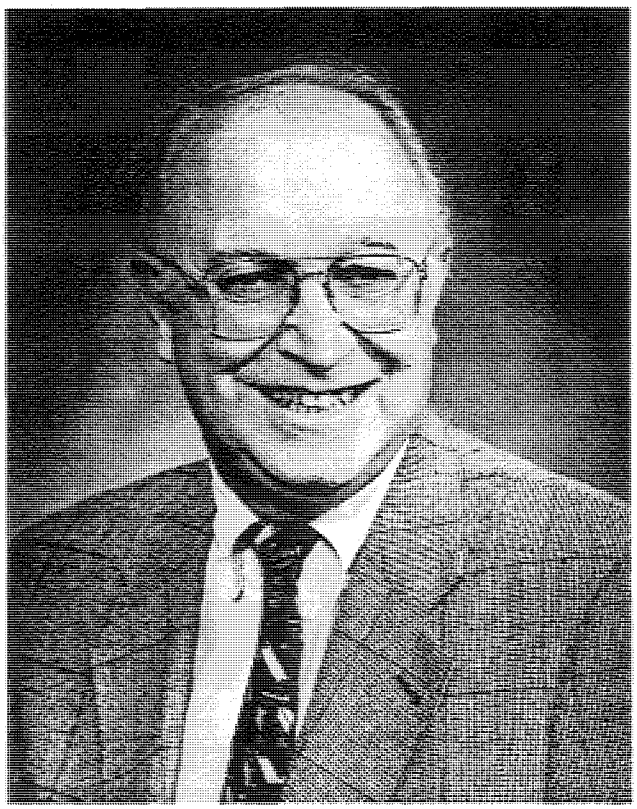
*An Interview with a Distinguished Pharmaceutical Scientist*

# Joseph R. Robinson[1]

Joseph R. Robinson, Ph.D. is Professor of Pharmacy (School of Pharmacy) and Professor of Ophthalmology (Medical School) at the University of Wisconsin-Madison. A graduate of Columbia University's College of Pharmacy (B.S., M.S.) and the University of Wisconsin-Madison (Ph.D.), he has served on the School of Pharmacy faculty at Madison, Wisconsin, since 1966. Dr. Robinson is a member of the editorial boards of many journals. He was awarded an honorary doctorate from the Royal Danish School of Pharmacy (1992), and is the recipient of the Ebert Prize (1989), the Maurice-Marie Janot Medal (1989), the Nagai Award (1990), the American Pharmaceutical Association (APhA) Research Achievement Award (1991), the American Association of Pharmaceutical Scientists (AAPS) Research Achievement Award (1991), the Controlled Release Society (CRS) Founders Award (1993), the AAPS Dale E. Wurster Pharmaceutical Research Award (1996), and the APhA Takeru Higuchi Research Prize (1997). He was the Ortho Distinguished Lecturer (1988), the Riegelman Lecturer (1988), the Kenneth Avis Distinguished Professor Lecturer (1991), the Bergy Lecturer (1991), and the 1993 Distinguished Lecturer in the Pharmaceutical Sciences at the University of Leiden in the Netherlands. Dr. Robinson is a past-president of both the Controlled Release Society (CRS) and the American Association of Pharmaceutical Scientists (AAPS). His interests are in the areas of controlled drug delivery, ocular drug disposition, and bioadhesives.



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

*Response:* There are many factors that contribute to success, including timing and a bit of luck. My career spans a time period where great changes were occurring in the field of pharmaceutics so that opportunities were plentiful. Moreover, I was fortunate to have received an excellent education at the University of Wisconsin and to be exposed to a culture that pioneered scholarly achievement in our field. In addition, I was even more fortunate to be able to join the faculty at this institution and to have colleagues who themselves were leaders in the field and who cherished independence. The research culture of an institution can play a pivotal role in success. Good institutions attract good people and expect them to perform. Naturally having a family that is willing to sacrifice for your success is essential and I have been blessed in that regard.

**ALTHOUGH YOU WERE TRAINED AS A PHYSICAL ORGANIC CHEMIST, WHY DID YOU CHOOSE THE PATH OF BIOLOGICAL RESEARCH? WHY DID YOU FOCUS INITIALLY ON OCULAR DRUG DELIVERY?**

*Response:* My major professor, the late Takeru Higuchi, was by training and interest a physical organic and analytical chemist. However, much of what he did was ultimately aimed at drug delivery, as we now define it, although he himself avoided moving close to the biological interface. His contemporaries, such as Dale Wurster, Edward Garrett, and Joseph Swintosky, were applying physical chemical principles to biological systems directly and that had an influence on me. I was also influenced by Stuart Eriksen, a young faculty member at Wisconsin. He, like Takeru Higuchi, thought "outside of the box." The reason why I focused on ocular drug delivery, as is often the case with young faculty, I needed research funding, and the National Eye Institute had funds available. At the time there was very little quantitative work in the literature on mechanisms of ocular drug disposition and drug delivery. It looked like a good opportunity to apply physical chemical principles to a biological system.

