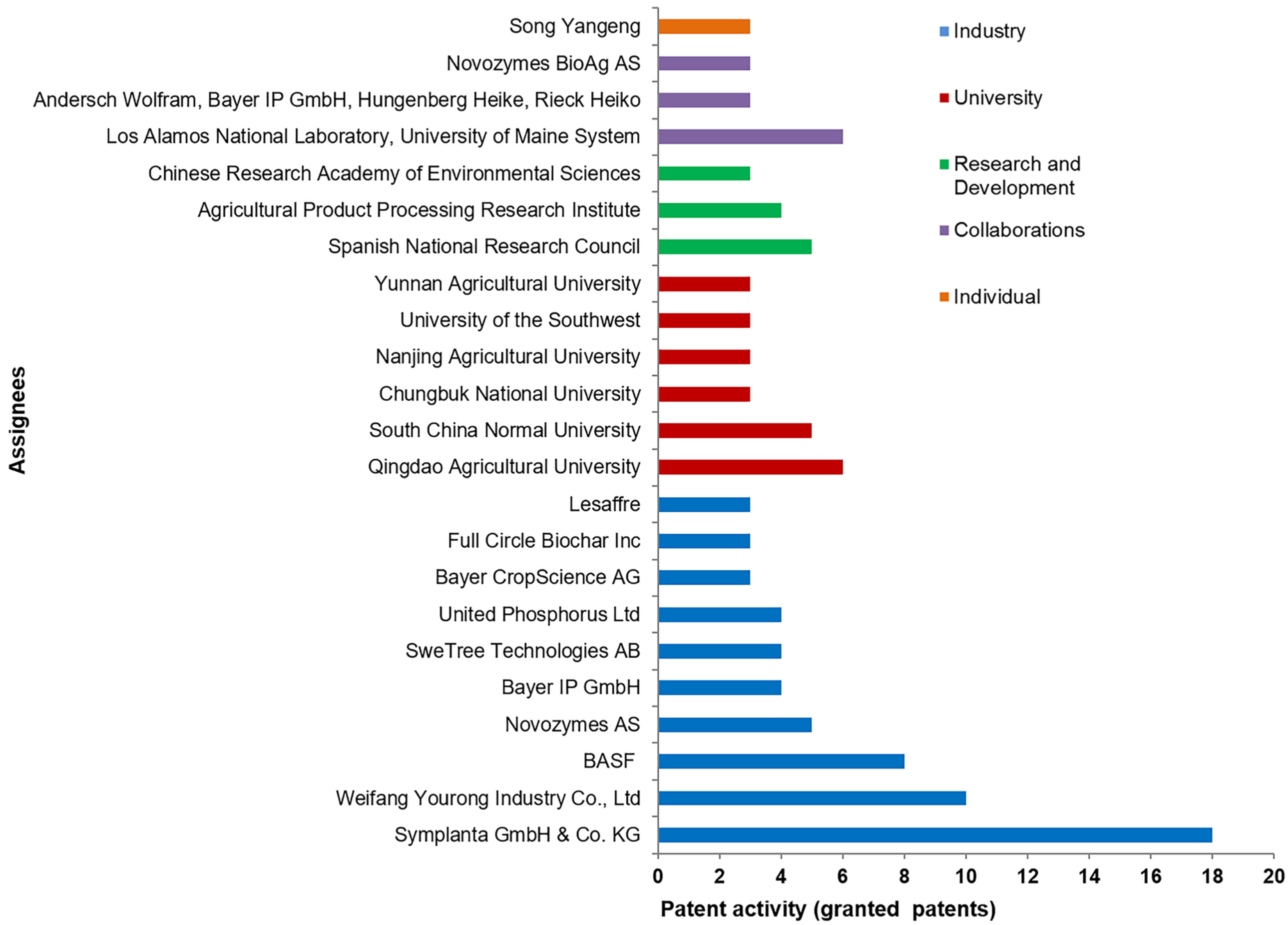

Fig. 3 Top-ranked assignees with at least 3 patents (patents granted) under five different categories of applicants

