BJHBS

Monobactams update on Aztreonam and Prospects for the Development of New Drugs

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Abstract

Introduction: Monobactams belong to the beta-lactam group and are drugs indicated for the treatment of infections caused by aerobic Gram-negative bacteria. Aztreonam is currently the only available representative of the group and, due to its clinical safety profile, efforts have been directed towards the development of new antibacterials in this class. Methodology: This is a narrative literature review that examines articles, books, and documents from various sources in Portuguese, English, and Spanish. The analysis focuses on relevant data regarding aztreonam and related compounds, addressing the main aspects of aztreonam – brief history, chemical structure, mechanism of action, pharmacokinetics, pharmacodynamics, spectrum of action, resistance mechanisms, drug interactions, clinical indications, dosage, use in special situations, and adverse effects – as well as presenting the potential of the aztreonam-avibactam combination and the development of new monobactams. Results and Discussion: Aztreonam has a unique chemical structure, containing a monocyclic beta-lactam ring. Its bactericidal action occurs through the inhibition of penicillin-binding protein-3 (PBP-3), affecting the cell wall synthesis of Gram-negative bacteria. In general, the drug is well-tolerated and causes mild adverse effects. Combinations like aztreonam-avibactam are promising for treating infections caused by multi-drug-resistant bacteria. Studies highlight the need for new compounds, such as LYS228 and BAL30072, which expand the spectrum of action and overcome resistance mechanisms. Conclusion: Aztreonam remains relevant in antimicrobial therapy against Gram-negative infections. The development of new monobactams is a strategy to address increasing bacterial resistance and improve the treatment of complex infections.

Keywords: aztreonam, beta-lactams, monobactams.

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BJHBS, Rio de Janeiro, 2025;24(1):38-48
DOI: 10.12957/bjhbs.2024.85386
Received on 30/11/2024. Approved on 18/03/2025.

Introduction

Beta-lactams are antimicrobial drugs that have the homonymous ring – which is responsible for antibacterial action – in their structure and whose scope includes four main groups of drugs: penicillin, cephalosporins, carbapenem and monobactams.[1] This latter group was described in 1975, in Japan, when researchers detected the production of beta-lactam antibiotics formed by a monocyclic structure – the monobactams –, by bacteria of the species *Nocardia uniformis*.[2]

Further research led to the production of aztreonam, the only drug available in this class, which stands out mainly for its stability against most beta-lactamases.[3] It is a bactericidal antibiotic that interferes with cell wall synthesis and causes bacterial lysis through interaction with penicillin-binding proteins (PBP) of sensitive microorganisms, inducing the formation of long bacterial filaments.[4,5] For some authors, the mechanism of action of aztreonam is similar to that of aminoglycosides, that is, it diffuses through the protein pores in the outer membrane, reaches the periplasmic space and penetrates the inner membrane by means of electron transport. Since this transport depends on energy, anaerobic environments do not permit the penetration of the drug into the cell, which reduces or completely stops its microbicidal action.[6,7]

Moreover, the low binding of the drug to PBP3 in gram-positive pathogens renders aztreonam ineffective against these etiological agents. Consequently, its spectrum of activity is limited to aerobic gram-negative bacteria, so other antimicrobials must be combined to broaden the coverage to include gram-positive and anaerobic bacteria.[7–9]

The medical importance of aztreonam lies in its in vitro activity against most strains of Enterobacteriaceae, even those that are multidrug-resistant, a context that represents a significant public health problem today.[10,11] In addition, aztreonam is able to act on Gram-negative non-sugar fermenters that cause healthcare-related infections – such as *Pseudomonas aeruginosa* – without the intrinsic nephrotoxicity of aminoglycosides.[1,8] In fact, the in-depth and constant study of aztreonam is of great importance, since it is effective against these pathogens (*Enterobacteriaceae* and *P. aeuruginosa*).[12]

Based on these considerations, the objectives of this article are [1] to review the most important features of aztreonam – historical, chemical, pharmacological (mechanism of action, pharmacokinetics, pharmacodynamics, spectrum of action, mechanisms of resistance and drug interactions) and therapeutic (clinical indications, dosage, use in special situations and adverse effects) aspects – and [2] discuss the prospects for the use of the aztreonam-avibactam association and for the development of new drugs of the monobactam class.

