Cephalosporins and its nomenclature

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Abstract-Cephalosporins are readily used as antibiotics since ages. The naming of these compounds is done in varied ways. This article shows the various forms of nomenclature in cephalosporins.

Keywords: Cephalosporins, nomenclature

Introduction

*Cephalosporium acremonium* is the first fungal source of cephalosporins which was isolated by Brotzu in 1948 [1] near a sewer outlet from the sea in the sardinian coast. Interestingly, the crude filtrate of its culture was observed to suppress the *in vitro* growth of *S. aureus*. Therefore, this filtrate was used for the treatment of typhoid fever as well as infections associated with staphylococcal. Further investigation in this direction lead to the development of five steroidal antibiotics which were called cephalosporins (P1-P5) [2-4] and one major antibiotic called cephalosporin N. Cephalosporin N was found to be significantly (2-6 times) active against gram negative organisms whereas activity against gram positive organisms was found to be very less (100 times lesser) [1,5,6]. In addition, the crude culture of this fungus was found to contain three other antibiotics called cephalosporin C, cephalosporin P and cephalosporin N [7-8].

The structure of Cephalosporin C (I) is depicted in Fig 1.1 which have characteristic D-α-amino acid moiety. Infrared spectroscopy of this molecule shows an absorption band at value of 5.62µ which confirms the presence of β-lactam ring which yields carbon dioxide on reaction with warm acid via hydrolysis.
The nucleus 7-aminocephalosporanic acid (7-ACA) resembles with 6-aminopenicillanic acid (6-APA) having a penam ring (2) instead of the cephem ring (3) found in the case of cephalosporins. Although, according to IUPAC rules, the numbering of 7-aminocephalosporanic acid (7-ACA) starts from nitrogen at 1 position (Fig 1.1) and in this chapter, the numbering according to IUPAC system has been followed for naming different cephalosporins. In literature [9], the numbering followed for both the penam and the cephem rings starts from sulfur atom, thereby the nitrogen atom is designated as 4 and 5 position in penam and cephem ring, respectively (Fig 1.2). The same has been approved vide IUPAC recommendations, 2004 [9] and has been used for the purpose of spectroscopic assignments in Chapter 2.
The \(\beta\)-lactam ring in penicillin is more constrained due to the presence of a five membered ring attached to it which contributes towards the degradation of the ring system in the presence of the nucleophiles like hydroxide ions as well as in the presence of metal ions. This ring system degrades at acidic pH also. This degradation is avoided clinically by buffering the solution of penicillins at pH 6.0-6.8. Due to the instability of the \(\beta\)-lactam ring, it can easily be attacked by \(\beta\)-lactamases which inactivates the antibiotic. Further development in this regard led to the discovery of cephalosporins wherein the \(\beta\)-lactam ring is appended to a six membered ring making the structure less strained and therefore less prone to nucleophillic attack or attack by \(\beta\)-lactamases. Greater stability of cephalosporins gives them broader range of activity than penicillins.

The modifications at the cephalosporin C (i.e. 7-aminocephalosporanic acid) nucleus lead to the formation of different type of derivatives which had more promising properties as antibacterial agents. Some of the derivatives which have been developed by such modifications are clavulanic acid, thienamycin, nocardicins, and cephemycins. These compounds were found to be of greater importance because of their wide range of activity against gram negative and gram positive strains.

**Nomenclature**

The chemical nomenclature of cephalosporins is somewhat complex than their penicillins counterparts due to the presence of a double bond in the dihydrothiazine ring and the substituents at 3-position. The fused ring system is designated by chemical abstracts the name as 5-thia-1-azabicyclo[4.2.0]oct-2-ene. Accordingly, the IUPAC names of all cephalosporins are derived from it by mentioning different substituents at different positions of this eight membered bicyclic system. Fig 1.3 represents the systematic IUPAC name for some of the cephalosporins.

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\text{a) } (6R,7R)-3-[(5\text{-methyl-1,3,4-thiadiazol-2-yl})\text{-amino}]\text{-carboxylic acid}
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\text{b) } (6R,7R)-7-[(2R\text{-amino-2-phenylacetyl})\text{-amino}]\text{-carboxylic acid}
\]
yl)thio[methyl]-8-oxo-7-[(1H-tetrazol-1-ylacetyl)amino]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid“

(cefazolin) (cefaclor)

Fig 1.3 Systematic IUPAC name of Cefazolin (4), Cefaclor (5), Cefixime (6) and Cefepime (7)

Cepham is the common name given to bicyclic ring system containing oxygen as part of lactom carbonyl. In this regard, 3-cephams is the common terminology used for the nomenclature of cephalosporins to identify the double bond position according to the numbering shown in Fig. 1.2. Although some cephalosporins, that have 3-acetoxy methyl group, have been named as derivatives of cephalosporanic acids [10].
Conclusion: The article shows the various types of nomenclature used for the cephalosporins. This study enables the easy IUPAC naming of the compounds.

References: