

# Behind the Scenes in Pharmacognosy: The Spirit of Cachaça

**T**his March, the Journal of Natural Products (J. Nat. Prod.) will publish a special issue dedicated to ASP Honorary Member Dr. Otto Sticher. This issue will include an article from the laboratory of ASP member Dr. Veronika Butterweck in the School of Life Sciences, Institute for Pharma Technology, at the University of Applied Sciences Northwestern Switzerland, Muttenz, Switzerland. The article, "Evaluation of Intestinal Permeability of Vicenin-2 and Lych-nopholic Acid from *Lych-nophora salicifolia* (Brazilian Arnica) Using Caco-2 Cells" describes work done on *Lych-nophora salicifolia*, an ingredient in Brazilian cachaça. We appreciate Dr. Butterweck taking the time to describe her laboratory's work in more detail. Please read the online article in J. Nat. Prod., November 26, 2013; doi: 10.1021/np400674t.

By Dr. Amy Keller

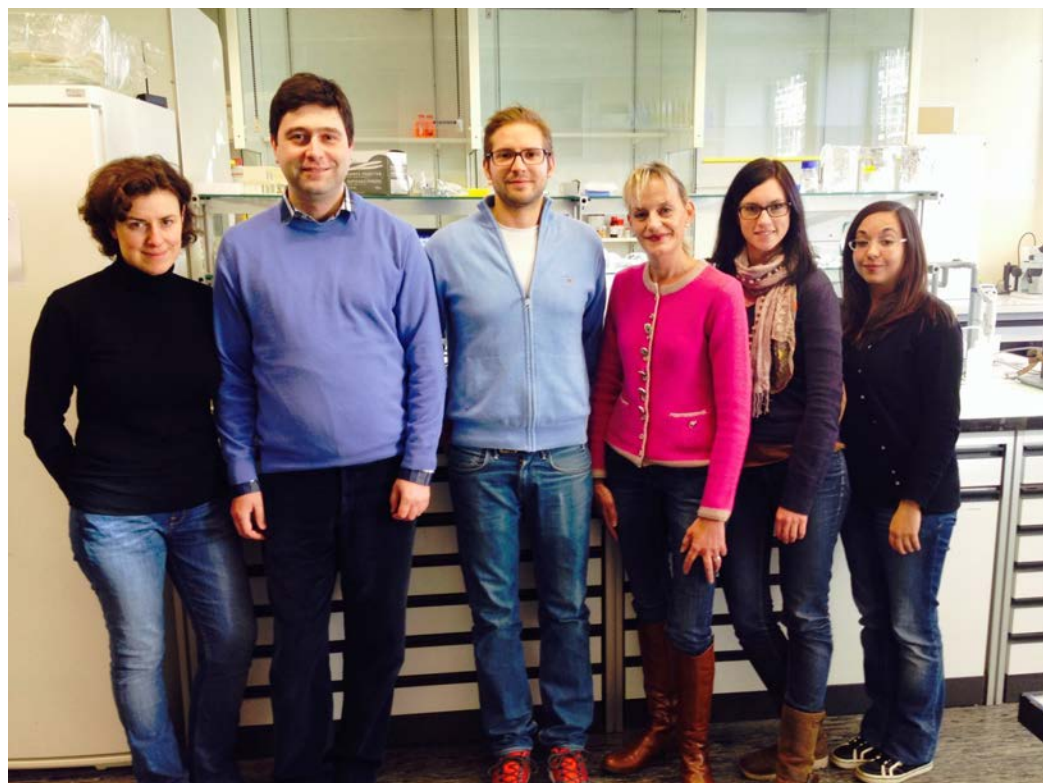
## How did you become interested in compounds from *Lych-nophora salicifolia* and cachaça?

*Lych-nophora salicifolia*, commonly known as "arnica," is used as an anti-inflammatory agent and as a flavoring agent in the Brazilian traditional spirit "cachaça." The *L. salicifolia* project was initiated by my colleague Dr. Norberto Peporine Lopes, Departamento de Física e Química, Faculdade de Ciências Farmacêuticas de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, Brazil. The phytochemical work on this plant and its compounds has been performed in his group.

One of the major focuses of my lab is on drug absorption, pharmacokinetics and herb-drug-interactions. Knowledge of the absorption characteristics and pharmacokinetics of a compound is essential for the correct in vivo interpretation of in vitro activities that are sometimes the basis of therapeutic claims. Thus, Dr. Lopes and I decided to bring our expertise together and start collaborating on the absorption characteristics and pharmacokinetics of active compounds from "cachaça" to correlate these data with the observed pharmacological effects.

