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Review article

Aspergillomarasmine, a promising adjuvant to overcome antibiotic resistance

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Abstract

Bacterial resistance to antibiotics poses a significant public health challenge. One mechanism by which bacteria acquire resistance is the synthesis of beta-lactamases that inhibit the activity of beta-lactam antibiotics. Metallo-beta-lactamases (MBL) are a class of these enzymes for which there are currently no clinically available inhibitors to restore the efficacy of beta-lactam antibiotics. Aspergillomarasmine A (AMA), a fungal metabolite, has emerged as a compelling candidate, selectively chelating Zn^{2+} to inactivate MBLs and restore β-lactam activity. This review integrates current knowledge gathered from electronic databases, including ScienceDirect, PubMed, Scopus, Web of Science, and Google Scholar, on the mechanism of action and potential role of AMA in antibiotic/adjuvant co-therapy. Evidence to date suggests that AMA's unique mode of action may limit the development of rapid resistance, although its clinical efficacy remains unproven. Accelerating AMA's preclinical and clinical evaluation is imperative to translate its promise role into a novel strategy against multidrug-resistant bacteria.

Keywords: Aspergillomarasmine A; Antibiotic resistance; Metallo-beta-lactamase inhibitor; Beta-lactam antibiotics.

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Abbreviation

AMA: Aspergillomarasmine; IMP: imipenemase; MBL: metallo-beta-lactamases; MDR: multidrug-resistant bacteria; NDM-1: New Delhi metallo-beta-lactamase-1; SBL: Serine-beta-lactamases; VIM-2: Verona integron-encoded metallo-beta-lactamase 2; WHO: World Health Organization.

1. Introduction

The emergence and dissemination of multidrug-resistant bacteria (MDR) are significant public health concerns, diminishing the efficacy of common antibiotics against widespread bacterial infections (Zahir et al., 2013; WHO, 2023). Recent data from the World Health Organization (WHO) indicate alarming resistance rates of 42% for third-generation cephalosporin-resistant *Escherichia coli* (*E. coli*) and 35% for methicillin-resistant *Staphylococcus aureus* across 76 countries.

For urinary tract infections caused by *E. coli*, one in five cases exhibited reduced susceptibility to standard antibiotics like ampicillin, co-trimoxazole, and fluoroquinolones in 2020 (WHO, 2023). This trend highlights the involvement of well-established molecular mechanisms of bacterial antibiotic resistance, such as decreased drug uptake, drug target alteration, drug inactivation, and drug efflux pumps activation (Mancuso et al., 2021).

One example of these processes, especially of that of antibiotic inactivation, is the synthesis of beta-lactamases, enzymes that degrade beta-lactam antibiotics (Mancuso et al., 2021). Of note, this family of antibiotics shares, as a common active group, a four-membered cyclic amide called the beta-lactam ring. Beta-lactamases catalyze the hydrolysis of these compounds by opening the cyclic beta-lactam pharmacophore (Palacios et al., 2020). According to the Ambler classification, β-lactamases are divided into four classes (A, B, C, and D) (Hall and Barlow, 2005; Mancuso et al., 2021).

Classes A, C, and D comprise serine β-lactamases (SBLs), and class B includes metallo-β-lactamases (MBLs) (Hall and Barlow, 2005). SBLs and MBLs lead to the same inactive hydrolytic products; however, they are distinguished by different catalytic mechanisms. SBLs utilize a serine residue as a nucleophile to attack the beta-lactam ring, whereas MBLs use a hydroxide ion, activated and stabilized by Zn^{2+} cofactors, to facilitate the hydrolysis (Koteva et al., 2022). Of interest, MBLs are a significant clinical problem because they are characterized by a broad substrate specificity by being able to inactivate almost all β-lactam-containing antibiotics, including those co-formulated with serine β-lactamase inhibitors (Ju et al., 2018; Sychantha et al., 2021).

Thus, this mini review provides an overview of these enzymes and describes the mode of action of an effective MBL inhibitor, which is aspergillomarasmine A. Many investigations have proven that this natural aminopolycarboxylic acid can counteract MBL-mediated resistance (King et al., 2014; Palacios et al., 2020; Sychantha et al., 2021; Koteva et al., 2022) and thus could be considered as a promising adjuvant of beta-lactam antibiotics.

