

3.3.1.2.3 Antipseudomonal Penicillins: Carboxypenicillins and Ureidopenicillins

In order to increase Gram-negative coverage and particularly against *Pseudomonas aeruginosa*, a carboxyl group was added to the penicillin structure to produce carboxypenicillins (ticarcillin). This modification enhanced Gram-negative coverage by improving its bacterial penetration through the cell wall. Their spectrum of activity includes *Enterobacter*, *Providencia*, *Morganella*, indole-positive *Proteus*, and *P. aeruginosa*.

To produce piperacillin, an ureido group plus a piperazine side chain was added. The Gram-negative coverage of piperacillin includes that of the carboxypenicillins plus coverage against *Klebsiella*, *Serratia*, and *Enterococcus* and increased anaerobic coverage (Miller 2002; Bush and Bradford 2016).

3.3.2 Cephalosporins

Cephalosporins are derivatives of the fermentation products of the fungus *Acremonium chrysogenum*. Its cephem core structure is called 7-aminocephalosporanic acid (7-ACA) (Figure 3.3). The chemical structure in radicals R1 and R2 define the different cephalosporin molecules as well as their antibacterial activities and pharmacokinetic properties (Garau et al. 1997; Fernandes and Prudêncio 2013).

Cephalosporins are more resistant against hydrolysis by beta-lactamases than penicillins; therefore, they showed a broader spectrum of activity and they are classified into five generations according to their antibacterial activity (Fernandes and Prudêncio 2013). In general, the first- and second-generation cephalosporins have good activity against Gram-positive microorganisms, and the third- and fourth-generation are more active against Gram-negative pathogens. However, *Listeria*, *Pasteurella* spp., enterococci, and all methicillin-resistant staphylococci are cephalosporin resistant (with the exception of fifth-generation cephalosporins).

3.3.2.1 First Generation

The following cephalosporins are included: cephalothin, cephapirin, cefazolin, cephalexin, cephradine, and cefadroxil. They are very active against Gram-positive cocci, except for enterococci and MRSA, moderately active against some Gram-negative rods (*E. coli*, *P. mirabilis*, and *Klebsiella*), and poorly active against *Moraxella catarrhalis*, *H. influenzae*, and *Neisseria* spp. Anaerobic bacteria are often sensitive, excluding *Bacteroides fragilis*. None of the drugs in this group penetrate the central nervous system (CNS), and they are not first choice drugs for any infection.

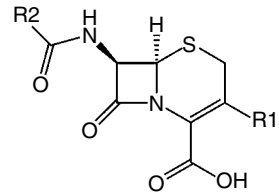


Figure 3.3 7-Aminocephalosporanic acid, core structure of cephalosporins.