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Increased Availability and Efficacy of Aminoglycosides

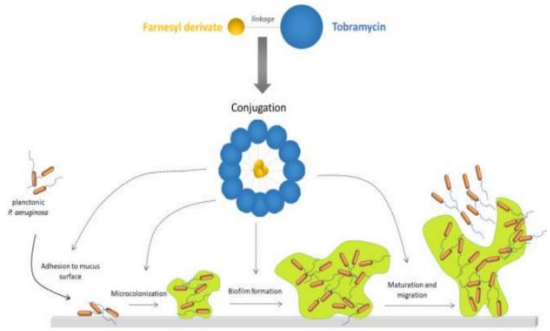
Keywords: Aminoglycosides, farnesyl conjugates, biofilm targeting, controlled release, antimicrobial therapy.

INVENTION NOVELTY

This innovation introduces a novel approach to enhance the efficacy of aminoglycoside antibiotics, such as tobramycin, through the covalent conjugation with farnesyl fractions. The resulting conjugates display reduced hydrophilicity, improved antibacterial activity, and self-assembly properties, enabling excipient-free drug assemblies with controlled release profiles. These conjugates release aminoglycosides in acidic environments like biofilms, where they exhibit superior antimicrobial efficacy and dual-action capabilities due to the quorum sensing inhibition (QSI) properties of farnesyl.

VALUE PROPOSITION

The technology offers a groundbreaking solution to combat gram-negative bacterial infections, such as those caused by *Pseudomonas aeruginosa*, with enhanced therapeutic efficiency and reduced toxicity. By enabling controlled drug release specifically in biofilms, the conjugates improve the eradication of resistant bacterial colonies while minimizing the need for high doses of antibiotics. Their excipient-free nature and self-assembly capabilities streamline production and enhance drug loading capacity, making them an ideal candidate for clinical applications targeting multidrug-resistant infections.



Excipient-free assemblies of Tombramycin and Farnesyl derivatives which prolong the availability of Tombramycin and enhance its efficiency in all stages of infection.

TECHNOLOGY DESCRIPTION

Aminoglycoside-farnesyl conjugates are synthesized in a one-step reaction with a 95% yield, using imine/enamine linkages between aminoglycoside amine groups and farnesyl aldehyde groups. These linkages are stable at pH > 6.0 and release aminoglycosides in acidic conditions, enabling targeted delivery within biofilms. The conjugates exhibit self-assembly properties, forming uniform nanoparticles with diameters tunable between 85 and 900 nm and a polydispersity index < 0.3. The dual-active conjugates leverage the antibacterial and antifungal properties of farnesyl while achieving up to 100% drug-loading capacity. Superior antimicrobial efficacy was demonstrated by MIC and MBEC assays against *E. coli* and *P. aeruginosa*, showing a 16-fold improvement over free tobramycin.

COMMERCIAL OPPORTUNITY

The invention is offered for licensing and co-development.

DEVELOPMENT STATUS

The antimicrobial activity was shown in standard in vitro assays. Studies on kinetics and mechanisms are ongoing. Synthesis of conjugates can be scaled up easily. Synthesis technique is applicable for other active ingredients.

PATENT SITUATION

The patent was granted in the EU (EP3 645 046 B1) on April 28, 2024, and in the USA (US 11,839,658 B2) on December 12, 2023

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