

An Interview with a Distinguished Pharmaceutical Scientist

George Zografi¹

Dr. George Zografi is the Edward Kremers Professor of Pharmaceutical Sciences, School of Pharmacy, University of Wisconsin-Madison. He received his B.S. in Pharmacy from Columbia University in 1956 and M.S. (1958) and Ph.D. in Pharmaceutical Chemistry from the University of Michigan in 1960. In 1972, after serving on the faculties of Columbia University and the University of Michigan, he joined the faculty of the University of Wisconsin. Dr. Zografi's research interests are focused in two areas: the properties of solids in the amorphous state and the surface chemistry of lipids, polymers, and proteins in monolayer and bilayer systems. He is the recipient of the APhA Ebert Prize (1984), the AAPS Dale E. Wurster Award for Pharmaceutics (1990), the AAPS Distinguished Scientist Award (1995), and the AACP Volwiler Research Achievement Award (1996). In 1989, he was elected to the Institute of Medicine of the National Academy of Sciences.

WHAT DO YOU THINK HOLDS THE KEY TO YOUR SUCCESS AS A PHARMACEUTICAL SCIENTIST?

Response: Whatever success I have had, I attribute primarily to the environments in which I was educated and where I have spent the last 38 years as an academic: Columbia University, the University of Michigan, and the University of Wisconsin. All of these universities provided me with excellent resources, students, faculty colleagues, and administrators. My interactions with many excellent industrial colleagues also have given me a very useful practical perspective for conducting my research in the pharmaceutical area.

WHAT DO YOU CONSIDER TO BE YOUR KEY RESEARCH ACCOMPLISHMENTS?

Response: I take greatest pride in the professional accomplishments of my former students and postdoctoral trainees in their scientific careers. As far as work in my laboratory, I particularly am pleased with our work on the surface phase behavior and viscoelastic properties of lipid and polymer monolayers spread at the air-water interface, and our more recent studies linking the physical and chemical instability of solids to molecular mobility caused by process-induced disorder and the absorption of water vapor.

WHAT WAS THE TURNING POINT IN YOUR DISTINGUISHED CAREER?

Response: When I joined the faculty of Columbia University in 1961, I met the distinguished surface chemist, Jack Schulman,



who generously introduced me to the study of surface monolayers and their potential as models for various self-assembled systems such as biological membranes. Another turning point was the summer of 1966 when I worked with Dr. Everett Hiestand at the Upjohn Co. on the possible effects of pharmaceutical processing on solid surface energetics. Both of these events set in motion the work we've done ever since.

WHO ARE THE INDIVIDUALS WHO MOST INFLUENCED YOUR RESEARCH CAREER?

Response: Besides the above-named individuals and my major professor at the University of Michigan, Albert M. Mattocks, I have been most influenced by the quality faculty colleagues and collaborators with whom I've worked. These include Lou Malspeis and Gil Hite (Columbia); Bill Higuchi and Tony Simonelli (Michigan); and Ken Connors, Joe Robinson, Jens Carsensen, and Hyuk Yu (Wisconsin). I also cannot say enough about the things I've learned from my graduate students and postdoctoral associates, as they developed independent approaches to their work in my laboratory.

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PHARMACEUTICAL SCIENTISTS ARE FACED WITH THE DILEMMA OF HAVING TO PUBLISH IN BIOMEDICAL OR BASIC SCIENCE JOURNALS AND HAVING TO PRESENT IN THEIR SPECIALTY MEETINGS IN ADDITION TO THE PHARMACEUTICAL SCIENCES VENUES. DOES IT MEAN CUTTING EDGE SCIENCE WILL NOT LIKELY BE FEATURED IN THE PHARMACEUTICAL SCIENCES FORUM?

Response: As an applied science area, pharmaceutical science should be using the best basic science possible to create its own "cutting edge" research, and this is what should be presented in the pharmaceutical sciences forum. If in the course of carrying out certain types of research a pharmaceutical scientist can see broader and more basic implications of the results, it is only natural that he or she would want to present this work outside of the pharmaceutical sciences. Quite a bit of my surface chemistry research, for example, has had more to do with understanding basic interfacial phenomena than with direct applications to pharmaceutical systems. When this has occurred, I have tended to go to journals such as, *Langmuir* or the *Journal of Colloid and Interface Science*. When I was studying the surface properties of drugs such as the phenothiazines, or the wetting of solid drugs and excipients, with direct pharmaceutical implications, I chose to publish in pharmaceutical journals. Correspondingly, I see no reason why our pharmaceutical meetings cannot continue to be venues for truly innovative pharmaceutical science, as our understanding of basic science expands.

