A PROPOSED NUMBERING SYSTEM FOR POLYETHER ANTIBIOTICS

JOHN W. WESTLEY

Chemical Research Department, Hoffmann-La Roche Inc., Nutley, New Jersey 07110, U.S.A.

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The structure, activity and biosynthesis of the streptomyces-produced polyether antibiotics were recently reviewed. Since that publication, more of these naturally occurring ionophores have been reported and because of the rapidly increasing number of compounds being added to the polyether class, a consistent system of numbering is needed as an aid in comparing the chemistry and biological action of these versatile antibiotics.

A common feature of the polyether antibiotics is the presence of a single carboxylic acid function at one end of the molecule which represents the last carbon added during the biosynthesis of the antibiotics' polyketide precursors. In the proposed system, this carbon is designated C-1 and the carbon backbone of the molecule is numbered consecutively to the terminal carbon. In the case of lasalocid, this terminal carbon (C-24) is derived from the methyl of the acetate unit involved in initiation of the compound's biosynthesis.

By analogy with lasalocid, the starting point in the biosynthesis of nigericin, grisorixin, salinomycin, antibiotic A204A and septamycin is C-30 (Fig. 1) suggesting that fifteen is the preferred number of sub-units in the biosynthesis of the carbon skeleton of the polyether antibiotics. An exception to the even numbered polyether backbones is lyso-cellin (C-23) indicating propionic acid as initiator and eleven sub-units involved in the biosynthesis of that particular antibiotic.

Another characteristic of the polyether antibiotics is the prevalence of C-alkyl groups. In the case of lasalocid, the four branched methyls present (in contrast to C-24) are propionate derived and the three ethyls are derived from the C-3, 4 carbons of butyric acid. The system proposed for numbering these branched alkyl groups follows the steroid model as illustrated for Ro 21-6150. The presence of a sugar-like function in I necessitates continuing the carbon numbering into the 2, 3, 6-trideoxy-4-O-methyl-D-erythrohexapyranose moiety (also present in salinomycin, septamycin and antibiotic A204A).

Oxygen and carbon atoms are differentiated in the proposed system with the oxygen numbers in parentheses as illustrated for antibiotic X-206. This will simplify assign-
Fig. 1. Structures of typical polyether antibiotics

Nigericin  \( R = \text{OH} \)  \( \text{C}_{40}\text{H}_{68}\text{O}_{11} \)

Grisorixin  \( R = \text{H} \)  \( \text{C}_{40}\text{H}_{68}\text{O}_{10} \)

Salinomycin  \( \text{C}_{42}\text{H}_{70}\text{O}_{11} \)

Antibiotic A204A  \( \text{C}_{49}\text{H}_{84}\text{O}_{17} \)

Septamycin  \( \text{C}_{48}\text{H}_{82}\text{O}_{16} \)

Lasalocid  \( \text{C}_{34}\text{H}_{54}\text{O}_{8} \)

Lysocellin  \( \text{C}_{34}\text{H}_{60}\text{O}_{10} \)
ment of trivial names for O-alkyl and desoxy analogues and can be used to distinguish methoxyls in those polyether antibiotics containing four or five -OMe groups such as septamycin and antibiotic A204A (Fig. 1). As proposed for the carbon system, the oxygen numbering would be continued in antibiotics having the hexapyranose moiety such as 1 in which the glycoside ether between C-41 and C-45 is O-12 and the methoxyl group is at O-13.

The system proposed in this communication (1 and 2) is easily applied to all the known antibiotics of the polyether class and the advantages of a universal method of numbering are self-evident.

References