Methodology

This paper is a narrative review that aims to describe a specific theme or point of view in a theoretical and contextual way[13] that is important for professional training – and also for lifelong learning –, since it provides readers with the ability to update knowledge in a shorter period of time, although it doesn't provide the methodological data that allows the reproducibility of the search for bibliographic references.[14] Therefore, the design of this study is distinct from a systematic review, which, despite being better structured, has the limitation of answering a specific question through a careful evaluation of studies that provide data – which are collected and analyzed –, in order to support the approach to the proposed question.[13] It should also be highlighted that the literature review is the first step in the synthesis of scientific knowledge, allowing gaps to be filled and opportunities for new research to be seized.[13,15]

Based on these concise notes, references were gathered from articles, books and published documents (produced by government agencies, scientific institutions and specialized bodies), in Portuguese, English and Spanish. The papers selected were read in full to summarize the relevant data, which allowed – through a critical analysis by the authors – the elaboration of results and discussion of the following topics: brief history; chemical structure; mechanism and spectrum of action; pharmacokinetics and pharmacodynamics; resistance mechanisms; drug interactions and adverse effects; clinical indications and dosage; use in special situations; and new monobactams.

Results and Discussion

Brief History

Beta-lactams represent a class of antibiotics of great clinical importance worldwide.[16] The first drug of this class was discovered in 1928 by Alexander Fleming, who noted that a culture of *Staphylococcus aureus* contaminated by a fungus, currently known as *Penicillium chrysogenum*, had its growth inhibited by the action of penicillin.[17]

The description of penicillin G was a milestone for the development of antimicrobial therapy. Since then, other beta-lactams have been made available for the treatment of different infectious conditions, thus revolutionizing the care of people with bacterial infections.[16,18] After the identification of penicillins and cephaloporins, other drugs emerged to increase the spectrum of action and potency of preexisting agents, including monobactams.[19]

The description of monobactams originates from the work of Aoki and collaborators, who identified a monocyclic beta-lactam antimicrobial—initially named nocardicin A—from the fermentation broth of a strain of *Nocardia uniformis subsp. tsuyamanensis*.[20] This isolated compound was the first monobactam discovered, although its antimicrobial potency was too low for clinical application.[4] Subsequent research led, about five years later, to the development of aztreonam—the first, and so far the only, monobactam approved for clinical use. Aztreonam is a synthetic drug developed in 1981, based on structural modifications of the natural monobactam produced by the Gram-negative bacterium *Chromobacterium violaceum*.[4,21]

Chemical Structure

The presence of a beta-lactam ring (β-lactam or beta-lactam), formed by four atoms (ring of four members) is the main characteristic of the chemical structure of aztreonam.[22,23] Lactams are cyclic amides, whose rings are characterized by nitrogen as a heteroatom directly linked to a carbonyl carbon. In the structure of a lactam, the first carbon atom attached directly to the carbonyl is designated alpha (α) and the next carbon atom is designated beta (β). Thus, the term β-lactam indicates that carbon β (in relation to carbonyl) is also bound to nitrogen, characterizing a ring formed by four atoms.[24] The β-lactam ring is present in the chemical structure of a series of antibiotic families called β-lactams antibiotics – including penicillins, cephalosporins, carbapenems and monobactams – and constitutes a fundamental structural portion of the antibacterial activity of all these classes.[25,26] Chemically, the simplest β-lactam, whose atoms that constitute the cycle are not bound to any substituents, is called azetidin-2-one (or 2-oxazetidine). Thus, β-lactams are structurally derivatives of azetidin-2-ones.[27] Aztreonam, whose chemical name is acid 2-[[[1-(2-amino-4-thiazolil)-2-[(2-methyl-4-oxo-1-sulfo-3-azetidinil)amino]-2-oxoetilideno] amino]oxy]-2-methyl-[2S-[2α,3β(Z)]], is a synthetic antibiotic of the monobactam class. Unlike penicillins, cephalosporins and carbapenems, for example, the chemical structures of monobact-

ams do not contain a second ring fused to the β-lactam ring. The name monobactam is thus a reference to the monocyclic structure of this class of β-lactams,[22] as shown in the figure below.

