# Chapter 9
# Bioprospecting with Brazilian Fungi

**João Vicente Braga de Souza, Diego Rayan Teixeira de Sousa, Jessyca dos Reis Celestino, Walter Oliva Pinto Filho Segundo, and Érica Simplício de Souza**

**Abstract** Fungi produce important substances for industrial utilization**.** Among these substances, colorants, biosurfactants, antibacterial compounds and enzymes are of particular relevance. Bioprospecting studies are important in order to identify fungal producers of these substances. Understanding that good producers of these substances can be found in places with high diversity and microbial competition is recognized widely and Brazil is perhaps the most biodiverse country for this type of work. The aim of this chapter is to present relevant research involving bioprospecting with Brazilian fungi.

## 9.1 Introduction

Brazilian researchers have initiated bioprospecting efforts to identify fungi that produce substances of industrial interest. Among these compounds, colorants, biosurfactants, antibacterial compounds and enzymes are of particular relevance. This chapter describes how the bioprospecting of these substances is being carried out in Brazil.

Brazil is the 5th largest country in the world and occupies 47 % of South America. This large territory contains different ecosystems such as the (a) Amazon rainforest (recognized as having the greatest biological diversity in the world), (b) Atlantic forest, (c) Cerrado savanna, (d) Caatinga (a desert in northeast Brazil) and (e) Araucaria forest, a temperate forest in the south. These conditions make Brazil a mega-diverse country (Brasil 2015).

The study of this diversity and its technological potential is mainly being performed by government-run universities and research institutes. Most of these institutions are located in the southeast region of Brazil, which is the most economically

---

J.V.B. de Souza (✉) • D.R.T. de Sousa • J.d.R. Celestino
W.O.P.F. Segundo • É.S. de Souza
Laboratório de Micologia, Instituto Nacional de Pesquisas da Amazônia - INPA,
Av. André Araújo 2936, 69080-97 Manaus, Amazonas, Brazil
e-mail: joao.souza@inpa.gov.br

R. Paterson, N. Lima (eds.), *Bioprospecting*, Topics in Biodiversity and
Conservation 16, DOI 10.1007/978-3-319-47935-4_9

developed region of the country. The results generated by these researchers typically have academic value, but unfortunately, very few of these findings have been applied to the industrial sector. Brazil significantly contributes to the scientific community via manuscripts, books, etc.; however, the country generates few patents (Glänzel et al. 2006; Leta et al. 2006).

Many of the chemicals that exhibit technological potential and could result in new patents, products and services are fungal and fungi play a very important role in environmental dynamics. The following discussion aims to examine the importance of these substances and presents some of the major related studies that have been conducted in Brazil.

## 9.2 Colorants

### *9.2.1 General*

Colorant additives are used to provide color to otherwise dull substances. They can be classified as insoluble pigments or soluble dyes; however, these terms are typically used interchangeably (Saron and Felisberti 2006; Mapari et al. 2010). Dyes have been used worldwide as food additives to enhance the marketability of products by making their color more attractive (Uenojo et al. 2007; Volp et al. 2009). This technique is utilized because the loss or reduction of a food product's natural color during processing or storage, which it is assumed, lessens their appeal to the consumer (Serdar and Knežević 2009).

Currently there is growing interest in the discovery of dyes of natural origin, because synthetic dyes have been reported as carcinogenic and mutagenic, as well as causing allergies (Gunasekaran and Poorniammal 2008; Polônio and Peres 2009). Examples are the amaranth and erythrosine dyes, which have been shown to be genotoxic although they are presumably safe (and permitted) at low concentrations (Düsman et al. 2012). Therefore, synthetic dyes face more severe legislation, which has reduced the number of substances that can be used in food due to their adverse health effects in the short and/or long term, further fueling the search for biocolorants.

Bacteria, yeasts, filamentous fungi and algae, can synthesize pigments, but fungi stand out for their high productivity and extracellular release of such metabolites (Mapari et al. 2010; Hailei et al. 2011). *Blakeslea trispora* is a non-toxigenic filamentous fungus isolated from tropical plants that can synthesize high concentrations of the yellow-orange carotene pigment (Dufossé 2006). There are other producing species, such as *Phycomyces blakesleeanus* and *Mucor circinelloides* and the yeast, *Rhodotorula* (Dufossé 2006; Oh et al. 2009; Takahashi and Carvalho 2010). Riboflavin, or vitamin B2, can be synthesized by the fungus *Ashbya gossypii* and is also used as a food colorant (Braga et al. 2011).

Bioprospecting of fungal-derived dyes has gained increasing prominence due to their reduced toxic properties and added medicinal values (Chengaiah et al. 2010). In the textile industry, replacing synthetic dyes with other non-synthetic sources is feasible and would also decrease environmental toxicity (Mirjalili et al. 2011).

Synthetic dye residues can contaminate soil and natural water sources and are responsible for causing serious problems of environmental pollution (Ali 2010; Mirjalili et al. 2011). Fungal pigments, in turn, are more readily biodegradable and are potential dyes for industrial application.

Among the producing fungi the literature has highlighted, *Aspergillus*, *Penicillium*, *Paecilomyces* and *Monascus* are prominent (Gunasekaran and Poorniammal 2008; Méndez et al. 2011). *Monascus* is a cosmopolitan genus, and species such as *M. ruber* and *M. purpureous* are known for production of orange and red pigments. Some *Penicillium* species are capable of producing chemicals of various colors, including azaphilones. The sclerotiorin pigment produced by *P. sclerotiorum* and chromophores of the anthraquinone-type red pigment, such as Red Arpink produced by *P. oxalicum* are used in the food industry (Gunasekaran and Poorniammal 2008; Petit et al. 2009; Celestino et al. 2014; Kumar et al. 2015).

### 9.2.2 Brazilian Situation

In Brazil, many fungi have been studied for their synthesis of pigments during fermentation as follows:

A *P. sclerotiorum* strain isolated from soil samples of the Brazilian Cerrado produced the yellow-orange pigment sclerotiorin (Hamano and Kilikian 2006; Kanokmedhakul et al. 2006; Lucas et al. 2010). Sclerotiorin was also obtained from *P. sclerotiorum* isolated from Amazonian soil that showed increased production of the metabolite when modified sources of carbon and nitrogen were added to the growth medium (Celestino et al. 2014).

