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# The challenges of introducing a new biofungicide to the market: A case study

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## Abstract

**Background:** Scientific literature contains many reports documenting the isolation and antagonist-testing of microorganisms with the potential for biological control in agriculture, however, very few have addressed all aspects involved in the long process that occurs before a potential strain, found and tested in laboratory, can reach commercialization.
**Results:** After a multi-institutional and multi-disciplinary effort to develop a biological control agent with remarkable technical characteristics and performance, the fungicide *Fungifree AB*® was recently introduced in Mexican market. This product that has no chemical residues and is environmentally friendly which can be used by mango, avocado, papaya and citrus fruits (and other crops in the short term) producers to increase crops quality, and therefore, to access world markets.
**Conclusions:** The successful introduction of *Fungifree AB*® in the Mexican market has been the result of a wide variety of factors: remarkable product technical characteristics, researchers' high scientific level, mango producers and exporters' interest in testing the product and commercial companies interested in its distribution.

**Keywords:** biofungicides, fungicides, *Fungifree AB*®, process biotechnology.

## INTRODUCTION

*Fungifree AB*® is a biofungicide that was recently introduced to the Mexican market. It has been registered in Mexico for the biological control of mango anthracnose and is in the process of being registered for use on a variety of other crops, including avocado, papaya and citrus fruits. This

biofungicide, completely developed in Mexico is the first of its class to reach the market. This paper describes the main aspects of the development of a project that, after 12 years, led to the commercialization of *Fungifree AB*® (Figure 1). The topics include not only the scientific/technological development, but also other aspects that were crucial for the success of the project, including the following: a) the founding of a technology-oriented spin-off company that scaled-up the production of the biofungicide; b) the registration of the product with the Mexican agricultural and health authorities; and c) the establishment of a collaboration with a commercial company that is widely distributing the product in Mexico and will do the same in other countries in the future.

The scientific literature contains many reports documenting the isolation and antagonist-testing of microorganisms with the potential for biological control in agriculture; however, very few have addressed the aspects involved in the long process that occurs before a potential strain, found and tested in the laboratory, can reach commercialization (Whitesides et al. 1994; Schisler and Slininger, 1997; Torres-Sánchez et al. 2004; Fravel, 2005; Serrano-Carreón and Galindo, 2007; Köhl et al. 2011). To the best of our knowledge, there are no reports in the literature documenting the innovation process that resulted in the commercialization of a biological control agent for phytopathogens. In particular, there are no reports describing such a process occurring in an emerging country like Mexico.

The objective of this paper is to describe a multi-institutional, multi-disciplinary effort to develop a biological control agent with remarkable technical characteristics and performance. *Fungifree AB*®, a product that has no chemical residues and is environmentally friendly, can be used by the producers of mango, avocado, papaya, and citrus fruits (and other crops in the short term) to increase the quality of their crops and, therefore, their access to world markets.

This paper describes how the project began, primarily from a scientific perspective, and summarizes the main technical aspects that required solutions to develop a product with high potential but not ready to become a saleable product. This paper also describes the intellectual property issues of the project and the crucial role of a fruit exportation company in giving added value to the project by confirming the effectiveness of the biofungicide at a commercial level. A technology-based company was established; this paper summarizes the challenges faced by that company during its incubation, and the successful licensing of the technology from the academic institutions and registration of the biofungicide with the Mexican authorities to make the product available for commercialization. The paper includes a description of the commercialization issues of a unique biological product enabling more sustainable agricultural practices that has a very wide range of uses. The paper concludes with a critical analysis of this case study and recapitulates the lessons learned by the multidisciplinary team that allowed introducing the biofungicide *Fungifree AB*® to the market.

## THE IMPORTANCE OF BIOLOGICAL CONTROL IN AGRICULTURA

The “green revolution” occurred during the second half of the last century and involved an extensive use of agrochemical pesticides to sustain increasing population growth. The pesticide industry flourished and the world’s crop production increased as losses due to pest and/or pathogen attack were significantly reduced. However, the intensive and frequently excessive use of chemical pesticides became a threat to public health and the environment. Furthermore, producers experience a significant reduction in chemical pesticide efficacy due to an increasing occurrence of resistance among the pest populations. Federal Agencies in developing countries, responding to such health threats and to the growing consumer demand for organically cultivated, fresh and processed fruits and vegetables, have established regulations to reduce, and, in many cases, eliminate the use of chemical pesticides for food production. Thus, farmers must address the need to produce more and healthier crops while reducing the application of chemical pesticides. Under current conditions, pests and diseases are responsible for 40% of crop losses. Thus, alternative pest management technologies are being evaluated to meet the food demands of the population in sustainable ways. In addition to plant crop resistance, various biological control methods based on natural pest suppressing organisms (Biological Control Agents: BCAs) are regarded as the main alternatives (Gerhardson, 2002). Indeed, since the beginning of this century, the agrochemical industry has shown a growing interest in both biotechnological strategies. However, while big agrochemical companies have mainly supported the development of genetically modified crops, the majority of BCAs manufacturing firms have sales of 1 to 2 million USD, most of which originate from intellectual property rights that are frequently attributable to non-profit or academic research (Guillon, 2004).

The pesticide market clearly shows the effects of regulation and consumer preferences. While chemical pesticide sales decreased 1.3% annually between 2003 and 2010, the compound annual growth rate (CAGR) for the biopesticide market was 15.6% over the same period (Figure 2). However, the transgenic seeds market in 2011 was 13.5 billion USD, compensating for most of the reduction in chemical pesticide sales, and had a CAGR of 7.6% (BCC Research Report, 2012). In Mexico, the use of biopesticides (*Bacillus thuringiensis*) substantially increased in the 1980s after resistance to chemical pesticides was observed in the Diamondback Moth.

The International Biocontrol Manufacturers' Association (IBMA) classifies BCAs as Macrobials, Microbials, Semio-chemicals and Natural Products that are used in two types of agriculture: organic farming and integrated crop farming. BCAs can be used in both types, but organic farming is a preferred market for biopesticides. Organic farming eliminates the use of synthetic pesticides, fertilizers, genetically engineered organisms and growth enhancers to stimulate soil and crops. In 2007, 32.2 million Ha of agricultural land was managed organically by more than 1.2 million producers (Table 1); these figures represent a growth of 41% compared to 2003. Almost two-thirds of the land under organic management is grassland (20 million hectares) used for extensive cattle breeding. The cropped area is 7.8 million hectares, one-quarter of the organically managed land. Olives (402,152 Ha), coffee (547,275 Ha) and grapes (121,835 Ha) are the most important crops that are organically cultivated (Willer and Kilcher, 2009).

**Table 1. Organic agricultural land and producers by region in 2007.**

| | Organically managed agricultural land (Ha) | Share of total agricultural land (%) | Producers |
|---|---|---|---|
| Africa | 870,329 | 0.1 | 529, 986 |
| Asia | 2,881,745 | 0.2 | 234,147 |
| Europe | 7,758,526 | 1. 9 | 213,297 |
| Latin America | 6,402,875 | 1.0 | 222,599 |
| North America | 2,197,077 | 0.6 | 12,725 |
| Oceania | 12,110,758 | 2.6 | 7,222 |
| **Total** | **32,221,311** | **6.4** | **1,229,526** |

Source: Willer and Kilcher (2009).

Integrated pest management takes advantage of all appropriate pest management options, including, but not limited to, the judicious use of pesticides to manage pest damage by the most economical means and with the least possible hazard to people, property and the environment (EPA, 2012). In this market, chemical and biological pesticides are complementary options for the farmer. However, most academic research evaluates potential BCAs with the aim of replace chemical pesticides, as can occur with bioinsecticides. This focus could be a mistake: biopesticides usually have great potential to prevent pest occurrences but very limited efficacy when the incidence of the pest is above a critical value. Each BCA must be evaluated to identify this critical pest incidence. Such information is relevant for defining integrated pest management strategies, including the rational application of chemical pesticides to provide efficient solutions to farmers avoiding chemical residuality.

## THE EXPORTERS' NEEDS AND THE EXPERIENCE OF AN EARLY USER OF THE NEW PRODUCT

An important portion of the exports of developing countries consists of fresh and manufactured agricultural products. The governments of such countries spend important economic resources to help the local producers penetrate the export market. However, farmers face the following problems:

a) A large proportion of the producers are very small or small in terms of the size of their orchards and, therefore, have limited technological and financial capacities.

b) In general, these producers are not fully aware of the characteristics, prices, needs, competitive issues and trends in the international markets.

c) It is common that, in regional markets, there is an oversupply or, due to the slow movement of the inventories, part of the harvest does not meet quality standards; therefore, the achievable commercial prices are low.

d) The logistics of export are not always optimal, and the relatively short shelf life of the products is an important restriction for exportation.

e) Air transport is very expensive, and the costs are not affordable for high-volume markets, restricting this option to high-price niches.

f) There is a lack of suitable production and postharvest technologies that would allow for high-quality products and longer shelf lives.

g) Global climate change is a reality; “perturbed” seasons (periods and intensities of rain) as well as increased temperatures and relative humidity are frequent, and as a result, the prediction of harvest time is inaccurate, increasing the risk in the rate of return of agricultural crops in export markets.

The previous points have a factor in common that is not always evident in the diagnosis of problematic exportation issues: the effect of phytopathogenic microorganisms. This factor is an important contributor to losses during the exportation of fruit, and it is present in the entire production chain: in the field, in packing installations, and in the transport and commercialization steps. Phytopathogens are an important cause of losses in the export of agricultural products. Despite the management practices of the producers and exporters in the different aspects of production, problems with the quality of the products can arise in the various steps of the production-commercialization chain. Such problems can occur even if a careful producer takes the precautions needed as early as in the flowering stage of the crop. For this reason, a biological product, such as the biofungicide whose development and introduction in the market is described in this paper, is very important, since it has provided the mango producers with an effective fungicide that is free of chemical residues. This development is very important because it emphasizes the importance of Mexican research institutions in establishing basic and applied research programs for the development of products that are useful for small- and medium-sized farms.