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**WHAT IS YOUR VIEW ON OCULAR DRUG DELIVERY AT THE PRESENT TIME?**

*Response:* Ophthalmology is largely a surgical and not a drug discipline and therefore the drug market size is perceived to be relatively small, but growing. Practically, this means there are a relatively small number of new drugs and thus the need for better ocular drug delivery systems is more general than specific. Nevertheless, strategies for ocular drug delivery are shifting somewhat from a technical to a cell/molecular biology approach, which I find vary exciting.

**WHAT ARE THE FUTURE CHALLENGES IN OCULAR DRUG DELIVERY?**

*Response:* The recent discovery of a gene for some forms of glaucoma suggests increasing activity in cell and genetic material delivery. Since it is difficult to deliver drugs to the back of the eye, various diseases involving the retina and macula are very hard to treat. Thus, topical delivery of drug to the front of the eye only results in low levels of drug making it to the back of the eye. The presence of a blood-vitreous humor barrier for many drugs suggests that in many cases an ocular implant in the back of the eye will be needed. Finally, blindness in third world countries from parasites can realistically only be treated with sustained release topical drugs. We continue to need effective topical drug delivery systems.

**YOU ARE ONE OF THE PIONEERS OF THE USE OF MUCOADHESIVES IN DRUG DELIVERY. WHAT MOTIVATED YOU TO PURSUE MUCOADHESIVE RESEARCH?**

*Response:* The front of the eye has considerable mucus and a defect in this mucus, or change in local conditions, can lead to dry eye. Ocular mucus is secreted by goblet cells in the conjunctiva. Although the mucus spreads across the cornea, it does not firmly attach to it. I was, and still am, interested in how mucus would attach firmly to one tissue (the conjunctiva) and not to a near neighbor (the cornea). It was a short step from mucus to mucomimetic (bloodhesive) polymers. It helped enormously that I had two extremely bright and talented graduate students, Kinam and Haesun Park, to initiate and execute the experimental work.

**WHAT IS YOUR VIEW ON THE STATUS OF MUCOADHESIVE RESEARCH AT THE PRESENT TIME?**

*Response:* We have had extensive work on the mechanism of attachment by people such as Nicholas Peppas (Purdue University) and Claus-Michael Lehr (University Saarland, Germany) and this work will continue. The first polymers were "off the shelf" chemicals for ease of regulatory approval but the newer multi-functional polymers, in which bioadhesion is only one of the attributes, gives considerable breadth to drug delivery strategies.

**WHAT ARE THE FUTURE CHALLENGES IN BIOADHESIVE RESEARCH?**

*Response:* The obvious first answer is specificity. Perhaps of greater importance is to find ways for bioadhesives to be effective in the gastrointestinal tract. At the moment the rather large amount of soluble mucus in the human gastrointestinal tract binds to any bioadhesive and limits its ability to attach to the tissue surface. Perhaps the greatest challenge in bioadhesive technology is the synthesis of new polymers with multi-functional properties. These properties include bioadhesion, rate control of drug release for a wide variety of drug properties, penetration enhancement, and enzyme inhibition.

**FROM MUCOADHESIVE RESEARCH, YOU UNDERTOOK A SERIES OF STUDIES ON GASTROINTESTINAL RESEARCH. WHAT PROMPTED THAT DEVELOPMENT?**

*Response:* The use of bioadhesive polymers in several routes of drug delivery has led to extraordinary improvements in contact time. Thus, in the eye a simple solution disappears from the front of the eye in a few minutes but can be extended to 10-12 hours with a bioadhesive. Vaginal contact time goes from a couple of hours to several days. The gastrointestinal tract has similar contact time constraints. However, the presence of food and mucus usually limits access of the bioadhesive polymer to the tissue surface. One way to limit this effect is to employ receptor targeting such as the work of Jindrich Kopecek (University of Utah) on targeting to sugar receptors in the colon.

**WHAT IS YOUR VIEW ON THE STATUS OF ORAL DELIVERY AT THE PRESENT TIME?**

*Response:* The most commonly used route, which is also the most complex, continues to vex those of us in drug delivery. It is easy to see progress in understanding the biological barriers in the oral route but equally easy to see that progress in new approaches or new systems is marginal. Thus, our biological barrier understanding now includes the cytochrome P450 metabolizing enzyme on the microvillus tips and the p-glycoprotein efflux system. Insofar as an exciting development in oral drug delivery, I am impressed with the novel peptide absorption work of Sam Milstein (Emisphere Technologies) which challenges conventional ideas of drug absorption.