Technology trends

Processes, products, and process-cum-products

Process patents are those that describe 'a method, a process, a preparation, a study, an experiment'; product patents, those that describe 'a utility model, a design, a system, a composition, a formulation'; and process-cum-product patents are those that describe 'a method and its application, a system and its application' (Fig. 4). Process patents were the most numerous (57%), followed by process-cum-products (29%), and products (14%). The most productive year was 2019, with 84 patents in the process-cum-product category, 79 patents in the process category, and 27 patents in the products category. The next most productive period was 2013–2018, during which more than 40 patents were applied or granted, the most numerous being process patents. Because process patents have been the most numerous overall, additional patents in the other two categories to convert the inventions into products for the end user probably now are needed.

Distribution of species of arbuscular mycorrhizal fungi

Our analysis of the distribution pattern of the fungi from 525 direct patents answered the four questions mentioned earlier. We found 149 patents with AMF information available either at the generic or species level and 376 patents with no information on the AMF used. We utilized information on all 525 patents to answer Q. 1. All other questions were answered based on an analysis of 149 patents. The answer to Q. 1 was 'Yes'; AMF were mentioned in 15.5% of patents as a single species and in 13% as a member of an AMF consortium. The remaining 71.5% gave no information on the AMF utilized.

The answer to Q. 2 is given in Fig. 5 which shows how AMF were distributed among process patents, product patents, and process-cum-product patents under both patents applied and patents granted categories. We found prominent occurrence of AMF utilized as part of an AMF consortium in both patent categories. Among the nature of inventions, process patents again outnumbered the product and process-cum-product patents.