The company “El Rodeo Fruit” is located in the main mango production region in Sinaloa. It has more than 26 years of experience in dealing with mango anthracnose problems. The company has determined that an important factor determining the incidence and severity of this disease is the rain occurring during the pre-harvest stages between flowering and harvest. In this 26-year period, there have been very critical years, such as 1997, 1998, 2005, and 2010, during which conditions associated with *El Niño* and *La Niña* caused rainy seasons considerably more intense than normal. In those years, there were a considerably higher number of reclamations, rejected shipments or, at least, severe penalties regarding the final prices of the fruit at the port of arrival. Reclamations mainly resulted from the damage caused by phytopathogens. Severe economic losses to the exporters occurred in consequence and, even more importantly, a significant damage to commercial relationships because of the poor image of the export brands and the lack of trust and decreased confidence on the part of the international clients. It took 2 to 3 years for the export company to recover trust from the clients in the export markets. However, when the situation returned to normal standards, a new heavy rain season occurred, and problems with the fruit quality arose again, causing new losses. This is why it is crucial to develop strategies for the application of biological alternatives, as well as conventional agrochemicals based on an extensive monitoring of the weather conditions and the building of reliable data bases of relevant parameters that could eventually help to predict the severity of the diseases caused by phytopathogens and other agents.

Another aspect that complicated the commercial situation was that, in early 2005, a large number of the countries to which “El Rodeo Fruit” was exporting started to restrict the use of chemical fungicides by establishing “maximum limits of residuality”. These restrictions made the export of mangoes even more difficult because if the limit was exceeded, the whole shipment could be rejected and incinerated.

An additional aspect is related to the logistics of shipment by sea (the most common method because of its affordability). The journey by ship can last from 15 to 23 days, and during this period, the high relative humidity, limited ventilation, and darkness in the containers favour the development of microorganisms that cause fruit deterioration and increase the possibility of a rejected arrival.

When “El Rodeo Fruit” became aware of the development of the biofungicide for mango anthracnose developed by UNAM and CIAD researchers, the company contacted them to inquire as to the possibility of using it in the company’s orchards, as well as in the orchards of the company’s suppliers (Figure 1). For four years (2006-2010) we encouraged (and supported) the farmers that had supply programs with “El Rodeo Fruit” to use the prototype of the biofungicide that was being produced at the Pilot Plant of the Institute of Biotechnology of UNAM (IBt-UNAM) in Cuernavaca (Mexico).

The mango producers gradually showed an increased interest in the biofungicide, and they convinced themselves of the relevant technical and high performance characteristics of the product (later named *Fungifree AB*®). The producers even added, empirically, a new attribute to the product: the higher level of “chapeo” (a characteristic of special brightness and colour of the fruit) in fruits treated with the biofungicide. No formal characterization has been made regarding this quality characteristic; however, it is customary that attributes given to a certain product by the producers increase the trust in the product. The demand for testing the product increased considerably, and the facilities at IBt-UNAM were not sufficient to produce the required sample amounts.

The producers now insist on the utilization of the biofungicide and request it before the flowering of the mango trees. These successful experiences have spread among other producers, who have shown interest in the use of the biofungicide. *Fungifree AB*® is now produced commercially (see below) by the company *Agro&Biotecnia* and is widely distributed by *FMC Agroquímica de México,* allowing all interested producers to use the product in their own orchards. In addition, it is hoped that the use of this biofungicide will lead to a more significant supply of high-quality markets for mango export companies, such as “El Rodeo Fruit”.

The widening range of applications (for avocado and papaya, for example) for *Fungifree AB*® will open new alternatives for companies, such as “El Rodeo Fruit”, that are interested in commercializing high-quality and residue-free Mexican “exotic” products for the international market.

## THE BEGINNING OF THE PROJECT

The main objective in the initial stage of the research was the selection and identification of microorganisms that were antagonistic to mango postharvest fungal pathogens (Figure 1). The study consisted of an extensive search of microorganisms, mainly bacteria and yeast, in the mango phyllosphere and the selection of potential antagonists of *Colletotrichum gloeosporioides*, one of the causal agents of mango anthracnose.

The choice of mango as a crop for potential anthracnose biocontrol was intentional for several reasons: 1) Mango orchards in Mexico are grown on approximately 175,000 Ha (FAO, 2007); 2) Mexico is one of the main mango exporters; and 3) anthracnose is the most economically significant disease of mango throughout the world.

Anthracnose is a major limiting factor in all major mango production areas. The fungus *C. gloeosporioides* can attack leaves, flowers and fruits. In the case of postharvest anthracnose, developing fruits are infected in the field, but infections remain quiescent until the onset of ripening, which occurs after harvest (Arauz, 2000). Postharvest anthracnose of mango can reduce the quality of the fruit, mainly by producing black spots that affect cosmetic standards.

The selection of candidates for anthracnose biocontrol was based on the biological relationship of antagonism between the fungal pathogen and bacteria and yeast from the mango's phyllosphere, because the canopy is an important infection and spore-production site for the fungus. This strategy allowed us to be much more selective regarding the action of the potential biocontrol agents on the fungal pathogen *C. gloeosporioides*.

The isolation of bacteria and yeast from the mango phyllosphere was conducted by extensive field sampling in mango orchards located in the north, central and south regions of Sinaloa, Mexico. Samples of mango leaves were collected, and their microbial populations were suspended in saline solution and plated on different culture media. The culture collection of isolates from the phyllosphere was based on colony morphology and colour. Approximately 200 isolates of bacteria and yeast were selected and preserved for screening to identify biocontrol candidates. The inhibition of mycelial growth of *C. gloeosporioides* was measured *in vitro,* and isolates with the highest levels of mycelial growth inhibition were selected for further tests. A group of seven bacterial isolates (6 *Bacillus* sp. and 1 *Pseudomonas* sp.) was selected based on the inhibition of mycelial growth of *C. gloeosporioides*.

The initial evaluation of antagonism was conducted in a small-scale *in vivo* field experiment. Bacterial isolates, selected on the basis of mycelial growth inhibition, were grown in nutrient media, adjusted to 3 x $10^8$ CFU/mL, and sprayed on mango trees before fruit maturity. According to the epidemiology of anthracnose in fruits, the flowering stage was selected as the critical period of infection to conduct the first application of the antagonistic microorganisms, followed by additional sprays during the period of fruit development. With this strategy, which was aimed at preventing mango postharvest anthracnose by several applications of the biocontrol agents, it was possible to protect the fruit from *C. gloeosporioides* infection, which could became latent and was only expressed at the ripening stage. Fruits collected from treated trees were evaluated postharvest for anthracnose, and a significant reduction in the incidence and severity of anthracnose was observed in fruits from trees sprayed with the isolate *Bacillus* sp. B-83.

In the case of the isolated yeasts, the biocontrol activity was evaluated through the application of yeast to artificially wounded mango fruits before inoculation with *C. gloeosporioides* (Arras, 1996). Application of one of the yeast isolates prevented the development of anthracnose symptoms in the fruit.

These promising results were presented at a meeting supported by the Mexican National Council for Science and Technology in 2000. At that meeting, scientists from CIAD and UNAM made contact for the first time, and a joint proposal was outlined to test the robustness of the initial results and to conduct additional studies. These further studies were designed: to identify a selected group of bacterial and fungal isolates; to select the optimal concentration of microorganism to be applied, the intervals of application, the proper time of application; to conduct semi-commercial- and commercial-scale experiments; and to test the efficacy during different agricultural cycles (Figure 1).

Several reviews have addressed aspects of maximizing the chances of developing a naturally occurring organism as a potential biocontrol agent (Hofstein et al. 1994; Wisniewsky et al. 2007; Nunes, 2012). The search strategy was to find bacteria and yeasts inhabiting the mango phyllosphere that met the prerequisite for biocontrol agent effectiveness: such an organism must colonize, survive, and multiply in the environment that is usually inhabited by the pathogen (Nunes, 2012).

## THE DEVELOPMENT OF THE PROJECT

After the initial contact between CIAD and IBt-UNAM researchers, the project formally began with the main purpose of selecting the most interesting bacterial isolates and developing the production processes at the scale of the laboratory bench (Figure 1). CIAD had a collection of potential candidates available for that purpose. At this stage (2001-2002), the project was the recipient of a grant from the Mexican Science and Technology Agency (CONACyT). These funds helped to support the research, primarily the fermentation studies at IBt-UNAM, and some preliminary field tests, performed by CIAD in the north western state of Sinaloa, México. Previous results revealed that two isolates (later characterized as *Bacillus subtilis* and *Rhodotorula minuta*) were the most promising. At that stage, the microorganisms were tested in the field as liquid concentrates that had been produced at the pilot plant of IBt-UNAM by centrifugation of the final fermentation broths. The biomass was produced in 10 and 100 liter fermenters, and the concentrates were kept under refrigeration (4ºC) until their use in the field. To illustrate the “proof of concept” of the potential biofungicides, the concentrates were shipped in the morning from Cuernavaca to Culiacan (more than 1000 Km apart) by air so that the formulation could be applied that same afternoon (Figure 1).

At the end of 2002, it was clear that the liquid biomass concentrates were limited for practical commercial applications. Therefore, a new grant with the main objective of developing solid formulations was obtained from the special fund of CONACyT and the Mexican Ministry of Agriculture (SAGARPA), which supports more technologically oriented projects. After three years of research, very reliable solid formulations were developed for a product containing the spores of *Bacillus subtilis* and a liquid product based on the vegetative cells of *Rhodotorula minuta* (Patiño-Vera et al. 2005). These two formulations were then used for more field trials, and the first paper from the project was published (Carrillo-Fasio et al. 2005). The project received the support of two more grants from the institutional research funding agency of UNAM (DGAPA-UNAM). This work was mainly devoted to the identification of the mechanism of action of the *Bacillus* (the production of nearly 50 compounds, some of which have antifungal activity), improving the yield and productivity of the fermentation stage, to the fine-tuning of some aspects of the solid and liquid formulations, and to establish the optimal doses and frequencies of application in additional field trials (Figure 1).