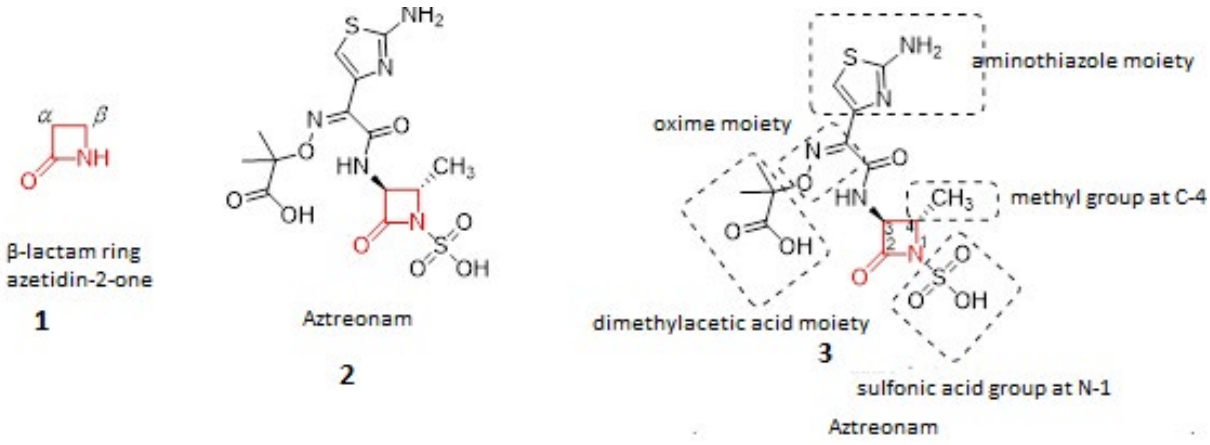

Figure 1. Chemical structure of the β-lactam ring and aztreonam
Source: The authors (2025).

All naturally occurring monobactams have a nitrogen-bound sulfonic acid (-SO3H) group (N-1) in the β-lactam ring, characterizing a structural portion of azetidin-2-one-1-sulfonic acid, along with a variety of substituents linked to carbon 3 of this ring. From the chemical structure of these natural monobactams, Structure-Activity Relationship (SAR) studies led to the development of the chemical structure of aztreonam. In this, the sulfonic acid group linked to N-1 promotes activation of the β-lactam ring. The substituting methyl group in carbon C-4 (β position) increases the stability of the β-lactam ring against the action of β-lactamases, promoting increased antibacterial activity. The aminotiazole oxime portion in the lateral acyl chain linked to C-3 of the β-lactam ring is responsible for potent activity against aerobic Gram-negative bacteria. The two methyl groups and the carboxylic acid group, which constitute the dimethyl acetic acid portion, linked to the oxime group, result in an optimization of the activity against a broad spectrum of Gram-negative bacteria.[22,28,29]

Mechanism and Spectrum of Action

Aztreonam is a bactericidal antibiotic whose mechanism of action is related to the presence of the beta-lactam ring, and it does not induce the production of beta-lactamases. This mechanism involves the interruption of bacterial cell wall synthesis and bacterial death through binding to penicillin-binding protein 3 (PBP-3). The polymerization process required for the formation of peptidoglycan—a key structural component of the bacterial cell wall—depends on the activity of various enzymes, including transglycosylases, transpeptidases, carboxypeptidases, and endopeptidases. PBPs, located on the outer surface of the plasma membrane, exhibit catalytic activity corresponding to these enzymes.[30] Their inhibition by antimicrobials—such as aztreonam—disrupts the synthesis and incorporation of peptidoglycan into the bacterial cell wall.[31] Since autolysins—autolytic enzymes responsible for breaking down the aged peptidoglycan to enable the construction of new cell wall layers—remain active, the ultimate consequence is the formation of defective walls, or even the failure to form them. This results in osmotic lysis of the bacterial cell, caused by the influx of water from the hypotonic external environment into the cell's interior.

