Biopolymers help save lives

Polymers and Medicine

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Synthetic and natural polymers are frequently used in medicine and pharmacology. At the Center of Polymer Chemistry in Zabrze, we have developed an original method for synthesizing a biodegradable and nontoxic nano-polymer that can be used as a carrier to improve the therapeutic properties of medicinal drugs

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NMR spectroscopy of the synthesized polymer conjugates

The field of biocatalysis in non-water environments was the subject of groundbreaking research by the Polish Professor Ernest A. Sym in the 1930s. After years of study at the university of technology in Lwów (now Lviv in Ukraine) and work at foreign universities, Professor Sym developed the field chiefly through his research at Warsaw University - work that was hailed in the literature as pioneering. He spent the WWII period in Warsaw, working at the State Hygiene Laboratory, and also helping produce explosive materials for the Polish Home Army (AK). After the war Professor Sym worked as director of the Chemistry Department at the University of Technology in Gdańsk and at Gdańsk University. The great esteem that his work earned him was shown by his election to become a member of the PAU (Polish Academy of Arts and Sciences) and by the State Award he received for papers published in leading research journals.

The Silesian group

Professor Sym's scientific career was unfortunately tragically cut short by a fatal car crash, and after his death his associate researchers went their separate ways in the world. Some continued their research in the United States, others at the Medical University of Warsaw, with several individuals ending up in the Silesia region (in Gliwice and Zabrze), where interdisciplinary centers drawing upon Prof. E. Sym's achievements were set up - such as the Institute of Oncology, the Silesian University of Technology, and the Center of Polymer Chemistry of the Polish Academy of Sciences.

This Silesian group forged ties to institutions of the US National Academy of Sciences, and Polish scientists were invited to pursue joint research. Under US grants, the Center of Polymer Chemistry in Zabrze researched topics in the 1990s that pertained to the synthesis of new biopolymers and their medical applications. This research collaboration was applauded by the US National Academy of Sciences and the International Union of Pure and Applied Chemistry (IUPAC), and it paved the way for joint US-Polish research projects.

After Poland's EU accession, the European Union assumed the funding of research at the Center of Polymer Chemistry in Zabrze, and in the years 2000-2004 the Center pursued two extensive research topics funded by the EU.

In cooperation with European and US partners, the Center of Polymer Chemistry organized two world symposia (in Warsaw in 1992 and in Kraków in 1997), each drawing

together more than 200 outstanding foreign and domestic scientists, with papers appearing in two English-language monographs published by the Center of Polymer Chemistry. The Polish organizers of these symposia were commended by the IUPAC, and some of them have also received honorary doctorates and medals from foreign universities.

In 2004, the EU founded the "BIOMAHE" (Biodegradable Polymeric Materials for Health and Environment) Center of Excellence at the Center of Polymer Chemistry in Zabrze.

Nanopolymer drugs

The research pursued at the EU Center of Excellence in Zabrze focuses on the synthesis of biopolymers and their applications as drug carriers. Synthetic and natural polymers have long been investigated for use as carriers useful in systems for controlling drug dosages (known as drug delivery systems, or DDS). The purpose of polymers in such a system is to deliver drugs to the target pathological cells, making drugs more effective, reducing their undesirable side effects, and simplifying dosage methods. In order to be used as drug carriers, polymers should have a well-defined structure and should be biodegradable, biocompatible, and not contain toxic additives. Unfortunately, certain natural polymers, such as poly-3-hydroxybutyrate (PHB) have turned out to contain certain quantities of toxic proteins and lipids (some 2.5%) and thus cannot be used in medicine, especially in drug delivery systems. Based on fundamental research and theoretical work, the Center of Polymer Chemistry has recently succeeded in developing a method for synthesizing a completely new, nontoxic polymer, nano-poly-3-hydroxybutyrate to be used as a drug carrier. Unlike methods applied so far, the new approach obtains poly-3-hydroxybutyrate using nontoxic components that are usable in medicine and pharmacology. This method has been patented in Poland and in the EU countries. Next we developed a method for combining this nontoxic synthetic polymer with certain drugs, especially from the large group of nonsteroid anti-inflammatory drugs (NSAIDs). We have developed methods for synthesizing conjugates of poly-3-hydroxybutyrate with such drugs as aspirin, ibuprofen, ketoprofen, naproxen, and diclofenac. This Polish drug manufacturing method, unique in the world, has also already been patented in Poland and abroad, and has proved to be exceptionally effective in treating inflammations and in the pharmacological prevention of oncological disorders. Specialist studies of the properties of such modified drugs at the Center of Oncology in Gliwice and the Institute of Industrial Organic Chemistry's branch in Pszczyna have indicated that they have highly useful therapeutic properties.

Prospects for the future

The drug modification methods developed at the Center of Polymer Chemistry, as part of the BIOMAHE European Center of Excellence, having obtained European patents, pave the way for original new ways of producing modified nanopolymer drugs. Foreign guests, professors and doctors are being hosted at the BIOMAHE European Center of Excellence in Zabrze on several-month research grants. During the first year of the European Center of Excellence's operations alone, training and grants were obtained by scientists from Austria, Rumania, Sweden, Hungary, and Italy, and the next group of scientists is now waiting for acceptance. The EU fully covers the costs of these foreign visitors' stay in Poland, as they pursue research using the Center's apparatus, equipment, and chemicals.

The aims of the work carried out by the European Center of Excellence at the Center of Polymer Chemistry are of great scientific as well as social significance. Such work follows the longstanding traditions of Polish research in the field, and the concrete results are much awaited by many clinical patients in need of new, more effective drugs.

Our research results, after being registered for patenting with the European Patent Office and published in renowned international journals, have sparked great interest from international research centers, and have generated offers to collaborate in the research field we have initiated. Aside from such foreign centers as the L&D Sherman Center for Research under the Department of Biomedical Engineering at the Technion (the Israel Institute of Technology) in Haifa, such interest has also been expressed by the Polish pharmaceutical industry, namely by the Foundation for the Development of Polish Pharmacology and Medicine, which subsidizes research projects in the pharmaceutical and medical sciences.

The use of polymers makes drugs more effective, reducing their side effects, and simplifying dosage methods

In short, the Center's research as outlined in this article – research which seeks new methods of drug modification in order to achieve new, original methods of obtaining wholly nontoxic oligo-3-hydroxybutyrates using our patented techniques – represents the continuation of Poland's longstanding traditions in this field, initiated years ago by world-famous Professor Ernest Sym. ■

Further reading:

V. Piddubnyak, P. Kurcok, A. Matuszowicz, M. Głowala, A. Fiszer-Kierzkowska, Z. Jedliński, M. Juzwa, Z. Krawczyk (2004). Oligo-3-hydroxybutyrates as potential carriers for drug delivery. *Biomaterials* 25, 5271.

Z. Jedliński (1999). Ring-opening Reactions of ß-Lactones with Activated Anions. *Acta Chem. Scand.* 53, 157.

Z. Jedliński (1998). Novel Electron Transfer Reactions Mediated by Alkali Metals Complexed by Macrocyclic Ligand. *Accounts Chem. Res.*, 31, 55.

Z. Jedliński, A. Czech, H. Janeczek. M. Kowalczuk (1995). Unusual electron transfer to styrene and α-methylstyrene mediated by potassium supramolecular complex with 18-crown-6. J. *Am. Chem. Soc.* 117, 8678.