## Who in your laboratory carried out the research?

The experimental work was carried out by first author Ms. Dayana Rubio Gouvea and Mr. Ar-thur de Barros Bello Ribeiro, two graduate students from Dr. Lopes' group who joined my lab in Basel, Switzerland, for four months in 2012 to carry out the absorption studies in Caco-2 cells. For their stay in Switzerland, both



From left to right: Ms. Mila Rusanova, Dr. Krasimir Rusanov, Mr. Jonas Wedler, Dr. Veronika Butterweck, Ms. Fabienne Thoenen, and Ms. Sheela Verjee.

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students were financially supported by the Brazilian Federal Agency for Support and Evaluation of Graduate Education (CAPES).

## Could you provide a brief explanation of the work and results in your own words?

Herbal medicines are multicomponent mixtures that contain several active compounds, thus, the determination of pharmacokinetic parameters is relatively complex. However, the pharmacological importance of vicenin-2 and lych-nopholic acid depends on their

availability for intestinal absorption and subsequent interaction with target tissues.

In this work, the absorption characteristics of vicenin-2 (a flavonoid C-glycoside) and lych-nopholic acid (a sesquiterpenoid) was investigated using Caco-2 cells. It was observed that lych-nopholic acid crosses the Caco-2 cell monolayer by passive diffusion. On the other hand, vicenin-2 was not transported, suggesting no absorption of this compound in Caco-2 cells.

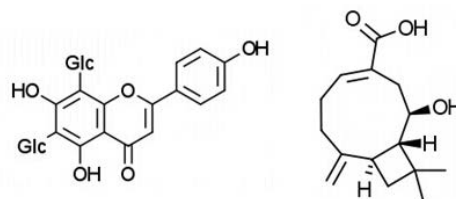
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### What implications might this work have on natural product science and health research in general?

It is necessary for the rational use of any drug to have a good understanding of the concentrations that will be achieved in the body after its administration. Of particular interest is the question to what degree and how fast the therapeutic agent is absorbed. Whereas there is usually detailed information available about the pharmacokinetics and biopharmaceutics of synthetic drugs, this is usually not the case for natural compounds. It cannot be emphasized enough that knowledge of the pharmacokinetics of a compound is important for the correct interpretation of its pharmacological effects. Our data could be used to predict the potential of drug development. Since lychopholic acid showed good permeability in the Caco-2 model, it might have a high absorption rate in vivo, thus it is a potential candidate for further drug-development studies. However, the C-glycoside vicenin-2 did not cross the cell monolayer and potential drug-likeness therefore can be excluded.



Vicenin-2 and lychopholic acid

### What is a favorite nonscientific activity of your lab?

We enjoy getting together for a traditional Swiss cheese fondue. This is a lot of fun, especially when it is cold outside. Very yummy!

### What is your lab's motto or slogan?

Never give up!

### What is your greatest extravagance in the lab?

The latest Olympus Live Cell Imaging system based on an Olympus IX-83 inverted microscope. Very cool! ■

## NCCAM Announces New Funding Initiative

By Dr. D. Craig Hopp

The National Center for Complementary and Alternative Medicine (NCCAM), in conjunction with the Office of Dietary Supplements (ODS), recently released a Funding Opportunity Announcement (FOA) entitled, "Center for Natural Products Innovation and Technology (U41)" (RFA AT-14-006). As the (NCCAM) has a strong interest in supporting research on improving natural product methodologies, the goal of this initiative is to challenge the research community to develop innovative solutions to some of the long-standing methodological obstacles that have plagued natural products research. Topics of interest for this FOA include:

- Innovative approaches for better characterization of network level pharmacological interactions between complex mixtures and complex biological systems
- Novel chemoinformatic technology for fingerprinting of complex mixtures
- Methodologies which can identify active components with reduced reliance on bioactivity guided fractionation
- Tools to quickly identify biological targets for natural products
- Novel approaches for rapid dereplication of active components in complex mixtures
- Innovative methodologies to detect contaminants or adulterants in complex mixtures
- Development of high content phenotypic assays capable of capturing multiple mechanisms of action
- Tools which can qualitatively and/or quantitatively establish presence of multiple active constituents (i.e. synergism) in a complex mixture.

This FOA was released simultaneously with the reissue of the ODS Botanical Research Centers FOA (RFA OD-14-001). NCCAM and ODS envision these two groups of grantees working together synergistically to advance the field of natural products research. However, the U41 grantee is not required to limit their focus to natural product sources typically associated with NCCAM. The technology being developed within the U41 could involve work with marine or microbial natural products as well as plant derived mixtures. The main point is that the technology should be broadly applicable.

NCCAM encourages the ASP community to consider applying for either of these programs. Please take a look and feel free to contact NCCAM program staff, Dr. Craig Hopp (hoppdc@mail.nih.gov) or Dr. John Williamson (williamsonjs@mail.nih.gov), with any questions.