The endophyte fungus *Phoma sorghina* found in association with *Tithonia diversifolia* (Asteraceae), produced anthraquinones with orange and yellow colors (Borges and Pupo 2006). Polyketides of red, yellow and lilac shades have been found in Ascomycetes isolated from Amazonian soil, flowers and sawdust (Durán et al. 2002). Another report listed three Amazonian strains of *Penicillium simplicissimum*, *Penicillium melinii* and *Aspergillus sclerotiorum* that produced xantoepocina pigments (yellow), atrovenetina (yellow) and neoaspergilico acid (yellow–green), respectively. These have high economic value and low toxicity (Teixeira et al. 2012).

## 9.3 Biosurfactants

### 9.3.1 General

Surfactants have industrial applications including detergency, emulsification, lubrication, foaming capacity, “wettability”, solubilization and dispersion. The use of these substances is increasing particularly in cleaning products (soaps and detergents), oils, cosmetics and toiletries (Nitschke and Pastore 2002). Commercially available surfactants are synthetic and are obtained from petroleum products, although they present toxicity and are non-biodegradable (Soberón-Chávez and Maier 2011). The growing environmental concerns among consumers, combined with new environmental control laws, have led to the search for alternative biosurfactants (Nitschke and Pastore 2002).

Biosurfactants are a structurally diverse group of surface-active substances produced by living organisms. These substances are amphiphilic and composed of a hydrophilic and a hydrophobic group. The hydrophilic group consists of mono, oligo or polysaccharides, peptides or proteins and typically contains hydrophobic mid-chain saturated hydrocarbons or unsaturated fatty acids (Marchant and Banat 2012).

The composition and variations of biosurfactants are classified according to their chemical composition and microbial origin, because they have different chemical structures, especially those produced in the presence of hydrocarbons. These can belong to seven groups: glycopeptides, lipopeptides, phospholipids, fatty acids, neutral lipids, surfactants and polymeric surfactants particulates (Shekhar et al. 2014).The production of biosurfactants by microorganisms is well studied and has been published in studies using bacteria and filamentous fungi (Bhardwaj 2013).

### *9.3.2 Brazilian Situation*

In Brazil, the most investigated topics are the use of agro-industrial waste as substrates for biosurfactant production and the bioprospecting of fungi for biosurfactants. It is expected that new and innovative products will be generated as a result. Although not bioprospecting in terms of using novel fungi, Luna et al. (2012) evaluated the use of industrial wastes from processing corn and peanuts as substrates for the production of biosurfactants from *Candida sphaerica* and obtained yields of up to 9 g/l. Katerine et al. (2013) investigated the potential use of waste from the bioethanol and fuel industry in the production of biosurfactants by mixed cultures and also obtained good yields. Two recent publications (Santos et al. 2013, 2014) reviewed the use of animal fat and corn steep liquor as substrates for biosurfactant production from *Candida lipolytica*. Silva et al. (2014) investigated the use of residues from corn and soybean processing industries with *Cunninghamella echinulata*, a fungus isolated from the Brazilian Cerrado. They showed that the biosurfactant could reduce and increase the vicosity of hydrophobic substrates and their molecules, suggesting a candidate for oil recovery. The residual glycerol from biodiesel production has been studied as a substrate by *Yarrowia lipolytica* for biosurfactant production (Ribeiro et al. 2013). Luna et al. (2012) investigated the environmental applications of biosurfactants produced by *C. sphaerica* and concluded that these biosurfactants have potential for use as adjuvants in the remediation/treatment of oily industrial effluents. Solid-state fermentation was also investigated for the production of biosurfactants by *Aspergillus fumigatus* (Castiglioni et al. 2013) on paddy rice bran and verified the importance of inducing substrates such as diesel oil.

With optimal nutritional conditions, *A. fumigatus* showed a good emulsifying activity and in experimental conditions, was able to provide a novel alternative for process optimizations in biosurfactants production. However, this fungus may be a human pathogen and should be avoided. In general, the data from these studies indicate that agro-industrial waste can be used for production of biosurfactants that have the potential to generate economically-promising bioprocesses.

Bioprospecting studies of biosurfactant-producing filamentous fungi have been conducted (Teixeira et al. 2012). Suzana et al. (2014) and Da Silva et al. (2014) isolated (a) *Pichia* strains from industrial effluents and (b) endophytic fungi using the biopanning technique (peptides affinity selection) in the plant *Myrcia guianensis* respectively. Both studies revealed high emulsification indexes, and that the strains were able to produce biosurfactants, demonstrating the potential of these organisms for bioremediation under a wide range of environmental conditions.

## 9.4 Antibacterials

The misuse of antibiotics for the treatment and prevention of infectious diseases has led to an increase in antimicrobial resistance (Michael et al. 2014). Millions of years ago, pathogenic bacteria modified their virulence to adapt to the host defense system (Beceiro et al. 2013). Evidence suggests that the development of antibiotic resistance by bacteria, over time, is a natural process, occurring in the absence of humans and animals (Arias and Murray 2009). While there was a marked decrease in the discovery of new antimicrobial agents in the last 30 years due to lack of research and development by large drug companies, the rate of bacteria resistant to multiple drugs (MDR) has alarmingly increased, resulting in a serious worldwide problem with consequences for the treatment of infectious diseases (Wright et al. 2014).

Bacterial resistance is a consequence of the evolution of bacteria and worsened with the ease of mobility of easy international travel. The (a) increasing world population; (b) misuse of antibiotics in human medicine, veterinary medicine and agriculture; (c) constant loss of antimicrobial efficacy and (d) decrease of new antimicrobial agents (Wright et al. 2014; Shaikh et al. 2015) contribute to the situation. In the 1980s and 1990s, many pharmaceutical companies refocused their research programs for new antimicrobial agents in more profitable areas, primarily focusing on gram-positive bacteria, due to the rapid rise of *Staphylococcus aureus* resistant to methicillin (MRSA). The increase in MDR gram-negative bacteria intensified the search for new antibiotics, as these also promised a good financial return for pharmaceutical companies (Theuretzbacher 2009).

Antimicrobials are generally classified by their molecular structure and mechanism of action in the bacterial cell. The β-lactams target Penicillin Binding Proteins PBPs, inhibiting the synthesis of peptidoglycans and the formation of the cell wall in susceptible bacteria. These glycopeptides act on the D-ala-D-wing of lipid II, inhibiting peptidoglycan synthesis. Macrolides, lincosamides, chloramphenicol and oxazolidones act on the 50S subunit of the ribosome and inhibits protein synthesis. Tetracycline and aminoglycosides affect the 30S ribosomal subunit, thus inhibiting protein synthesis. The fluoroquinolones inhibit topoisomerases (DNA gyrase and topoisomerase IV), thus inhibiting DNA replication (Silver 2011).