An invited paper published in Spanish in a non-scientific Mexican journal (Galindo et al. 2005) that is read by agribusiness professionals was crucial by making our project known to an innovative Mexican company ("El Rodeo Fruit") that exports mangoes to the USA, Europe and Japan. The researchers were contacted by this company, which was looking for alternatives for controlling mango anthracnose to obtain as much export-quality fruit as possible. Although Mexico is a major mango exporter worldwide, only approximately 14% of its production is exported, mainly due to the limited amounts of high-quality fruits that are available from Mexican mango producers.

"El Rodeo Fruit" offered to conduct field trials of the solid formulation (Figure 1). Semi-commercial- and commercial-scale experiments were performed, and the efficacy of our product was confirmed (Serrano-Carreón et al. 2010). One of the most important results was that 85% of the mangoes (postharvest) treated with the later commercialized product *Fungifree AB*® were free of anthracnose and of the quality required for export to Japan, while only 27% could be exported after a conventional fungicide-based regional treatment (Figure 3). However, more important than confirming the previously obtained results at the smaller scale, these tests developed an increasing trust in the product by mango producers and exporters. "El Rodeo Fruit" helped to make the product known and available for free to producers. In turn, these producers, as is usual in this field, promoted the biofungicide among other mango producers. *El Rodeo Fruit*, being aware of the efficacy of the product, offered its suppliers a bonus in the price of the fruits, provided they used the biofungicide and documented the experience. The data generated and, perhaps more importantly, the actual involvement of the producers, provided a more commercial perspective to the project, based on semi-commercial and commercial field trials that were developed and witnessed by the producers themselves.

In parallel, by the end of 2005, the technology developed for the production and formulation of a solid biofungicide for the biological control of mango anthracnose based on *Bacillus subtilis* spores was at the stage where it could be transferred to a company interested in scaling it up for production and commercialization (Figure 1). Several efforts were made by the researchers to advertise the project and search for potential companies interested in the technology. These efforts included the publication of a paper in a journal read by the people in the Mexican agroindustry (Galindo et al. 2005), numerous presentations at conferences and congresses, and meetings with associations of mango producers and the like. Two companies producing agrochemicals showed some interest and participated in preliminary negotiations; however, by the beginning of 2007, transfer of the technology had not been achieved yet.

The development of the biofungicide resulted not only in a very reliable and effective product but also in some important byproducts. The training of highly qualified personnel and the development of sophisticated techniques and equipment for the precise quantification of mango anthracnose are among the most important of these byproducts.

During the nearly twelve years of development of the project, 13 students have been involved in scientific aspects of the project: five BSC students developed their theses and 8 MSC students obtained their degree working in subjects associated with the project. Biologists, agronomical engineers, biochemists, and chemical and biochemical engineers have participated in work associated with the project.

The other important byproduct was the development of image-based analytical techniques for high precision evaluation, of the symptoms of anthracnose (black spots on the mango surface). This byproduct is quite useful because the current techniques for evaluating anthracnose are based only on subjective hedonic scales. By using sophisticated image analysis techniques, the area of the dots caused by anthracnose can be precisely evaluated (Corkidi et al. 2006). A robust prototype of the instrument has been built and tested under the conditions prevailing in a mango orchard (Corkidi-Blanco et al. 2010).

## INTELLECTUAL PROPERTY (IP) STRATEGY AND TECHNOLOGY LICENSING

A good understanding of the real meaning and utility of a patent or how the patent system works is not widespread in Latin America; however, most people see the patent as a type of magic key that opens the commercialization doors for an invention. Patent lawyer firms are busy with the procedures for the entrance of foreign international PCT (Patent Cooperation Treaty) applications into their respective national patent systems but do not draft patent applications, especially in biotechnology. When a researcher wants to generate a patent, he/she needs to find a Technology Transfer Office because it is difficult for a patent lawyer and a scientist to understand each other for the drafting of the patent application. It is as if they speak different languages; therefore, the inventor needs to meet a person (patent manager) who can speak both languages and is able to link the technical/scientific work with the legal patent system. This need is particularly true in the field of biotechnology (Eisenberg, 2003). In addition, there is very little experience in technology transfer from universities or academic institutions to the private industry. There is a clear disjoint between academic R&D goals and market needs, and industry in developing countries normally lacks R&D capacity. Accordingly, innovation is poor.

Because direct commercialization is not part of their mission, technology transfer/licensing has not been an important goal for universities. Indeed, technology transfer/licensing is a complex task that involves evaluating the technology to obtain an estimate of the nature of the negotiation (a marketing study will provide important information) and contacting a variety of companies related to the corresponding technological field. The creation of a spin-off company (as in the case of *Agro&Biotecnia*) is also an option for transferring the technology. Once a company has shown interest, a preliminary agreement must be drafted to set all the main terms to be negotiated, which includes the following: the technology involved; the products of the technology; the IP rights and their management; exclusivity; the field of use; the territory; further development and regulation; the amount to be paid and the schedule of payments; term and termination; confidentiality; governing law; and other terms that the parties may consider relevant.

Once the preliminary agreement is set, the parties begin to negotiate terms until they reach an agreement. Subsequently, one of the parties drafts an agreement contract proposal based on the pre-agreed terms, and the parties negotiate the minor terms of the draft agreement until they have a final version for execution. A final negotiation round starts after the university lawyers have reviewed the agreement contract and requested modifications.

The task is too complex to be conducted by the researchers themselves, and the involvement of a specialized technology transfer office, is highly recommended. The Instituto de Biotecnología (IBt) of UNAM has been concerned with IP protection of the technology that its researchers generate and the transfer of this technology to the private sector since the IBt-UNAM was created in 1985. IBt created a technology innovation unit in 1987, the Technology Transfer Office, which perform these two important tasks.

When IBT's inventors of the *Fungifree AB*® technology thought that they had an industrially applicable technology to solve the anthracnose problem in mangoes, they did not have to perform all of this work related to IP protection and the licensing process; IBt's Technology Transfer Office took on the task for them. Otherwise, it is possible that the inventors may not have followed through with the project.

A study of the state of the art was initially performed, which helped the inventors to give proper direction to the last stages of the project. When the project was ready, a second study of the state of the art was performed to ensure that the invention was patentable (it is novel, non-obvious, and has industrial applicability) and determines the fastest and best strategy to obtain the patent (Reiter et al. 2011). After conducting the study of the new biofungicide, the IP strategy was addressed to protect the

solid formulations. The invention description was drafted and discussed with the inventors, and a PCT application (WO2008/048081) was filed in 2006 with claims that protect a solid, dry formulation containing *B. subtilis* for the biological control of *C. gloeosporioides* (Figure 1). The results of an international search and the opinion of the international examiner concluded that the invention was new, innovative and industrially applicable because no documents that limited its scope were found. However, it is important to realize that the patent (once it is granted) is not a magic key. It will not automatically allow the commercialization of the invention. It will only allow its owner to restrict third parties from commercially exploiting the invention. In the case of technology developers such as universities, the patent is a useful tool for negotiating the transfer of the technology to a third party, generally a company (Kalanje, 2005). Companies usually know their business very well, and when consider taking an invention to the marketplace, they only invest in technology that is well protected against third parties that may imitate their product.

The licensing of the technology was promoted within the national agroindustry while the PCT application was in its international phase (2006-2008). These efforts were unsuccessful and this situation prompted the creation of the *Agro&Biotecnia* company (see below), which was incubated by two IBt inventors. Because the technology was developed (as previously mentioned) in collaboration with the CIAD, an inter-institutional agreement was negotiated and executed in 2009 to establish the co-ownership of the invention and the responsibility of the IBt Technology Transfer Office for the patent management and the technology out-licensing (Figure 1).

During 2011, after the incubation of *Agro&Biotecnia* (including the production of the first commercial batch of the biofungicide and product registration with the Mexican authorities) the company contacted the IBt Technology Transfer Office to formalize the technology license. A term-sheet was negotiated, including an upfront payment divided into several incremental payments, which allowed the company to capitalize because, as a spin-off, the company had a quite limited capital. Therefore, the more expensive payments were deferred to the moment when the company would be commercializing the product. The terms also included a differential royalty rate: a higher one for the crop tested by the developers and a lower one for additional crops that the company might test. The pre-agreed terms in the term-sheet were set in a license agreement contract which, after some negotiation, resulted in a contract version that was ready for review by UNAM's legal counsel. It is important to highlight that, although UNAM, and particularly IBt, is one of the most experienced institutions in technology transfer to the private sector in Mexico, this was the first case in which the company was a spin-off (with some UNAM academics as partners), and UNAM did not have (and, to date, does not have) a clear policy covering this situation.

Thus, when UNAM's legal counsel reviewed the document, it was particularly severe, identifying several legal and formal issues that required another round of discussion to solve. Additionally, they identified a conflict of interest: the university researchers that were simultaneously the inventors and partners in the company would receive a double benefit: one as the inventors (because UNAM's rules are that inventors shall receive 40% of UNAM income for technology exploitation) and one as the company partners. The researchers proposed, and UNAM counsel accepted, to convert the share of royalties legally belonging to them into operating budget for their laboratories.

Finally, at the beginning of 2012, a license agreement was executed to license and transfer the technology from UNAM to *Agro&Biotecnia* to allow the commercial exploitation of the technology through the sale of the product *Fungifree AB*® (Figure 1).

## A CRITICAL DECISION: STARTING A SPIN-OFF COMPANY

At the end of 2007, the researchers had enough evidence to support the following conclusions: a) the *Bacillus subtilis* (strain 83), isolated from mango tree foliage, had commercial potential as a biological control agent; b) a robust pilot-scale production technology was ready to be scaled-up to industrial level; c) there is market demand for high-quality mangoes, the amount of which can be increased using the biological control agent; and d) the companies to which the technology package was offered did not have enough interest to invest in the production and registration to put a new product on the market.

