

Modern Research on Chinese Medicine Intervention in Drug-Resistant Bacterial Infections

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Abstract. The issue of resistant bacteria caused by such agents as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE) has only been aggravating in recent years, and there is the problem of the lag in antibiotic development, as well as such obvious side effects. The primary mechanisms of resistance of resistant bacteria are target mutation and resistant enzyme production. There is a positive impact of traditional Chinese medicine on interfering with the resistant bacterial infections, which is not only able to directly damage the bacterial structure, prevent bacterial metabolism and gene expression, but also indirectly control the immune system of the body. This paper focuses on traditional Chinese medicine (TCM) interventions for drug-resistant bacterial infections. It notes the growing threat of infections from MRSA, VRE, etc., while highlighting the limitations of Western antibiotics (slow development, side effects). It explains drug-resistant mechanisms, then outlines TCM's anti-resistant effects—directly damaging bacterial structures and indirectly regulating immunity. It introduces two TCM strategies (single herbs, compound formulas) and mentions clinical applications of TCM-antibiotic combinations (plus compatibility contraindications). Finally, it points out current TCM research gaps, concluding TCM may offer new directions for treating drug-resistant infections.

Keywords: Traditional Chinese Medicine, drug-resistant bacteria, MRSA/VRE

1. Introduction

In recent years, the problem of infections caused by drug-resistant bacteria has become increasingly severe. The clinical isolation rate of drug-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin resistant enterococci (VRE) continues to rise. According to the China Bacterial Resistance Monitoring Network (CHINET 2024), the detection rate of MRSA in *Staphylococcus aureus* is still as high as 28.6%, while VRE has exceeded 15.7% in *Enterococcus faecalis* [1]. VRE and MRSA can cause serious respiratory infections, skin and soft tissue infections, and other diseases, posing a great threat to patients' health, while also imposing a heavy burden on the healthcare system and socio-economic development. At present, drug-resistant bacteria have been listed by the World Health Organization (WHO) as one of the "most severe challenges to global public health security in the 21st century".

Western medicine mainly relies on new antibiotics in the treatment of drug-resistant bacterial infections, but the development speed of antibiotics is far behind the rate of bacterial resistance, and

long-term use of antibiotics can easily cause side effects such as intestinal microbiota imbalance, which has obvious limitations [2]. Compared to this, traditional Chinese medicine has great potential in reversing drug resistance, reducing adverse drug reactions, and synergistically enhancing efficacy with traditional antibiotics due to its multi-component and multi-target characteristics. In this context, exploring the treatment methods of traditional Chinese medicine for drug-resistant bacteria has important practical significance.

2. Drug resistance mechanisms of drug-resistant bacteria

Bacteria can demonstrate their drug resistance through target mutations and the production of resistant enzymes. Some targets of bacteria, such as penicillin binding proteins (PBPs), undergo genetic mutations that decrease their affinity for antibiotics, making them ineffective [3]. Taking MRSA as an example, the PBPs gene changes to produce PBP2a, which has extremely low affinity for β -lactam antibiotics, making it difficult for these antibiotics to inhibit the synthesis of bacterial cell walls. Many superbugs can produce resistance enzymes, among which β -lactases can hydrolyze the β -lactam ring of β -lactam antibiotics, causing them to lose their antibacterial activity. *Escherichia coli*, which produces extended spectrum β -lactams (ESBLs), can decompose various β -lactam antibiotics such as cephalosporins, resulting in significant therapeutic effects on these antibiotics [4].

3. Mechanisms of Chinese medicine against drug-resistant bacteria

The mechanisms by which traditional Chinese medicine resists drug-resistant bacteria are diverse [5], including both direct effects on bacteria and indirect regulation of the body's immune system. On the one hand, it can directly act on bacteria themselves by disrupting their structural integrity. For example, some components of traditional Chinese medicine can alter the permeability of bacterial cell membranes, leading to leakage of intracellular substances and bacterial death; At the same time, it can also inhibit key metabolic processes of bacteria, such as interfering with energy metabolism, blocking nucleic acid synthesis, etc., hindering the replication of bacterial genetic material, and thereby inhibiting its growth and reproduction; In addition, traditional Chinese medicine can also reduce the production of antibiotic resistant enzymes by regulating the expression of bacterial related genes (such as inhibiting the activity of genes related to antibiotic resistant enzyme synthesis), thereby reducing the production of antibiotic resistant enzymes and restoring antibiotic sensitivity to bacteria. On the other hand, traditional Chinese medicine not only directly acts on bacteria, but also assists in resistance by enhancing the patient's own immune system, such as regulating immune cell function, enhancing the body's immune response, and helping the body more effectively eliminate drug-resistant bacteria.

