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Phosphinate prodrugs: Past, present and future

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Phosphinic peptides have been widely used for the study of proteases so as to elucidate their function in health and disease by acting as reversible, non-toxic, potent and selective inhibitors. Some of the most interesting targets are Angiotensin Converting Enzyme (blood pressure regulation) and Matrix Metalloproteases (cancer). Nevertheless, the use of phosphinates as drugs presents a challenge with respect to their drug delivery. At physiological pH, phosphinates are negatively charged and due to their polarity are unable to penetrate cell membranes. To overcome this problem, esters can be used as prodrugs. These esters should meet several requirements, such as chemical stability/solubility of the prodrug in the gastrointestinal tract, good permeability across cell membranes and finally the efficient release of the drug at the target. Several kinds of such phosphinate esters have been developed and have been used in clinical trials. We have recently designed and developed a new class of phosphinate esters and their biological evaluation is underway.

Biography

Magdalini Matziari is a lecturer at Xi'an-Jiaotong Liverpool University, Department of Chemistry. After receiving a Chemistry degree from the University of Ioannina in 1996, she pursued graduate studies in the University of Athens, Greece, where she received a M.Sc. (1999) and a Ph.D. degree (2001) in Organic Chemistry, orientated to the synthesis of metalloproteases inhibitors. She received the award of Unesco-L'Oréal, for "In Women in Science" concentrating excellence program in 2006 for her contribution in the Material Science area. In her graduate and postdoctoral research, she developed new methods of synthesis and diversification of phosphinic pseudo-peptides. Her current research interests include design and synthesis of protease inhibitors, the chemistry of phosphorus-based compounds and amino acid derivatives. Currently, she is working on the development of antivirals towards HIV and hepatitis, as well as drug delivery systems.

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