Fungi are used for the discovery of new bioactive natural products because they are a source of compounds with different biological activities and can produce antiviral, antimicrobial and insecticidal substances with relevance in the industrial, agricultural and pharmaceutical sectors (Vieira et al. 2011). Most of the classes of antimicrobial agents used today were discovered from actinomyces in the soil (Aminov 2010). However, there are many antimicrobials produced by fungi currently used in therapy, including (a) cephalosporins produced by *Cephalosporium acremonium*; (b) penicillins produced by *Penicillium chrysogenum*, *Aspergillus nidulans* and *Cephalosporium acremonium*; (c) pleuromutilin produced by *Pleurotus mutilus* and *P. passeckerianos*; and (d) fusidic acid produced by *Fusidium coccineum* and *Acremonium fusidioide*s (Wright et al. 2014).

### *9.4.1 Brazilian Situation*

Brazil is carrying out bioprospecting of antibiotics produced by endophytes fungi, the production of nanoparticles with antimicrobial activity and optimizing antimicrobial activity. Using a bioprospecting approach, Orlandelli et al. (2012) investigated the production of antimicrobials, including terpenes by the endophytic fungus *Piper hispidum*. They observed that some of the isolates produced antimicrobials and three produced terpenes. Vaz et al. (2012) investigated the endophytic fungi on plants belonging to Brazilian flora (i.e. *Myrciaria floribunda*, *Alchornea castaneifolia* and *Eugenia* aff. *bimarginata*) and *Emericellopsis donezkii* and *Colletotrichum gloesporioides* produced an antimicrobial with an MIC similar to that of conventionally used antimicrobials. Santos et al. (2015) investigated the fungi from the leaves of *Indigofera suffruticose* Miller. (Fabaceae) where *Nigrospora sphaerica* and *Pestalotiopsis maculans* showed antimicrobial activity against gram positive (*Staphylococcus aureus*, *Bacillus subtilis*) and gram negative (*Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa*) bacteria. Flores et al. (2013) investigated the production of 3-nitropropionic acid by endophytic *Phomopsis longico* from *Trichilia elegans* A. JUSS spp. and found that it had activity against *Mycobacterium tuberculosis*.

Important investigations have also been carried out in the biogenesis of nanoparticles. Rodrigues et al. (2013) demonstrated the ability of *Aspergillus tubingensis* and *Bionectria ochroleuca* to produce silver nanoparticles with antimicrobial activity. Ishida et al. (2014) used a similar approach and obtained similar results by using *Fusarium oxysporum*.

The influence of the bioprocess factors on the production of metabolites with antimicrobial activity has also been studied. Bracarense and Takahashi (2014) using *A. parasiticus,* investigated modulation in the production of antibiotics, including kojic acid, showing growth inhibition against *A. flavus, C. albicans*, *E. coli* and *S. aureus*. However, *A. parasiticus* is a well-known aflatoxin producing fungus and should be avoided for bioprospecting procedures. Pigments of Brazilian fungal origin were also assessed for biological activity. Teixeira et al. (2012) investigated the biological activity of the dyes produced by *Aspergillus* and *Penicillium* isolated from the Amazon forest and found that many of these showed biological activity, with the pigments produced by *A. sclerotiorum* and *P. simplicissimum* being particularly important.

The cited studies present a panorama of bioprospecting and screening of endophytic fungi; however, clinical evaluation of these substances is required to determine the therapeutic potential for these preliminary findings.

## 9.5 Enzymes

The enzyme industry is part of biotechnology that has developed rapidly, especially during the previous four decades. Since ancient times, enzymes found in nature have been used in the production of foodstuffs such as cheese, beer, wine and vinegar (Saxena 2015). The use of fungi for the production of enzymes has led to a highly diverse industry with significant economic importance.

Fungi produce enzymes that are critical to their survival. These can act extracellularly or intracellularly to contribute to the digestion of food or in defense (Lange et al. 2012). These enzymes have not escaped the eyes of bio-engineering researchers. They are still being studied and occupy important positions in various industries, including the food, pharmaceutical and chemical industries (Kirk et al. 2002; Choi et al. 2015).

Fungal enzymes have been produced by the biotechnology industry in large quantities and low cost, and these enzymes can be modified according to desired characteristics. Enzymes of animal and plant origin have more complicated procurement mechanisms and modification procedures (Freedonia 2015). Multidisciplinary teams of chemists, microbiologist, biochemical engineers, biochemists and experts in other areas have come together to complement the knowledge that each area has on enzymes to improve their practices and develop technological innovations (Monteiro and Silva 2009).

The consumer markets are based on enzymes intended for industrial fabrics and cleaning products, foods and drinks and animal feed. The main industrial enzymes are proteases, amylases, lipases, cellulases, xylanases and phytases, and the largest producers are often European, e.g. International (Finland), Gist-Brocades (the Netherlands), and Novo Nordisk (Denmark), with Genencor, USA also a major player (Mussatto et al. 2007). Novo Nordisk controls about half of the global market where costs for production are decreasing, while the demand continually increases (Sanderson 2011; Jemli et al. 2014).

Brazil has an enormous diversity of microorganisms that can be exploited for the production of different enzymes of industrial interest in various areas (Table 9.1).