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2. Methodology

This review compiles scientific evidence on aspergillomarasmine A as a MBL inhibitor. A targeted literature search was conducted in ScienceDirect, PubMed, Scopus, Web of Science, and Google Scholar, using relevant keywords including aspergillomarasmine A, antibiotic resistance, metallo-β-lactamases, β-lactamases, β-lactamase, and metallo-β-lactamase inhibitor. Results were cross-checked to eliminate duplicates and screened by title, abstract, and full text according to predefined criteria. Eligible studies were analyzed in detail, and the extracted data were synthesized to perform this review. Chemical structures were drawn using Simplified Molecular Input Line Entry System software (SMILES) and verified from the PubChem databases (https://pubchem.ncbi. nlm.nih.gov/compound).

3. Results

3.1. Metallo- β-lactamases

MBLs, also known as class β carbapenemases, are zinc-dependent periplasmic enzymes that catalyze, except monobactams, the hydrolysis and inactivation of all other classes of antibiotics from the β -lactam family, namely penicillins, cephalosporins, and carbapenems (Ju et al., 2018; Sychantha et al., 2021). However, it is interesting to note that not all carbapenemases are MBLs. Some are serine beta–lactamases such as *Klebsiella pneumoniae* carbapenemase and oxacillinase 48, producing carbapenem-resistant Enterobacterales which belong to class A and D of the Amber classification, respectively (European Centre for Disease Prevention and Control, 2025). Moreover, the MBLs are responsible for the antibiotic resistance demonstrated by many bacteria (*Klebsiella pneumoniae*, *Acinetobacter* spp., *Pseudomonas* spp.) against antibiotics from the carbapenem family, such as meropenem, imipenem, and ertapenem (Palacios et al., 2020).

Moreover, among the factors that make MBLs particularly interesting are (i) the rapid rate at which new variants are isolated; (ii) their ubiquity, as they are isolated from nosocomial and environmental sources; and (iii) the transferability of their coding genes (plasmids, integrons), allowing these enzymes to be disseminated worldwide, thereby exacerbating the geographical spread of resistance (Palacios et al., 2020; Mojica et al., 2022). Furthermore, based on molecular criteria, MBLs are divided into three subclasses (B1, B2, and B3), which indeed have two metal-binding sites (site 1 and site 2) but differ in active site residues, metal content requirement, and substrate profile (Palacios et al., 2020; Mojica et al., 2022; Longhi et al., 2022).

Undoubtedly, enzymes of subclass B1 require two Zn^{2+} ions to be fully active and have a broad substrate spectrum. Genes encoding these enzymes are transferred by mobile genetic elements. In contrast, enzymes of subclass B2 are encoded by chromosomal genes, are active with a single Zn^{2+} ion, and are carbapenem-specific, showing low hydrolytic capacities against penicillins and cephalosporins. B3-type enzymes can be active with one or two Zn^{2+} ions and have a broad substrate spectrum (Palacios et al., 2020). However, the most clinically significant enzymes belong to subclass B1, notably the New Delhi metallo- β-lactamase-1 (NDM-1), Verona integron-encoded metallo-beta-lactamase 2 (VIM-2), and imipenemase (IMP) (Sychantha et al., 2021; Mojica et al., 2022).

Zn^{2+} ions are key elements in the catalytic reaction mechanism of MBLs. The zinc ions in MBLs activate a water molecule, leading to the formation of a functional hydroxyl ion in the active site, promoting nucleophilic attack on the antibiotic. This attack causes the cleavage of the C-N bond of the beta-lactam ring, thereby leading to the hydrolysis of the beta-lactam (Palacios et al., 2020; Mojica et al., 2022). Furthermore, there is no pharmacological inhibitor (clavulanic acid, tazobactam, sulbactam, avibactam, vaborbactam, relebactam)–approved for clinical use and co-formulated with another beta-lactam antibiotic to extend its utility in combination therapies–capable, to date, of reversing resistance and resensitizing bacteria to carbapenem antibiotics (Palacios et al., 2020; Sychantha et al., 2021; Mojica et al., 2022). This makes MBLs a significant threat to human health (Sychantha et al., 2021). The activity spectrum of the aforementioned drug combinations is limited to bacteria producing SBLs. This leaves the growing clinical challenge of MBLs unaddressed, indicating the need for therapies targeting MBLs (Palacios et al., 2020).

