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Determination of antibacterial activity of resveratrol on some pathogenic bacteria

Nihal Mısır[1*], Serpil Uğraş[2]

*[1]*Düzce University, Faculty of Arts and Sciences, Department of Biology, Düzce, Türkiye.*
[2]*University of Health Sciences, Hamidiye Faculty of Pharmacy, Department of Basic Pharmaceutical Sciences, Division of Pharmaceutical Microbiology, Istanbul, Türkiye.*

*Corresponding author : nihal151400@gmail.com
Orcid No: https://orcid.org/0009-0006-4807-4406

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Abstract: This study aims to investigate the antibacterial effect of resveratrol, a natural polyphenol, on some pathogenic bacteria. Resveratrol is a compound found in plants such as red grapes and is known for its antioxidant, anti-inflammatory and antimicrobial properties. Due to these properties, it is considered as a potential agent in the prevention and treatment of bacterial infections. In this context, in this study, it was aimed to determine the antibacterial effects and effective dosage of resveratrol on *Salmonella typhimurium, Staphylococcus epidermidis, Pseudomonas aeruginosa, Yersinia pseudotuberculosis, Proteus vulgaris, Enterococcus faecalis, Enterobacter cloaceae, Escherichia coli,* and *Listeria monocytogenes*. Antibacterial activity studies were performed by agar well diffusion method. As a result of antibacterial activity studies, inhibition zones with a diameter of 14.0 ± 1.0 mm for *S. epidermidis*, 15.0 ± 0.5 mm for *E. faecalis*, 15.0 ± 0.5 mm for *E. cloaceae* and 16.0 ± 0.5 mm for *L. monocytogenes* were measured at 500 µg\mL dosage of resveratrol. However, resveratrol was found to have a bacteriostatic effect against *S. typhimurium, P. aeruginosa, Y. pseudotuberculosis, P. vulgaris* and *E. coli*. According to these results, it can be said that resveratrol may be effective against some pathogenic bacteria and may contribute to the development of new strategies for its use as an antibiotic adjuvant, although its use in terms of both food safety and public health is foreseen.

Keywords: Resveratrol, pathogenic bacteria, inhibition, antibacterial effect

1 Introduction

Bacterial infections pose a significant threat to both public health and food safety. The widespread use of antibiotics in the treatment of bacterial infections has particularly led to an increase in antibiotic resistance, making the development of alternative treatment strategies essential (Patel and Scott 2011). In this context, compounds derived from natural sources have emerged as a promising area for the discovery of new antibacterial agents (Das and Kapmaz 2019). Resveratrol, a natural polyphenol, is found naturally in plants and is most abundant in the skins of red grapes, blueberries, raspberries, mulberries, and peanuts (Das and Kapmaz 2019). Studies have reported that resveratrol has antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. Additionally, it serves as a protective compound in plants against stress, infections, or ultraviolet (UV) radiation (Karameşe and Dicle 2022). Resveratrol attracts attention due to its numerous potential health benefits, particularly its protective effects against heart diseases, diabetes, cancer, and neurodegenerative diseases (Faydaoğlu and Sürücüoğlu 2013). Moreover, it has been shown to be effective against bacterial infections, making it important to consider as an alternative or adjuvant to antibiotics (Das and Kapmaz 2019). Although the literature indicates that resveratrol is effective against many pathogenic bacteria, the effects on various bacteria are not fully understood. However, studies have shown that resveratrol is effective against both Gram-positive and Gram-negative bacteria. The antibacterial activity of resveratrol is known to be mediated through mechanisms such as inhibiting bacterial cell wall synthesis, disrupting membrane permeability, or affecting bacterial metabolism (Karameşe and Dicle 2022).

Studies have observed that resveratrol possesses inhibitory properties against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa* (Karameşe and Dicle 2022). Additionally, it has been revealed through studies that resveratrol can inhibit the biofilm-forming capabilities of bacteria, which makes them more resistant to antibiotics, and thus may be effective in the treatment of infections (Karameşe and Dicle 2022). In the face of the dramatic rise in antibiotic-resistant pathogens, the use of such molecules as direct or indirect antibiotic adjuvants is of great importance. Antibiotic adjuvants are known to inhibit bacterial resistance mechanisms and make pathogens susceptible to the effects of antibiotics, thereby extending the lifespan and efficacy of existing antibiotic stocks and suggesting the development of new strategies (Vestergaard and Ingmer 2019). This study investigates the antibacterial efficacy of resveratrol against *Salmonella typhimurium*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Yersinia pseudotuberculosis*, *Proteus vulgaris*, *Enterococcus faecalis*, *Enterobacter cloacae*, *Escherichia coli*, and *Listeria monocytogenes* bacteria and determines the effective dosage.