**Table 9.1** Studies on enzyme production by fungi in Brazil

| Industrial enzymes | Microorganisms | Authors | Methodology |
|---|---|---|---|
| Amylase | Filamentous fungi | De Castro et al. (2010) | Solid State Fermentation |
| Amylase | *Lichtheimia ramosa* | Silva et al. (2013) | Solid State Fermentation |
| Amylase | Filamentous fungi | Pasin et al. 2014) | Submerged Fermentation |
| Amylase | *Candida parapsilosis,*<br>*Rhodotorula mucilaginosa,*<br>*Candida glabrata* | De Oliveira et al. (2015) | Solid State Fermentation |
| Amylase | *Pycnoporus sanguineus* | Onofre et al. (2015) | Semi Solid Fermentation |
| Cellulase | *Aspergillus niger* | Cunha et al. (2012) | Submerged Fermentation,<br>Semi Solid Fermentation |
| Cellulase | *Aspergillus fumigatus* | Moretti et al. (2012) | Submerged Fermentation |
| Cellulase | *Acremonium strictum* | Goldbeck et al. (2013) | Submerged Fermentation |
| Cellulase | *Penicillium funiculosum* | Maeda et al. (2013) | Submerged Fermentation |
| Cellulase | *Lasiodiplodia theobromae,*<br>*Trichoderma* sp.<br>*Fusarium* sp. | Faheina Junior et al. (2015) | Submerged Fermentation |
| Lipase | *Penicillium sp.* | Griebeler et al. (2009) | Solid State Fermentation |
| Lipase | *Penicillium sp.* | Rigo et al. (2010) | Solid State Fermentation |
| Lipase | Yeast | Bussamara et al. (2010) | Submerged Fermentation |
| Lipase | *Aspergillus sp.* | Colla et al. (2010) | Submerged Fermentation |
| Lipase | *Aspergillus candidus* | Cyndy et al. (2015) | Solid State Fermentation |
| Phytase | Filamentous fungi | Guimarães et al. (2006) | Submerged Fermentation |
| Phytase | *Aspergillus niger* | Spier et al. (2011) | Solid State Fermentation |
| Phytase | *Paecilomyces variotii* | Madeira et al. (2011) | Solid State Fermentation |
| Phytase | *Lichtheimia blakesleeana* | Neves et al. (2011) | Solid State Fermentation |
| Phytase | *Penicillium chrysogenum* | Ribeiro Corrêa et al. (2015) | Recombinant Expression |
| Protease | *Myceliophthora sp.* | Zanphorlin et al. (2010) | Solid State Fermentation,<br>Submerged Fermentation |
| Protease | *Duddingtonia flagrans* | Braga et al. (2011) | Submerged Fermentation |
| Protease | Filamentous fungi Yeast | Rodarte et al. (2011) | Solid State Fermentation |
| Protease | *Mucor hiemalis* | Ribeiro et al. (2015) | Submerged Fermentation |
| Protease | Filamentous fungi | Mendes et al. (2015) | Solid State Fermentation |
| Xylanase | Filamentous fungi | Simões et al. (2009) | Submerged Fermentation,<br>Solid State Fermentation |
| Xylanase | *Aspergillus sp.* | Peixoto-Nogueira et al. (2009) | Semi Solid Fermentation |
| Xylanase | *Neosartorya spinosa* | Alves-Prado et al. (2010) | Solid State Fermentation |
| Xylanase | *Lichtheimia blakesleeana* | Neves et al. (2011) | Solid State Fermentation |
| Xylanase | *Myceliophtora thermophile* | Moretti et al. (2012) | Solid State Fermentation |
| Xylanase | *Rhizomucor* sp.<br>*Myceliophthora* sp. | Cassia Pereira et al. (2015) | Solid State Fermentation |

However, enzyme technology is clearly overdue in the country, which is paradoxical. According to the Bio-Economy Agenda of Brazil, the enzyme industry is of great importance to the Brazilian economy, being directly linked to the “Third Industrial Revolution”. Brazil is one of the countries that can benefit from the development of a national enzyme technology because it has a huge amount of renewable raw materials that can be transformed enzymatically into products with high added value and would be useful for strategic sectors of the economy (Harvard Business Review 2013).

A study by the US Research Industry Freedonia group estimated that world demand for enzymes will grow 6.3 % annually to $7 billion by 2017. The increase in per capita income in countries such as China and India will support consumer demand for higher value products, which can be achieved with enzymes such as detergents and foodstuffs. Advances in biotechnology will also boost demand for enzymes (Freedonia 2015).

With the advent of biofuels, studies related to the production of these compounds involving enzymes has become increasingly common (Cadete et al. 2014; Damaso et al. 2014; Aguieiras et al. 2015; Carvalho et al. 2015; Duarte et al. 2015). In addition, it is possible to obtain enzymes of industrial interest using certain waste (or byproducts) as substrates. The need for these enzymes by the world market has spurred studies in several parts of Brazil that go beyond the basic techniques of fermentation and genetic engineering to meet the future demand for renewable energy (Delabona et al. 2012; Valencia and Chambergo 2013; Ióca et al. 2014; Katoch et al. 2014; Souza et al. 2014). Brazil is underexplored for the production of enzymes of industrial interest. The country imports most of the enzymes it uses. Imports were $119 million, while exports reached $52 million. The Brazilian market for enzymes was estimated in 2011 at approximately $200 million (Ministério Do Desenvolvimento, Indústria e Comércio Exterior 2012). From 2007 to 2011, imports have tripled, while exports grew only moderately. To address this, Decree 6041/2007 established the Biotechnology Development Policy and includes the production and industrial use of enzymes (Bon et al. 2008). The current focus on enzymes research in Brazil has been applied in the food industry, antibiotic production, products for cleaning industries, effluent treatment and biofuel production e.g. biodiesel, bioethanol and biogas.

## 9.6 Conclusions

Brazil is experiencing tremendous growth in the biotech sector, as the main challenge of the current policy in science and technology is to ensure domestic firms participate more intensively in conducting and funding research activities to engender technological autonomy for the country. Innovative companies are being created that seek international competitiveness (Rezaie et al. 2008; Resende 2012). The enormous potential of the Brazilian biodiversity means that new substances and products can be discovered, resulting in the improvement of society's quality of life (Ribeiro and Raiher 2013; Corrêa et al. 2014; Ferreira et al. 2015). In this context, the scientific community, society and governing bodies should strengthen their relationships in a shared vision to invest in the development of technologies to expand domestic production and export of enzymes.

## References

Aguieiras ECG, Cavalcanti-Oliveira ED, Freire DMG (2015) Current status and new developments of biodiesel production using fungal lipases. Fuel 159:52–67. doi:10.1016/j.fuel.2015.06.064

Ali H (2010) Biodegradation of synthetic dyes—a review. Water Air Soil Pollut 213:251–273. doi:10.1007/s11270-010-0382-4

Alves-Prado HF, Pavezzi FC, Leite RSR et al (2010) Screening and production study of microbial xylanase producers from Brazilian Cerrado. Appl Biochem Biotechnol 161:333–346. doi:10.1007/s12010-009-8823-5

Aminov RI (2010) A brief history of the antibiotic era: lessons learned and challenges for the future. Front Microbiol 1:134. doi:10.3389/fmicb.2010.00134

Ana PADO, Maria AS, Heloiza FA-P et al (2015) Bioprospecting of yeasts for amylase production in solid state fermentation and evaluation of the catalytic properties of enzymatic extracts. Afr J Biotechnol 14:1215–1223. doi:10.5897/AJB2014.14062

