PROPOSAL TO NAME THE VANCOMYCIN-RISTOCETIN LIKE GLYCOPEPTIDES AS DALBAHEPTIDES

Sir:

The appearance of novel pathogens refractory to established drugs (such as many coagulase-negative Staphylococci, corynebacteria, *Clostridium difficile*) and the resurgence of old but modified pathogens (such as the multiresistant *Staphylococcus aureus* and the highly gentamicin-resistant Enterococci) has stimulated the search and development for novel antibiotics. Thus, in the past few years we have witnessed the discovery of numerous antibiotics active on refractory microorganisms, some of which are now under clinical development. Many of these antibiotics have in common a peptidic structure and the presence of sugars and sometimes fatty acid residues.

Particularly numerous is a sub-group of peptidic antibiotics, the vancomycin-ristocetin type, often referred to as "glycopeptides". Close to one hundred natural and a large number of semisynthetic molecules of this subgroup have been described to date[1].

The term glycopeptide is used in the natural product literature[2,3] to describe such diverse substances as the antibacterial vancomycin, and related compounds; the antiblastic bleomycins and congeners; the potentiator of β-lactams, antibiotic SQ28504; the broad spectrum antibiotic myomycin; the inhibitors of angiotensin converting enzyme, muraceins; the antibacterial ramoplanin (A16686), just to cite a few. These substances have in common only the presence in their molecule of at least two amino acids bound by a peptidic bond and a sugar (or modified sugar) residue. It is clear that the so called vancomycin-ristocetin like glycopeptides and their aglycones form a distinct subclass, for which, however, no specific descriptive name is available.

A term is descriptive of a set of objects if it describes the distinctive character of the set, *i.e.* one which is both unique and common to all members of the set. The distinguishing feature of the glycopeptides of the vancomycin-ristocetin type is their modified linear heptapeptidic structure which forms the basis for their specific mechanism of action, *i.e.* complexation with the D-alanyl-D-alanine terminus of the peptidoglycan pentapeptide[4]. For this reason, we have proposed to call these substances dalbaheptides from D-alanyl-D-alanine-binding antibiotics with heptapeptide structure[1].

Here we would like to reiterate this proposal as follows: The term dalbaheptides would refer to all members of the vancomycin-like glycopeptides including the aglycones. Furthermore, one would refer to glycodalbaheptides (*e.g.*, vancomycin, ristocetins, avoparcins, orienticins) and lipoglycodalbaheptides (*e.g.*, teicoplanins, kibdelins, parvodicins).

The use of these terms would help to separate this class of antibiotics from all the unrelated glycopeptides such as those cited above and others such as ramoplanin, a glyco(lipodepsi)peptide[5].

This latter substance is not a linear heptapeptide and although an inhibitor of cell wall biosynthesis, does not interact with the D-alanyl-D-alanine containing structures of the cell wall[6]. Therefore it does not belong to the dalbaheptide subclass. The exclusion of ramoplanin from dalbaheptides would intuitively support the notion of a difference in cellular target and lack of cross-resistance between this group and ramoplanin. Indeed, strains of Enterococci with plasmid-mediated high level resistance to vancomycin are cross-resistant to all tested dalbaheptides (although at different levels) but are sensitive to ramoplanin (P. COURVALIN; personal communication. Also our data).

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