

The Prospect of Daphnetin against Drug-Resistant Bacteria

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Abstract

The increasing risk of antibiotic resistance put forward urgent requirements for novel drugs to treat infection diseases. The objective of this study is to perform a review of the advantages of daphnetin against drug resistant bacteria.

Key words: Daphnetin; Drug-resistant bacteria; *H. pylori*.

INTRUDUCTION

Antibiotics have saved millions of patients and brought a revolution in the field of infectious diseases [1]. However, due to the overuse and inappropriate use, an enormous threat has been posed here that many antibiotics are no longer effective [2]. Millions of people are affected with antibiotic-resistant bacteria infection, among which about one percent died from the infection [2]. Without action, bacterial infections that can now be shrugged off with a simple course of treatment could again become common causes of death and we will return to the “pre-antibiotic era” [3]. Moreover, the production of new antibiotics (especially the antibiotics against Gram-negative bacteria) has diminished progressively over the past 20 years and too few new drugs have moved from the laboratory into clinical trials [4]. Leading to the treatment of infections caused by drug-resistant pathogens become more complicated and limited [5]. For example, vancomycin and daptomycin- the ‘last resort’ antibiotics against methicillin-resistant *Staphylococcus aureus* infections, have found their resistant strains. Polymyxins have been considered as one of better choices for carbapenem-resistant Gram-negative pathogens. However, mutations of *pmrA/B*, *phoP/Q* and *mgrB* genes located in the chromosome and plasmids carrying the *mcr-1* gene make these drugs no longer effective. So, what should we do when facing these drug-resistant strain infections?

SHORT COMMUNICATION

Numerous chemical compounds purified from medicinal plants are considered to be potential solutions of drug-resistant strain infection. Literally thousands of the compounds alone and combined with antibiotics have been tested against drug-resistant bacteria. Daphnetin (7, 8-dihydroxycoumarin) is a major bioactive component extracted from medicinal plant-Daphne koreana Nakai. It has been used clinically to treat Buerger’s disease in China for many years. Moreover, its anti-tumor, -malarial, -inflammatory properties were investigated due to its inhibition effects on tumor invasion and migration, lipopolysaccharide -induced inducible nitric oxide synthase and cyclooxygenase 2 expressions and reactive oxygen species production, and protein alkylation. Based on these multiple pharmacological profiles, the antibacterial spectrum of daphnetin was also investigated. Although its antibacterial activity was found to be weaker than some antibiotics, daphnetin has some specific advantages as a novel agent against drug-resistant bacteria (e.g. metronidazole resistant *H. pylori* and methicillin resistant *S. aureus*). (1) It is stable in different environments and is not easy to develop resistance. (2) The activity against drug-resistant bacteria is almost equal to the one against drug-sensitive bacteria. (3) It has stronger activity against Gram-negative bacteria than Gram-positive bacteria. (4) The specific mechanisms of daphnetin against *H. pylori* were related to increase

of DNA damage and phosphatidylserine translocation, decrease of its attachment to gastric epithelial cells and inhibition of its urease activity. (5) No toxic effects and genetic toxicity were found. (6) It improves human immunity and reduces pathogens colonization.

CONCLUSION

Although daphnetin antibacterial activity was weak, the rapid emergence of resistance bacterial strains has forced it to be reevaluated in assisting antibacterial aspect because of its advantages in reducing virulence and colonization ability of pathogens and its protective effect on human cells. Taken together, our review suggests that daphnetin has a potential to be a novel, safe, and effective agent for the prevention and/or treatment of infection diseases induced by drug-resistant bacteria.

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