Arias CA, Murray BE (2009) Antibiotic-resistant bugs in the 21st century — a clinical superchallenge. N Engl J Med 360:439–443. doi:10.1056/NEJMp0804651

Beceiro A, Tomás M, Bou G et al (2013) Antimicrobial resistance and virulence: a successful or deleterious association in the bacterial world? Clin Microbiol Rev 26:185–230. doi:10.1128/CMR.00059-12

Bhardwaj G (2013) Biosurfactants from fungi: a review. J Pet Environ Biotechnol 04:1–6. doi:10.4172/2157-7463.1000160

Bon EPS, Jr NP, Gottschalk LMF et al (2008) Bioprocessos para produção de enzimas. In: Enzimas em Biotecnologia – Produção, Aplicações e Mercado, 1rd edn. Interciência, Rio de Janeiro, pp. 95–122

Borges WDS, Pupo MT (2006) Novel anthraquinone derivatives produced by *Phoma sorghina*, an endophyte found in association with the medicinal plant *Tithonia diversifoli*a (Asteraceae). J Braz Chem Soc 17:929–934. doi:10.1590/S0103-50532006000500017

Bracarense AAP, Takahashi JA (2014) Modulation of antimicrobial metabolites production by the fungus *Aspergillus parasiticus*. Braz J Microbiol 321:313–321. doi:10.1590/s1517-83822014000100045

Braga FR, Araújo JV, Soares FEF et al (2011) Optimizing protease production from an isolate of the nematophagous fungus *Duddingtonia flagrans* using response surface methodology and its larvicidal activity on horse cyathostomins. J Helminthol 85:164–170. doi:10.1017/S0022149X10000416

Brasil (2015) Instituto Brasileiro de Geografia e Estatística. In: Ministério do Planejamento, Orçamento e Gestão. http://www.sidra.ibge.gov.br. Accessed 7 Jan 2015

Bussamara R, Fuentefria AM, De Oliveira ES et al (2010) Isolation of a lipase-secreting yeast for enzyme production in a pilot-plant scale batch fermentation. Bioresour Technol 101:268–275. doi:10.1016/j.biortech.2008.10.063

Cadete RM, Fonseca C, Rosa CA (2014) Novel yeast strains from Brazilian biodiversity: biotechnological applications in lignocellulose conversion into biofuels. In: Biofuels in Brazil: fundamental aspects, recent developments, and future perspectives 1rd edn. Springer International Publishing, New York, pp 255–279

Carvalho AKF, Rivaldi JD, Barbosa JC, de Castro HF (2015) Biosynthesis, characterization and enzymatic transesterification of single cell oil of *Mucor circinelloides* – a sustainable pathway for biofuel production. Bioresour Technol 181:47–53. doi:10.1016/j.biortech.2014.12.110

Cassia Pereira J, Paganini Marques N, Rodrigues A et al (2015) Thermophilic fungi as new sources for production of cellulases and xylanases with potential use in sugarcane bagasse saccharification. J Appl Microbiol 118:928–939. doi:10.1111/jam.12757

Castiglioni G, Stanescu G, Rocha LAO, Costa JAV (2013) Analytical modeling and numerical optimization of the biosurfactants production in solid-state fermentation by *Aspergillus fumigatus*. Acta. Sci Technol 36:61–67. doi:10.4025/actascitechnol.v36i1.17818

Celestino JDR, De Carvalho LE, Lima MDP et al (2014) Bioprospecting of Amazon soil fungi with the potential for pigment production. Process Biochem 49:569–575. doi:10.1016/j.procbio.2014.01.018

Chengaiah B, Rao KM, Kumar KM et al (2010) Medicinal importance of natural dyes-a review. Int J Pharm Tech Res 2:144–154

Choi J-M, Han S-S, Kim H-S (2015) Industrial applications of enzyme biocatalysis: current status and future aspects. Biotechnol Adv 33:1443–1454. doi:10.1016/j.biotechadv.2015.02.014

Colla LM, Rizzardi J, Pinto MH et al (2010) Simultaneous production of lipases and biosurfactants by submerged and solid-state bioprocesses. Bioresour Technol 101:8308–8314. doi: 10.1016/j.biortech.2010.05.086

Corrêa RCG, Rhoden SA, Mota TR et al (2014) Endophytic fungi: expanding the arsenal of industrial enzyme producers. J Ind Microbiol Biotechnol 41:1467–1478. doi:10.1007/s10295-014-1496-2

Cunha FM, Esperança MN, Zangirolami TC et al (2012) Sequential solid-state and submerged cultivation of *Aspergillus niger* on sugarcane bagasse for the production of cellulase. Bioresour Technol 112:270–274. doi:10.1016/j.biortech.2012.02.082

Cyndy MF, Odacy CDS, Minelli AS et al (2015) High-level lipase production by *Aspergillus candidus* URM 5611 under solid state fermentation (SSF) using waste from *Siagrus coronata* (Martius) Becari. African. J Biotechnol 14:820–828. doi:10.5897/AJB2014.14339

Da Silva M, Nascimento C, Junior S, Albuquerque P (2014) Biosurfactant production by *Myrcia guianensis* endophytic fungi. BMC Proc 8:213. doi:10.1186/1753-6561-8-S4-P213

Damaso MCT, Machado CMM, Rodrigues DDS et al (2014) Bioprocesses for biofuels: an overview of the Brazilian case. Chem Biol Technol Agric 1:1–8. doi:10.1186/s40538-014-0006-0

De Castro AM, De Andréa TV, Dos Reis CL, Freire DMG (2010) Use of mesophilic fungal amylases produced by solid-state fermentation in the cold hydrolysis of raw babassu cake starch. Appl Biochem Biotechnol 162:1612–1625. doi:10.1007/s12010-010-8942-z

De Oliveira APA, Silvestre MA, Alves-Prado HF et al (2015) Bioprospecting of yeasts for amylase production in solid state fermentation and evaluation of the catalytic properties of enzymatic extracts. Afr J Biotechnol 14:1215–1223. doi:10.5897/ajb2014.14062

Delabona PDS, Pirota RDPB, Codima CA (2012) Using Amazon forest fungi and agricultural residues as a strategy to produce cellulolytic enzymes. Biomass Bioenergy 37:243–250. doi:10.1016/j.biombioe.2011.12.006

Dos Santos IP, Da Silva LCN, Da Silva MV et al (2015) Antibacterial activity of endophytic fungi from leaves of *Indigofera suffruticosa* Miller (Fabaceae). Front Microbiol. doi:10.3389/fmicb.2015.00350

