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Synthesis of novel furan-based antituberculars potentially targeting the methionine aminopeptidases (*Mt*MetAP1a)

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Methionine aminopeptidase (MetAP) carries out an essential function of protein N-terminal processing in many bacteria and is a promising target to develop novel antitubercular agents. MetAP is divided into two subtypes, namely type 1 and type 2. Eukaryotic cells have both subtypes, and prokaryotic cells have only one, which codes for a type 1 MetAP. *Mycobacterium tuberculosis* has two MetAP genes and both belong to type 1 MetAP: *Mt*MetAP1a and *Mt*MetAP1c, which are essential for its *in vivo* survival and pathogenicity1.

As furan-based compounds have shown to be promising antitubercular agents as MetAPs inhibitors2, we planned the design and synthesis of new derivatives functionalizing 2 and 5 positions of the furane ring (Figure 1), starting from our hit compound, MM40. This latter is the most potent competitive MbtI inhibitor to date identified and exhibited a promising antibiotic activity. MbtI is the salicylate synthase from *Mycobacterium tuberculosis* which catalyzes the first step in mycobactins biosynthesis, that is a validated target for fighting tuberculosis3. These compounds could be synergically able to act on MetAPs and MbtI, leading to new antituberculars.

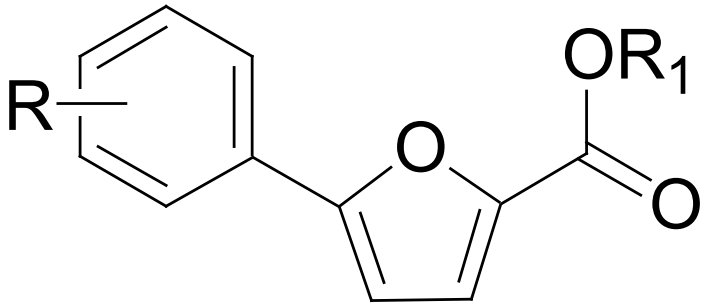

Figure 1. General structure of the new derivatives

Biography

Arianna Gelain graduated in Medicinal Chemistry and Technology and achieved her PhD degree in Medicinal Chemistry at University of Milan. She is researcher at Departement of Pharmaceutical Science and assistant professor at faculty of pharmacy. She is co-author of 31 papers, 6 reviews, published in peer reviewed journals and 1 book chapter.

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