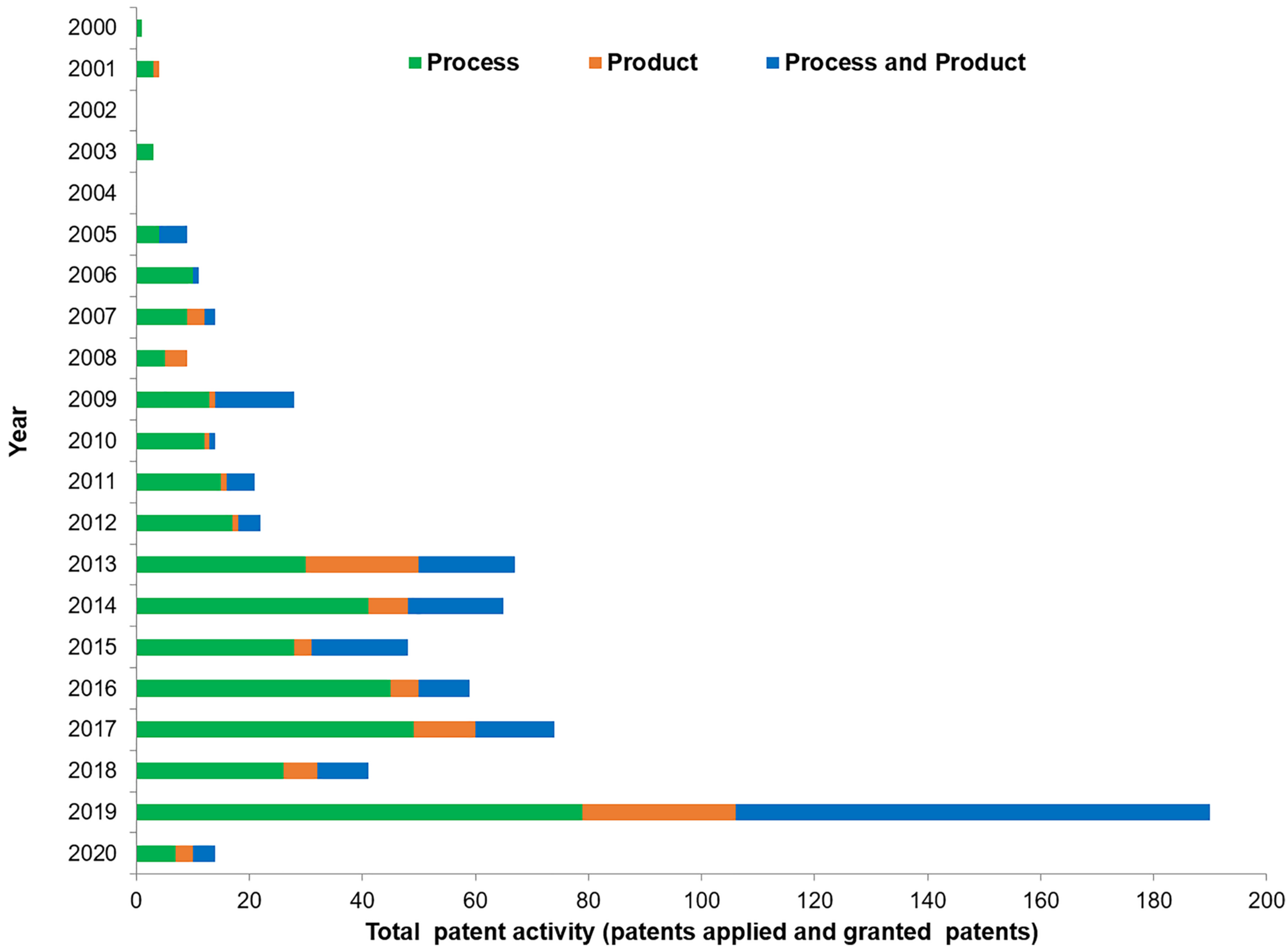

Fig. 4 Number of patents applied or granted from 2000 to April 2020, by year, under category of invention: process, product, or process-cum-product

Among process patents (Fig. 5a and b), in total, those mentioning a single species were more numerous than those that mentioned consortia of microorganisms. The most commonly mentioned species were *Glomus intraradices* and *G. mosseae*, followed by *G. versiforme*. In product patents, however, consortia were more numerous than individual species taken together, although the most frequent species were again those of the genus *Glomus*, namely *G. intraradices*, *G. etunicatum*, and *G. clarum*. In the third category (process-cum-product), single species taken together again outnumbered consortia.

As can be seen from Fig. S2, members of *Glomus* were the most numerous (82.5%) and far outnumbered *Rhizophagus* (3.9%), *Scelerocystis* (3.9%), *Gigaspora* (2.9%), and *Acaulospora* (2.5%). Other genera combined accounted for less than 1.5% of the total. The five most prominent species (accounting for at least 5%; Fig. 6), either as single species or as members of consortia, were *G. mosseae* (26.6%), *G. intraradices* (24.7%), *G. etunicatum* (10.4%), *G. versiforme* (6.9%), and *G. fasciculatum* (5%).

Other microbes and plants

Bacteria were the most common microorganisms associated with AMF, the most common among them being *Bacillus licheniformis*, *B. subtilis*, *Bradyrhizobium japonicum*, *Pseudomonas fluorescens*, and *Rhizobium meliloti*. The most common in terms of application were nitrogen-fixing bacteria, phosphate-solubilizing bacteria, and plant-growth-promoting rhizobacteria. Among fungi other than AMF, *Trichoderma harzianum* was the most common. As to hosts, tobacco was the most commonly mentioned host in the patents. Other frequently featured plants were rice, honeysuckle, clover, cannabis, alfalfa, chrysanthemum, grapes, maize, peony, salvia, sorghum, soybean, and wheat.