Duarte SH, del Peso Hernández GL, Canet A et al (2015) Enzymatic biodiesel synthesis from yeast oil using immobilized recombinant *Rhizopus oryzae* lipase. Bioresour Technol 183:175–180. doi:10.1016/j.biortech.2015.01.133

Dufossé L (2006) Microbial production of food grade pigments. Food Technol Biotechnol 44:313–323

Durán N, Teixeira MFS, De Conti R, Esposito E et al (2002) Ecological-friendly pigments from fungi. Crit Rev Food Sci Nutr 42:53–66. doi:10.1080/10408690290825457

Düsman E, Berti AP, Soares LC, Vicentini VEP et al (2012) Principais agentes mutagênicos e carcinogênicos de exposição humana. SaBios-Revs Saúde e Biol 7:66–81

Faheina Junior GDS, Amorim MVDFS, Souza CG De et al (2015) Strategies to increase cellulase production with submerged fermentation using fungi isolated from the Brazilian biome. Acta Sci Biol Sci 37:15-22. doi: 10.4025/actascibiolsci.v37i1.23483

Ferreira MC, Vieira MDLA, Zani CL et al (2015) Molecular phylogeny, diversity, symbiosis and discover of bioactive compounds of endophytic fungi associated with the medicinal Amazonian plant *Carapa guianensis* Aublet (Meliaceae). Biochem Syst Ecol 59:36–44. doi:10.1016/j.bse.2014.12.017

Flores AC, Pamphile JA, Sarragiotto MH, Clemente E (2013) Production of 3-nitropropionic acid by endophytic fungus *Phomopsis longicolla* isolated from *Trichilia elegans* A. JUSS ssp. elegans and evaluation of biological activity. World J Microbiol Biotechnol 29:923–932. doi:10.1007/s11274-013-1251-2

Freedonia (2015) World enzymes: market environment. The freedonia Group. http://www.freedoniagroup.com/brochure/28xx/2824smwe.pdf. Acessed 03 Dec 2015

Glänzel W, Leta J, Thijs B (2006) Science in Brazil part 1: A macro-level comparative study. Scientometrics 67:67–86. doi:10.1007/s11192-006-0055-7

Goldbeck R, Ramos MM, GAG P, Maugeri-Filho F (2013) Cellulase production from a new strain *Acremonium strictum* isolated from the Brazilian biome using different substrates. Bioresour Technol 128:797–803. doi:10.1016/j.biortech.2012.10.034

Griebeler N, Polloni AE, Remonatto D et al (2009) Isolation and screening of lipase-producing fungi with hydrolytic activity. Food Bioprocess Technol 4:578–586. doi:10.1007/s11947-008-0176-5

Guimarães LHS, Peixoto-Nogueira SC, Michelin M et al (2006) Screening of filamentous fungi for production of enzymes of biotechnological interest. Braz J Microbiol 37:474–480. doi:10.1590/S1517-83822006000400014

Gunasekaran S, Poorniammal R (2008) Optimization of fermentation conditions for red pigment production from *Penicillium sp*. under submerged cultivation. Afr J Biotechnol 7:1894–1898. doi:10.4314/ajb.v7i12.58846

Hailei W, Zhifang R, Ping L et al (2011) Improvement of the production of a red pigment in *Penicillium sp*. HSD07B synthesized during co-culture with *Candida tropicalis*. Bioresour Technol 102:6082–6087

Hamano PS, Kilikian BV (2006) Production of red pigments by *Monascus ruber* in culture media containing corn steep liquor. Braz J Chem Eng 23:443–449

Harvard Business Review (2013) Bioeconomia: Uma Agenda Para o Brasil. Brasilia: CNI 40p

Ióca LP, Allard PM, Berlinck RGS (2014) Thinking big about small beings – the (yet) underdeveloped microbial natural products chemistry in Brazil. Nat Prod Rep 31:646–675. doi:10.1039/c3np70112c

Ishida K, Cipriano TF, Rocha GM et al (2014) Silver nanoparticle production by the fungus *Fusarium oxysporum*: nanoparticle characterisation and analysis of antifungal activity against pathogenic yeasts. Mem Inst Oswaldo Cruz 109:220–228. doi:10.1590/0074-0276130269

Jemli S, Ayadi-Zouari D, Hlima HB, Bejar S (2014) Biocatalysts: application and engineering for industrial purposes. Crit Rev Biotechnol 36:246–258. doi:10.3109/07388551.2014.950550

Kanokmedhakul S, Kanokmedhakul K, Nasomjai P et al (2006) Antifungal azaphilones from the *Fungus Chaetomium* cupreum CC3003. J Nat Prod 69:891–895. doi:10.1021/np060051v

Katerine A, Lobato DCL, Almeida AF et al (2013) Biosurfactant production from industrial residues using microorganisms isolated from oil wells. Int Rev Chem Eng 5:310–316. doi:10.3109/07388551.2014.950550

Katoch M, Salgotra A, Singh G (2014) Endophytic fungi found in association with *Bacopa monnieri* as potential producers of industrial enzymes and antimicrobial bioactive compounds. Braz Arch Biol Biotechnol 57:714–722. doi:10.1590/s1516-8913201402502

Kirk O, Borchert TV, Fuglsang CC (2002) Industrial enzyme applications. Curr Opin Biotechnol 13:345–351. doi:10.1016/S0958-1669(02)00328-2

Kumar A, Vishwakarma HS, Singh J, Kumar M (2015) Microbial pigments: production and their applications in various industries. Int J Pharm Chem Biol Sci 5:203–212

Lange L, Bech L, Busk PK et al (2012) The importance of fungi and of mycology for a global development of the bioeconomy. IMA Fungus 3:87–92. doi:10.5598/imafungus.2012.03.01.09

Leta J, Glänzel W, Thijs B (2006) Science in Brazil. Part 2: sectoral and institutional research profiles. Scientometrics 67:87–105. doi:10.1007/s11192-006-0051-y

Lucas E, Machado Y, Ferreira A et al (2010) Improved production of pharmacologically-active sclerotiorin by *Penicillium sclerotiorum*. Trop J Pharm Res 9:365–371. doi:10.4314/tjpr.v9i4.58930

Luna JM, Rufino RD, Campos-Takaki GM, Sarubbo LA (2012) Properties of the biosurfactant produced by *Candida sphaerica* cultivated in low-cost substrates. Chem Eng Trans 27:67–72. doi:10.3303/CET1227012