The high selectivity of aztreonam for Gram-negative bacteria is due to its strong affinity for the PBPs of these organisms. Its minimal or absent in vitro activity against Gram-positive and an-

aerobic microorganisms results from the weak binding of the drug to the PBPs of these bacteria. However, compared to other monobactam antibiotics, the bactericidal and bacteriostatic concentrations (inhibitory concentrations) of aztreonam have been observed to be very similar.[4]

Aztreonam has specificity against aerobic Gram-negative bacteria. It has high resistance to inactivation by beta-lactamases, both those of plasmid and chromosomal origins (all class B and most classes A and D), which makes this antibiotic efficient even against cephalosporin-resistant microorganisms. Most *Enterobacteriaceae* of community origin are normally sensitive to aztreonam, even at low concentrations (less than 1µg/ml).[32] Currently, Gram-negative bacilli of nosocomial origin may present resistance to aztreonam. It has exclusive activity against aerobic Gram-negative bacteria, except the strains producing beta-lactamases KPC, extended spectrum (ESBLs) and ampicilinase class C (AmpC).[6,21,33] However, most strains of *Enterobacteriaceae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Aeromonas spp.* and *Pasteurella multocida* show sensitivity at low concentrations of this drug. *P. aeruginosa* generally requires high inhibitory concentrations and about a third of the strains of this bacterium are currently resistant to aztreonam. Most strains of *Burkholderia cepacia*, *Stenotrophomonas maltophilia*, *Citrobacter freundii*, *Enterobacter aerogenes* and *Campylobacter jejuni* are resistant to the drug, as are *Legionella pneumophilia*, *Mycoplasma spp.*, *Acinetobacter spp.* and *Chlamydia spp*.[8,21,32–34]

Pharmacokinetics and Pharmacodynamics

Aztreonam may be administered intravenously (IV), intramuscularly (IM), inhaled, and intraperitoneally. Bioavailability after oral administration is <1%. Its mean serum elimination half-life is two hours in patients with normal liver and kidney functions. Aztreonam has 56% serum protein binding and good tissue distribution, penetrating most tissues and body fluids, including bones, prostate, bronchial secretion and liquor. About two-thirds of the drug is eliminated unchanged in the urine, with glomerular filtration and tubular secretion playing approximately equal roles. Serum clearance of aztreonam after a dose of 1g IV was linearly related to clearance of urinary creatinine.[21,32,34,35]

Like other beta-lactams, aztreonam is characterized by a time-dependent bactericidal effect. Data obtained in animal models suggest that the efficacy of aztreonam is related to a time interval greater than the minimum inhibitory concentration (MIC) (t>MIC) of 50% to 60% of the dose interval. Nevertheless, limited pharmacodynamic data suggest that the efficacy of aztreonam in humans is more closely related to the ratio of the area below the time-concentration curve (AUC) over the MIC (AUC/MIC).[35]

Resistance Mechanisms

Resistance to aztreonam is usually due to the action of beta-lactamase enzymes, which hydrolyze the beta-lactam ring. Two molecular mechanisms employed by beta-lactamases may occur: action of the nucleophile serine (class A and D beta-lactamases) or production of chromosomal or plasmid AmpC. Class B beta-lactamases (metalobeta-lactamases) are unable to hydrolyze aztreonam.[36–38]

Other mechanisms of resistance to aztreonam were described: increased expression of efflux pumps (mainly MexAB-OprM); and a deficiency of porin OmpK35 that causes a decrease in membrane permeability.[33,37]

Drug interactions and Adverse Effects

Aztreonam should not be administered concomitantly with sodium naphthyline, cefradine and metronidazol[39] (AZANEM® patient package insert). For the verification of other possible drug interactions, sites that are specialized in this subject (e.g. Drug Interactions Checker – https://www.drugs.com/drug_interactions.html and Drug Interactions – www.greghi.com.br/index.php) should be consulted.