The top technologies

Innovation has touched many different aspects of AMF in agriculture (Fig. 7). These aspects can be grouped into nine main categories including AMF as biofertilizers (39% of

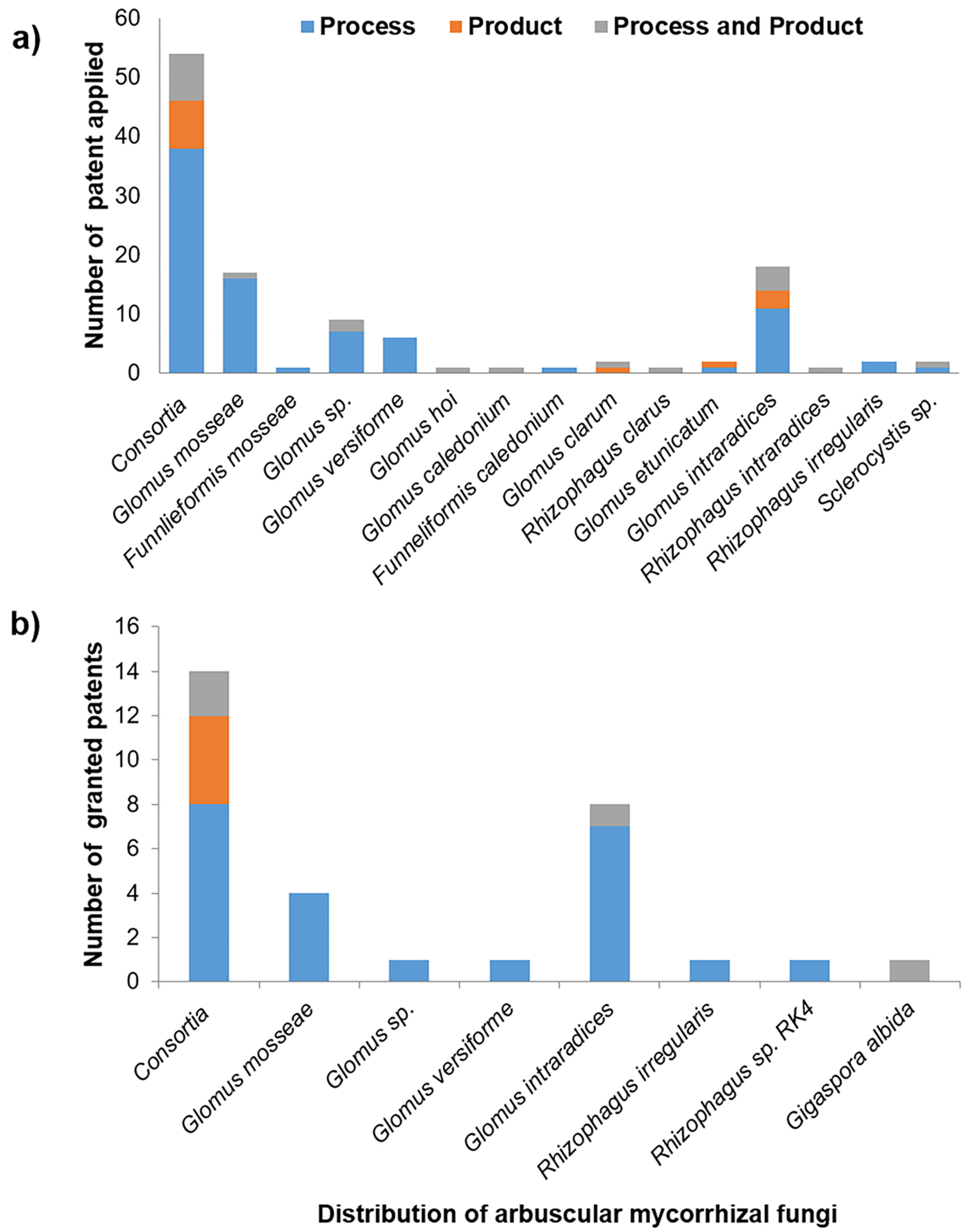

Fig. 5 Number of directly related patents with different species of arbuscular mycorrhizal fungi by category of invention. **a)** Patents applied. **b)** Granted patents

the patents), their applications (21%), improvement in AMF formation (3%), devices (7%), detection and identification (3%), production methodologies (14%), formulations (9%), transgenics (2%), and extraction of plant-growth-promoting compounds (2%) from AMF.

