Design, synthesis and biological evaluation of Pfa-M1 inhibitors as potential antimalarial agents

Mounir Al Masri*[1]

[1]Chimie organique et bioorganique (COB) – CNRS : UMR7015, Université de Haute Alsace - Mulhouse, Ecole Nationale Supérieure de Chimie de Mulhouse – 3 Rue Alfred Werner 68093 MULHOUSE CEDEX, France

Résumé

The M1 aminopeptidases catalyze the cleavage of amino acids from the N-terminus of proteins or peptides. They belong to the sub family MA (E) and are also known as Gluzincins with one essential catalytic zinc ion in the active site. M1 aminopeptidases are widely distributed in animal cells, plants, bacteria, parasites and fungi. These enzymes play important biological roles (e.g. angiotensin system, immune system, and in inflammation) and are involved in many associated diseases[1],[2]. Our research group has previously reported the development of potent and selective inhibitors of APN/CD13. This allowed us to identify aminobenzosuberone core as a promising scaffold that demonstrates an exceptional selectivity towards the M1 aminopeptidase family.
In this work we focus on the development of potent and selective inhibitors of *Pfa*-M1. This M1 aminopeptidase plays a major role in *plasmodium* life cycle[3], [4]; it is involved in the last step of hemoglobin breakdown by hydrolyzing dipeptides into essential amino-acids[5].

Hereby, we present our most recent advances in the syntheses of the aminobenzosuberone analogues, SAR studies, 3D structures as well as pharmacological and pharmacokinetic data.

Mots-Clés: SAR studies, 3D structures, pharmacological and pharmacokinetic data.

*Intervenant