When administered IV, aztreonam is a well-tolerated drug; however, about 2% of patients may develop phlebitis, usually after a week of use. When administered IM, the most commonly described adverse effects are pain and edema at the site of application. Rash was reported in 1% of the treated patients. Nausea, vomiting, diarrhea, dysgeusia, thrombocytopenia, leukopenia, elevated serum aminotransferases and changes in alkaline phosphatase and prothrombin activity are rarely reported adverse events.[4]

The antimicrobial should be used with caution in patients with a history of hypersensitivity to penicillins and cephalosporins, although cross-sensitivity is very unusual with the use of aztreonam.[4,40,41] However, in patients with a history of hypersensitivity to ceftazidime, administration of aztreonam should be even more cautious, since both antibiotics share an identical side chain. Although it can cause hepatotoxicity in children and infants, its use is generally well tolerated in this age group.[6]

Clinical Indications and Dosage

Aztreonam is indicated in the treatment of infections caused by aerobic Gram-negative bacilli, especially those acquired in the community, and the need for association with other antimicrobials for coverage of Gram-positive and anaerobic bacteria should be considered. When used to treat urinary tract, gynecological, pulmonary and osteoarticular infections, good cure rates are obtained.[4] In hospital infections, aztreonam is indicated in the treatment of pneumonia and urinary infections caused by sensitive bacteria.[6,42] In short, aztreonam represents an option in the treatment of infections caused by sensitive Gram-negative bacilli, without the potential for nephrous/ototoxicity that is inherent in the use of aminoglycosides.[1,32]

When combined with clindamycin, chloramphenicol and metronidazole, aztreonam can be used to treat intra-abdominal infections – such as peritonitis, appendicitis and liver, intra-abdominal, subphrenic and parietal abscesses[4,43] – in view of the action of these drugs in anaerobes. Moreover, it represents an alternative in the treatment of meningoencephalitis caused by *H. influenzae*, *N. meningitidis* and *Enterobacteriaceae*, especially in patients with a history of allergy to penicillins and cephalosporins.[1,33]

Aztreonam is generally used in the treatment of infections by *P. aeruginosas* or *Enterobacteriaceae*;[44] however, when compared to other beta-lactams, its use has been associated with an increase in lethality to patients with septic shock and the need for association with other antibiotics in infections by *Pseudomonas spp*.[45]

Although aztreonam is an option in the treatment of patients allergic to penicillin, more detailed research is needed regarding this hypersensitivity; if an IgE-mediated allergic reaction prior to penicillin is confirmed by a penicillin skin test or duly documented history, the probability of real cross-reactivity should be borne in mind, especially in patients with cystic fibrosis.[7]

A small clinical trial demonstrated that aztreonam 2g, via IM, is likely effective in the treatment of uncomplicated but ineffective gonococcal urethritis in the eradication of *N. gonorrhoeae* from the oropharynx. This treatment may be useful for rectal infections, but further research is needed before aztreonam can be recommended in the treatment of gonorrhea in this topography.[46] Although clinical data from more than three decades ago were used, a recent meta-analysis concluded that aztreonam could be an effective alternative in the treatment of urogenital gonorrhea, particularly among those with beta-lactam allergies. However, more data on the efficacy of treatment for pharyngeal and rectal infections, as well as information on the MIC distribution of contemporary isolates, are required before recommending this antimicrobial.[47]

Aztreonam (formulation containing lysine) can be administered by inhalation (nebulization) in the treatment of chronic infections by *P. aeruginosa* in patients with cystic fibrosis, at a dose of 75mg, three times a day.[48]

In patients allergic to beta-lactams, aztreonam associated with vancomycin was effective in the treatment of febrile[9] neutropenia, despite not being considered the antimicrobial scheme of choice for this clinical indication.[33]