Patents related to AMF as fertilizers include AMF as components of both composite (24%, fertilizers of organic or biological origin) and compound (29%; composition that contain some percentage of conventional chemical fertilizers of N, P, and K) fertilizers. Some patents are for plant-specific (47%) AMF as biofertilizers. Other applications include role of AMF in land restoration (for example, iron tailings, coal mines, desserts, and urban landscaping), bioremediation of land and water bodies (using mycorrhizal plants for removing heavy metals such as cadmium, petroleum products, polyaromatic hydrocarbons, and phosphor-gypsum), and protection from biotic (fungal and other plant diseases, pests, and weeds) as well as abiotic sources of stress (such as saline or alkaline soils and very low temperatures).

Due to the beneficial roles of AMF in agriculture, patents have been applied or granted for colonization promoting agents and for methods that improve root colonization both *in planta* and in hydroponic systems. Compounds have been explored and patented including mannitol, monosaccharides and/or disaccharides that stimulate mycorrhizal or root development, improve mycorrhizal interactions (for example L-amino acids and acyl homoserine lactone), or stimulate the *myc* growth

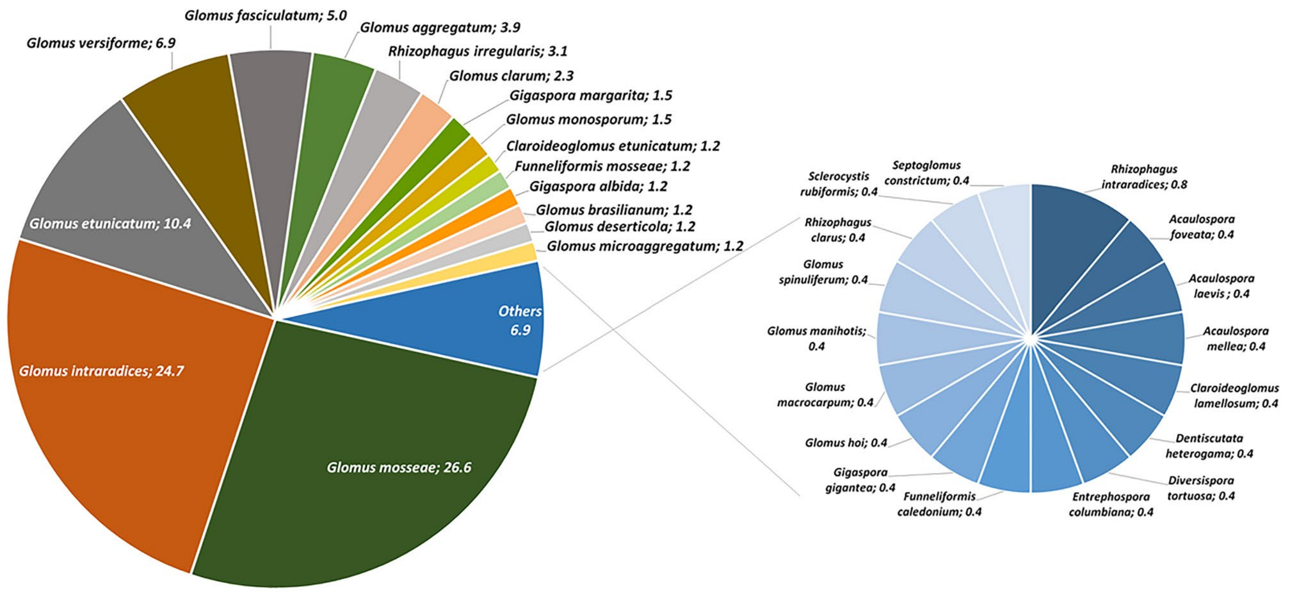

Fig. 6 Proportion (%) of different species of arbuscular mycorrhizal fungi as named (not taxonomically revised) in directly related patents

factor or multiplication rate of AMF. Additionally, transgenics have proved important to mycorrhizal symbiosis as evident from applications for patents for (1) a gene that promotes mycorrhizal propagation and increases plant biomass, (2) the LsSYMRK gene for increasing phosphorus absorption and its efficient re-use, and (3) the SWEET1b gene for promoting mycorrhization in *Medicago sativa* and modifying LysM receptors in target plants.

