

Zincophorin – biosynthesis in *Streptomyces griseus* and antibiotic properties

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Abstract

Zincophorin is a polyketide antibiotic that possesses potent activity against Gram-positive bacteria, including human pathogens. While a number of total syntheses of this highly functionalized natural product were reported since its initial discovery, the genetic basis for the biosynthesis of zincophorin has remained unclear. In this study, the co-linearity inherent to polyketide pathways was used to identify the zincophorin biosynthesis gene cluster in the genome of the natural producer *Streptomyces griseus* HKI 0741. Interestingly, the same locus is fully conserved in the streptomycin-producing actinomycete *S. griseus* IFO 13350, suggesting that the latter bacterium is also capable of zincophorin biosynthesis. Biological profiling of zincophorin revealed a dose-dependent inhibition of the Gram-positive bacterium *Streptococcus pneumoniae*. The antibacterial effect, however, is accompanied by cytotoxicity. Antibiotic and cytotoxic activities were completely abolished upon esterification of the carboxylic acid group in zincophorin.

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