SUSTAINABLE USE OF THE BRAZILIAN BIODIVERSITY: CHEMICAL AND PHARMACOLOGICAL PROSPECTION ON HIGHER PLANTS

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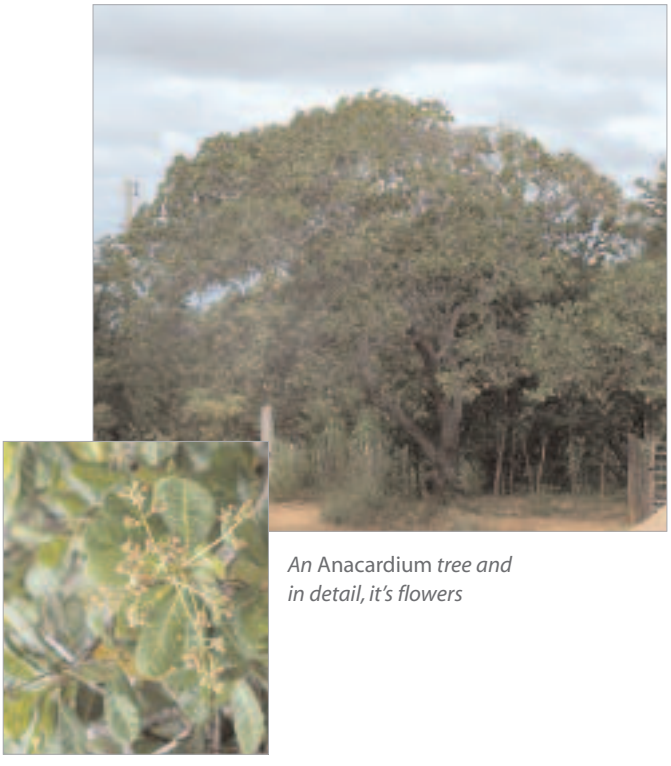
The apparent incompatibility between chemical and pharmacological investigation of a plant specie can be solved with the strong determination by dealing rationally with the problem.

The research groups on Natural Products Chemistry from the Chemistry Institute (IQ-Araraquara/Unesp), on Pharmacology, from Institute of Biosciences (IB/Unicamp) and Institute of Biosciences (IB-Botucatu/ Unesp) and on Biological Sciences, from School of Pharmaceutical Sciences (FCF-Araraquara/Unesp) have started collaboration some years ago, and have already produced a significative amount of work, with relevant results on the investigation of plant species with anti-ulcer, anti-oxidant, analgesic, anti-inflammatory and antimicrobial activities.

These results arose from an approach that includes ethno botanical and ethno pharmacological research, pharmacological, microbiologic and mutagenic assays with crude extracts or infusions, chemical screening to determine new chemical classes of compounds, isolation and structural determination of compounds and use the compounds or enriched fractions to determine the possible pharmacological action mechanisms involved with the detected properties.

This project deals with the integrated chemical and pharmacological investigation of plant extracts, including species that composes the bioma Cerrado, a savannah like vegetation, of the State Sao Paulo, comparatively to the Bioma Cerrado of other Brazilian States, like the State of Tocantins, which it is also under our investigation.



An Anacardium *tree and in detail, it's flowers*

Plant extracts are among the most attractive sources for developing new drugs and have been shown to produce promising results in the treatment of several diseases. The Brazilian Cerrado is one of highest biogeography regions of the world and also the most threatened. It includes several thousands of native vascular plants species grouped in hundreds of families. Many of these plants are commonly used as natural remedies by people living in these areas to treat many illnesses. An ethnopharmacogical inventory made at this region is the starting point of our project, which involves the chemical and pharmacological investigation of extracts and infusions of ca. 30 plant species belonging to the genera *Alchornea, Anacardium, Ananas, Byrsonima, Davilla, Guapira, Indigofera, Miconia, Mouriri, Neea, Qualea* and *Strychnus*. Fractionment of these plant extracts will be followed by structural determination of the secondary metabolites, as well as the establishment of the qualitative and quantitative chromatographic fingerprint.

SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

To perform the phytochemical step we used chromatographic techniques, mainly those for the analysis of polar substances (GPC, XAD2, DCCC, HSCC, HPLC, etc). To determine the structure of the isolated compounds we used modern spectrometric methods (NMR, IR, UV, MS).

To evaluate the biological activities, the possibility of toxicicity and genotoxicity effects of each specie were determined. Simultaneously, we evaluated the activity of the extracts and pure substances (or enriched fractions) against different experimental models of peptic ulcer disease which operate by distinct mechanism of ulcerogenesis in man. The analgesic and anti-inflammatory activities were examined by using of chemical and thermal pain models and the classic inflammatory assays in rats or in mice. Through these models, we quickly evaluated the presence or absence of these activities. The antimicrobial activity was assayed against Gram positive and Gram negative bacteria, and also on the *Mycobacterium genus*, with emphasis on the etiological agent of tuberculosis, *M. tuberculosis*. The determination of the antiulcerogenic mechanisms was investigated through the effect of the isolated substances (or enriched fractions) on specific receptors, enzymes and substances produced in response to the gastric lesion, such as the expression of the new epidermic growing factor. Simultaneously, the antioxidant activity of extracts/substances was also evaluated, mainly those related to the possible mechanisms of the antiulcerogenic activity. Furthermore, assays for the detection of mucus, prostaglandins, somatostatin, gastrin and others involved with mechanisms of gastric secretion were also be evaluated. Assays against *Helycobacter pylori*, the most important bacterial pathogen of humans involved in the pathogenesis of peptic ulcer disease, were also performed. Finally, assays to detect the production of NO, H2O2 and TNF were performed with extracts, substances and enriched fractions to evaluate their potential immunostimulating activity.

The compounds isolated and identified were catechins, flavonoids, saponins, terpenes, steroids, alkaloids, phenolic compounds and proanthocyanidins.

The results indicated plant species with promising activities, like antiulcer, anti-inflammatory, immunomodulatory, antimicrobial, antioxidant, anti tuberculosis and antitumour, most of them with no acute toxicity and no mutageniticity. This approach led to a better understanding of the biological activities observed in crude extracts and enriched fractions. Additional experiments are in progress to further evaluate the activity of the isolated compounds and also to investigate the mechanisms of action related to the biological activities observed.

MAIN PUBLICATIONS

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