This situation was frustrating, because the researchers had in their hands a technology with a high potential to be useful to farmers, but they did not have the resources to bring it to the market. For a

technologist, the final objective of his/her work is to transform the acquired knowledge into viable solutions for real problems. Thus, storing the technology package in a desk was not an option. Dr. Serrano and Dr. Galindo made a critical decision: they founded a company and identified the limiting step to close the loop: market demand → technological solution → product on the market. In some research fields, this decision could be far from the conventional way of thinking. However, since the merge of biotechnology, an increasing number of biotechnologists have become entrepreneurs. Despite this general trend, in developing countries, this decision remains infrequent. The researchers searched for a partner with experience in the fields of quality control and manufacturing in biotech companies and found C. Roberto Gutiérrez, a biotechnologist, who has more than 25 years of experience in industry and currently is working in one of the most important Latin-American fermentation companies (Fermic). Therefore, *Agro&Biotecnia* was formally born in March 2008 (Figure 1), and its first goal was to offer a technological solution to improve the efficiency and safety of the production of agriculture goods, with mangoes as the first example, by putting the biofungicide on the market. The financing of the new company was supported in part by a grant from the CONACyT-Morelos State Fund, which supports the development of new companies, as well as *Agro&Biotecnia* resources.

In some countries, starting a new company may be an easy process. Unfortunately, this is not the case in Mexico. Although the government has sought mechanisms to simplify and facilitate the creation of companies, it is still a long and sinuous process involving a significant number of steps.

The development of the *Agro&Biotecnia* business plan was supported during its incubation at the CeMITT (Centro Morelense de Innovación y Transferencia Tecnológica), which allows the company founders to work with professionals from different areas that are involved in the creation of a new company. The collaboration with these professionals gave the founders the ability to self-evaluate their capabilities and weaknesses. The analysis enabled them to define the company profile and a general operating strategy. The advice of professionals in strategic planning was also very important, helping the company to identify the strengths of *Agro&Biotecnia* and assisting the company team in finding mechanisms to overcome weaknesses in basic areas of the business, such as commercialization and distribution.

The interaction between the company founders and communication and design professionals lead to the naming of the biofungicide as *Fungifree AB*®, and the relationship with regulatory professionals supported the company in registering the product and the trademark with the Mexican authorities (Figure 1).

## INCUBATING THE SPIN-OFF COMPANY

A spin-off is a technology-based company that is also often linked to a university. It contributes to the transfer of scientific findings to the social sector in the form of innovative products. Thus, the new products (which have a high added value) that have been developed by skilled minds and hands can offer great benefits to the society. The term "spin-off" is an Anglo-Saxon word that expresses the idea of the creation of new businesses within existing companies or organizations, whether public or private entities, acting as facilitators or incubators, gaining independence in legal, technical and commercial issues (Universia). A spin-off frequently starts with the production of prototypes of goods/services issued from academic activities and the best of innovative technological developments. Such a company involves hard work and financial investment in research and development.

Given the business opportunity, it is advisable to start the company in a business incubator, especially if the new company comes from a university. Business incubators are organizations that are generally installed within scientific and technological parks. They offer a number of resources that are managed by experts able to guide new entrepreneurs with good ideas for the design and accomplishment of a business plan. The services offered by incubators include physical space, such as offices or laboratories, shared services and departments and teams, coaching and counselling, and networking for possible partnerships or investment activities. The incubator's consultants perform a transfer of know-how to new entrepreneurs with innovative business ideas. The strengths and weaknesses of the spin-off are identified to facilitate the necessary resources to allow the rapid growth of the new business. In a business incubator, different business components are evaluated: the future market, the technology, the human resources, the competitive advantages, the global or regional approaches, the

feasibility, and the assessment of the innovativeness of the idea. Among the three types of incubators that exist in Mexico (Traditional, Intermediate Technology, and High Technology), the high-tech incubators support the incorporation of companies in advanced sectors, such as information technology and communications, microelectronics, micro-electromechanical systems (MEMs), biotechnology, and food and pharmaceutical industries, among others (Sistema Nacional de Incubación de Empresas, SNIE).

To access a high-tech business incubator, entrepreneurs must have an innovative good/service, which is analyzed and selected by a project evaluation committee. Once an incubator has accepted an innovative project, the business goes through a process of development that is usually divided into three stages: pre-incubation, incubation and post-incubation (CeMITT). In the pre-incubation stage, the company defines the business model, conducts market research and defines the strategic plan. The incubation starts by preparing the business plan (designing models that work in various areas, such as production, marketing, finance, administration, human resources, graphic and industrial design) and the attention to crucial points (intellectual property issues, technology transfer, and legal issues); the incubation takes between 12 and 18 months. Then, there is a post-incubation period. In this stage, the project is tracked, and areas of opportunity are strengthened. This period is considered to be a critical phase; it takes at least six months, and requires advice from specialists in various areas, as the launch of the company should occur in this phase.

The first achievement of a spin-off is making the decision that a business idea must be converted into a company (the business vision), followed by the integration of a team of researchers with entrepreneurial spirit. The foundation of the new company is the most important issue. *Agro&Biotecnia* S de RL MI was founded in March 2008 and started its incubation at the CeMITT in May 2008. For the new entrepreneurs, one of the major challenges was to establish a win-win negotiation between the research center (the owner of the patent and/or the technology) and the owners of the new company (the authors of the patent or the development) for technology transfer through licensing the technology. In Latin-American countries, this is a delicate negotiation for a spin-off company stemming out from a university. Experience is limited and seldom documented, and concerns about conflicts of interest are always present. After almost 3 years of negotiations, *Agro&Biotecnia* signed a technology license agreement with UNAM in early 2012 (Figure 1).

Another challenge for the new entrepreneurs was to define a business plan that established the basic direction of the new company. In Mexico, as well as in other countries, obtaining registrations from governmental agencies is a challenge in terms of time, logistics and economic resources; therefore, obtaining such registrations is a main bottleneck in the process of starting a spin-off.

It was crucial to obtain initial working capital from government organizations or private investors (angel investors or strategic partners). In 2008, *Agro&Biotecnia* obtained a grant from the special Fund of CONACyT (National Council of Science and Technology) and the Morelos State Government. An integrated set of activities that allowed for the important achievement of the birth of the company was needed. Those activities, including the protection of trademarks and patents, conducting large-scale production and the registration of the product (including the required toxicological and biological efficacy evaluations), were performed during the incubation period. The process of registering *Fungifree AB*® with the Mexican authorities (SAGARPA and COFEPRIS) lasted approximately 2.5 years and was completed during 2011 (see below). The incubation of the company at CeMITT lasted approximately two years, and the company finished the incubation program at the end of 2010 (Figure 1).

## THE CRUCIAL ISSUE OF PRODUCT REGISTRATION

Product registration with the regulation authorities is an essential formality required to legally commercialize a product. Registration should be obtained in every country where the commercialization of the product is intended. *Fungifree AB*® is considered to be a microbial plaguicide by the Mexican authorities. Sanitary registration is a Mexican government certificate that guarantees the quality, efficacy and safety of a marketable product. In Mexico, two governmental authorities are involved in the granting of the sanitary registration of bioplaguicides: The Ministry of Agriculture (SAGARPA) and the National Commission for the Prevention of Sanitary Risks (COFEPRIS), a division of the Mexican Ministry of Health. SAGARPA is responsible for supervising the evaluation, through field

tests, of the biological efficacy of the bioplaguicide. If the product shows significant control of the disease claimed in the application, SAGARPA submits a positive report to COFEPRIS. Biological efficacy tests of *Fungifree AB*® were performed in mango orchards in southern Sinaloa from January to July 2009, and the report was submitted to SAGARPA in September 2009. A positive opinion was issued by SAGARPA in June 2010 (Figure 1). In parallel, COFEPRIS supervises the sanitary risk assessment of the product. In this case, the applicant must provide independent proofs (issued by certificated laboratories) of product safety and quality, including the following issues: composition, physico-chemical properties, use-related physical properties, biological properties, toxicological and eco-toxicological assessments, and stability. Such information defines the risk level assigned to the product (in the case of *Fungifree AB*®, the lowest level of risk was obtained), and together with a positive biological efficacy report issued by SAGARPA, the final registration can be granted (Figure 4). Sanitary registration was obtained in April 2011. To summarize, the sanitary registration of the product occurred approximately three years after the first administrative procedures (Figure 1). It should be noted that the entire process is intended for each formulation for a particular botanical group and for a particular disease. If registration of the formulation for different diseases and/or botanical groups is required, the number of biological efficacy evaluations increases accordingly, although safety and quality tests are no longer needed if the formulation remains unaltered. As an example, *Fungifree AB*® was initially registered for anthracnose control in mango, and the registration cost was nearly US$ 40,000.

## THE COMMERCIALIZATION ISSUES

At the beginning of 2011, many of the innovative aspects of the new biofungicide were set up: a) a spin-off company was negotiating with UNAM the use of the technology, and b) the company had scaled-up the production technology and obtained the registration of the product. The only missing aspect was how to commercialize the product.

The *Agro&Biotecnia* vision and mission statement remarks that it is mainly a technology company, aimed at the development of innovative products for the agricultural sector. The company had no experience in commercialization issues and decided to establish a strategic alliance with a company having experience and prestige in that field.

*Agro&Biotecnia* was contacted by various agrochemical companies operating in Mexico. A very fruitful and strategic agreement was finally signed between *Agro&Biotecnia* and *FMC Agroquímica de México*.

*FMC Agroquímica de México* is a company with the business principles of providing Mexican fields with high impact solutions to productivity and positioning its portfolio in an increasingly environment- and farmer-friendly way. This philosophy is global for the *FMC Corporation*, and it is based on consumer trends indicating high demand for naturally treated crops. Additionally, the company is aware that its mission is to provide tools that promote the marketing of their crops based on excellent quality and sustainable welfare. Therefore, FMC is committed to social responsibility, which has given a substantial boost to its *Grow Organic* line.

