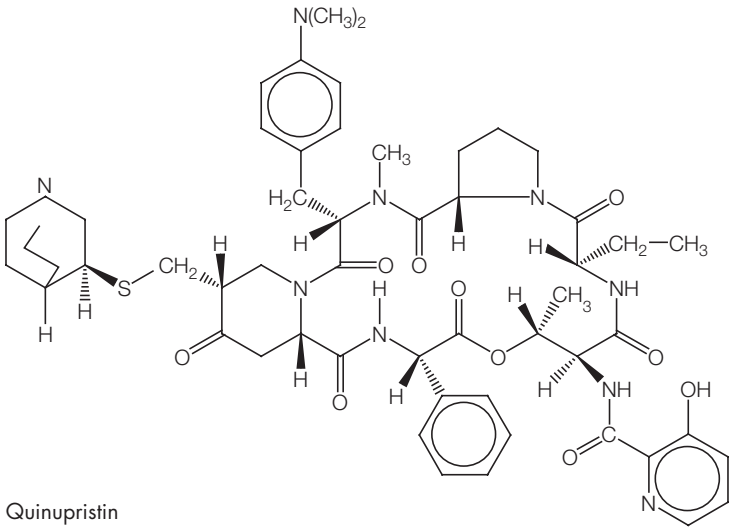


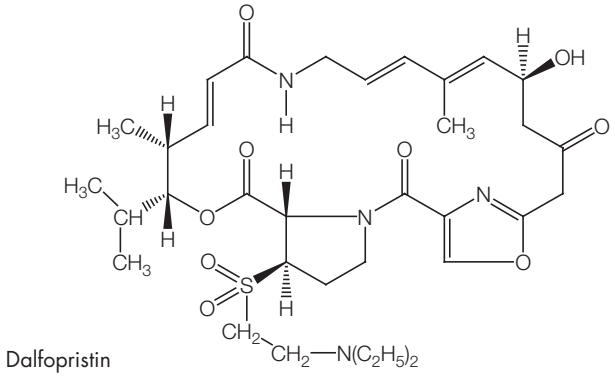


Figure 77.1. Chemical structure of quinupristin and dalfopristin.

*Acinetobacter* species are commonly resistant to quinupristin–dalfopristin because of cell wall impermeability (Maraki *et al.,* 2014; Bouanchaud, 1996, 1997; Von Eiff *et al.,* 2000).

## 2b. Emerging resistance and cross-resistance

The mechanisms of resistance in staphylococci and *Enterococcus faecium* to quinupristin–dalfopristin are summarized in Table 77.2. Two genes, *vat(D)* and *vat(E),* confer resistance to group A streptogramins, and another two (*vgb* and *erm*) confer resistance to group B streptogramins. These genes have been found in *Enterococcus* species. Quinupristin–dalfopristin resistance, which was caused by a combination of *erm* and *vat* genes, was first found among *S. aureus* clinical isolates in China (Yu *et al.,* 2014). Resistance to streptogramins is mediated by three possible mechanisms: drug inactivation by enzymes, efflux or active transport of the antibiotic out of the cell, and plasmid-coded conformational alterations in ribosomal target binding site (Nadler *et al.,* 1999). The third is the most common expression of bacterial resistance to streptogramins. Constitutive or induced expression of macrolide–lincosamide–streptogramin B resistance occurs in some staphylococcal species (Eliopoulos *et al.,* 1998; Luh *et al.,* 2000). Drug inactivation can occur in some staphylococcal and enterococcal species by production of a quinupristin-inactivating hydrolase or a dalfopristin-inactivating acetyltransferase. Some species of coagulase-negative staphylococci and *E. faecium* become resistant by active efflux of dalfopristin (Cocito *et al.,* 1997; Johnson and Livermore, 1999). Emerging resistance during the treatment of infections caused by vancomycin-resistant *E. faecium* has generally been to both components of the formulation (Linden *et al.,* 1997). The antibiotic susceptibility of glycopeptide-resistant enterococci was investigated in a Tertiary Greek Hospital. Seventy consecutive glycopeptide-resistant enterococci were tested. Sixty-two isolates were identified as *E. faecium* (88.6%), and 8 (11.4%) as *E. faecalis*. All strains were susceptible to linezolid and daptomycin, whereas 17.1% (12/70) and 11.4% (8/70) were resistant to quinupristin–dalfopristin and tigecycline, respectively. All *E. faecalis* isolates were resistant to quinupristin–dalfopristin, and 4 of 62 (6.5%) *E. faecium* isolates were resistant to quinupristin–dalfopristin (Sambatakou *et al.,* 1998).

There is no reported cross-resistance between quinupristin–dalfopristin and these agents when tested by the MIC method. This is probably due to the mechanism of action of quinupristin–dalfopristin, which differs from that of other classes of antibacterial agents such as beta-lactams, aminoglycosides, glycopeptides, quinolones, macrolides, lincosamides, and tetracyclines (Sambatakou *et al.,* 1998; Finch, 1996, Schmitz *et al.,* 1999).