Aztreonam (2 grams IV every 8h, infused in 3h) administered concomitantly with ceftazidime-avibactam (2.5 grams IV every 8h, infused in three hours) is an option in the treatment of infections caused by carbapenem resistant enterobacteria (CRE) producers of metallo-β-lactamases and in the rescue treatment of infections caused by *S. maltophilia*.[49–52]

In the treatment of infections of moderate severity, the recommended dose of aztreonam is 1 to 2 grams, by IV or IM, every 8 or 12 hours. In more severe infections, the suggested dose is 2 grams, IV, every 6 or 8h (maximum dose of 8 grams/day). In children, the suggested dose is 30mg/kg, IV, every 6 to 8h (maximum dose of 8 grams/day). In preterm infants (<2kg), the recommended dose is 30mg/kg, IV, every 12h.[32,33]

Currently, given the increasing number of hospital infections caused by multidrug-resistant bacteria, the use of aztreonam should be rationalized to preserve its efficacy. Aztreonam-avibactam (ATM-AVI) is a promising new therapeutic option to combat multidrug-resistant Gram-negative bacteria, including those that produce metallo-β-lactamases. Therefore, avoidance of the use of aztreonam in infections caused by multidrug-resistant bacteria is recommended, especially in community-acquired infections, in order to minimize selective pressure and reduce the risk of resistance. Furthermore, in critically ill patients with severe hospital infections, the therapeutic decision should be guided by in vitro sensitivity testing and rigorous monitoring of the clinical response.[52, 68]

Use in Special Situations: Pregnant women, lactating women, liver failure and kidney failure

Aztreonam proved to be a highly safe and effective drug (risk category A), according to pharmacokinetic and clinical studies carried out in the perinatal period (period between 22 completed weeks of gestation and 7 days after birth), in addition to having no side effects and no abnormal laboratory records.[39,53] Aztreonam is found in small amounts in breast milk and is considered an acceptable drug for use in lactating women.[33]

The half-life of aztreonam is slightly increased in hepatopaths, but there is no need to adjust doses in patients with chronic hepatopathy if there is no concomitant renal failure.[21,35]

Aztreonam is depurated through continuous venous hemofiltration, hemodialysis and peritoneal dialysis.[21] For patients with creatinine clearance between 10 and 30ml/min, the initial dose is recommended at the usual intervals on the first day of treatment, followed by half the initial dose at the usual intervals on subsequent days. For patients with creatinine clearance less than 10ml/min, the initial dose is recommended at the usual intervals on the first day of treatment, followed by a quarter of the initial dose at the usual intervals on subsequent days. A supplementary dose of 0.5 grams should be administered after each hemodialysis session.[32,44]

Aztreonam-Avibactam and new monobactams

Since their description, beta-lactams have been one of the most important and used antibiotic classes in the world. However, their overuse has led to the appearance of multidrug-resistant bacteria, many of which are no longer susceptible to existing drugs. This phenomenon reinforces the need for compliance with the principles of rational use of antimicrobials.[54] Therefore, strategies must be devised to overcome bacterial resistance,[55] the most efficient of which is the modification of the chemical structure of drugs already in use, promoting a change in their biological activity.[27]

Seeking the development of new monobactam agents with greater stability against the action of beta-lactamases and better activity against Gram-negative bacteria, Thu and collaborators (2021) synthesized six new compounds based on the structure of aztreonam. The azetidin-2-one ring with sulfonic acid group in N-1, which constitutes the central portion of the aztreonam molecule, was conserved in all of the synthesized compounds. The modifications made to the model compound consisted of: (i) introduction of a second methyl group in C-4 of the beta-lactam ring to increase the steric impediment in this position and, consequently, increase stability against beta-lactamases; (ii) replacement of the apolar geminal dimethyl group attached to the alpha carbon and the carboxylic acid group with a phenyloxy group aims to increase the polarity of this region of the molecule and enhance its interaction with bacterial macromolecules.; and (iii) introduction of a piperidine ring linked to the phenyloxy group through a urea portion, a structure that could act as siderophore and favor the entry of the compound into Gram-negative bacteria via bacterial iron absorption systems. The compounds differed from each other by the stereochemistry of a stereogenic center in the piperidine ring and the position in the nitrogen atom in this same ring, and also by the configuration (Z or E) of the double bond of the oxoimine portion. Two of these compounds showed higher potency against almost all bacteria tested compared to aztreonam.[27]