As part of its strategic plan, *FMC Agroquímica de México* decided to enter the organic market with its *GROW ORGANIC* line (integrating *Fungifree AB*®); this decision was based on the potential value of the sector, considering that the Mexican market is approaching a figure of approximately $560M USD (not including herbicides). The company sees a great opportunity driven by new consumer trends and regulatory pressures for traditional chemistry to migrate to (or be replaced by) more sustainable new practices.

There is no doubt that the marketing of these products is more challenging, particularly with regard to convincing the farmer to make an increased investment and change his production habits. For this reason, over the last five years, the FMC Company has been very active in evaluating various biological products and companies that could be integrated as partners in the strategic plan. For each of these products and companies, the following factors have been established as the most important:

a) Biological effectiveness has to be comparable to the traditional chemical products that will be replaced.

b) Offering outstanding quality and a differentiated value proposal.

c) A shelf life of over 2 years without refrigeration (ideal).

d) A partner sharing a vision and/or business model and growth based on innovation and research.

e) The cost-benefit holistically includes the value chain, *i.e.*, greater benefit than cost.

Both *Agro&Biotecnia* and *Fungifree AB*® are in line with the above-mentioned factors. Therefore, *Fungifree AB*® arrived in Mexico as a valuable tool for the export market and for those producers who have had anthracnose as this product represents a solution for declining profits and marketing difficulties.

Among the key communication tools for product positioning, FMC has used different channels to achieve greater brand recognition. There has been an expectation campaign involving mailing and social networks. The plan included sending information to a large number of potential clients, including opinion leaders, key suppliers, technical consultants and growers.

*Fungifree AB*® was launched in the framework of the Guanajuato Agro-Exhibition 2012, which was held from 07 to 10 November 2012 in the city of Irapuato, Guanajuato, México (Figure 5). This exhibition was a very important showcase because it is the most important event for the industry in Mexico. FMC participated in two spaces within the Agro-Exhibition; one space was within the commercial plant and included detailed product information via virtual screens. In another space on the field, visitors could observe the effects and benefits of the applications on zucchini. The forum included the participation of the main actors of the project described in this paper (UNAM, CIAD-Culiacán, *Agro&Biotecnia* and FMC) in an event titled "*Fungifree AB*®*,* solutions for Mexican Fields", in which the product was formally presented to the Mexican market. It should be noted that the following quote is written on the label of *Fungifree AB*®: “Product formulated with technology of the IBt-UNAM and CIAD-Culiacán” (Figure 1). In this way, FMC reiterates its confidence in the Mexican talent and public institutions that worked together to bring tangible benefits to the fields of our country and, thus, confirm the FMC goal of being a company that promotes sustainable agriculture.

## WIDENING THE USES OF THE BIOFUNGICIDE *FUNGIFREE AB*®

*Fungifree AB*® is currently (December, 2012) registered for use on mango anthracnose; however, SAGARPA has endorsed the biological effectiveness for other fruits, including avocados, papaya and citrus fruits (Figure 1). Some of the effectiveness tests are described below.

### Application to avocados

Anthracnose (*Colletotrichum gloeosporioides*) is one of the most important diseases of fruit trees, causing damage during flowering, fruit development and postharvest. During postharvest, the disease causes the most important damage (4 to 60% loss) due to the development of fruit spots and shortening of the shelf life. Mexico is the largest avocado producer worldwide. Recently, the export market for Mexican avocado has substantially increased to the U.S., Europe and Japan, reaching up to 200,000 tons of the nearly one million tons produced annually in the country. Unfortunately, anthracnose incidence has increased significantly worldwide, and importers are implementing measures to encourage farmers to improve the management of the disease and to reduce the use of chemicals.

Today, there are very few products registered for anthracnose management. Consequently, the Association of Avocado Producers and Packers of Michoacán (APEAM) are currently leading a project to support companies in registering new molecules or products to contend with avocado anthracnose. The evaluation of the effectiveness of *Fungifree AB*® was part of this important project in 2011 (Figure 1).

In collaboration with APEAM in the state of Michoacán, several experimental trials have shown that *Fungifree AB*®, when periodically applied to foliage at the rates of 2 or 3 g/L, prevents anthracnose

and reduces the severity values of untreated fruits from 21% to only 2.5 and 3.8%, respectively. Regional treatments and copper hydroxide resulted in values of 5.0 and 6.7% severity, respectively, while the control treatment showed 21 % anthracnose-severity (Figure 6). Official trials, aiming to extend the registration of *Fungifree AB*® for use in the control of avocado anthracnose, conducted in Tancítaro, Michoacán, showed that three applications of *Fungifree AB*® (2 or 3 g/L) were significantly better in anthracnose reduction than copper hydroxide at 4 g/L (Figure 7). These results demonstrated that *Fungifree AB*® performs better than or equal to the chemical treatments that are conventionally used to manage the disease. Therefore, once the product is registered for this crop, *Fungifree AB*® will definitely be a new alternative for producers and exporters of this important fruit.

**Application to papaya**

Papaya is also susceptible to the attack of *C. gloeosporioides,* and this crop is perhaps one of those with the highest use of agrochemicals. The global trend, as in other crops, is to reduce the use of chemicals. Therefore, farmers are searching for sustainable alternatives. Tests conducted in the states of Colima and Veracruz confirmed that *Fungifree AB*® applied at intervals of 7-10 days prevents papaya anthracnose with similar efficacy to the most commonly used chemical treatments (Figure 8). *Fungifree AB*® seems to be a good alternative, and its registration for papaya anthracnose control is in progress.

## ***FUNGIFREE AB*® NEW PERSPECTIVES**

In the international literature, the use of *Bacillus subtilis* in foliar applications for preventing foliar diseases in vegetables and fruit trees is well documented. *B. subtilis* is a well-known producer of a wide array of antibiotics that prevent disease development through their effects on the cell walls of pathogens. However, several environmental factors influence the efficacy of *B. subtilis*, making necessary the use of periodic applications during crop development. This necessity causes the farmers to despair because they seek a more rapid effect, especially when the disease is unpredictable, and because they are used to applying curative instead of preventive strategies.

The natural habitat of *Bacillus subtilis* is the soil; however, there is limited information on its use as an antagonist of soil pathogens. In addition to antibiotics, *B. subtilis* produces root growth promoters and other compounds that enhance the uptake and assimilation of nutrients by the roots. This ability can be exploited in greenhouse seedling production through the mix of the product with the substrate as well as drench applications after transplanting or in furrows for crops such as potatoes and sugarcane. Preliminary assessments of the effect of *Fungifree AB*® (8 and 10 g /L) showed an increase in roots and aerial biomass, making this product an attractive option for seedling production (Figure 9). These results led us to perform an evaluation of *Fungifree AB*® as antagonist to *Phytophthora capsici* in *jalapeño* (chili pepper) seedlings, variety Champion. Different biofungicides were mixed and incorporated with the substrate, and seeds, previously inoculated by immersion for 5 min in a solution containing 5800 CFU/mL of *Phytophthora capsici,* were then sown.

The results indicated that *Fungifree AB*® at 12 g/L was the best treatment, with only 8% of the plants affected, followed by a dose of 8 g/L with 10% of the plants affected; the untreated control exhibited 28% damaged plants (Figure 9). A short-term development project will include new assessments in various vegetables to determine the appropriate application rate for obtaining efficient plant disease control.

Planting potatoes and sugar cane, where the seed is deposited at the bottom of the row and then plugged, is suitable for the establishment of *Bacillus subtilis* in soil. Preliminary trials in potato indicate a positive effect of *Fungifree AB*® sprays, yielding an improved quality of the tuber, which, in turn, improves commercialization opportunity of this crop.

In summary, the potential use of *Fungifree AB*® is not only in the prevention of anthracnose on fruit trees but also in the prevention of powdery mildew in vegetable crops. In the short term, we will evaluate its use when mixed with substrate or drenched in furrow applications with regard to protection against diseases and growth promotion; to enhance quality and yield; and, most importantly, to be part of integrated pest management strategies to achieve more sustainable production systems.

## A CRITICAL ANALYSIS OF THE CASE STUDY

The success of putting *Fungifree AB*® on the market is the result of a wide variety of factors and actors. To analyze this case study, two main categories should be considered: the people and institutions involved, and their environment.

### a) Actors

**Researchers of CIAD & IBt-UNAM.** At the beginning of the project, the main purpose of the researchers was to find a viable solution for a common problem in Mexican fields: mango anthracnose. There were many research groups working on the isolation and testing of antagonist microorganisms with potential for biological control in Mexican agriculture. However, the relationship between these two high-level research groups yielded the following: a) an effective microorganism for the biological control of mango anthracnose; b) a pilot process to produce the BCA; and c) a stable formulation. Furthermore, the pilot process allowed for the possibility of testing the microorganism at a scale that could attract the attention of mango producers.

**El Rodeo Fruit.** The interest of this Mexican fruit exportation company in searching for and evaluating innovative alternatives for controlling mango anthracnose to improve the quality of their mangoes provided the researchers with two basic tools: a) the point of view of mango exporters (which have the largest risk of product rejection due to the postharvest nature of the disease); and b) the possibility of evaluating the strain at a commercial level and under well-controlled experimental conditions. “El Rodeo Fruit” is a company whose characteristic of continuous searching for innovative solutions to daily problems was fundamental in establishing the collaboration between farmers and distribution companies with real problems and academic technologists interested in evaluating solutions for them.

**Agro&Biotecnia.** The company was initially founded with the main objectives of introducing the biofungicide in the Mexican market, scaling-up the technology to an industrial level and registering the product with the Mexican authorities. The foundation of the company offered the researchers a way to evaluate a technological solution from a commercial point of view and to put a product into the market.

**Centro Morelense de Innovación y Transferencia Tecnológica (CeMITT).** This centre was created as a business incubator to facilitate the development of technology-based companies. In particular, the first Director of the centre (Dr. Antonio del Rio) offered *Agro&Biotecnia* a favourable environment for the transition from academic to entrepreneurial ideology. Indeed, the collaboration with professionals in regulatory, law, administrative and business fields allowed *Agro&Biotecnia* to develop the organizational structure necessary to operate as a formal company.

