Chloramphenicol glycoside derivative: a way to overcome its antimicrobial resistance and toxicity

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Triggered by the urgent need to tackle the global crisis of multidrug-resistant bacterial infections, in this work, we present a way to overcome chloramphenicol resistance by introducing modifications based on the glycosylation of its hydroxyl groups. The synthesized derivatives demonstrate complete resistance to the action of recombinant chloramphenicol acetyltransferase (CAT) from *Escherichia coli* and efficacy against methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli* ESBL, and *Pseudomonas aeruginosa* ATCC 27853. Glycosylation gives chloramphenicol an additional advantage - the stable glycosidic form is less toxic to human dermal fibroblasts and has significantly better water solubility than non-glycosylated chloramphenicol. Using a specific glycosidase, chloramphenicol can be almost immediately released from the stable prodrug at the site of polybacterial infections.

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