4. Treatment strategies of Chinese medicine for drug-resistant bacteria

4.1. Single-herb therapy

Some traditional Chinese medicines contain active ingredients against drug-resistant bacteria and can be used for monotherapy. The active ingredient berberine in Huanglian inhibits bacterial metabolism and interferes with DNA synthesis; Inhibiting TraA protein and blocking plasmid conjugation transfer to exert anti drug resistance, Allicin in garlic has a good inhibitory effect on MRSA [6]. Allicin in garlic exerts broad-spectrum antibacterial activity by disrupting the bacterial cell membrane structure, leading to leakage of cellular contents [7].

4.2. Compound therapy

Traditional Chinese medicine formulas often achieve better anti drug resistance effects through the synergistic action of multiple components. Taking Huanglian Jiedu Tang as an example, its main ingredients include Huanglian, Huangqin, Huangbai, Gardenia, etc., which contain various blood entering components such as berberine, baicalin, and geniposide. The construction of a "component target pathway" network in network pharmacology revealed that the top five targets with the highest moderate values in Huanglian Jiedu Tang were PBP2a, MurA, SarA, WalK, and SigB. They precisely target molecular targets related to bacterial structure, metabolism, and drug resistance. Firstly, the core component of Huanglian, berberine, binds to the phospholipid bilayer on bacterial cell membranes, leading to ion imbalance, protein leakage, and bacterial apoptosis by altering membrane permeability and potential, disrupting bacterial structural integrity [8]. Secondly, flavonoids such as baicalin in Huangqin inhibit bacterial proliferation and biofilm formation by suppressing DNA topoisomerase and nucleic acid synthesis pathways [9]. Thirdly, the compound regulates the Src/Csf1R signaling pathway as a whole, reducing the expression of drug-resistant enzymes (such as β -lactam), enhancing host immune response (such as macrophage function), reducing inflammation, and restoring antibiotic sensitivity. These mechanisms not only explain their significant inhibitory effect on drug-resistant bacteria such as MRSA, but also highlight the network effect of traditional Chinese medicine formulas, forming a synergistic effect of "destruction+inhibition repair" [10].

5. Clinical application of Chinese medicine

At present, the synergistic strategy of traditional Chinese medicine and antibiotic combination therapy has become the main clinical application for patients with severe drug-resistant bacterial infections. The combination of Huanglian Jiedu Tang and vancomycin in the treatment of MRSA pneumonia is a typical case [11]. Vancomycin is a commonly used antibiotic in the treatment of MRSA infections, and Huanglian Jiedu Tang can enhance the antibacterial effect of vancomycin while reducing the possible nephrotoxicity and other side effects caused by vancomycin. Clinical studies have found that patients in the combination therapy group experience faster symptom improvement and higher bacterial clearance rates [12]. When traditional Chinese medicine is used in combination with antibiotics, there will inevitably be compatibility taboos. Some components of traditional Chinese medicine may interact with antibiotics, affecting their efficacy or increasing the risk of adverse reactions, such as hepatotoxic traditional Chinese medicine+hepatotoxic antibiotics: traditional Chinese medicines such as Huangyaozi, Polygonum multiflorum (raw), and Atractylodes macrocephala have the risk of liver damage; Antibiotics such as erythromycin, chloramphenicol, rifampicin, isoniazid, etc. may also cause liver damage. The combination of the two can increase the metabolic burden on the liver and significantly increase the risk of drug-induced hepatitis. Renal toxic traditional Chinese medicine+nephrotoxic antibiotics: Traditional Chinese medicines such as Aristolochia lactiflora (containing aristolochic acid), Radix Menispermaceae, and Tripterygium wilfordii have a risk of kidney damage; Antibiotics such as aminoglycosides (gentamicin, streptomycin) and cefotaxime may also damage renal tubules. Combined use can directly superimpose nephrotoxicity and may lead to acute kidney injury. Traditional Chinese medicine that affects coagulation function+antibiotics with bleeding risk: Traditional Chinese medicine such as Danshen, Chuanxiong, and Danggui (those with strong blood activating effects); Antibiotics such as cefoperazone and cefoperazone may inhibit vitamin K synthesis and increase the risk of bleeding. The combination of the two may cause gum bleeding, skin bruising, and in severe cases,

gastrointestinal bleeding. Therefore, in clinical applications, strict research and monitoring of the compatibility of traditional Chinese medicine and antibiotics are necessary to ensure the safety and effectiveness of medication [13].

