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Glycopeptide Antibiotics

Mechanism of Action and Recent Developments

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4.1 Introduction

Glycopeptide antibiotics are an important class of antibiotics that inhibit bacterial cell wall biosynthesis. Vancomycin (Figure 4.1a) was the first member of this class of antibiotics to be discovered by Eli Lilly and approved for clinical use by the Food and Drug Administration (FDA) in 1958 (Butler et al. 2014). The discovery of vancomycin came at a time when resistance to most widely used antibiotics, β-lactam, had emerged. It has been used as the antibiotic of last resort for treatment of multidrug-resistant Gram-positive bacterial infections since then. It is still vital for the treatment of Gram-positive bacterial infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile*. Later in 1988, teicoplanin (Figure 4.1a), which was discovered in the Lepetit Research Center (Milan, Italy), was approved for use in Europe for treating similar Gram-positive infections (Butler et al. 2014). The glycopeptides were isolated from the soil bacteria *Actinomycetales*. Numerous other glycopeptides have been discovered since then, which never made it to the clinic. A year after the discovery of vancomycin, ristocetin was isolated. Although it seemed to be a promising antibacterial agent, it was discontinued from clinical use because it caused platelet aggregation in patients missing a platelet factor in platelet-type von Willebrand disease (Jenkins et al. 1974; Meyer et al. 1974). Glycopeptides such as actaplanin and avoparcin were shown to promote growth in farm animals. The use of avoparcin was banned due to

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