IN THE 1960'S MANY OF YOUR COLLEAGUES WHO WERE TRAINED IN THE PHYSICAL SCIENCES CHOSE TO PURSUE BIOLOGICAL RESEARCH. DID YOU CONSIDER THIS OPTION?

Response: From the very beginning, my research in surface chemistry was motivated by my interest in biological membranes and related biological self assemblies, particularly the relationships of small molecules (drugs) with these systems. Indeed, at one point I seriously considered applying for a NIH Career Development Award in Psychopharmacology because of my work with the phenothiazines and model membranes. Upon deep reflection, however, I realized that I was most interested in the thermodynamic and kinetic aspects of relatively simple model systems for both biophysical and materials understanding, and that I was really a "physical pharmacist."

WHAT IS YOUR VIEW ON THE CURRENT STATUS OF RESEARCH IN THE MATERIALS SCIENCE OF PHARMACEUTICALS?

Response: The importance placed on rapid preclinical development of new drugs, as well as the use of increasingly complex drug delivery systems, has created the necessity for more understanding of solid material characteristics including solubility, interfacial behavior, stability, mechanical properties, and compatibility with drugs and biological tissues. We need to have people in the pharmaceutical sciences that can bring the enormous amount of basic information being generated by the current "materials sciences revolution," to bear on these pharmaceutical issues. If we are to predict such physical and

chemical behavior, we need sound molecular understanding and predictive models. For a variety of reasons, research of this type in the pharmaceutical industry has declined significantly, so I hope that more people in pharmaceutical academia can see this as an important activity. The biggest barrier, of course, is the difficulty of obtaining "unrestricted" research funding to support such work in academia. I hope that the pharmaceutical industry together with NSF will increasingly recognize the need for funding such "basic" applied research on pharmaceutical materials.

WHAT IS THE KEY TO DEVELOPING SUCCESSFUL COLLABORATIVE RELATIONSHIPS?

Response: I never actively collaborated in research until 1982 when I joined with Prof. Hyuk Yu, a polymer chemist, here in Madison to study the dynamic properties of small molecules and polymers spread as monolayers at the air/water interface. In 1990, I joined with Steve Bym at Purdue on a program concerned with the role of molecular mobility in crystalline and amorphous solid-state stability; and in 1992 I joined with Dr. Francis Tsao, a pulmonary biochemist, to study the biophysical aspects of lung surfactant. In all of these cases each of us brought our own expertise and perspective to a general set of issues. Mutual respect, open give and take, similar standards of operating, and total dedication to the issues being studied, without excessive concern for who gets the credit, seem to be paramount for a successful collaboration. I've thoroughly enjoyed these collaborations and my students have benefitted greatly in the process.

YOU HAVE SERVED AS THE DEAN OF THE SCHOOL OF PHARMACY, UNIVERSITY OF WISCONSIN AND ALSO AS THE PRESIDENT OF THE AMERICAN ASSOCIATION OF COLLEGES OF PHARMACY. WHAT IS YOUR VIEW ABOUT SCIENTISTS TAKING UP ADMINISTRATIVE AND PUBLIC SERVICE RESPONSIBILITIES?

Response: This is a very difficult situation because administrative work, of its very nature, has to interfere with one's professional progress as a research scientist. It reduces the time available for contemplation and reading, as reflected in fewer publications, less grant proposals, and limited ability to attend scientific meetings. Likewise, professional organizational work uses time that could otherwise be spent on scholarship. Having said this, however, I must also say that there is a broader community within an institution or profession that requires leadership and administration. If top-flight scholars do not give some percentage of their entire career to "professional citizenship," who will provide leadership in a manner that goes beyond management of resources, recognizing the unique and fragile nature of our schools and organizations. It's a bit old fashioned to say that we all owe some level of such citizenship to those who follow us, but I sincerely believe this to be true.

HOW HAS YOUR PHILOSOPHY OF EDUCATING GRADUATE STUDENTS BEEN CHANGED OVER THE YEARS?

