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Semisynthetic glycopeptide antibiotics

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Stellingen

Bijbehorende bij het proefschrift

Semisynthetic Glycopeptide Antibiotics

1. Although the ‘low-hanging’ fruit in antibiotic discovery may have been plucked a long time ago, this does not mean we cannot utilize this ‘fruit’ to achieve the development of novel antibiotics (*This thesis*)
2. There is no ‘text book’ way of designing improved glycopeptides. It relies on a subtle interplay between the nature and positioning of the substituent(s) (*Chapter 1*)
3. The guanidino lipoglycopeptides have the potential to be the new ‘best in class’ glycopeptide antibiotics, if an improved therapeutic window is proven (*Chapter 2 and 3*)
4. If synergy is proven between glycopeptide and synergist, it is worth assessing the potency once covalently linked (*Chapter 1 and 4*)
5. Semisynthesis is a more viable strategy compared to total synthesis in the development of glycopeptide antibiotics.
6. While MIC is valuable measure for initial activity assessment, one should keep in mind the relevance for therapeutic intervention in patients, as growth phase and environment can be vastly different.
7. Although a compound might kill bacteria, that does not yet make it an antibiotic. Potency compared to a control antibiotic as well as selectivity/toxicity need to be established as well.
8. Antibiotics have a unique set of physicochemical properties compared to ‘standard’ drugs. When selecting libraries to screen to discover new antimicrobials, this differentiation, as well as differences for compound with Gram-positive and Gram-negative activity, must be taken into account. (*J. Med. Chem.* 2008, 51, 10, 2871–2878)
9. We have a global responsibility to ensure improved antibiotic stewardship to prevent potential outbreaks, especially in low- and middle-income countries, as drug-resistant microorganisms do not abide to borders. (*The Lancet.* 2022, 399, 10325, 629-655)
10. MIC should be pronounced as ‘em-ai-si’, not ‘mik’. You would not pronounce IC₅₀ as ‘ik₅₀’.
11. Just as medicine approved in the clinic should not be advertised, products with no evidence of medical benefit should most definitely not be allowed to advertise those unproven claims.
12. PhD students should be exposed more to potential career options outside of academia, as most of them end up in other career paths.