

Professor Edward Borowski and Molecular Aspects of Chemotherapy

Professor Edward Borowski was born in 1928 in Wilno. He moved to Gdańsk in 1945 to start studying at the Chemical Faculty, Gdańsk University of Technology. As a 3rd-year student, he was in 1948 appointed a Research Assistant at the Department of Organic Chemistry and this date marks the onset of his academic career. His research at that time was focused on discovery of novel antibiotic substances by random screening of soil samples. These studies resulted in discovery of tetaïne, the first ever antibiotic isolated in Poland and in getting PhD for this achievement in 1954. In 1957 Edward Borowski went to the USA where he got a position of a Postdoctoral Fellow at the Institute of Microbiology, Rutgers University, New Brunswick, N.J., in laboratory of the Nobel Prize winner, Professor Selman A. Waxman. In Prof. Borowski's opinion the experience gained at Waxman's lab was of a great importance for his further career. Coming back to the Gdańsk University of Technology in 1960, E. Borowski was given a position of a Head of the Department of Biochemistry (converted later into Department of Pharmaceutical Technology & Biochemistry), and started building his research team. Small at the very beginning, it rapidly expanded and quickly became a large group combining scientists who represented different specializations: organic chemists, biochemists, biophysicists and microbiologists. In the eighties the group was joined by quantum chemists who had been using modern computational technologies for drug design. All these researchers combined their efforts towards studies on molecular basis for the rational design of potential chemotherapeutics for the control of eukaryotic systems, especially antifungal and anticancer agents. Such a multidisciplinary approach was entirely pioneering at that time. Professor Borowski and his Molecular Chemotherapy Group quickly became a leading Polish center of studies on molecular aspects of chemotherapy, well known and appreciated by the world scientific community in this field. In the meantime, Professor Borowski was nominated for several years a Director of the Institute of Organic and Food Chemistry and Technology at his mother faculty. As a matter of fact, he did not enjoy those administrative duties, as they had taken too much time that could be much better spent on doing research.

The scientific record of Professor Borowski is very impressive. It comprises nearly 800 scientific publications, including 340 peer-reviewed articles in journals and books, 380 conference communications and 70 patents. His works were cited by other authors nearly 1100 times in the period 1981–2000. Such a citation record places Prof. Borowski among the most cited Polish scientists. Detailed enumeration of all achievements of Professor Borowski and his research group is undoubtedly beyond the scope of this article but the most important of them include:

1. Isolation and characterization of original peptide antibiotics: tetaine [1] and edeine complex [2]. Studies on the mechanism of action of tetaine led to the proposal of the enzyme, glucosamine-6-phosphate synthase, as a new target for antifungal chemotherapy [3] and to the later rational design and development of highly effective antifungal oligopeptides, containing selective inhibitors of this enzyme [4]. Edeines are well known for their broad spectrum of activity and an unique mode of action as universal inhibitors of translation [5].
2. Discovery and isolation of 4 polyene macrolide antifungal antibiotics and determination of structures of over 20 polyene macrolides, including Amphotericin B [6], known as a "golden standard" in antifungal chemotherapy. Papers of Borowski and his coworkers constitute about 80% of world scientific bibliography on this subject.
3. Fundamental works on molecular basis of action and selectivity of antifungal polyene macrolides [7, 8] led to the development of several derivatives of Amphotericin B (AMB) exhibiting qualitatively improved selective toxicity in comparison to the mother antibiotic, including a methyl ester of N-methyl-N-fructopyranosyl-AMB, as the most promising compound [9].
4. Presentation of a novel concept of mechanism of cardiotoxicity of anthraquinone anticancer agents (AAA). Borowski and coworkers provided evidence for generation of oxygen radicals due to participation of AAA in intracellular single-electron transfer (SET) processes [10] and pointed out that substrate properties of AAA in respect to NADH/NADPH-dependent oxidoreductases are the main factor determining SET potential of these compounds [11].
5. Demonstration of directions of possible chemical modifications of some clinically useful anticancer agents leading to the development of derivatives highly active against multidrug-resistant cancer cells [12] and new modulators of cancer drug efflux membrane proteins that could be used in combination with existing anti-tumor drugs.
6. New technologies of production of several β -lactam antibacterial antibiotics, developed in the seventies of the previous century and a new method of synthesis of an important anticancer agent Novantrone [13], implemented in industrial practice in the nineties.

