

Silver microproducer

Fungus is used to produce metallic nanoparticles that can be employed as antibacterial substances

A study coordinated by Professor Nelson Durán of the University of Campinas Institute of Chemistry (IQ-Unicamp), indicates that the fungus *Phoma glomerata* can produce silver nanoparticles, which may be effective against microorganisms. This is part of an effort to develop new drugs to fight diseases caused by fungi and bacteria. According to Durán, antimicrobial nanoparticles have many advantages over conventional antibiotics, including a decrease in adverse effects.

“Taking into consideration their antimicrobial activity and the aspects involved in production, such as the use of low-cost culture methods, with good yields and non-toxic waste products, it is possible that in the near future, silver nanoparticles could be used as drugs, or in combination with antibiotics, to increase their effect,” says biologist Marta Cristina Teixeira Duarte. Duarte, a researcher at the Unicamp Multidisciplinary Center for Chemical, Biological and Agricultural Research (CPQBA), participated in the study by carrying out *in vitro* tests on the antifungal activity of the nanoparticles. They will probably be used initially to treat dermatomycoses. The ingestion of nanoparticles is not being considered at the moment as their toxicity to humans is unknown.

In the article published in 2015 in the *IET Nanobiotechnology* journal, the authors, including Durán and Duarte, suggest that silver nanoparticles are a new hope for treating infections caused by antibiotic-resistant bacteria. According to Durán, silver nanoparticles have a relatively large surface compared to their volume. This means that most of the atoms are on the surface of the nanoparticle, which increases its antimicrobial efficiency due to its greater capacity to interact with other substances. The use of the fungus *Phoma* spp. represents a new strategy to replace — and improve

Cultivation of *Fusarium oxysporum*, a fungus used to develop a drug against nail infections



— the physical and chemical methods that often use substances toxic to the environment.

Durán says that, to overcome these obstacles, scientists seek inspiration in nature and are increasingly using biological systems such as plants, bacteria, algae and fungi to carry out synthesis. Research up to now has indicated that fungi has the ability to reduce metal cations (ions with a positive charge) in order to form nanoparticles with different sizes and properties.

Durán's group chose fungi because they are eukaryotes (organisms or cells whose nucleus is enveloped in a membrane), which are more robust and have sophisticated biological machinery. Additionally, it is easy to control their growth and a large variety of strains is available. The properties of these organisms that allow them to extract metals from the extracellular medium, which can be reduced or oxidized via the removal or addition of electrons, also contributed to their selection. "We proposed the term 'myconanotechnology' to define the field of research involving synthesis of nanomaterials by fungi," says Durán.

EFFICIENT PROTOTYPE

The fungus *Fusarium oxysporum* was studied in addition to *Phoma* spp. "The projects sought to determine which was the most efficient and economical," explains Durán. "But their performance was very similar." The first study compared the efficiency of existing antibiotics with that of the silver nanoparticles produced by the microorganism. Studies on *F. oxysporum* began before those on *Phoma*, so they are more advanced.

An antifungal prototype (gel and enamel) to fight onychomycosis (nail infections) has been developed using the nanoparticles produced by this species. "Now, with the support of the FAPESP Innovative Research in Small Businesses Program (PIPE), we will attempt production on a larger scale, for use in the treatment of important neglected, fungal diseases in humans." The new drug is being studied by the company Donaire, in Americana, São Paulo state.

Durán recounts that the work was begun in his laboratory in 2013 by Indian researcher Mahendra Rai of Amravati University, who was in Brazil

with FAPESP support, and who also co-authored the article published in IET Nanobiotechnology. The exchange had begun a few years earlier, in a partnership program between the two countries, financed by the National Council for Scientific and Technological Development (CNPq). "He visited us several times and I visited him a few times in his country," he says. "The goal was to generate biological silver nanoparticles for medical and agricultural applications. As a result, we published articles on antibacterial and antifungal substances and obtained a patent in Brazil for a film to protect fruit (see Pesquisa FAPESP Issue No. 176)."

According to Professor Elson Longo of the Institute of Chemistry, São Paulo State University (Unesp), Araraquara, and coordinator of the Center for Research and Development of Functional Materials, one of FAPESP's Research, Innovation and Dissemination Centers (RIDC), Durán's work is innovative and has great potential for transformation into a product. "The market will determine if this technological development is viable," says Longo, one of the first Brazilian researchers to work with nanotechnology. "There is similar work in the

early stages all over the world." I know of no similar study in Brazil." According to Longo, the principal advantage of this line of research is the use of fungi as labor, which makes it a low-cost, innovative method. "Since there are many products that require different types of metallic silver (clusters, nanoparticles, microparticles, silver anchored to different substrates, associated with other compounds), obtaining a better or worse result with the metal depends on the use," says Longo. ■ **Evanildo da Silveira**

Projects

1. *Development of a pharmaceutical product based on silver nanoparticles for treatment of onychomycosis* (No. 2013/50289-7); **Grant Mechanism:** Innovative Research in Small Businesses Program (PIPE); **Principal Investigator:** Patricia Pulcini Rosvald Donaire (Donaire Consultoria); **Investment:** R\$83,153.50.

2. *Biosynthesis of silver nanoparticles by selected species of Phoma and their activity against multi-drug-resistant microbes* (No. 2012/03731-3); **Grant Mechanism:** Visiting researcher project; **Principal Investigator:** Nelson Eduardo Durán Caballero (Unicamp); **Visiting Researcher:** Mahendra Rai (Amravati University); **Investment:** R\$167,241.52.

Scientific article

Mahendra, R. et. al. Three *Phoma* spp. synthesized novel silver nanoparticles that possess excellent antimicrobial efficacy. *IET Nanobiotechnology*. V. 9, No. 5, p. 280-7. Oct. 2015.

THE USE OF FUNGI AS LABOR COULD RESULT IN A CHEAP AND INNOVATIVE PRODUCTION SYSTEM TO PRODUCE SILVER NANOPARTICLES FOR MEDICINE AND AGRICULTURE