Innovations in devices and utility models have not lagged: 28 patents were added to this category from 2013, almost all (24) from China. Devices have been built for studying different phenomena (intercropping, absorption and translocation of

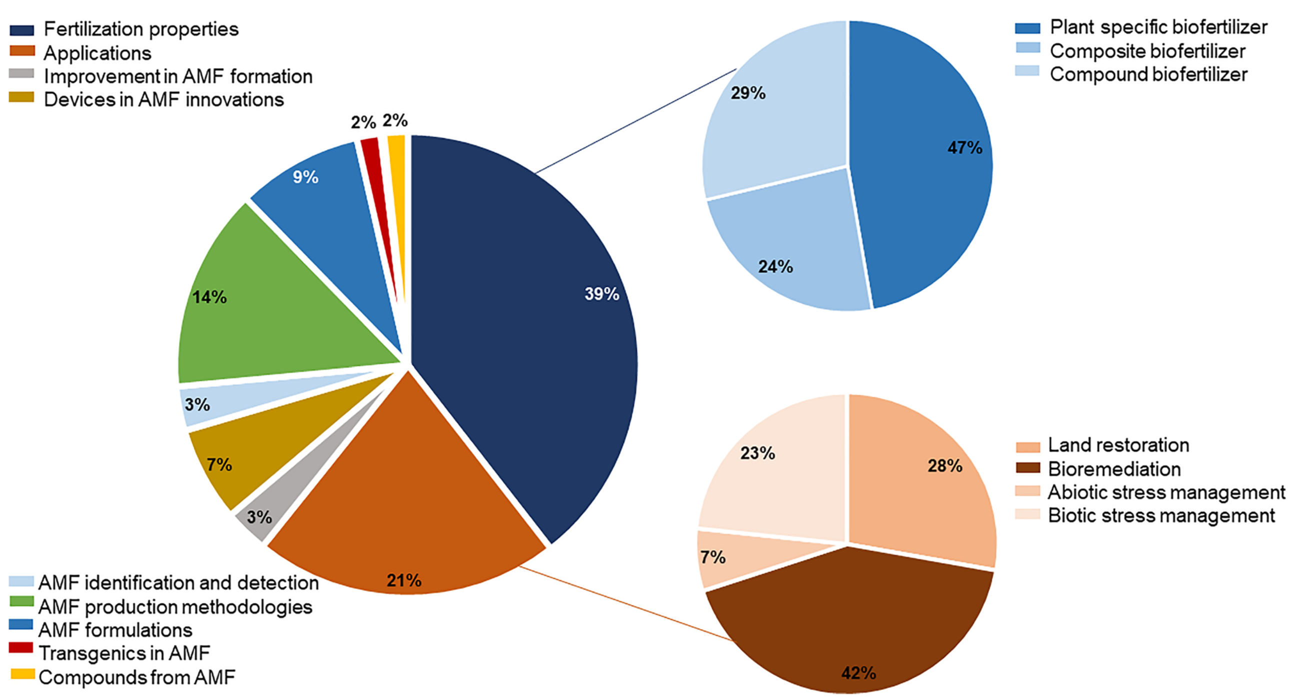

Fig. 7 Top technology percentage in granted patents involving arbuscular mycorrhizal fungi from 2000 to April 2020

water, root damage), isolating and viewing (spores, phyto-ecological monitoring), cultivating (mycorrhizal plants and those inoculated with beneficial bacteria), detecting (carbon transfer among plants, labelled isotopes, test apparatus for fungi), and extraction (root exudates in situ).

Since 2009, patents related to techniques for detecting and identifying AMF have increased. Fluorescence- and chemical-based staining procedures that are environmentally friendly have been patented as well as those related to molecular methods including the use of quantitative reverse transcription—polymerase chain reaction (qPCR) and special primers. Leaf markers to detect root colonization by AMF have been developed and patented (International Publication Number: WO2019166437A1, applied by Max-Planck-Gesellschaft zur Förderung der Wissenschaften e.V., Munich, Germany).