Studies have also shown that investigating the activity of aztreonam against beta-lactamases is important for supporting the discovery of new enzyme inhibitors. The selectivity of these enzymes increases with more hydrophobic compounds, and the addition of a chlorine atom has been shown to enhance the antibacterial activity of the synthesized drugs.[56]

Aztreonam associated with avibactam (non-beta-lactamase inhibitor) has in vitro activity against class A beta-lactamase-producing enterobacteria (including ESBLs and KPC), class B (metalobeta-lactamases), AmpC, some of class D (OXA-48) and *S. maltophilia*.[50,57–60] Nevertheless, such a combination is not effective in vitro against *Acinetobacter spp.* and some strains of *P. aeruginosa*, which could be explained by the presence of other resistance mechanisms, in addition to the production of beta-lactamases.[61,62] Moreover, aztreonam-avibactam is more susceptible to the "inoculum effect" than the combination of ceftazidime with avibactam.[63] Currently, aztreonam-avibactam is under evaluation in phase III clinical trials and may be useful in treating

patients allergic to penicillin, sparing the use of carbapenems. In addition, its use can be considered in patients at high risk of developing pseudomembranous colitis, since aztreonam hardly alters the intestinal anaerobic microbiome, due to the lack of activity of the drug against such bacteria.[37]

Two new monobactams incorporated a siderophore substructure to facilitate their absorption. The siderophore dihydropyridone substituent of BAL30072 confers a potent inhibitory activity against *Acinetobacter spp.*, *Burkholderia spp.* and *Pseudomonas spp.* as well as many species of Enterobacteriaceae. BAL30072 is highly resistant to hydrolysis by metalobeta-lactamases and is an AmpC inhibitor. BAL30376 is a triple combination antibacterial, consisting of a monobactam siderophore (analogous to aztreonam, with a dihydropyridone iron-chelating group), a class C beta-lactamase inhibitor (BAL29880, a structurally unique monobactam) and clavulanic acid. It has *in vitro* activity against the enzymes AmpC and ESBLs, and also against strains of *P. aeruginosa* resistant to carbapenemas, among other Gram-negative MDR.[64]

LYS228 is a new monobactam that has in vitro activity against metallobete-lactamases (NDM). However, due to changes in its chemical structure, it is also active against beta-lactamases of group A (KPC) and D, through its binding to PBP3.[3,65] Pharmacokinetic studies have shown that such an antimicrobial is safe and well tolerated.[65] It is currently in stage of phase II clinical trials (treatment of complicated urinary tract and intra-abdominal infections).[3]

Another recently developed monobactam, AIC499, has broad antimicrobial activity in vitro against strains of Gram-negative bacteria (*E. coli* and *P. aeruginosa*) and greater resistance to most beta-lactamases.[64,66] *In vitro* studies and the use of animal models have shown that a new antimicrobial, monosulfactam 0073, is a promising candidate for use as a single antibiotic against serine beta-lactamases and metalobete-lactamases produced by Gram-negative MDR.[67]

Conclusions

The scope of this article was to review of the main aspects of monobactams – which concentrated on the chemical, pharmacological and therapeutic aspects of aztreonam – and provide an update on the aztreonam-avibactam association and the current state of development of new monobactams.

Scientific efforts, in the form of new studies aimed at this group of drugs – whose action on aerobic Gram-negative bacteria is an important issue today –, may contribute to the development of innovative perspectives in terms of antimicrobial therapy, thus diversifying the possibilities of response to the increasing bacterial resistance to drugs, while especially expanding the potential for health care of people victimized by different infectious conditions.

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