SAR Determination of GE81112A

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In the past 50 years, not a single novel antibiotic class against Gram-negative bacteria has been marketed. The lack of new drugs combined with a steady increase in antibiotic resistance, may lead to a significant increase in mortality in the near future. These pathogens rated “critical” due to antibacterial resistance by the WHO. Whereas all belonging to the group of Gram-negative bacteria, therefore the development of novel drugs against these microorganisms is of utmost importance.

GE81112 is a tetrapeptidic natural product (cf. figure 1) with a rare bioactivity against Gram-negative bacteria. The physicochemical properties of this compound suggest it to be an ideal starting point for a medicinal chemistry campaign with the aim of turning this natural product into a lead candidate for drug development.

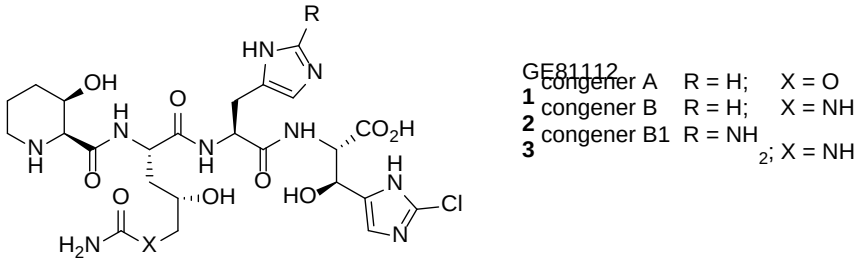

Figure 1: Structure of the three congeners of GE81112.

It is our current goal to establish the SAR by total synthesis of selected derivatives. Furthermore, variation of physicochemical properties and incorporation of various structural motifs should provide insight into the relationship between structure, bacterial uptake and frequency of resistance.

Some of these derivatives will aim at changing the tissue distribution in order to provide a viable advanced lead candidate for different applications such as urinary tract infections or septicemia.