**Commercialization Company, FMC Agroquímica de México.** FMC is a world-class international marketing company with wide experience in distributing agrochemicals in Mexico and the commitment to providing farmers with innovative and sustainable solutions. FMC has an increasing interest in introducing biological products to the market that can be used in IPM strategies or for organic production. FMC provided the missing link in the commercialization structure of *Fungifree AB*®: distribution, farmer consultancy, and sales. The input of FMC in the expanding applications (and registrations) of *Fungifree AB*® has been critical for opening and, hopefully, increasing the market of the product.

### b) Conditions/environment

There is a worldwide interest in identifying safer and environmentally friendly alternatives for the production of agricultural goods. This interest has been evident to researchers for many years; however, the variety of non-chemical agricultural inputs and their market share remain low. Today, the production and consumption of biological biopesticides accounts only for a minor percentage of the total business. However, the biopesticide market has shown a remarkable growth, indicating that consumers are open to this class of innovative solutions. Many of these products have been developed by small companies founded by researchers and put into the market by larger companies; however, there are very few examples of such cases in Latin America.

The lack of successful events in developing countries is associated with the complexity of the process through which companies are founded, the scarcity of governmental financial support to encourage the development of innovation-based industry and a culture in which different actors are themselves not directly responsible for completing the technology transfer.

## LESSONS LEARNED

Many lessons were learned during the 12 years of the project leading to the commercialization of *Fungifree AB*®. The first, and perhaps more important of these lessons, was recognizing that in the innovation process, several actors (from the academic, industrial and service sectors) with very different professional backgrounds, abilities and even jargon, are required. Although this may be well known to experts who study the innovation process, it was not clearly evident to the researchers, particularly at the beginning of the project.

The other lesson was that scientific papers are not necessarily the most important part of the process of innovation. This concept might also be well known to experts in the field of innovation, but was not obvious to the actors of the innovation process. From the academic point of view, the important activity usually ends when the scientific paper is published. In the case of the development of *Fungifree AB*®, very few papers were published in international journals, which, for maintaining the scientific productivity of the academic participants, required them to publish papers in other lines of research. Researchers having only one line of research would have experienced problems in maintaining the usual standards regarding the publication rate required for a conventional academic career.

The other important lesson learned is associated with an old saying: “if you keep doing the same things, you will continue getting the same results”. If we (as researchers) had performed the usual steps researchers take (*i.e.*, mainly publishing papers and hoping that somebody else would complete the innovation process), the project described in this paper would be in a file in a drawer. Turning researchers into entrepreneurs is not an easy task, and it has many obstacles arising from many aspects of the process, including the University.

Perhaps one of the most critical lessons learned concerned the registration of the product with the Mexican authorities. This registration would have been impossible if only the academic view had been taken into account. This step was very likely the one that made the product attractive to a big commercial company. Before having the registration, despite the high intrinsic value of the technology, as well as the remarkable technical characteristics of the biofungicide, the product had little commercial value. Registration is costly, requires a long time, and is an unknown world for academic researchers. Therefore, successful development requires money, patience and entrepreneurial thinking. In this case, the incubation of *Agro&Biotecnia* provided a major boost to obtain the specialized consultancy needed to induce the transition of the project from a purely academic exercise to an entrepreneurial one.

Another lesson came from the mango producers and the mango exporters. If a high-quality product is available to them and they can test it, trust will be generated not only in the product but also in the companies and the people involved in producing and distributing the product.

Small companies, such as BCA producers in general, do not have the resources (physical, economic and human) to successfully – and quickly – introduce a new product to the agricultural market. Thus, a joint venture between *Agro&Biotecnia* and *FMC Agroquímica de México* brought together the main strengths of both companies: technical knowledge and market expertise.

An overall lesson is that the commercial development of a relevant bioproduct is possible in emerging countries, such as Mexico. This result is not only due to the personal merits of the actors involved, but is also associated with the high technical and scientific level of some of the Mexican research groups, particularly in the biotechnology field (see for example Bolívar, 2004; Boyer et al. 2009).

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## REFERENCES

ARRAS, G. (1996). Mode of action of an isolate of *Candida famata* in biological control of *Penicillium digitatum* in orange fruits. *Postharvest Biology and Technology,* vol. 8, no. 3, p. 191-198. **[CrossRef]**

ARAUZ, L.F. (2000). Mango anthracnose: Economic impact and current options for integrated management. *Plant Disease,* vol. 84, no. 6, p. 600-611. **[CrossRef]**

BCC RESEARCH REPORT. (2012). Agricultural Biotechnology: Emerging Technologies and Global Markets. p. 138.

BOLÍVAR, F. (2004). *Fundamentos y casos exitosos de la biotecnología moderna*. México, D.F., El Colegio Nacional, 355-672 p.

BOYER, L.V.; THEODOROU, A.A.; BERG, R.A.; MALLIE, J.; CHÁVEZ-MÉNDEZ, A.; GARCÍA-UBBELOHDE, W.; HARDIMAN, S. and ALAGÓN, A. (2009). Antivenom for critically ill children with neurotoxicity scorpion stings. *The New England Journal of Medicine,* vol. 360, no. 20, p. 2090-2098. **[CrossRef]**

CARRILLO-FASIO, J.A.; GARCIA-ESTRADA, R.S.; MUY-RANGEL, M.D.; SAÑUDO-BARAJAS, A.; MÁRQUEZ-ZEQUERA, I.; ALLENDE-MOLAR, R.; DE LA GARZA-RUÍZ, Z.; PATIÑO-VERA, M. and GALINDO-FENTANES, E. (2005). Control biológico de antracnosis (*Colletotrichum gloeosporioides* Penz.) y su efecto en la calidad poscosecha del mango (*Mangifera indica* L.) en Sinaloa, México. *Revista Mexicana de Fitopatología,* vol. 23, no. 1, p. 24-32.

CORKIDI, G.; BALDERAS-RUÍZ, K.A.; TABOADA, B.; SERRANO-CARREÓN, L. and GALINDO, E. (2006). Assessing mango anthracnose using a new three-dimensional image analysis technique to quantify lesions on fruit. *Plant Pathology,* vol. 55, no. 2, p. 250-257. **[CrossRef]**

CORKIDI-BLANCO, G.; ROJAS-DOMÍNGUEZ, A.; BALDERAS-RUÍZ, K.A.; SANGABRIEL-MENDOZA, J.C.; SERRANO-CARREÓN, L. and GALINDO-FENTANES, E. (2010). Una nueva herramienta para la caracterización precisa y cuantitativa de la antracnosis del mango, de utilidad para fitopatólogos, productores y exportadores. *Claridades Agropecuarias,* vol. 198, p. 39-47.

EISENBERG, R. (2003). Patenting genome research tools and the law. *Comptes Rendus Biologies*, vol. 326, no. 10-11, p. 1115-1120. **[CrossRef]**

Environmental Protection Agency U.S. (EPA). (2012). Integrated Pest Management (IPM) Principles. [cited November 20, 2012]. Available from Internet: www.epa.gov/opp00001/factsheets/ipm.htm.

FAO. (2007). FAOSTAT Agriculture Data. Rome, Italy: *Food and Agriculture Organization of the United Nations*. [cited November 14, 2012]. Available from Internet: http://faostat3.fao.org/home/index.html.

FRAVEL, D.R. (2005) Commercialization and implementation of biocontrol. *Annual Review of Phytopathology,* vol. 43, no. 1, p. 337-359. **[CrossRef]**

GALINDO, E.; CARRILLO-FASIO, A.; GARCÍA-ESTRADA, R.S. and PATIÑO, M. (2005). Tecnología para el control biológico de la principal enfermedad del mango (antracnosis) y el efecto en su calidad poscosecha. *Claridades Agropecuarias,* vol. 148, p. 50-59.

GERHARDSON, B. (2002). Biological substitutes for pesticides. *Trends in Biotechnology,* vol. 20, no. 8, p. 338-343. **[CrossRef]**

GUILLON, M. (2004). Current World situation on acceptance and marketing of biological control agents (BCAs). [cited November 18, 2012]. Available from Internet: www.ibma.ch/IBMA_Public_Positions/20041028_Presentation_BCAs_Thailand_Indonesia_Cuba.pdf.

HOFSTEIN, R.; FRIEDLENDER, B.; CHALUTZ, E. and DROBY, S. (1994). Large scale production and pilot testing of biological control agents for postharvest diseases. In WILSON, C.L. and WISNIEWSKI, M.E. eds. *Biological Control of Postharvest Disease, Theory and Practice*. USA, CRC Press. p. 89-100.

KALANJE, C.M. (2005). Role of Intellectual Property in Innovation and New Product Development. [cited November 6, 2012]. Available from Internet: www.wipo.int/sme/en/documents/ip_innovation_development.htm.

KÖHL, J.; POSTMA, J.; NICOT, P.; RUOCCO, M. and BLUM, B. (2011). Stepwise screening of microorganisms for commercial use in biological control of plant-pathogenic fungi and bacteria. *Biological Control,* vol. 57, no. 1, p. 1-12. **[CrossRef]**

NUNES, C.A. (2012). Biological control of postharvest diseases of fruit. *European Journal of Plant Pathology*, vol. 133, no. 1, p. 181-196. **[CrossRef]**

PATIÑO-VERA, M.; JIMÉNEZ, B.; BALDERAS K.; ORTÍZ, M.; ALLENDE, R.; CARRILLO, A. and GALINDO, E. (2005). Pilot-scale production and liquid formulation of *Rhodotorula minuta*, a potential biocontrol agent of mango anthracnose. *Journal of Applied Microbiology,* vol. 99, no. 3, p. 540-550. **[CrossRef]**

REITER, T.A.; DE YOUNG J.K.; MACPHAIL S. and FASSE, J.P. (2011). Strategies for expediting examination of US patent applications. *Industrial Biotechnology*, vol. 7, no. 5, p. 349-353. **[CrossRef]**

SCHISLER, D.A. and SLININGER, P.J. (1997) Microbial selection strategies that enhance the likelihood of developing commercial biological control products. *Journal of Industrial Microbiology and Biotechnology,* vol. 19, no. 3, p. 172-179. **[CrossRef]**

SERRANO-CARREÓN, L. and GALINDO-FENTANES, E.G. (2007). Control biológico de organismos fitopatógenos: Un reto multidisciplinario. *Ciencia,* vol. 58, no. 1, p. 77-88.