3.2. Aspergillomarasmine A: A Potent Inhibitor of Metallo-β-lactamases

To overcome the mentioned therapeutic impasse, a leading strategy was undertaken consisting of directly inhibiting MBLs. Thus, many compounds were reported, including cyclic boronates, thiols, chelators, dicarboxylic acids, and other agents (Table 1) (Boyd et al., 2020).

Cyclic boronates are inhibitors that target both SBLs and MBLs (Boyd et al., 2020). Recently, two bicyclic boronates, xeruborbactam (QPX7728) and taniborbactam (VNRX-5133), are of great interest (Boyd et al., 2020; Zhang et al., 2025). They are the only candidates in clinical trials (He et al., 2024; Kang et al., 2024).

These compounds possess a bicyclic structure and a carboxyl group analogous to those found in β-lactam antibiotics, allowing them to replicate the initial binding mode of β-lactam antibiotics to the active sites of SBLs and MBLs, therefore exhibiting potent inhibitory activity against a broad spectrum of β-lactamases (Zhang et al., 2025). Xeruborbactam (QPX7728) exhibits a 50% inhibitory concentration of enzymatic activity (IC_{50}) for the NDM-1, MBL is around 55 ± 25 nM, compared with 14±4 nM for VIM-1, while the IC_{50} for IMP-1 is considerably higher, at 610±70 nM (Boyd et al., 2020).

The combination of xeruborbactam and meropenem has completed Phase I clinical trials (Zhang et al., 2025). This significantly lowered bacterial counts in murine thigh and lung infection models with carbapenem-resistant *K. pneumoniae*, *P. aeruginosa*, and *A. baumannii* compared to meropenem alone (Boyd et al., 2020).

Table 1. Some encouraging β-lactamase inhibitors (inspired on studies of Zhang et al., 2025, and Mojica et al., 2022)

Inhibitor	Clinical trial phase	β-lactam partner	Chemical type	Inhibition profile of the inhibitor						References
				Serine β-lactamases				Metallo β-lactamases		
				Class A (extended spectrum β-lactamase)	Class A (KPC)	Class C	Class D	Sublass B1	Sublass B3	
Taniborbactam	Phase III trials	Cefepime	Cyclic boronates	S	S	S	S	S	NS	Zhang et al., 2025; Boyd et al., 2020 ; Mojica et al., 2022
Xeroborbactam	Phase I trials	Meropenem	Cyclic boronates	S	S	S	S	S	NS	Zhang et al., 2025; Boyd et al., 2020 ; Mojica et al., 2022
Dipeptide L-captopril	-	Meropenem	Thiol	NS	NS	NS	NS	S	S	Brem et al., 2016
EDTA	-	Imipenem	Chelator	NS	NS	NS	NS	S	S	Boyd et al., 2020; Yoshizumi et al., 2013
QA	-	Meropenem	Chelator	-	-	-	-	S	S	Liu et al., 2025
Aspergillomarasmine A	-	Meropenem	Tetracarboxylic acid	NS	NS	NS	NS	S	NS	King et al., 2014; Rotondo and Wright, 2024
Tavaborole	-	Meropenem	Benzoxaborole	S	S	S	S	S	-	Zhang et al., 2025
Emerione A	-	Meropenem	Polyketide	-	-	-	-	S	-	He et al., 2022

-: not performed; S: inhibitory activity shown; NS: inhibitory activity not shown; KPC: *K. pneumoniae* carbapenemases; EDTA: ethylenediaminetetraacetic acid

Taniborbactam shows promising results in phase III clinical trials when combined with the fourth-generation cephalosporin, cefepime, for treating complicated urinary tract and intra-abdominal infections (Boyd et al., 2020; Kang et al., 2024; Zhang et al., 2025). It is a reversible competitive inhibitor of VIM and NDM MBLs, with a low inhibitor constant (Ki), and rapid dissociation from MBLs. Nevertheless, it does not act against IMP types (Boyd et al., 2020; Kang et al., 2024). The safety of cefepime-taniborbactam has been confirmed in healthy volunteers (NCT02955459) (Boyd et al., 2020), and there is a strong potential for FDA approval, pending clearance of additional chemistry, manufacturing, and control data (Zhang et al., 2025).

