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Design, synthesis and testing of novel classes of inhibitors against metallo-β-lactamases: Towards drug leads to combat antibiotic resistance

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Nowadays, antibiotic resistance incidence is increasing as antibiotics are overprescribed. Since bacteria are able to evolve resistance to new antibiotics (by β-lactamases production) and can transfer genes for antibiotic resistance between unrelated species, standard treatments become ineffective. β-Lactamases are classified into serine-β-lactamases (SBLs) and metallo-β-lactamases (MBLs). It is well known that clavulanic acid can effectively inhibit serine β-lactamases (SBLs). Nonetheless, society is in urgent need of metallo-β-lactamases (MBLs) inhibitors as clinically approved inhibitors for MBLs are not yet available. IMP-1, a clinically significant MBL has been reported to cause infections such as pneumonia and wound infections. In this research, novel inhibitors against IMP-1 MBL were designed base on the excellent competitive inhibition properties of L-captopril and D-captopril. Synthesis of the designed IMP-1 inhibitors was completed via three steps reaction (methylation, coupling, and base hydrolysis to remove both methyl ester and thioester). All synthesised compounds including the novel inhibitors and their precursors were tested against IMP-1 enzyme. Potent compounds were selected for further testing to determine the inhibition constant, Ki value.

Biography

Yusralina Yusof has obtained her Bachelor degree from Keio University, Japan in 2005 and Master degree from the same university in 2007. She worked in Universiti Malaysia Sarawak, Malaysia for 5 years before starting PhD research at The University of Queensland, Australia.