SERRANO-CARREÓN, L.; BALDERAS, K.; WONG, M.A.; ROSAS, D.R. and GALINDO-FENTANES, E.G. (2010). Biofungicidas para el control de la antracnosis del mango: Logrando frutos de alta calidad internacional para mercados exigentes. *Claridades Agropecuarias,* no. 208, p. 28-37.

TORRES-SÁNCHEZ, E.; CÁRDENAS-COTA, H. M. and DE LA TORRE-MARTINEZ, M.M. (2004). Biocontrol de plagas agrícolas y enfermedades de las plantas. In: BOLIVAR-ZAPATA, F.G. ed. *Fundamentos y casos exitosos de la biotecnología moderna*, México, El Colegio Nacional, p. 505-528.

WHITESIDES, S.K.; DAOUST, R.A. and GOUGER, R.J. (1994). Commercialization of biological control agents: an industry perspective. In: WILSON, C.L. and WISNIEWSKY, M.E. eds. *Biological Control of Postharvest Diseases - Theory and Practice*. USA, CRC Press, p. 107-121.

WILLER, H. and KILCHER, L. (2009). *The World of Organic Agriculture. Statistics and Emerging Trends 2009*, IFOAM, p. 299.

WISNIEWSKY, M.; WILSON, C.; DROBY, S.; CHALUTZ, E.; EL.GHAOUTH, A. and STEVENS, C. (2007). Postharvest biocontrol: New concepts and applications. In: VINCENT, C.; GOETTEL, M.S. and LAZAROVITZ, G. eds. *Biological control: A global perspective.* United Kingdom, CABI International, p. 262-273.

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# Figures

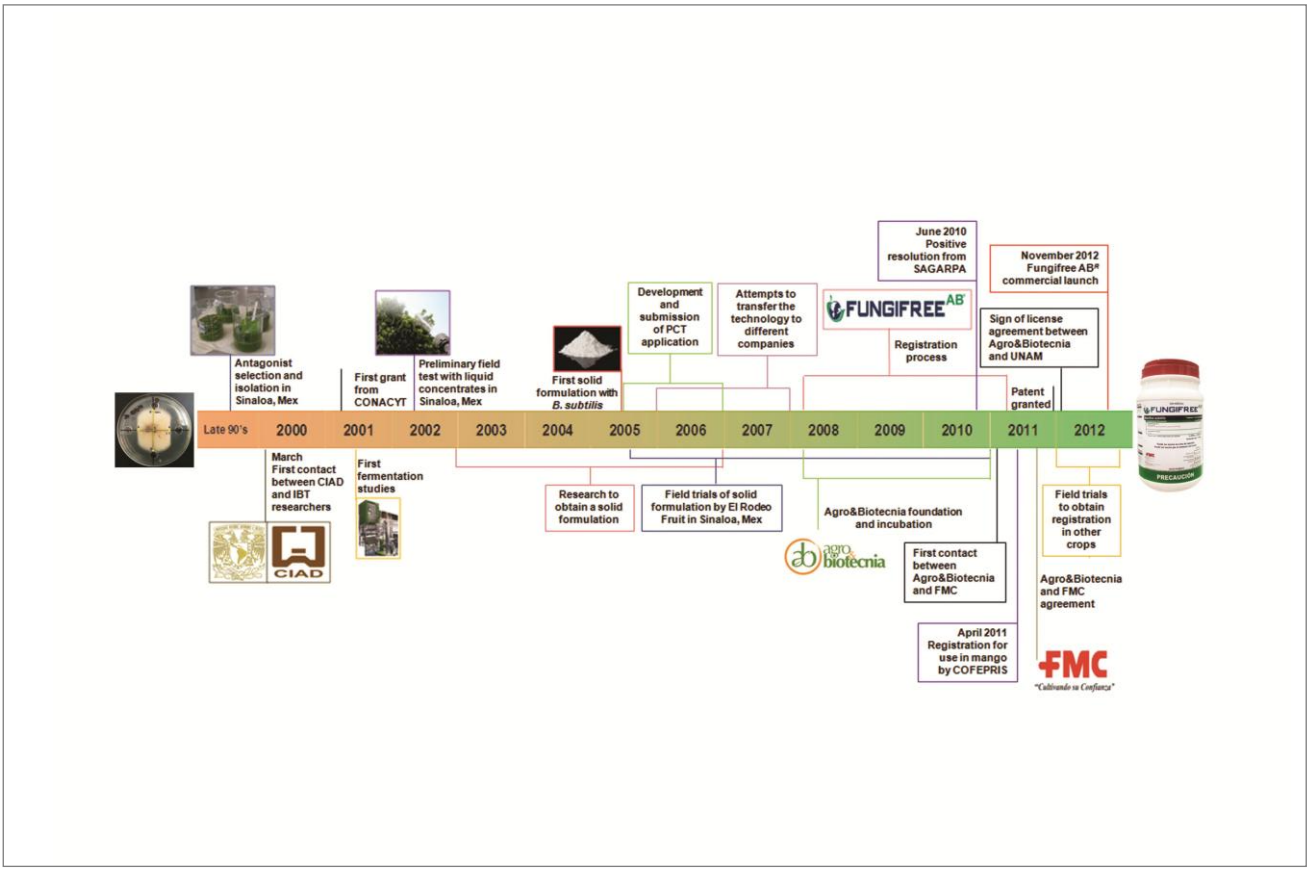



**Fig. *1 Fungifree AB*® development.**

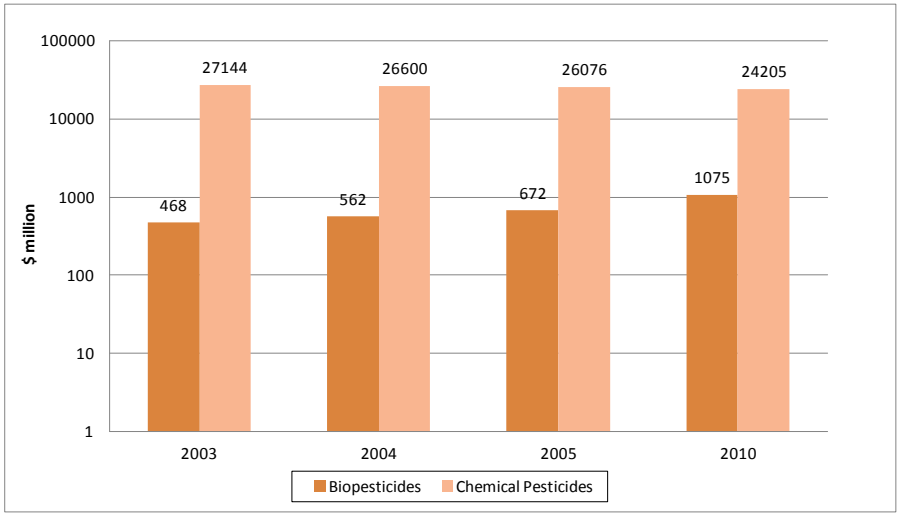



**Fig. 2 Market trend for biological and chemical pesticides.** Source: BCC Research Report, 2012.

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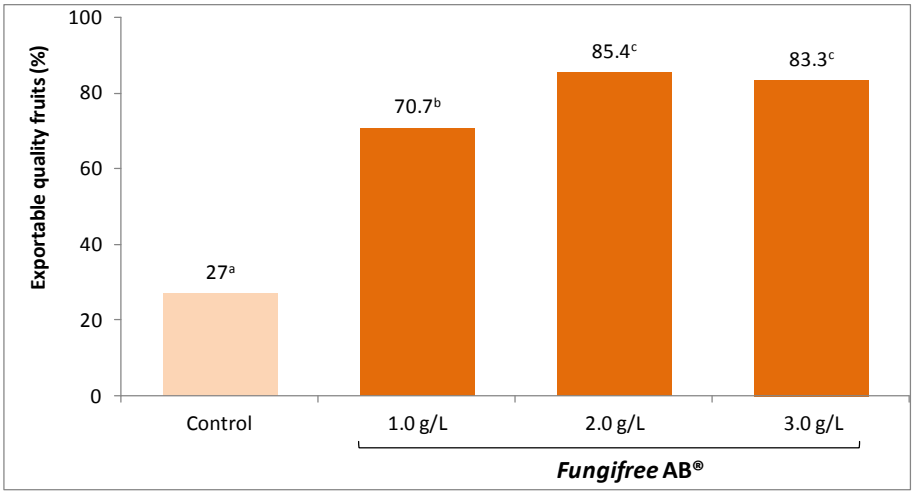



**Fig. 3 Increased production of export-quality mangoes using *Fungifree AB®.*** Data adapted from Serrano-Carreón et al. (2010). Identical letters indicate that there were no significant differences between the samples (p = 0.05).

