

## THE CONSERVATION AND SUSTAINABLE USE OF BRAZILIAN CERRADO AND ATLANTIC FOREST FOR POTENTIAL DRUGS PROSPECTION

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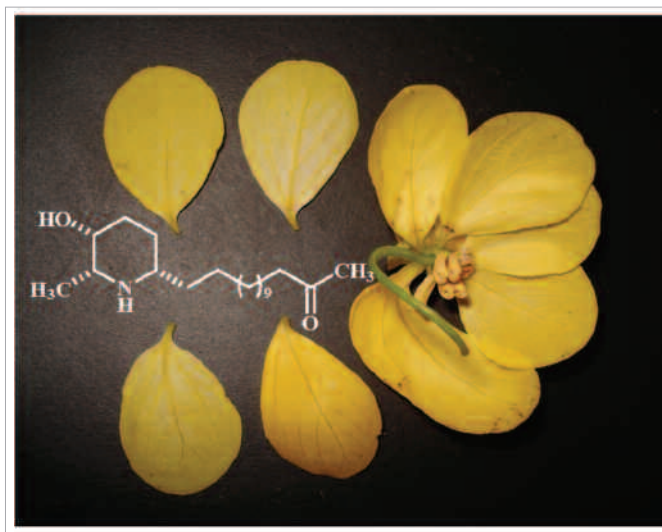


Photo: Marcos Pivatto

The main goal of this project is to search lead molecules from plant species and endophytic fungi occurring in the State of São Paulo, especially in the Cerrado and Atlantic Forest. The main interested compounds include antioxidant, anti-inflammatory, antifungal, anticancer, antimalarial and antiacetylcholinesterase. Besides drug discovery, biodiversity conservation, and sustainable economic growth, this project also supports the advances in natural product chemistry knowledge such as: (i) to evaluate, correlate and develop chemical methodologies to study intra- and inter-specific variability in some selected bioactive species, (ii) to develop micro propagation and cell cultures of rare plants producing active compounds and (iii) to study biosynthetic

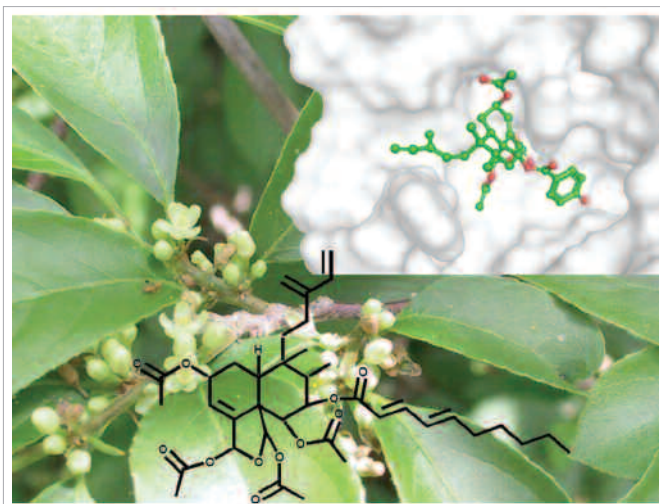
pathways and particularly to determine the activity of phenyltransferases, terpene cyclases and cytochrome P-450 oxido-reductases for kinetic studies and further proteomic and functional analysis. This should lead to the cloning of genes for heterologous over expression in other plants, to conduct studies on structure activity relationships (SAR) of lead compounds previously identified and to sustain and maintain the virtual database already initiated in phase I.

## SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

The first bioprospecting efforts have resulted in a storage bank of 2,000 plant extracts and more than 150 isolates of endophytic fungi, most of these from bioactive plant species belonging to approximately 88 different families. These plant species are mostly represented by Angiosperms occurring in Cerrado and Atlantic Forest (the two major biomes of São Paulo State). All the plant material samplings were performed in function of the restricted polices from CGEM.

All stored extracts (ca 774 from Cerrado plants and 1226 from Atlantic Forest) were screened with *Cladosporium cladosporioides* and *C. sphaerospermum*. From these, 800 extracts inhibited fungi growth, (nystatin 0.1mg/mL as positive control), indicating a great potential to find antifungal compounds (Graphic 1). Acetylcholinesterase (AChE) thin-layer chromatography assay (TLC) method was used to screen several extracts, and after the development of this test in an appropriate solvent, the presence of active compounds related to the reference of AChE inhibition (galanthamine as positive control) were detected in ca. 354 extracts, representing 17.7 percent of the total extracts (Graphic 2). The potential anticancer activity of extracts was tested against a panel of cell lines using *in vitro* 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The preliminary antifungal screening, with human pathogen fungi, was tested against the strains *C. albicans*, *C. krusei*, *C. parapsilosis* and *C. neoformans* showed promising activity. From pure compounds assayed, 50 percent has shown promising activity, and these compounds are being tested in additional enzymatic and receptors bioassays. Although all plant extracts and endophytic fungi still have to be bioassayed in other assays, these results have indicated that bioprospection is a promising tool for exploring Brazilian biodiversity.

Photo: Alberto Cavalheiro



## MAIN PUBLICATIONS

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