purifying proteins with new chromatographic techniques

BY PAUL SORENSON AND JOSEPH CARLSON

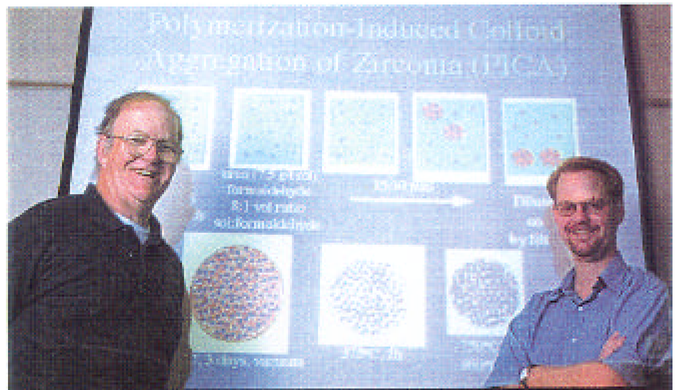
LIKE FARMERS SEPARATING wheat from chaff, scientists developing new drugs must find ways to isolate useful proteins from other molecules, including undesirable toxins and molecular debris. Liquid chromatography, the technique normally used in this process, is limited by the type and temperature of material with which it can be used. But a team of IT researchers is developing new materials that will remove those limitations and broaden chromatography's effectiveness across a wide range of applications.

Liquid chromatography works through selective adsorption, explains chemistry professor Peter Carr, who leads the team of researchers developing the new technique. In a chromatograph, particles of silica gel are packed together in a dense columnar mass that acts as a selective adsorbent. As fluid moves through the column, molecules of different types pass through it at varying rates. By carefully adjusting the surface chemistry of the silica particles, scientists can design chromatographic media to purify and analyze a wide range of substances, including proteins and amino acids.

Scientists use Chromatography to purify proteins and separate mixtures of complex molecules. Researchers have engineered a new medium that improves its effectiveness with a broad range of chemical materials.

Although liquid chromatography has been widely used for years, Carr and Alon McCormick, an associate professor of chemical engineering and materials science, discovered that the technique could be improved by using zirconia as the chromatographic media rather than silica. For example, zirconia-based liquid chromatographs can function at higher temperatures and process materials under more acidic and basic conditions.

According to Carr, zirconia-based chromatographs are also more useful in biotechnology applications because, unlike those based on silica filtering agents, they can be sterilized with a strong base to remove pyrogenics, the toxic by-products of protein harvesting that "stick like hell to everything."



Peter Carr and Alon McCormick

The new media will also improve liquid chromatography's applications in environmental and chemical analysis, forensic science, biochemistry, and industrial chemistry laboratories, he adds.

Carr began exploring the use of zirconia in liquid chromatography during a collaboration with 3M in the early 1980s. The company eventually pulled out of the project, leaving Carr to continue the research with McCormick and other colleagues, including Professor Michael Flickinger and Assistant Professor Anuradha Subramanian, at the University's Biological Process Technology Institute.

Since then, Carr and McCormick have focused on the complex chemical analysis and modifications required to develop zirconia as effective chromatographic media, earning several patents for their work.

In 1995, the University licensed several of those patents to ZirChrom Separations, a company founded by Carr and a former graduate student to manufacture the zirconia-based chromatographs. According to Clayton McNeff, ZirChrom's vice president and director of research, most of the company's sales are to large pharmaceutical corporations like Novartis.

ZirChrom also has earned state and federal research grants to develop the technology further. With that funding, the company is sponsoring a collaboration with McCormick to discover ways to improve the raw colloidal materials used to create the zirconia. Another grant supports a joint project with Subramanian to develop techniques for purifying monoclonal IgG antibodies and other larger molecules.

Future University-industry collaborations are inevitable, says Carr. "The biotechnology applications alone [for this new technique] are staggering," he says. "We've only just begun exploring the possibilities." ■

FOR MORE INFORMATION visit the Biological Process Technology Institute web site at http://biosci.cbs.umn.edu/bpti

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