Some of the above mentioned achievements resulted in part from the international scientific collaboration. Professor Borowski has established highly successful and effective links between his group and more than 20 foreign academic and research institutions. In 1984 he organized in Gdańsk the International Symposium on Molecular Aspects of Chemotherapy as a new forum for the exchange of scientific information among researchers interested in rational drug design. This initiative met with an interest and thus the 1984 conference became the first in the series of eight such events, organized always in Gdańsk in the period of 1984–2001.

Professor Borowski has built a well recognized scientific school. He has been a supervisor of 42 PhD thesis, his 7 co-workers got the DSc degree and 3 of them became full professors. For his academic achievements Professor Borowski has been

awarded many times in Poland and abroad. In 1997 he was the first ever laureate of the Hevelius Award, established to honor especially distinguished scientist of the Pomeranian region. Member of editorial boards of several scientific periodicals, including a highly prestigious journal *Antimicrobial Agents & Chemotherapy* and Polish Journal of Chemistry. Elected many times a member of Scientific Councils of many research institutes and a current member of the Committee of Drug Science, Polish Academy of Sciences. Despite the fact that science is Professor Borowski's primary love, he has also found some time to be a very active President of the Gdańsk branch of the Association of Friends of Wilno and the Wilno Region (Professor Borowski's homeland, now in Lithuania). In his free time he has enjoyed hunting and farming.

In 1998 Professor Borowski celebrated the 50th anniversary of beginning of his scientific career. In the same year he passed the position of a head of the department to Professor Jerzy Konopa but remained a leader of the Molecular Chemotherapy Group. For those who know Professor Borowski a bit closer it was obvious that his formal retirement could not mean any real abandonment of the scientific activity, so that nobody should be surprised that this activity has never actually decreased. His current subject of special scientific interest is a phenomenon of multidrug resistance and chemotherapeutic strategies of its overcoming. Professor Borowski is highly active in arrangements of scientific consortia for the purpose of participation in the 6 Framework Programme of EU.

The members of the Professor Borowski's research group, including myself, have always known that our joint work is difficult from time to time but always interesting. The Professor's ideas are sometimes controversial but always stimulating. Following them has been for us a kind of a scientific adventure – may be sometimes not highly practical but often exciting. Professor Borowski has inoculated at least some of us with his a bit romantic attitude to science – not so abundant nowadays. We are highly grateful to him for this gift.

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LITERATURE

1. Borowski E., *Acta Biochim. Polon.*, **4**, 231 (1957).
2. Wojciechowska H., Ciarkowski J., Chmara H. and Borowski E., *Experientia*, **28**, 1423 (1972).
3. Borowski E., Andruszkiewicz R., Bontemps-Gracz M., Chmara H., Milewski S., Zaremba, M. and Borowski J., 6th Mediterranean Congress of Chemotherapy, Taormina, Italy 1988, Abstr. 358, p. 164.
4. Andruszkiewicz R., Milewski S., Zieniawa T. and Borowski E., *J. Med. Chem.*, **33**, 132 (1990).
5. Woynarowska B., Chmara H. and Borowski E., *Drugs Exptl. Clin. Res.*, **5**, 181 (1979).
6. Borowski E., Zieliński J., Zimiński T., Falkowski L., Kołodziejczyk P., Jereczek E. and Adlerkreutz, H., *Tetrahedron Lett.*, **45**, 3909 (1970).
7. Borowski E. and Cybulska B., *Nature*, **213**, 1034 (1967).

8. Malewicz B. and Borowski E., *Nature*, **281**, 80 (1979).
9. Grzybowska J., Sowiński P., Gumieniak J., Zieniawa T. and Borowski E., *J. Antibiotics*, **50**, 709 (1997).
10. Tempczyk A., Tarasiuk J., Ossowski T. and Borowski E., *Anti-Cancer Drug Design*, **2**, 371 (1988).
11. Tarasiuk J., Garnier-Suillerot A., Stefańska B. and Borowski E., *Anti-Cancer Drug Design*, **7**, 329 (1992).
12. Dzieduszycka M., Martelli S., Arciemiuk M., Bontemps-Gracz M., Kupiec A. and Borowski E., *Bioorg. Med. Chem.*, **10**, 1025 (2002).
13. Dzieduszycka M., Stefańska B., Kołodziejczyk P., Borowski E. and Martelli S., *Il Farmaco*, **42**, 219 (1987).



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