If AMF are to win widespread economic acceptance, technologies for mass multiplication of propagules are essential and some of those have been patented, including in situ (using hydroponics, container-grown plants, or those growing in the field), in vitro transformed plants or plant-based techniques, liquid media, nutrient films, and soil tanks and even technologies that use gas–liquid phase reactors (mist based).

Another category of application includes products for prolonged shelf life and different formulations of AMF including the following: liquids, capsules, free-flowing solid forms based on silt or symbiotic clay or other substrates, water-soluble solids, powders, granules, magnetized carrier, and porous chitin-polyhydroxy-alkanoate nanofibres. Other formulations include seeds coated with mycorrhizal fungi and those suitable for in-furrow application involving polyethylene glycol.

Other than these major technologies, the quest for novel mycorrhizal fungus species has been intensified: a patent was secured for a strain of *Rhizophagus irregularis* AH01 (deposit number 12157 at CGMCC: China General Microbiological Culture Collection Center). Six patents in the USA patent *G. intraradices* to produce lipo-chito-oligosaccharides (LCOs) as plant growth promoters.

Thus, over the past two decades, technological developments related to AMF have revolved around their use as biofertilizers, in bioremediation and stress management, and technologies for mass multiplication, production, improved processes, detection, and superior formulations.

Challenges and opportunities

Based on our overview of patents related to AMF, we speculate upon the forces that drive AMF technology to benefit researchers, industry and related stakeholders, policymakers, investors, and even governments.

Government investments and policies to promote translational research and innovation

China dominates the AMF patent landscape, but a majority of Chinese patents are filed locally; relatively few are subjected to any assessment on a global scale. Heavy investment by the Chinese government in biotechnology research and state ownership of universities and R&D institutes probably explain the country's dominance—investments that other countries may do well to emulate.

The state can encourage innovation by offering grants, tax relief, and capital allowance and by lowering corporate tax on profits from such innovations. Funding to mycorrhiza-based start-ups and shareholding by the state is yet another way of supporting innovations. Innovations related to the use of mycorrhiza-based biofertilizers and coated seeds in agriculture can be supported by policies that encourage these applications. Given that AMF help in the uptake of phosphorus, policies that support farming on phosphorus-depleted land will spur the search for efficient fungal isolates, strategies to improve mycorrhizal efficiency, and development of mass propagation techniques.

Industrial interventions for buying and building

Industry has contributed the most to innovation and can be encouraged to do even more if large industrial conglomerates can partner with or acquire small-scale industries. Among such potential large conglomerates are Agrinos AS, AgriLife, Symborg SL, Suståne Natural Fertilizer Inc., Valent Biosciences, Symbiom Ltd., Asfertglobal, and Privi Life Sciences Pvt. Ltd. Industry can also step up its investments on R&D related to AMF.

Next-generation biofertilizers and production technologies

A short shelf life of AMF products can limit market acceptability, so innovative methods and formulations (including those based on nanotechnology) are needed to extend shelf life. Indigenous species of mycorrhizal fungi can offer enhanced biological responses and therefore need increased attention in the near future. Combining AMF with slow-release fertilizers may encourage adaptation. As the volume and diversity of applications of AMF continue to increase, quality production of mycorrhizal spores will increase in importance. Although in vitro techniques of spore production are available, innovations are required in on-site, cost-effective bioreactors for large-scale production that can be operated without special training to manufacture ready-to-use products for farmers. Innovations are required for applications in sectors other than agriculture, for example in identifying and developing marketable by-products.

Consortia comprising not only AMF but microorganisms different from AMF, such as bacteria can serve as especially effective biofertilizers and need to be identified and developed. Innovations need to look beyond AMF and even beyond biology to explore other factors or components that will act synergistically with existing products or processes and which can be deployed in precision farming.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Research involving human participants and/or animals This article does not contain any studies with human or animal subjects.

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