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Inhibitory Actions of Catechins, Pro-anthocyanidins, and Flavonols Against Pathogens Resistant to Multiple Drugs: Flavonoid Forcefields

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Abstract: *There is an urgent requirement for the development of novel and creative antimicrobial techniques to fight against the menace of emerging drug-resistant microorganisms. This research evaluates the antibacterial activity of three flavonoid compounds against resistant strains of S. aureus, P. aeruginosa, and S. typhi: catechins, pro-anthocyanidins, and flavonols. By recognized antimicrobial susceptibility techniques, both the MIC and MBC were determined to show considerable antibacterial activity. Flavonols exhibited the highest zones of inhibition, with peak inhibition measuring 24.4±0.03 mm. It also reflected the most significant bactericidal and inhibitory effect, especially against S. aureus. Flavonoids may provide scaffolds for the development of novel antibacterial drugs. Flavonoids may be the weapon of choice to fight against bacterial strains that are resistant to conventional antibiotics since they offer a natural substitute that is not only safe but efficacious as well.*

Key Words: Flavonoids, Antibacterial Activity, Multidrug Resistance

Introduction

The prevalence of multidrug-resistant (MDR) bacterial infections is rising, posing a growing threat to global health (Azeem, Hanif, Mahmood, Ameer, et al., 2023). This indicates that research into novel antimicrobial medications is necessary as established antibiotics are losing their efficacy(Abid et al., 2022). Due to their many pharmacological properties and low propensity to induce resistance, natural chemicals have garnered a lot of interest as possible treatments. Flavonoids are a class of polyphenolic chemicals found in fruits, vegetables, and plants(Azeem et al., 2022). They have potent antibacterial, anti-inflammatory, and antioxidant effects(Azeem, Hanif, Mahmood, Siddique, et al., 2023). This study aims to assess the antibacterial activity of three different flavonoids: pro-anthocyanidins, flavonols, and catechins against three common MDR pathogens: Pseudomonas aeruginosa (P. aeruginosa), Staphylococcus aureus (S. aureus), and Salmonella typhi (S. typhi) (Usman Abid et al., 2023). MDR bacterial strains, such as the ones this study looked at, can have disastrous clinical outcomes because they are resistant to different antibiotic regimens(H. M. U. Abid et al., 2024). Drugs like ampicillin, trimethoprim-sulfamethoxazole, and chloramphenicol which were once thought to be effective against the typhoid fever-causing bacteria, S. typhi, have become less effective. In a similar vein, S. aureus poses a significant risk in clinical and community contexts, particularly the methicillin-resistant strain (MRSA)(S. Abid et al., 2024). Due to its inherent resistance mechanisms, P. aeruginosa is a commonly occurring hospital-acquired infection that is extremely difficult to treat. It is resistant to many medications. Against these challenges, pharmacological exploration of flavonoids as potential antibacterial agents offers a viable avenue. Flavonoids have shown modes of action in bacterial cells that include nucleic acid synthesis, cytoplasmic membrane function, and reduction of energy metabolism, all of which may decrease the likelihood of resistance emerging. Because early research has demonstrated that catechins, pro-anthocyanidins, and flavonols are potent antimicrobial agents capable of interfering with bacterial cell functions and structures that are critical to the survival and pathogenicity of the organism,

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these compounds are the focus of this work (Khan et al., 2024). This study aims to investigate the MIC and MBC values of flavonoids against MDR strains of S. typhi, S. aureus, and P. aeruginosa, with the goal of highlighting the therapeutic potential of natural compounds in the management of resistant bacterial infections. In addition to advancing the quickly expanding field of antimicrobial research, this paves the way for the future development of medicines based on flavonoids, which will help address the urgent need for new antimicrobial strategies in the fight against drug-resistant organisms.

Methodology

The antimicrobial susceptibility evaluation of flavonols, pro-anthocyanidins, and catechins against multidrug-resistant S. typhi, S. aureus, and P. aeruginosa was conducted using a simple, previously published, and slightly modified method of RM. Humphries and Consorts eight To put it briefly, 120°C sterilizes the medium. Mueller-Hinton Each sterile petri dish was aseptically filled with twenty milliliters of agar. The mixture was then left to solidify at 37 °C. After being diluted, the bacterial cultures in the nutrient broth attained an optical density of 0.5. All bacterial cultures were fully developed in nutrient broth after 24 hours at 37°C. After preparing Muller Hinton (MH) agar plates, 100µl of the bacterial suspension (1×105 CFU/ml) was spread onto the plates using a sterile cotton swab. Each MH agar plate had three mm-diameter wells drilled into it using an aseptic borer. After directly injecting 4 mg/ml (100µl) of flavanol, pro-anthocyanidin, and catechin solutions into bores, plates were incubated at 37°C for 24 hours. As a positive control, one well was used, and ciprofloxacin (10 µg) was cultured there for the entire day. Each sample's zone of inhibition was measured 24 hours later. Three runs of the experiments were carried out. Bacterial ZOI was compared with ciprofloxacin (positive control) in compliance with CLSI guidelines from 2016. Three rounds of additional analysis were performed on the strains affected by the complex.