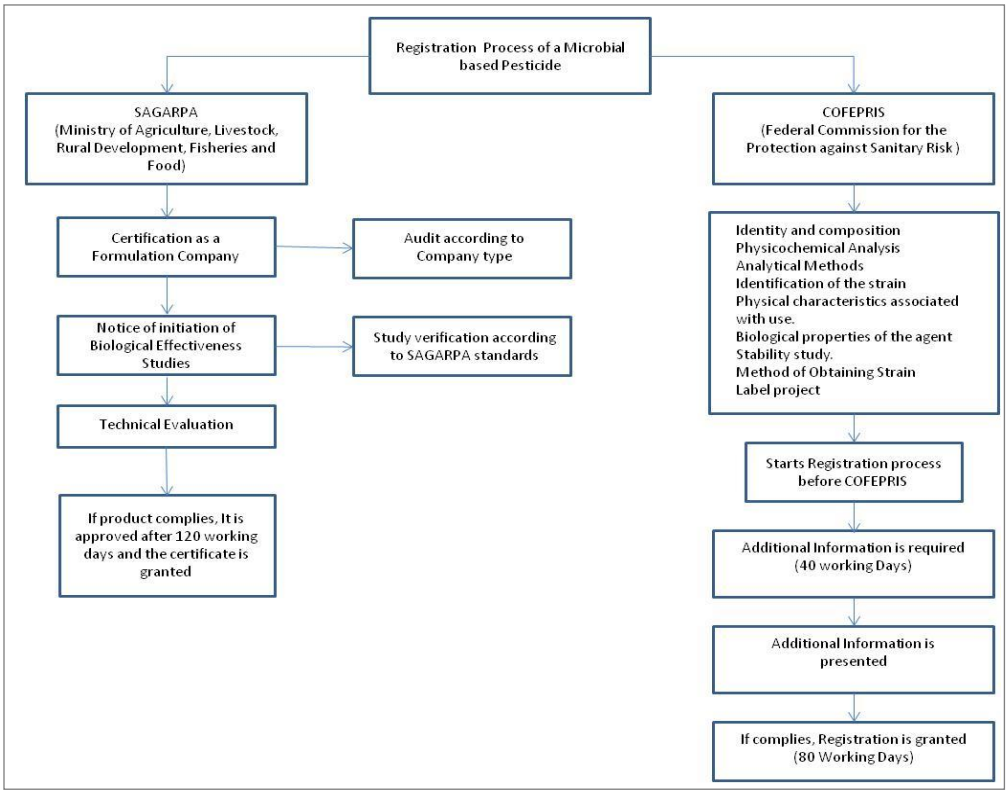



**Fig. 4 Sanitary registration flow chart.**




**Fig. 5 *Fungifree AB*$^{R}$ commercial launch in Irapuato, Guanajuato, México, November 2012.**

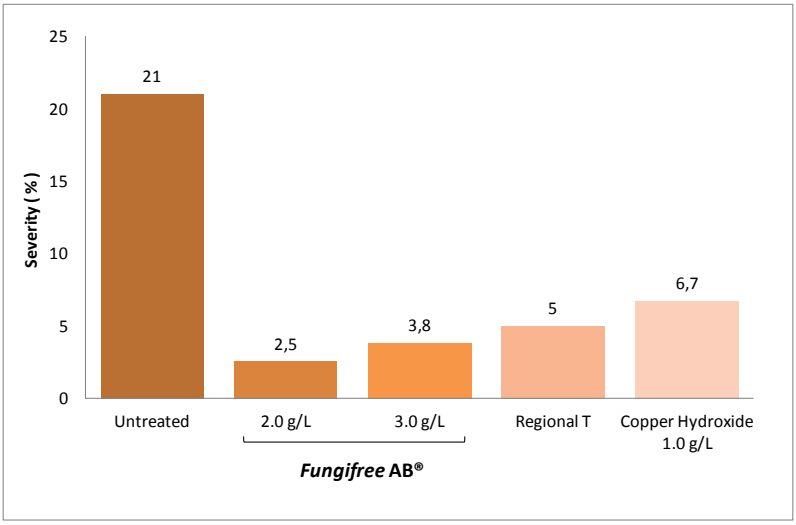



**Fig. 6 Anthracnose severity on avocado fruits var. Hass, at 10 days after harvest treated with *Fungifree AB*® at two doses and standard treatments.** Number of sprays: 6, interval between applications: 30-35 days, water volume: 2100 L/ha, sample size: 100 fruits/experimental unit). Experiments developed at "La Barranca", Tancítaro, Michoacán, México, from March to September 2011 by *FMC Agroquímica de México*. Regional T: Copper Hydroxide 1.0 g/L / Folpet + Copper Hydroxide 2.5 g/L / Copper oxicloride 1.5 L/L. Borderless mix, Calcium Hydroxide 6 g/L / Copper Sulphate 10.0 g/L.

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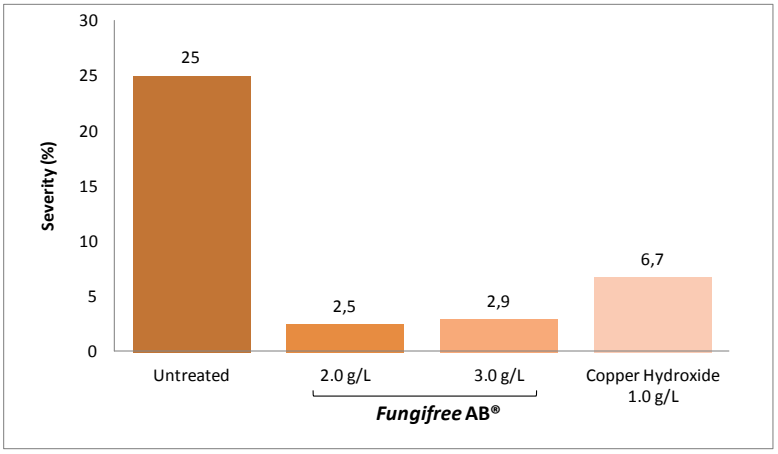



**Fig. 7 Effects of two doses of *Fungifree AB*® on anthracnose severity of avocado fruits var. Hass measured 10 days after harvest.** Number of sprays: 3, interval between applications: 30 days, water volume: 2000 L/ha, sample size: 100 fruits/experiemental unit). Experiments developed at "El Puerto", Tancítaro, Michoacán, México, from September to December 2011 by Bertha Tlapal, Universidad Autónoma de Chapingo.

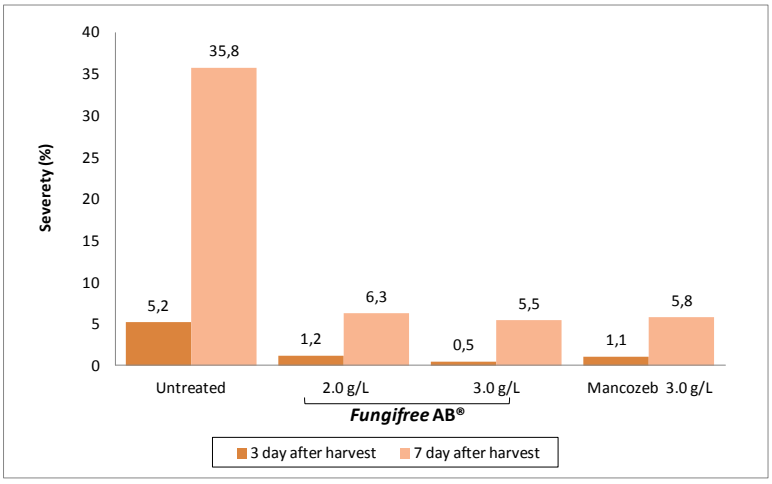



**Fig. 8 Effects of two doses of *Fungifree AB*® on anthracnose severity of papaya fruits var. Maradol.** Number of sprays: 4, interval between applications: 7 days, water volume: 500 L/Ha, sample size: 60 fruits/experimental unit). Experiments developed at Cotaxtla, Veracruz, México, from January to February 2012, by Bertha Tlapal, Universidad Autónoma de Chapingo.

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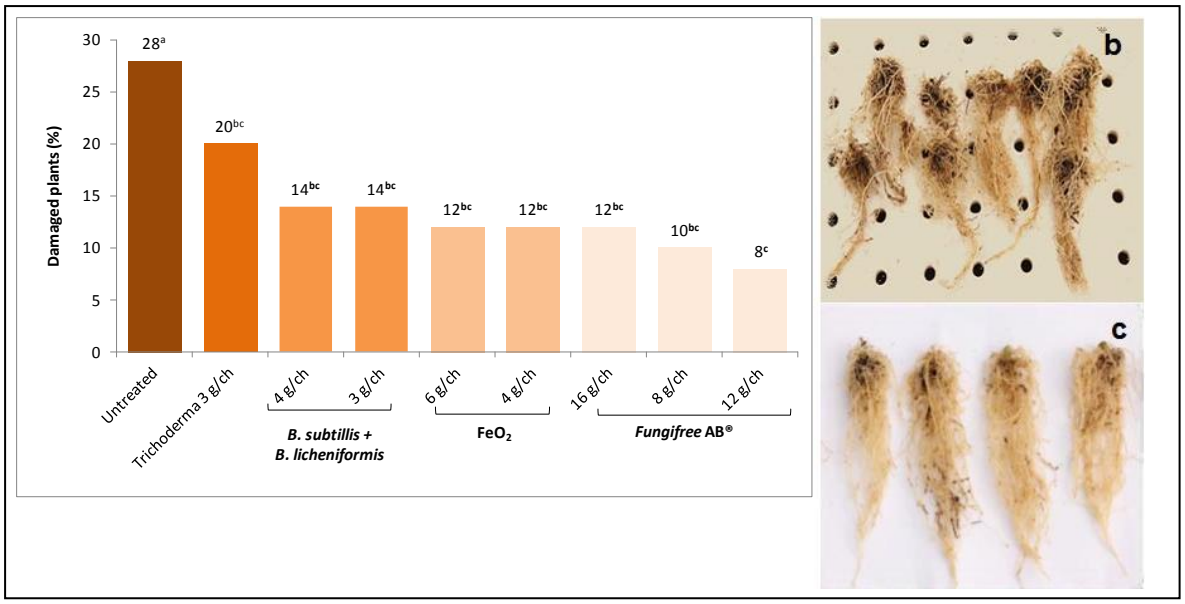



**Fig. 9 (a) Effect of different biofungicides in the control of *Phytopthora capcici* damage on *jalapeño* (chili pepper) seedlings var. Champion.** Experiments developed at *Agrosome Greenhouse*, Zamora, Michoacán, México, 2012. Dried roots of *jalapeño* (chili pepper) (b) Untreated and (c) treated with *Fungifree AB*®.

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