**WHAT ARE THE FUTURE CHALLENGES IN ORAL DRUG DELIVERY?**

*Response:* Assuming good technology to solubilize and stabilize problem drugs, the remaining issues can be succinctly summarized as ability to spatially place and maintain the drug at a desired location, ability to control tissue absorption, and ability to control residence time. These are formidable, but not insurmountable, obstacles.

**WHAT WAS THE TURNING POINT ON YOUR CAREER?**

*Response:* For me, the turning point was coming to the University of Wisconsin in the early 1960's to continue my education and meeting faculty who were devoted to or consumed by research. Many of these faculty were engaged in "high risk" research (as opposed to derivative) and clearly sent the message that failure was alright as long as the research problems were significant.

I must relate a story about my research. My thesis advisor, Takeru Higuchi, felt strongly that in general biological systems were too crude to make meaningful research contributions. When I began to do more biologically related work, I am certain that Takeru Higuchi was disappointed in me. Several years later, in a brief conversation he told me "I was doing good work." Note, he did not say great or exceptional work, but good work. I took that as a high compliment and his approval was very important to me.

**WHO ARE THE TWO OR THREE INDIVIDUALS WHO HAVE MADE A DIFFERENCE IN YOUR CAREER?**

*Response:* In my early career Takeru Higuchi was my mentor and role model. He was not only a good scientist but a wonderful father figure who was always there when I needed him. The next two were later in my career; they were Bob Langer (MIT) and Sung Wan Kim (University of Utah). Bob's career is legendary in both quantity and quality of pioneering work in drug delivery and he has consistently challenged drug delivery dogma; Sung Wan Kim, who is equally prodigious in his research and has made giant contributions in both biomaterials and drug delivery, is my guru in the world of polymers.

**YOU WERE PRESIDENT OF TWO SCIENTIFIC ORGANIZATIONS: THE CONTROLLED RELEASE SOCIETY AND THE AMERICAN ASSOCIATION OF PHARMACEUTICAL SCIENTISTS. WHY DID YOU VOLUNTEER YOUR SERVICES TO THOSE TWO SCIENTIFIC ORGANIZATIONS?**

*Response:* I believe that scientists have an obligation to engage in public service. Organization without leadership will flounder and I am vain enough to believe I can change things that in my view need changing. A good role model in this regard is Les Benet (UCSF) who founded AAPS. I was fortunate to serve on the Executive Committee of AAPS when it was formed. Presidents before Les complained about the relationship of the Academy of Pharmaceutical Sciences to its parent organization the American Pharmaceutical Association. Les did not complain; he did something about it. He created an organization that could be a home for all pharmaceutical scientists. We have all encountered prominent scientists who when approached to run for an office in a scientific organization beg off with the excuse they are too busy. I find that excuse unacceptable because we are all busy and basically each of us has an obligation to serve in some capacity.

**DO YOU FEEL THAT WE ALL HAVE AN OBLIGATION TO BE A VOLUNTEER IN SCIENTIFIC ORGANIZATIONS? IF NO, WHY?**

*Response:* I have already commented on my strong feelings that we have an obligation for public service in some capacity. A scientific organization exists to serve scientists through publications and meetings and to promote our sciences within the science community and to government agencies. These things are best done by scientists. In a world where travel time is shortened so that international meetings are common and communication is exceedingly rapid, there is a blurring of disciplinary lines; and our science is often viewed as dangerous and out of control, the need for strong scientific organizations is of utmost importance.

**WHAT WOULD BE YOUR ADVICE TO OUR JUNIOR PHARMACEUTICAL SCIENTISTS WHO ARE ABOUT TO EMBARK ON THEIR CAREERS?**

*Response:* Find an area where you can make a difference, choose research problems that are important and meaningful, and surround yourself with colleagues who are equal to or better than you. This is not a snappy answer but is intended to convey important advice. Senior scientists can make a difference in a career by offering fair and constructive critical comments. Seek out a respected senior scientist and discuss the what and why of your research.

**WHAT WOULD BE YOUR ADVICE TO OUR SENIOR PHARMACEUTICAL SCIENTISTS IN THEIR RELATIONSHIP TO JUNIOR COLLEAGUES?**

*Response:* Meaningful advice is never forgotten. Knowing the impact that a senior colleague has had on each of our careers, and the life-long gratitude we feel because of that advice, we should each welcome an opportunity to mentor a colleague. Thank you very much.