

# Medicinal Chemistry & Computer Aided Drug Designing

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## Development of new antibiotics targeting shikimate kinase: From concept to practice

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According to the World Health Organization, antibiotic resistance is becoming a public health emergency of unknown proportions. Therefore, there is a great interest in the discovery of novel drugs and therapies to tackle antimicrobial resistance, in particular drugs that target unexplored essential processes for bacterial survival. For this purpose, a detailed knowledge of the catalytic mechanism, the binding determinants and the essential motion for catalytic turnover of selected enzymes involved in biosynthetic pathways or processes that do not have mammalian homologs, but are essential for bacterial survival, can be valuable for the rational design of these mimetics (inhibitors) that can be used as drugs. Our research group is studying the possible development of new antibiotics whose mode of action is based on the selective and effective inhibition of an essential enzyme in bacteria that does not have any counterpart in human cells, shikimate kinase (SK). This enzyme is essential in relevant pathogenic bacteria such as *Mycobacterium tuberculosis*, *Helicobacter pylori* and *Pseudomonas aeruginosa* and catalyzes the stereospecific phosphorylation of the C3 hydroxyl group of shikimic acid by transferring the  $\gamma$ -phosphate group of ATP to the hydroxyl group to provide shikimate 3-phosphate and ADP. Here, we report results from NMR, biochemical, structural and molecular dynamics simulation studies that help understand the catalytic mechanism of the SK enzyme. Based on these results, several competitive inhibitors of the enzyme were designed. Our recent results on this project will be presented.

### Biography

Concepción González-Bello has obtained her PhD at the University of Santiago de Compostela (USC, Spain) in 1994. She did two Pre-Doctoral stays in the University of Gent (Belgium) with Professor Vandewalle and in the Scripps Research Institute (USA) with Professor Nicolaou. After a Postdoctoral stay in the University of Cambridge (UK) with Professor Abell, she joined USC as an Assistant Professor, was promoted to Associate Professor in 2003 and obtained the Spanish habilitation to Full Professor in 2011. She is Author of more than 65 papers and several book chapters. She is a Member of the ChemMedChem International Advisory Board.

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