Resistance and target of aminopolyol peptide antibiotic paenilamicin

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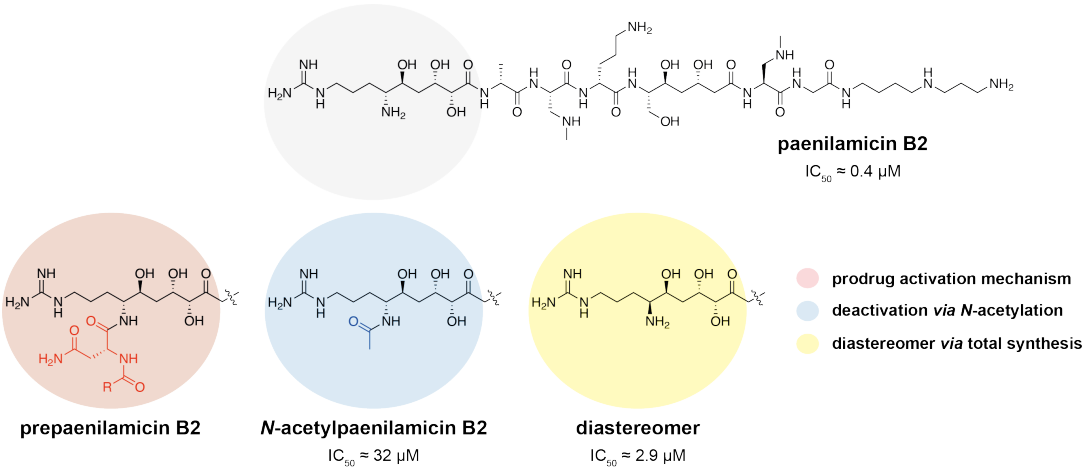
The Gram-positive bacterium *Paenibacillus larvae* is the causative agent of the devastating honey bee disease American Foulbrood. Paenilamicin is an unusual cationic antibacterial and antifungal peptide, which is encoded by a PKS-NRPS hybrid gene cluster found in *P. larvae*.[1] The biosynthesis of paenilamicin is proposed to follow a prodrug strategy[2] by activating prepaenilamicin by a membrane-bound peptidase PamJ, which is presumably involved in a resistance mechanism. Genome mining has revealed a gene in the paenilamicin gene cluster encoding an acetyl-CoA-dependent *N*-acetyltransferase PamZ that indicates an additional self-resistance mechanism by deactivating paenilamicin through regioselective *N*-acetylation.[3] *P. larvae* has developed a dual self-resistance strategy towards paenilamicin to protect itself from harm while defending its ecological niche. In addition, the access to the total synthesis of paenilamicin and its diastereomers has enabled the evaluation of the biological activity.[4] Paenilamicin has indicated an IC_{50} of approx. 0.4 µM in an *in vitro* translation inhibition activity assay and is proposed to be a potential ribosome inhibitor. In sum, these findings revealed the N-terminal fragment of paenilamicin as an important pharmacophore.



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