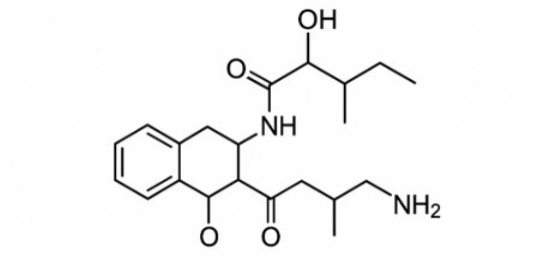

Figure 1. Chemical structure of aspergillomarasmine A

On the other hand, many studies have focused on discovering MBL inhibitors from natural sources since the identification of the fungal metabolite, aspergillomarasmine A, as a potent anti-NDM-1 inhibitor (He et al., 2022). Therefore, this review highlights the potential of aspergillomarasmine A.

Its significance as an MBL inhibitor has been recognized since a screening for NDM-1 inhibitors was conducted in 2014 from a collection of naturally active compounds produced by microorganisms. It is reported that a fungal-derived molecule synthesized by the fungus *Aspergillus versicolor* in 1956 acts as an effective inhibitor capable of degrading two major carbapenemases, namely NDM-1 and VIM-2 (King et al., 2014). This molecule is known as aspergillomarasmine A (AMA), a tetracarboxylic compound consisting of one molecule of aspartic acid linked to two molecules of alanine (Figure 1) (King et al., 2014).

3.2.1. Historical and pharmacological background

Previously, in the early 1960s, AMA was known for its wilting and necrotic effects on plant leaves. This molecule was re-evaluated in the 1980s as an inhibitor of angiotensin-converting enzyme (ACE) and in the early 1990s as a preclinical candidate for blocking the activation of human endothelin, a vasoconstrictor peptide that modulates the muscular contraction of blood vessels (King et al., 2014).

Earlier studies revealed that AMA is well-tolerated and has low toxicity in mice (the lethal dose for 50% of tested animals, LD_{50}, is 159.8 mg per kg intravenously, compared to EDTA at 28.5 mg per Kg) and does not influence mean auricular blood pressure (King et al., 2014).

3.2.2. In vitro and in vivo activity of aspergillomarasmine A

It is worth noting that AMA itself is not an antimicrobial, but it acts in combination with β- lactam antibiotics to inhibit catalysis by MBLs, especially VIM and NDM (Li et al., 2022). Indeed, AMA shows potent and rapid inactivation of the enzymatic activity of MBLs, with low IC_{50} values against NDM-1 and VIM-2 at approximately 4 and 9.6 µM, respectively (King et al., 2014).

While at 8µg/ml, the inhibitor restores fully the activity of meropenem *in vitro* against over 88% of various bacterial strains of Enterobacteriaceae, *Acinetobacter baumannii,* and *Pseudomonas aeruginosa* possessing either VIM or NDM resistance genes (King et al., 2014). AMA also restores, *in vivo*, meropenem activity in mice infected with strains of *Klebsiella pneumoniae* expressing NDM-1 (King et al., 2014; Koteva et al., 2022).

Even more, AMA (at ≤0.5–64 µg/ml) can also be used as an adjuvant with other β-lactam antibiotics against VIM or NDM producers Enterobacteriaceae (Rotondo et al., 2020; Li et al., 2022).

3.2.3. Aspergillomarasmine A's mechanism of action

It appears that this molecule is a selective zinc chelator, a key element acting as the indispensable catalytic cofactor for the action of MBLs. Indeed, a study conducted in 2021 demonstrated that AMA induces the loss of a Zn^{2+} ion from a low-affinity binding site of NDM-1. NDM-1 deprived of Zn^{2+} is rapidly degraded, contributing to the efficacy of AMA as a potentiator of beta-lactams (Koteva et al., 2022).

Based on these results, it has been demonstrated that AMA is a non-toxic compound that presents, when combined with a carbapenem, a therapeutic potential to counteract bacterial resistance mechanisms mediated by carbapenemases, with emphasis on NDM-1 and VIM (King et al., 2014; Li et al., 2022).

