Behind the Scenes in Pharmacognosy

From the Madagascar Rain Forest to the Hills of Virginia

by Amy Keller

In March of this year, the *Journal of Natural Products* published, "Cytotoxic Triterpenoid Saponins of *Albizia gummifera* from the Madagascar Rain Forest", authored by Shugeng Cao and others in the laboratory of Dr. David Kingston. This article appeared in the March 2007 issue in honor of Dr. Kenneth L. Rinehart. Dr. Kingston graciously answered our questions regarding this multi-faceted study.

The Virginia Tech *Albizia* team: Dr. David Kingston, Andrew Norris, Yanpeng Hou, and Dr. Shugeng Cao (left to right, back to front).

How did you become interested in *Albizia gummifera*?

We did this work as part of the Madagascar International Cooperative Biodiversity Group (ICBG). In this group our botanical colleagues at Missouri Botanical Garden (MBG) and Centre d'Application des Recherches Pharmacutiques (CNARP) make essentially random collections of plants from the northern part of Madagascar, and chemistry colleagues at CNARP prepare extracts of these plant collections. We then screen these extracts for activity against the A2780 ovarian cancer cell line, and select the most promising extracts to work on. An extract of *Albizia gummifera* showed significant activity in this assay, and thus was selected for fractionation studies.

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What is it like to be part of an International Cooperative Biodiversity Group? How did you become involved with this kind of cooperative research?

The ICBG program has been one of the hardest but also one of the most rewarding things I have done. It is hard because the program is very complex; we have seven independent Associate Programs working together in Madagascar, and just keeping up with all the e-mails, managing all the budgets, and writing all the reports seems to be a full time job! But it is rewarding because we have been able to do much more than simply discover new chemical compounds. For example, we have done a lot of good work in the development area, with bridges built, wells dug, and storage buildings constructed. We have enhanced the capabilities of CNARP by the establishment of a malaria bioassay unit, purchase of a new HPLC and other equipment, assisted in the establishment of the Diego protected area, and have greatly extended our knowledge of the plant life of Madagascar with the identification of several new species and the publication of guides to the ferns and plants of Zahamena.

I became involved in the ICBG program back in 1992, when the first RFA was announced for the formation of different ICBG programs. Dr. Mark Plotkin, who was then at Conservation International, called me up one day to ask if I was interested in collaborating with him in an ICBG application, and I agreed to do this. Because of my experience with NIH grants I was "elected" the Program Leader, and Mark and I between us assembled a team to work in Suriname. Our grant application received the best priority score I have ever had (I think it was something like 120), and we began our work in Suriname. Later we added Madagascar to the program, and eventually we moved all our work there.

Who in your laboratory carried out the research? Did this study involve fieldwork in Madagascar?

The chemical work in my laboratory was all done by an extremely skilled colleague and ASP

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member, Dr. Shugeng Cao. Shugeng did an outstanding job of analyzing some very complicated NMR spectra and elucidating the structures of the compounds. The bioassay work was done by my former laboratory technician, Mr. Andrew Norris. The botanical collection program was headed up by Dr. James S. Miller of MBG, and the actual collection was carried out by Fidy Ratovoson and Jeremi Razafitsalama of MBG. The extraction program at CNARP was headed by Rabodo Andriantsiferana, and the actual extraction was made by Vincent E. Rasamison. And finally some of the bioassay work was done by our collaborators at Eisai Research Institute, Karen TenDyke, and ASP member Dr. Ted Suh.

Could you provide a brief explanation of the work and results in your own words? In what way are the data in your paper new?

We succeeded in isolating three new triterpenoid saponins with good potency against the A2780 ovarian cancer cell line. They are highly complex structures with several sugar units linked in some cases by prenyl-type linker units, and the structure elucidation of these compounds, carried out on 3 – 18 mg of sample, was a real tour de force.

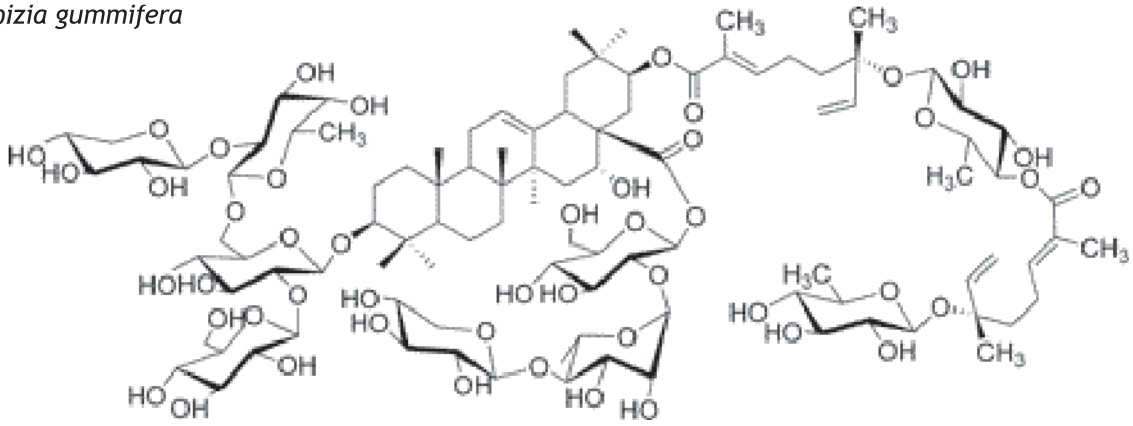
What impact does this research have, in terms of the cytotoxic compounds of *A. gummifera*?

In spite of their good potency they, sadly, are unlikely to become drug development candidates because compounds of this type have not proved to be successful in the past. Interestingly compound **3** was tenfold more potent against the HT-29 colon cancer cell line than compound **1** even though they have very similar activity against the A2780 ovarian cancer cell line, so clearly there are some subtle effects on antiproliferative activity which we do not understand.

Albizia gummifera

Your article appeared in a special issue of the *Journal of Natural Products* dedicated to Dr. Kenneth Rinehart. What impact did Dr. Rinehart have on your research in general? How did he influence you?

I did not work personally with Dr. Rinehart, but he was a great role model for me in my early years in natural products chemistry in this country. Since I was doing natural products chemistry in a chemistry department, I was encouraged by the fact that he was a successful natural products chemist in a chemistry department and I aspired to emulate him.



Gummiferaoside A