Madeira JV, Macedo JA, Macedo GA (2011) Detoxification of castor bean residues and the simultaneous production of tannase and phytase by solid-state fermentation using *Paecilomyces variotii*. Bioresour Technol 102:7343–7348. doi:10.1016/j.biortech.2011.04.099

Maeda RN, Barcelos CA, Anna LMMS, Pereira N (2013) Cellulase production by *Penicillium funiculosum* and its application in the hydrolysis of sugar cane bagasse for second generation ethanol production by fed batch operation. J Biotechnol 163:38–44. doi:10.1016/j.jbiotec.2012.10.014

Mapari SAS, Thrane U, Meyer AS (2010) Fungal polyketide azaphilone pigments as future natural food colorants? Trends Biotechnol 28:300–307. doi: http://dx.doi.org/10.1016/j.tibtech.2010.03.004

Marchant R, Banat IM (2012) Microbial biosurfactants: challenges and opportunities for future exploitation. Trends Biotechnol 30:558–565. doi: http://dx.doi.org/10.1016/j.tibtech.2012.07.003

Mendes MMGS, Pereira SA, Oliveira RL et al (2015) Screening of Amazon fungi for the production of hydrolytic enzymes Afr J Microbiol Res 9:741–748. doi: 10.5897/A

Méndez A, Pérez C, Montañéz JC et al (2011) Red pigment production by *Penicillium purpurogenum* GH2 is influenced by pH and temperature. J Zhejiang Univ Sci B 12:961–968. doi:10.1631/jzus.B1100039

Michael CA, Dominey-Howes D, Labbate M (2014) The antimicrobial resistance crisis: causes, consequences, and management. Front Public Heal 2:145–145. doi:10.3389/fpubh.2014.00145

Ministério Do Desenvolvimento Indústria E Comércio Exterior (2012) Diagnóstico de referência sobre serviços de escalonamento de biotecnologias no Brasil. Fundação Bio-Rio, Rio de Janeiro

Mirjalili M, Nazarpoor K, Karimi L (2011) Eco-friendly dyeing of wool using natural dye from weld as co-partner with synthetic dye. J Clean Prod 19:1045–1051. doi:10.1016/j.jclepro.2011.02.001

Monteiro VN, Silva RN (2009) Aplicações Industriais da Biotecnologia Enzimática. Revista processos químicos 3:9–23

Moretti MMS, Bocchini-Martins DA, Silva DR et al (2012) Selection of thermophilic and thermotolerant fungi for the production of cellulases and xylanases under solid-state fermentation. Braz J Microbiol:1062–1071. doi:10.1590/s1517-83822012000300032

Mussatto SI, Fernandes M, Milagres AMF (2007) Enzimas: Poderosas ferramentas na indústria. Ciência Hoje 41:28–33

Neves MLC, Da Silva MF, Souza-Motta CM et al (2011) *Lichtheimia blakesleeana* as a new potencial producer of phytase and xylanase. Molecules 16:4807–4817. doi:10.3390/molecules16064807

Nitschke M, Pastore M (2002) Biossurfactantes: Propriedades e aplicações. Quím Nova 25:772–776. doi:10.1590/s0100-40422002000500013

Oh J, Jeong H, Oh S (2009) Characterization of optimal growth conditions and carotenoid production of strain *Rhodotorula mucilaginosa* HP isolated from larvae of *Pieris rapae*. Entomol Res 39:380–387. doi:10.1111/j.1748-5967.2009.00250.x

Onofre SB, Santos ZMQ, Kagimura FY, Mattiello SP et al (2015) Cellulases produced by the endophytic fungus *Pycnoporus sanguineus* ( L .) Murrill. Afr J Agric Res 10:1557–1564. doi:10.5897/AJAR2015.9487

Orlandelli RC, Alberto RN, Almeida TT et al (2012) In vitro antibacterial activity of crude extracts produced by endophytic fungi isolated from *Piper hispidum* Sw. J Appl Pharm Sci 2:137–141. doi:10.7324/JAPS.2012.21027

Pasin TM, Benassi VM, Moreira EA et al (2014) Prospecting filamentous fungi for amylase production: standardization of *Aspergillus japonicus* culture conditions. British. Biotechnol J 4:482–498. doi:10.9734/bbj/2014/7659

Peixoto-Nogueira SC, Michelin M, Betini JHA et al (2009) Production of xylanase by Aspergilli using alternative carbon sources: application of the crude extract on cellulose pulp biobleaching. J Ind Microbiol Biotechnol 36:149–155. doi:10.1007/s10295-008-0482-y

Petit P, Lucas EMF, Abreu LM et al (2009) Novel antimicrobial secondary metabolites from a *Penicillium sp*. isolated from Brazilian cerrado soil. Electron J Biotechnol. doi:10.2225/vol12-issue4-fulltext-9

Polônio MLT, Peres F (2009) Consumo de aditivos alimentares e efeitos à saúde: desafios para a saúde pública brasileira. Cad Saúde Pública 25:1653–1666. doi:10.1590/S0102-311X2009000800002

Resende V (2012) The biotechnology market in Brazil. US Dept Commer 9. https://www.nccommerce.com/Portals/5/Documents/ITD/Biotech%20Market%20in%20Brazil.pdf. Acessed 03 Dec 2015

Rezaie R, Frew SE, Sammut SM et al (2008) Brazilian health biotech fostering crosstalk between public and private sectors. Nat Biotechnol 26:627–644. doi:10.1038/nbt0608-627

Ribeiro MDFDS, Raiher AP (2013) Potentialities of energy generation from waste and feedstock produced by the agricultural sector in Brazil: the case of the state of Paraná. Energ Policy 60:208–216. doi:10.1016/j.enpol.2013.05.004

Ribeiro Corrêa TL, De Queiroz MV, De Araújo EF (2015) Cloning, recombinant expression and characterization of a new phytase from *Penicillium chrysogenum*. Microbiol Res 170:205–212. doi:10.1016/j.micres.2014.06.005

Ribeiro J, Da Lima JRC, Maria L, Lopes DA (2013) Utilization of crude glycerol by *Yarrowia lipolytica* IMUFRJ 50678 in bioproduct production. J Chem Chem Eng 7:1087–1093

Ribeiro RCDS, Ribeiro TRDS, De Souza-Motta CM et al (2015) Production and partial characterization of proteases from *Mucor hiemalis* URM3773. Acta Sci Biol Sci 37:71. doi:10.4025/actascibiolsci.v37i1.21016