2.Materials and Methods

2.1 Resveratrol

In this study, the antibacterial efficacy of resveratrol (Resveratrol-(4-hydroxyphenyl-13C6, Merck), a natural polyphenol, was determined (Figure 1). A 30% aqueous solution of DMSO (Dimethyl sulfoxide - C2H6OS, Merck) was used as the solvent for resveratrol. The final concentration of resveratrol was prepared fresh before each use at 5 mg/mL.

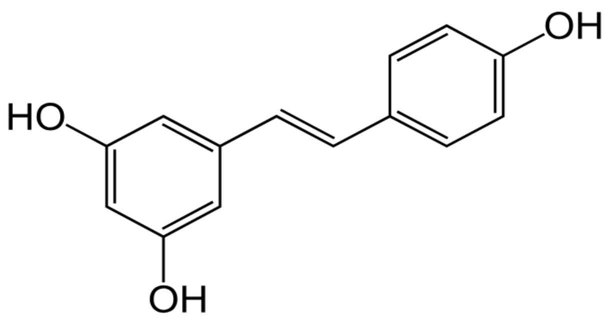

Figure 1. Chemical Structure of Resveratrol

2.2 Test Bacteria Used in the Study

A total of nine different bacteria were used as test bacteria in antibacterial activity studies (Table 1). The bacteria were grown in Nutrient Broth (NB, Merck) and Nutrient Agar (NA, Merck) for 16-18 hours at 37°C.

Table 1. Indicator Bacteria

Test Bacteria	Source
Salmonella typhimurium	ATCC 14028
Staphylococcus epidermidis	ATCC 12228
Pseudomanas aeruginosa	ATCC 27853
Yersinia pseudotuberculosis	ATCC 911
Proteus vulgaris	ATCC 13315
Enterococcus faecalis	ATCC 29212
Enterobacter cloaceae	ATCC 13047
Escherichia coli	ATCC 35218
Listeria monocytogenes	ATCC 7644

ATCC; American Type Culture Collection

2.3 Antibacterial Activity Test

The antimicrobial activities of resveratrol were determined using the agar well diffusion method (Aytar and Oryaşın 2019). The test bacteria included *Salmonella typhimurium*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Yersinia pseudotuberculosis*, *Proteus vulgaris*, *Enterococcus faecalis*, *Enterobacter cloacae*, *Escherichia coli*, and *Listeria monocytogenes* the bacteria were inoculated into Nutrient Broth (NB) and incubated in a shaking water bath at 37°C for 16-18 hours. After incubation, the absorbance of the microbial cultures was measured at a wavelength of 600 nm using a spectrophotometer (Mapada, UV3100PC). The prepared cultures were diluted with sterilized dH2O to approximately 1 × 10^8 CFU/mL. A volume of 50 µL of the diluted bacterial cultures was added to 20 mL of soft Nutrient Agar (NA), spread onto the plate, and then allowed to gel. Wells were then created on the agar surface. A volume of 100 µL of the resveratrol (5 mg/mL) solution was added to the wells. Ciprofloxacin (30 µg/disk; Bioanalyse) was used as a positive control.

3. Results and Discussion

As a result of this study, inhibition zones were measured for resveratrol (500 µg/mL) with values of 14.0 ± 1.0 mm for *Staphylococcus epidermidis*, 15.0 ± 0.5 mm for *Enterococcus faecalis*, 15.0 ± 0.0 mm for *Enterobacter cloacae*, and 16.0 ± 0.5 mm for *Listeria monocytogenes*. When compared to the control group, it can be stated that the antibacterial activity was low. However, resveratrol was found to have a bacteriostatic effect against *Salmonella typhimurium*, *Pseudomonas aeruginosa*, *Yersinia pseudotuberculosis*, *Proteus vulgaris*, and *Escherichia coli* (Table 2 and Figure 2).

Bacteriostatic effect is a type of effect that stops the growth and reproduction of bacteria. The bacteriostatic effect of resveratrol can occur through mechanisms such as disrupting the cell membrane, affecting gene expression, and influencing metabolic pathways (Altıok and Bayraktar 2009).