The MIC (Minimum Inhibitory Concentration) values of the previously chosen flavonols, pro-anthocyanidins, and catechins against S. aureus, S. typhii, and P. aeruginosa were ascertained using a previously described dilution procedure. Test tubes were filled with five milliliters of nutritional broth and a loop that held bacterial culture. A pre-made broth was combined with samples ranging in concentration (2, 5, 10, 15, 20, and 30 µg/mL), and the mixture was incubated at 37 °C for the full day. For every sample, a minimum inhibitory concentration (MIC) was established. The experiment was then run three times to yield the mean ± standard deviation (n = 3).

A similar protocol was proposed for the MBC (Minimum Bactericidal Concentration) test. Essentially, a 1 ml culture was moved from the MIC tubes into the nutrient agar and incubated at 37°C for the entire day. Every sample's MBC was ascertained by figuring out the concentration at which 100% of the bacterial growth inhibition was observed. Ciprofloxacin (10 ug/ml) was a positive control that demonstrated efficacy against all bacterial species.

Results

In the current study, S. aureus and S. typhii P.aeroginosa were isolated from foot ulcer ulcers. The lowest and maximum Zone of Inhibition (ZOI) values for flavonols, catechins, and pro-anthocyanidins are shown in Table 1. It was discovered that the maximum zone of flavonoid inhibition for G-ve bacteria, specifically S. typhii and P. aeruginosa, was 18.4±0.02. Conversely, S. aureus exhibited the largest zone of flavonoid inhibition, measuring 24.4±0.03, in G +ve bacteria. The enhanced ZOI of flavonols against P. aeruginosa may be due to holes in the outer membrane of G-ve bacteria. G+ve bacteria are more susceptible to flavonols because they do not have an outer membrane, such as S. aureus. The MIC and MBC values of flavonols are also incredibly low in comparison to the other two flavonoids.

Conclusion

This study highlights the pro-anthocyanidins, flavonols, and catechins' strong antibacterial properties as well as their capacity to effectively halt the development of bacteria that are resistant to drugs. The findings support the addition of flavonoids to the repertoire of antibacterial agents, potentially providing a safe and efficient way to counteract the growing threat of antibiotic resistance.

Table 1

ZOI, MIC, and MBC of Catechins, Pro-anthocyanidins, and flavonols against pathogenic bacteria.

Sample	Bacterial strains	MIC (µg/100µl)	MBC (µg/100µl)	Zone of Inhibition
Catechins		3.2±0.02	4.56±0.01	16.1±0.02

Pro-anthocyanidins	*S. Typhii* (Gram-ve)	2.9±0.03	4.02±0.03	14.4±0.04
flavonols		2.8±0.04	3.84±0.03	12±0.01
Catechins		3.22±0.03	6.25±0.03	14.5±0.01
Pro-anthocyanidins	*P. aeruginosa* (Gram -ve)	3.12±0.02	6.25±0.02	16.5±0.02
flavonols		2.24±0.04	3.125±0.04	18.4±0.02
Catechins		4.76±0.04	6.44±0.02	21.1±0.01
Pro-anthocyanidins	*S. aureus* (Gram +ve)	5.25±0.02	6.22±0.02	18.5±0.03
flavonols		3.125±0.02	5.44±0.04	24.4±0.03

MIC=Minimum inhibitory concentration MBC= Minimum bactericidal concentration

Figure 1

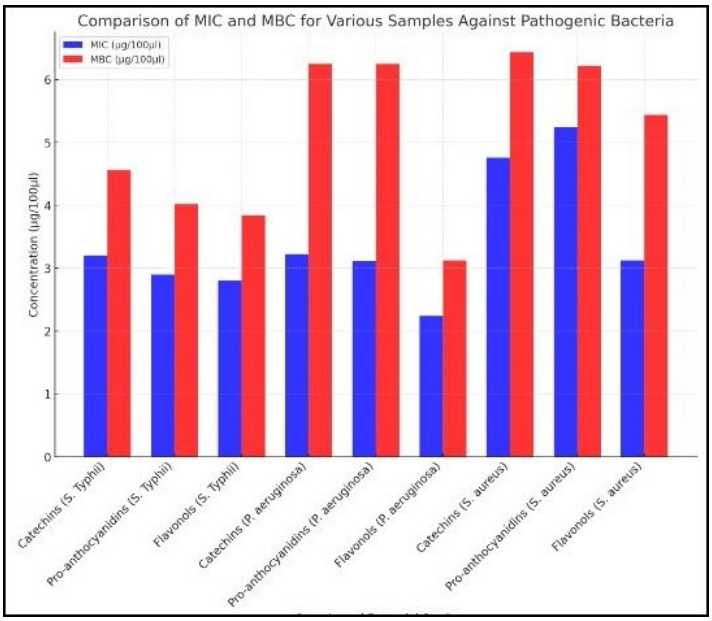

Figure 2 Bar graph showing the comparison of Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) for catechins, pro-anthocyanidins, and flavonols against various pathogenic bacteria. Each set of bars represents the MIC and MBC values for a specific sample against a specific bacterial strain, with MIC values in blue and MBC values in red. The labels on the x-axis indicate the sample and the bacteria.

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