Rigo E, Ninow JL, Di Luccio M et al (2010) Lipase production by solid fermentation of soybean meal with different supplements. LWT Food Sci Technol 43:1132–1137. doi:10.1016/j.lwt.2010.03.002

Rodarte MP, DR D, DM V, RF S (2011) Proteolytic activities of bacteria, yeasts and filamentous fungi isolated from coffee fruit (*Coffea arabica* L.). Acta Sci Agron 33:457–464. doi:10.4025/actasciagron.v33i3.6734

Rodrigues AG, Ping LY, Marcato PD et al (2013) Biogenic antimicrobial silver nanoparticles produced by fungi. Appl Microbiol Biotechnol 97:775–782. doi:10.1007/s00253-012-4209-7

Sanderson K (2011) Chemistry: enzyme expertise. Nature 471:397–398. doi:10.1038/nj7338-397a

Santos DKF, Rufino RD, Luna JM et al (2013) Synthesis and evaluation of biosurfactant produced by *Candida lipolytica* using animal fat and corn steep liquor. J Pet Sci Eng 105:43–50. doi:10.1016/j.petrol.2013.03.028

Santos DKF, Brandão YB, Rufino RD et al (2014) Optimization of cultural conditions for biosurfactant production from *Candida lipolytica*. Biocatal Agric Biotechnol 3:48–57. doi:10.1016/j.bcab.2014.02.004

Saron C, Felisberti I (2006) Ação de colorantes na degradação e estabilização de polímeros. Quím Nova 29:124–128. doi:10.1590/s0100-40422006000100022

Saxena S (2015) Microbial enzymes and their industrial applications. Appl Microbiol:121–154. doi:10.1007/978-81-322-2259-0_9

Serdar M, Knežević Z (2009) Simultaneous LC analysis of food dyes in soft drinks. Chromatographia 70:1519–1521. doi:10.1365/s10337-009-1340-4

Shaikh S, Fatima J, Shakil S et al (2015) Antibiotic resistance and extended spectrum beta-lactamases: types, epidemiology and treatment. Saudi J Biol Sci 22:90–101. doi: http://dx.doi.org/10.1016/j.sjbs.2014.08.002

Shekhar S, Sundaramanickam A, Balasubramanian T (2014) Biosurfactant producing microbes and their potential applications: a review. Crit Rev Environ Sci Technol 45:1522–1554. doi:10.1080/10643389.2014.955631

Silva CADA, Lacerda MPF, Leite RSR, Fonseca GG (2013) Production of enzymes from *Lichtheimia ramosa* using Brazilian savannah fruit wastes as substrate on solid state bioprocessess. Electron J Biotechnol doi: 10.2225/vol16

Silva NAR, Luna M, Santiago A et al (2014) Biosurfactant-and-bioemulsifier produced by a promising *Cunninghamella echinulata* Isolated from caatinga Soil in the Northeast of Brazil. Int J Mol Sci 15:15377–15395. doi:10.3390/ijms150915377

Silver LL (2011) Challenges of antibacterial discovery. Clin Microbiol Rev 24:71–109. doi:10.1128/CMR.00030-10

Simões MLG, Tauk-tornisielo SM, Tapia DM (2009) Screening of culture condition for xylanase production by filamentous fungi. Afr J Biotechnol 8:6317–6326

Soberón-Chávez G, Maier R (2011) Biosurfactants: a general overview. In: Soberón-Chávez G (ed) Biosurfactants SE. Springer, Berlin/Heidelberg, pp. 1–11

Souza FHM, Meleiro LP, Machado CB et al (2014) Gene cloning, expression and biochemical characterization of a glucose- and xylose-stimulated β-glucosidase from Humicola insolens RP86. J Mol Catal B Enzym 106:1–10. doi:10.1016/j.molcatb.2014.04.007

Spier MR, Fendrich RC, Almeida PC et al (2011) Phytase produced on citric byproducts: purification and characterization. World J Microbiol Biotechnol 27:267–274. doi:10.1007/s11274-010-0455-y

Suzana CSM, Viviane OA, Claudia MM (2014) Pichia spp. yeasts from brazilian industrial wastewaters: physiological characterization and potential for petroleum hydrocarbon utilization and biosurfactant production. Afr J Microbiol Res 8:664–672. doi:10.5897/AJMR2013.6037

Takahashi JA, Carvalho SA (2010) Nutritional potential of biomass and metabolites from filamentous fungi. Curr Res Technol Educ Top Appl Microbiol Microb Biotechnol 2:1126–1135

Teixeira MFS, Martins MS, da Silva JC et al (2012) Amazonian biodiversity: pigments from *Aspergillus* and *Penicillium*-characterizations, antibacterial activities and their toxicities. Curr Trends Biotechnol Pharm 6:300–311

Theuretzbacher U (2009) Future antibiotics scenarios: is the tide starting to turn? Int J Antimicrob Agents 34:15–20. doi: http://dx.doi.org/10.1016/j.ijantimicag.2009.02.005

Uenojo M, Roberto M, Junior M, Pastore M (2007) Carotenóides: Propriedades, aplicações e biotransformação para formação de compostos de aroma. Quím Nova 30:616–622. doi:10.1590/s0100-40422007000300022

Valencia EY, Chambergo FS (2013) Mini-review: Brazilian fungi diversity for biomass degradation. Fungal Genet Biol 60:9–18. doi:10.1016/j.fgb.2013.07.005

Vaz ABM, Brandão LR, Vieira ML et al (2012) Diversity and antimicrobial activity of fungal endophyte communities associated with plants of Brazilian savanna ecosystems. African J. Microbiol Res 6:3173–3185. doi:10.5897/AJMR11.1359

Vieira MLA, Hughes AFS, Gil VB et al (2011) Diversity and antimicrobial activities of the fungal endophyte community associated with the traditional Brazilian medicinal plant *Solanum cernuum* Vell. (Solanaceae). Can J Microbiol 58:54–66. doi: 10.1139/w11-105

Volp ACP, Renhe IRT, Stringueta PC (2009) Pigmentos naturais bioativos. Aliment e Nutr 20:157–166

Wright PM, Seiple IB, Myers AG (2014) The evolving role of chemical synthesis in antibacterial drug discovery. Angew Chem Int Ed 53:8840–8869. doi:10.1002/anie.201310843

Zanphorlin LM, Facchini FDA, Vasconcelos F et al (2010) Production, partial characterization, and immobilization in alginate beads of an alkaline protease from a new thermophilic fungus *Myceliophthora sp*. J Microbiol 48:331–336. doi:10.1007/s12275-010-9269-8