3.2.4. Limitations

MBLs have similar structures and active sites to some human enzymes. Hence, MBL inhibitors can target other metalloproteins in the human body and inactivate them (Kang et al., 2024). On that account, the hazard of inhibiting human metalloenzymes needs vigilant investigation because affecting these proteins may preclude clinical development of AMA (Boyd et al., 2020).

Another concerning limitation of AMA's use is its inactivity against certain MBLs of subclass B1, such as São Paulo metallo-1 (SPM-1), Adelaide imipenemase (AIM), or IMP-1, which exhibit strong zinc affinity (Mojica et al., 2022).

Another point to underline is that the analysis of NDM alleles has shown that NDMs are under evolutionary pressure for limiting $Zn^{2+}$and could escape chelator action by incorporating mutations that provide a higher affinity for Zn^{2+} binding. This natural selection event could be exacerbated by the misuse and overuse of antibiotics, pushing the boundaries of bacterial resistance. Consequently, this aspect needs to be considered when evaluating the use of metal chelators to combat MBLs (Palacios et al., 2020).

4. Conclusion

The potential of AMA as an MBL inhibitor that selectively sequesters Zn^{2+}holds great promise as a new avenue for antibiotic/adjuvant co-therapy to address the recent emergence of MBLs in clinical settings. While the clinical efficacy of AMA remains to be established, current findings suggest that multidrug-resistant bacteria are unlikely to rapidly develop resistance mechanisms. Advancing this candidate through rigorous preclinical and clinical evaluation is an urgent priority to fully assess its therapeutic potential and strengthen the antibacterial arsenal.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data availability statement

The datasets presented in this study are available upon reasonable request from the corresponding author.

References

Boyd SE, Livermore DM, Hooper DC, Hope WW. **2020.** Metallo-β-lactamases: structure, function, epidemiology, treatment options, and the development pipeline. Antimicrob Agents Chemother 64 (10): e00397-20. https://doi.org/10.1128/AAC.00397-20

Brem J., van Berkel S. S., Zollman D., Lee S. Y., Gileadi O., McHugh P. J., Walsh T. R., McDonough M. A., Schofield C. J. **2016**. Structural basis of metallo—lactamase inhibition by captopril stereoisomers. Antimicrob Agents Chemother. 60:142 150. doi:10.1128/AAC.01335-15

European Centre for Disease Prevention and Control. Carbapenem-resistant Enterobacterales, third update. **2025**. ECDC: Stockholm; 2025. DOI 10.2900/8752612

Hall B. G., Barlow M. **2005**. Revised Ambler classification of β-lactamases, Journal of Antimicrobial Chemotherapy. 55 (6), 1050–1051, https://doi.org/10.1093/jac/dki130

He Y., Zhou S., Sun W., Li Q., Wang J., Zhang J. **2022.** Emerione A, a novel fungal metabolite as an inhibitor of New Delhi metallo-β-lactamase 1, restores carbapenem susceptibility in carbapenem-resistant isolates. Journal of Global Antimicrobial Resistance: 216–222. https://doi.org/10.1016/j.jgar.2021.12.019

Ju L. C., Cheng Z., Fast W., Bonomo R. A., Crowder M. W. **2018**. The Continuing Challenge of Metallo-β-Lactamase Inhibition: Mechanism Matters. Trends Pharmacol Sci. 39(7), 635–647. doi:10.1016/j.tips.2018.03.007

Kang S. J., Kim D. H., Bong-Jin Lee B J. 2024. Metallo-β-lactamase inhibitors: A continuing challenge for combating antibiotic resistance. Biophysical Chemistry 309: 107228. doi.org/10.1016/j.bpc.2024.107228

King A. M., Reid-Yu S. A., Wang W., King D. T., De Pascale G., Strynadka N.C., Walsh T. R., Coombes B. K., Wright G. D. **2014**. Aspergillomarasmine A overcomes metallo-β-lactamase antibiotic resistance. Nature. 510, 503 – 519. https://doi:10.1038/nature13445

