An innovative antibacterial drug discovery system and its results: lysocin E

Takeo Kohda (Silk Strand Pharmaceuticals, Co. Ltd.)
Hiroshi Hamamoto (Yamagata University)
Kazuhisa Sekimizu (Teikyo University, Silk Strand Pharmaceuticals, Co. Ltd.)

1. Summary

Lysocin E is a groundbreaking antibacterial substance discovered through a unique screening process using silkworms, showcasing novelty in both its structure and mechanism of action (Hamamoto et al. Nature Chem Biol, 2015). Lysocin E is a cyclic peptide produced by the soil bacterium *Lysobacter* sp. Lysocin E exerts its rapid and potent bactericidal activity by binding to menaquinone in the bacterial cell membrane, leading to the disruption of *Staphylococcus aureus* cell membranes, including MRSA and VRSA.

2. Status of development

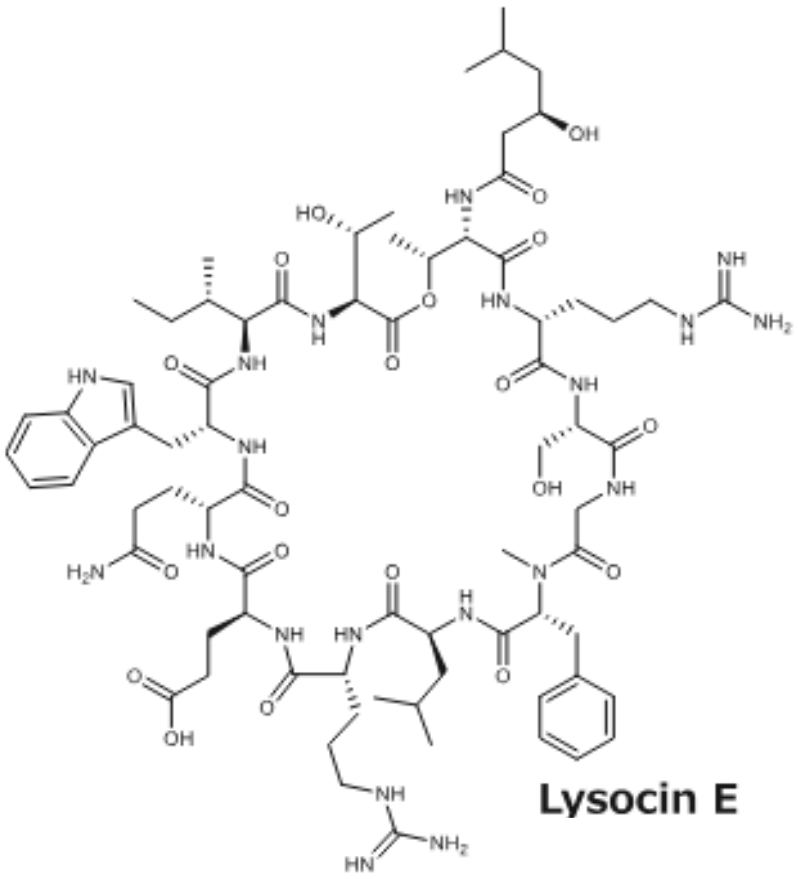
Lysocin E is currently in the preclinical development stage. GLP-compliant non-clinical safety trials are planned for initiation by the end of 2025. Concurrently, manufacturing methods and specifications for the active pharmaceutical ingredients and drug products are being developed for clinical trials.

3. Property of Lysocin E

The defining feature of Lysocin E is its rapid and potent bactericidal activity, capable of reducing MRSA bacteria to undetectable levels within minutes, outperforming existing antibacterials, such as vancomycin and linezolid. This advantage stems from Lysocin E's unique mechanism of action. Lysocin E binds to menaquinone specifically present in the bacterial cell membranes then immediately perturbs the integrity of the membrane, culminating in the eradication of the target bacteria such as *Staphylococcus aureus* and *Mycobacterium*, which use menaquinone as the sole cofactor in their electron-transport chain. Another notable feature of Lysocin E is that its antibacterial activity is further enhanced through its interaction with host factors (Hamamoto et al. Nature Commun, 2021). While the MIC of Lysocin E is comparable to that of existing antibacterials *in vitro*, its therapeutic efficacy has been proven to be approximately 100-fold more potent through mouse infection models.

4. Conclusion

Lysocin E is a distinctive and potent novel antibacterial drug candidate originating from Japanese academia. Our goal is to develop Lysocin E into a pharmaceutical product and make a significant contribution to global AMR countermeasures. The discovery of Lysocin E was made possible through the utilization of a unique platform technology which employs silkworms for screening efficacy and safety. This platform technology allows for the continuous generation of antibacterial and antifungal drug candidates with diverse characteristics.



Lysocin E