Table 2. Antibacterial Activity Properties of Resveratrol on Test Bacteria

	Inhibition Zone (mm)	
Test Bacteria	**Resveratrol**	**Control**
S. typhimurium	BS	36.0 ± 1.0
S. epidermidis	14.0 ± 1.0	20.0 ± 2.0
P. aeruginosa	BS	29.0 ± 1.6
Y. pseudotuberculosis	BS	26.0 ± 0.5
P. vulgaris	BS	36.0 ± 3.0
E. faecalis	15.0 ± 0.5	29.0 ± 1.2
E. cloaceae	15.0 ± 00	35.0± 1.0
E. coli	BS	35.0 ± 0.6
L. monocytogenes	16.0± 0.5	30.0 ± 1.5

BS: Bacteriostatic Effect, Control; Ciprofloxacin (30 µg/disk)

Figure 2. Inhibition Zones 1; *Salmonella typhimurium*. 2; *Staphylococcus epidermidis*. 3; *Pseudomonas aeruginosa*. 4; *Yersinia pseudotuberculosis*. 5; *Proteus vulgaris*. 6; *Enterococcus faecalis*. 7; *Enterobacter cloaceae*. 8; *Escherichia coli*. 9; *Listeria monocytogenes*.

Studies have shown that resveratrol has an inhibitory effect against various Gram (+) and Gram (-) bacteria. Some research has indicated that resveratrol exhibits antibacterial activity against *Staphylococcus aureus*, particularly antibiotic-resistant strains (MRSA), as well as *E. coli* and *Pseudomonas aeruginosa*. Resveratrol is being investigated for its direct antibacterial properties against antibiotic-resistant bacteria and as a potential adjunctive therapeutic agent (Paulo et al. 2010; Vestergaard et al. 2019).

Moreover, studies have demonstrated that resveratrol has a bacteriostatic effect against Gram (+) bacteria such as *Bacillus cereus* and *S. aureus*. However, the mechanisms underlying the antibacterial efficacy of resveratrol have not yet been fully elucidated (Paulo et al. 2010). Additionally, it has been reported that resveratrol can suppress biofilm formation in *S. aureus* (Cui et al. 2024). There are also studies indicating that resveratrol mitigates the pathogenic and inflammatory activities of *Porphyromonas gingivalis* and *Streptococcus mutans*. It is noted that resveratrol significantly reduces acid production and tolerance related to the virulence characteristics of *S. mutans*, inhibiting polysaccharide synthesis (Uysal et al. 2022).

Resveratrol has been shown to possess antibiofilm properties at low concentrations for some bacteria and, when combined with vancomycin, disrupts the expression of surface proteins, capsular polysaccharides, and genes associated with quorum sensing (QS). it has been shown that resveratrol exhibits stronger activity against established biofilms (Cui and Wang 2024). Resveratrol is a naturally occurring polyphenolic compound belonging to the stilbene family, found in grapes, blackberries, blueberries, cranberries, blackcurrants, peanuts, Japanese knotweed, pine trees, legumes, and *Theobroma cacao* (cocoa). It is also present in related by-products such as red wine, dark chocolate, and fruit juices (Cui and Wang 2024).

Resveratrol has garnered attention not only as a potential natural antimicrobial agent but also for its possible functional and therapeutic applications. Therefore, its potential for use in both clinical applications and food preservation positions it as a polyphenol worthy of further research in the future. In this context, it suggests that at higher doses, resveratrol may exhibit bactericidal effects while also providing the opportunity for use as an antibiotic adjuvant due to its ability to inhibit bacterial growth.

4. Conclusion

In this study, the antibacterial effects of resveratrol against pathogenic bacteria such as *Salmonella typhimurium*, *Staphylococcus epidermidis*, *Pseudomonas aeruginosa*, *Yersinia pseudotuberculosis*, *Proteus vulgaris*, *Enterococcus faecalis*, *Enterobacter cloacae*, *Escherichia coli*, and *Listeria monocytogenes* have been identified. Supporting this study, literature suggests that resveratrol could be a significant antibacterial agent against bacteria.

Although the antimicrobial effects of resveratrol are promising, there is a need for a comprehensive elucidation of this efficacy. In particular, it is essential to identify the antimicrobial activities of resveratrol against different microorganisms. Synergistic effect studies are important to investigate whether the combination of resveratrol with other antimicrobial agents enhances its antibacterial efficacy. Previous research has shown that resveratrol exhibits synergistic effects with some antibiotics, and it is necessary to optimize these effects with appropriate dosages. Such combination studies could potentially offer solutions to serious public health issues, such as antibiotic resistance, by enhancing the effectiveness of antibiotics.

Specifically, the combination of antibacterial agents and natural compounds has the potential to reduce toxicity and slow down the development of antimicrobial resistance, as they can be effective at lower doses. The low toxicity of resveratrol is anticipated to provide an advantage for its use in food safety or medical applications. However, it should be noted that further research is needed regarding the potential of resveratrol for use in combination with antibiotics and its synergistic effects.

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