Koteva K., Sychantha D., Rotondo C. M., Hobson C., Britten J. F., Wright G. D. **2022**. Three-Dimensional Structure and Optimization of the Metallo-β-Lactamase Inhibitor Aspergillomarasmine A. ACS Omega. 7, 4170−4184. http://pubs.acs.org/journal/acsodf

Li X., Zhao J., Zhang B., Duan X., Jiao J., Wu W., Zhou Y., Wang H. **2022**. Drug development concerning metallo-β-lactamases in gram-negative bacteria. Front. Microbiol. 13, 959107. doi: 10.3389/fmicb.2022.959107

Longhi, C., Maurizi, L., Conte, A. L., Marazzato, M., Comanducci, A., Nicoletti, M., Zagaglia, C. **2022**. Extraintestinal Pathogenic *Escherichia coli*: Beta-Lactam Antibiotic and Heavy Metal Resistance. Antibiotics, 11(3), https://doi.org/10.3390/antibiotics11030328

Liu M., Wu C.,1, Zhang X., Wang Y., Wei Y., Hu Y., Sun Z., Chen C., Ma Y. **2025**. Discovery of a dual-action compound for metallo-β-lactamase inhibition and biofilm clearance to reverse CRE resistance. Journal of Inorganic Biochemistry 273: 113028. https://doi.org/10.1016/j.jinorgbio.2025.113028

Mancuso G., Midiri A., Gerace E., Biondo C. **2021**. Bacterial Antibiotic Resistance: The Most Critical Pathogens. Pathogens. 10, 1310. https://doi.org/10.3390/pathogens10101310

Mojica M. F., Rossi M-A., Vila A. J., Bonomo R. A. **2022**. The urgent need for metallo-β-lactamase inhibitors: an unattended global threat. Lancet Infect Dis. 22, e28–34. https://doi.org/10.1016/S1473-3099(20)30868-9

Palacios A. R., Rossi M-A, Mahler G. S., Vila A. J. **2020**. Metallo--Lactamase Inhibitors Inspired on Snapshots from the Catalytic Mechanism. Biomolecules. 10, 854. doi:10.3390/biom10060854

Rotondo C. M., Sychantha D., Koteva K., Wright G. D. **2020**. Suppression of beta-lactam resistance by aspergillomarasmine A is influenced by both the metallo-beta-lactamase target and the antibiotic partner. Antimicrob. Agents Chemother. 64, e01386-19. doi: 10.1128/AAC.01386-19

Rotondo C. M., Wright G D. **2024**. Efficacy of aspergillomarasmine A/meropenem combinations with and without avibactam against bacterial strains producing multiple β-lactamases. Antimicrobial Agents and Chemotherapy 68 (9). DOI 10.1128/aac.00272-24

Sychantha D., Rotondo C. M., Tehrani K. H. M. E., Martin N. I., Wright G. D. **2021**. Aspergillomarasmine A inhibits metallo-β-lactamases by selectively sequestering Zn^{2+}. J. Biol. Chem. 297(2), 100918. https://doi.org/10.1016/j.jbc.2021.100918.

WHO. 2023. Antimicrobial resistance. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance (Accessed 21/01/2025)

Yoshizumi A., Ishii Y., Kimura S., Saga T., Harada S., Yamaguchi K., Tateda K., Livermore DM, Woodford N, Livermore DM. **2013**. Efficacies of calcium–EDTA in combination with imipenem in a murine model of sepsis caused by Escherichia coli with NDM-1 β-lactamase. J Infect Chemother 19: 992–995. https://doi.org/10.1007/s10156-012-0528-y

Zahir I., Houari A., Bahafid W., Iraqui M., Ibnsouda S. **2013**. A novel *Alcaligenes faecalis* antibacterial-producing strain isolated from a Moroccan tannery waste. African Journal of Microbiology Research. 7(47), 5314-5323. DOI: 10.5897/AJMR2013.6029

Zhang Y., Yang S., Deng Z., Song H., Xie N., Tian Y., Qin S., Liu J., Guo Y., Wang D., Liu J., Wu C., Shen J.,Ma S., Wang Y., Liu D. **2025**. Antifungal agent tavaborole as a potential broad-spectrum serine and metallo-β-lactamases inhibitor. eBioMedicine;116: 105754. https://doi.org/10.1016/j.ebiom.2025.105754