Response: There is nothing more exciting to me than the discovery that comes with doing research. However, I believe that

those of us in academia are obliged to practice our profession in the context of the major function of any university, which is education and training. We should be creating new knowledge; but if it is done with graduate students and postdoctoral trainees, their education is the bottom line even if it takes longer and is less efficiently carried out. I've always felt that when doing research with students, the specific project is less important than the process by which they develop and carry out the research project as independently as possible. I've always worked on the premise that a properly educated Ph.D. in the area of pharmaceuticals only needed a basic course background and good research training (including possible postdoctoral training) to be able to find a niche in academia or the pharmaceutical industry. Indeed, I have observed this to be the case with literally hundreds of Ph.D. graduate students with whom I've had contact over the years. Lately, however, I sense an increased tendency on the part of companies and some major professors to favor developing graduate students who have very specific applied knowledge and even some product development skills as part of their thesis work. I believe that this approach can lead to a regrettable situation for the education of new Ph.D.'s if it becomes more widespread, since it will limit the depth to which they can react to changes in science and technology over a career.

HOW HAS YOUR PHILOSOPHY OF MENTORING JUNIOR FACULTY CHANGED OVER THE YEARS?

Response: When I was a junior faculty member in 1961–67 in 2 research-intensive institutions, I was advised by two deans that a significant commitment to teaching and service was essential and that such balance in my activities would not hurt my prospects for promotion as long as what I did do in the way of research was of a high quality. Today, new faculty members are expected to come to their position after postdoctoral experience with well-developed research plans and, perhaps, even some research funding. In return, research-intensive universities invest in considerable start-up funding and other resources, with associated reduced teaching loads, to get them off to a good start toward tenure. Thus, young people today enter a very different academic climate than existed even 10 years ago. Consequently, as a mentor today I find it very difficult to encourage such faculty, before tenure, to become active academic citizens or to spend a significant percentage of their time developing innovative approaches to their teaching, knowing on what basis they will ultimately be judged. It is my hope that what little they are able to do in teaching and service will be done conscientiously and with the interests of students and their institution in mind.

WHAT WOULD BE YOUR ADVICE TO OUR JUNIOR PHARMACEUTICAL SCIENTISTS EMBARKING ON THEIR CAREERS IN THE PHYSICAL PHARMACY AREA?

Response: If they were entering the academic area, I would advise them to work hard to find important basic questions and

problems related to drug product development and drug delivery systems that are being ignored, or where they feel that they can make a unique basic contribution. They should avoid following trends unless, as I said, they have something new to offer. To be in a position to address such questions and to receive funding, it is essential that young faculty in physical pharmacy be conversant with the chemical physics, physical chemistry, and materials science literature and to move beyond the pharmaceutical arena in their reading and attendance at scientific meetings. This is the only way that they will be able to bring new ideas to our field.

WHAT IS THE PLACE OF ENTREPRENEURSHIP IN ACADEMIA?

Response: From my perspective, this is not a black and white issue because the term entrepreneurship means different things to different people. If one of the fruits of a scientist's academic research is a unique discovery that can be patented, it can be very nice for the investigator and the University from a financial perspective. Universities increasingly see this as an alternative source of unrestricted research funding, so perhaps this even will become an expectation of all faculty in future years. How such activity affects a faculty member's ability to be involved in research rather than spending time on the product development of this patent would interest me. Are remaining responsibilities to students and to the academic program in general being met? Consequently, to the extent that the basic mission of the University might be compromised by such activity, even with a financial return to the University, I would question its place without very strict guidelines as to the impact on academic programs.

WHAT ARE THE FUTURE CHALLENGES FACING THE PHARMACEUTICAL SCIENCES?

Response: From the fruits of the biological and materials revolution, the pharmaceutical industry will greatly expand in its impact and financial success in the coming decades. It is truly an exciting period to be part of it all. The pharmaceutical sciences need to continue to attract talented people who can bring basic science concepts and information to bear on the important problems to be faced in providing cost-effective quality products. Such people must come from a variety of disciplines with strong research, education, and training. The industry and AAPS must provide the stage and resources which will be required to bring these people together. A balance between "good science" and "commercial payoff" will be needed if true scientific and technological progress will be made in this area with a major societal impact. Innovation in pharmaceutical research must come from academia and imaginative "start-up" companies, since the larger and larger pharmaceutical companies will increasingly be less interested and unable to meet these scientific needs, except perhaps through the funding of other companies and institutions.