6. Conclusion

Traditional Chinese medicine, as a treatment for drug-resistant bacteria, has the advantages of low drug resistance and immune regulation. Traditional Chinese medicine has complex ingredients, making it difficult for bacteria to develop resistance. Moreover, it can regulate the body's immune system and exert an overall anti bacterial effect. However, the exploration of the mechanism of action of traditional Chinese medicine against drug-resistant bacteria in existing basic research is not deep enough, and many mechanisms are not fully understood. In terms of clinical experience, there is a lack of large-scale and multi center clinical studies, and the standardization of clinical applications needs to be improved. In terms of industrialization, the extraction and pharmaceutical processes of active ingredients in traditional Chinese medicine need to be optimized to improve the quality and stability of traditional Chinese medicine. Despite many problems, traditional Chinese medicine still plays an important role in the crisis of drug-resistant bacteria and is expected to provide new directions for the treatment of drug-resistant bacterial infections. In the future, we should strengthen the basic research on the resistance of traditional Chinese medicine to drug-resistant bacteria, deeply explore its mechanism of action, carry out more high-quality clinical studies, accumulate rich clinical experience, optimize the industrialization process of traditional Chinese medicine, promote the modernization of traditional Chinese medicine, and better serve the treatment of drug-resistant bacterial infections.

References

- [1] National Bacterial Resistance Surveillance Network. (2024, Nov.18). <https://www.carss.cn/Report/Details/978>
- [2] Sun, Y. (2021). Experimental study on tetrahedral framework nucleic acid carrying antibiotics against drug-resistant bacteria [Master's thesis, Sichuan University].
- [3] Mo, L., & Wang, Q. N. (1997). Study on the affinity of oxacillin to penicillin-binding protein of *Staphylococcus aureus* TACC25923. *Chinese Journal of Antibiotics*, 22(4), 294-297.
- [4] Wang, J. (2012). Structure and function study of New Delhi metallo- β -lactamase NDM-1 from super bacteria [Doctoral dissertation, Nankai University]. <https://doi.org/10.7666/d.Y2525260>
- [5] Mechanism of bacterial drug resistance. (2010). *Scientific Chinese*, (11), 72-72.
- [6] Wang, X. H. (2013). Research progress on clinical study of berberine. *Journal of Frontiers of Medicine*, (27), 380-381.
- [7] Zhou, L., Qian, Y. F., Lyu, L. H., et al. (2025). Inclusion of allicin by cyclodextrin loaded in pullulan/polyvinyl alcohol nanofiber membrane and its antibacterial properties. *Advanced Textile Technology*, 33(6), 91-99.
- [8] Zhang, R. (2023). Determination of coptisine content and study on its antibacterial mechanism against avian *Pasteurella multocida*.
- [9] Lu, Q., Wang, J. S., Du, N., et al. (2025). Research progress on pharmacological effects and application of baicalin. *Clinical Rational Drug Use*, 18(10), 176-180.
- [10] Gong, M. F., & Fu, S. H. (2018). Current status and development strategy of anti-resistant compound antibiotics research and development at home and abroad. *Chinese Journal of Antibiotics*, 43(1), 15-21.
- [11] Xiao, N., Duan, H. H., & Wang, Y. (2025). Mechanism of Huanglian Jiedu Decoction in treating *Staphylococcus aureus* pneumonia. *Tianjin Journal of Traditional Chinese Medicine*, 42(4), 511-518.
- [12] Feng, Y. B., Chen, H., & Zhang, X. A. (2025). Research progress on modern clinical application and mechanism of Huanglian Jiedu Decoction. *Journal of Liaoning University of Traditional Chinese Medicine*, 27(6), 201-207.
- [13] Xu, Y. (2022). Rationality evaluation of combined medication of Shuanghuanglian injection and ampicillin sodium for injection.