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COMBINATION THERAPY: HERBAL PRODUCTS WITH ANTIBIOTICS IN COMBATING BACTERIAL RESISTANCE - A MINI-REVIEW OF THE LITERATURE

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Abstract: The use of antibiotics is crucial in combating bacterial infections and has had a significant impact on the health-related quality of human life since their introduction.
Over the past few decades, many commonly used antibiotics have become less effective due to the emergence of drug-resistant bacteria, creating a significant global public health concern. An alternative approach to treating infectious diseases involves using plant extracts individually or in combination with antibiotics. Thus, this review aims to emphasize, through a study of the current literature, the role of synergistic action between plant products and antibiotics in combating bacterial resistance. PubMed and Google Scholar are used as the search engines, and the latest studies are considered. The main classes of compounds with antimicrobial activity include flavonoids, isoquinoline alkaloids, terpenoids, volatile oils, and polyphenols. They target multiple bacterial processes, including protein synthesis, cell wall integrity, deoxyribonucleic acid (DNA) replication, metabolic pathways, efflux pump activity, and cell viability. Research from 2001 to 2024 demonstrates that phytochemicals can reduce antibiotic minimum inhibitory concentrations (MICs) by 0.25 µg/mL to 63.4 µg/mL-fold against World Health Organization (WHO) priority pathogens, with fractional inhibitory concentration (FIC) indices as low as 0.03-0.5. Despite robust preclinical evidence, significant bioavailability challenges and the absence of large-scale clinical trials remain barriers to clinical translation.

Keywords: plant products, antibiotics, drug-resistant bacteria, synergism, bioactive compounds, efflux pump.

INTRODUCTION

Bacterial infections have plagued humanity throughout history. For much of recorded history, infections were attributed to supernatural forces or bodily imbalances, with treatments relying primarily on herbal remedies and basic surgery. Several major bacterial diseases have caused significant pandemics: leprosy (Hansen's disease), one of the oldest known infectious diseases, with skeletal evidence dating back millennia; tuberculosis (caused by *Mycobacterium tuberculosis* complex), found in ancient human remains with bone lesions and genomic data; and the Plague, (caused by *Yersinia pestis*), which led to the most devastating pandemics in recorded history.

Antibiotics are medications that are used to combat or prevent bacterial infections by either eradicating bacteria (bactericidal) or stopping their growth and reproduction (bacteriostatic) (Souza et al., 2025).

They target specific, essential processes or structures in bacterial cells while exhibiting selective toxicity, which minimizes harm to human cells (Souza et al., 2025).

The main mechanisms include: inhibition of cell wall synthesis (β-lactams, glycopeptides), inhibition of protein synthesis (aminoglycosides, macrolides, tetracyclines), inhibition of nucleic acid synthesis (fluoroquinolones, rifamycins), disruption of the cell membrane integrity (polymyxins), inhibition of metabolic pathways (sulfonamides, trimethoprim) (Birlutiu & Birlutiu, 2025).

Antimicrobial resistance threatens to result in ten million deaths annually by 2050 unless a global response is implemented (De Kraker et al., 2016). Thus, in the last few years, numerous authors have documented the requirement for new antimicrobial agents to supplement the existing inventory of anti-infective promoters (Martínez et al., 2011; Wise et al., 2011). Despite the remarkable studies and advancements in cure and prevention measures, infectious diseases remain the top cause of death worldwide, especially in emerging countries. The threat of dangerous pathogens is constantly rising. According to a WHO report, infectious diseases, including co-infections like Human Immunodeficiency virus (HIV) and worms, account for over 70% of premature deaths in 22 African countries (Soares et al., 2016).

The primary factors driving increased resistance include: antibiotic abuse and overprescription (including inappropriate use for viral infections); use of antibiotics in animal feed for disease prevention and growth enhancement; and spread of resistant bacteria from humans and animals into the environment, including food chains. In order to combat human microbial pathogens, new molecular technologies and information are needed.

The WHO published an updated list on May 17, 2024, identifying 15 priority pathogen families grouped

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into three priority categories (critical, high, and medium) to guide research and development of new treatments and measures:

Critical Priority: Carbapenem-resistant *Acinetobacter baumannii*, third-generation cephalosporin-resistant *Enterobacterales*, rifampicin-resistant *Mycobacterium tuberculosis*.

High priority: Drug-resistant *Neisseria gonorrhoeae*, Methicillin-resistant *Staphylococcus aureus* (MRSA), and carbapenem-resistant *Pseudomonas aeruginosa*.

Medium priority: Group A and B streptococci and *Streptococcus pneumoniae* (*WHO Bacterial Priority Pathogens List 2024*, 2024).

In the past, there have been various recommendations for overcoming antibiotic resistance. One of the optional strategies to accomplish this goal is to mix phytochemicals with deteriorating antibiotics (Bazzaz et al., 2016; Betts & Wareham, 2014). These natural agents can act independently or synergistically with antibiotics to enhance antibacterial activity against a wide range of bacteria (Bazzaz et al., 2016; Tenover, 2006; Walsh, 2003). This approach offers several potential advantages: restoring efficacy to antibiotics that have lost effectiveness, reducing required antibiotic doses (potentially minimizing side effects), and targeting multiple bacterial mechanisms simultaneously to reduce resistance development.

According to studies, the bioactive compounds would target protein synthesis, cell wall biosynthesis, membrane structure, bacterial DNA replication, metabolic pathways, as well as efflux pump permeability, by inhibiting respectively disrupting them (Abass et al., 2022).

This review aims, through the study of the current literature, to emphasize, on the one hand, the main herbal products and their main bioactive compounds with antimicrobial activity and, on the other hand, the role of synergistic action between plant products and antibiotics in combating bacterial resistance.

METHODS

PubMed and Google Scholar were used as databases in this study. Studies were reviewed by 2025 using the keywords *plant products, antibiotics, drug-resistant bacteria, synergism, phytochemicals,* and *efflux pump.* The inclusion criteria for this review were: relevant articles written in English, from 2001- 2025, related to synergism of herbal products and antibiotics in combating bacterial resistance.

RESULTS AND DISCUSSIONS

Most of the herbal products contain a complex blend of components and thus have various antimicrobial properties. Results of the present study showed that the main bioactive compounds belong to terpenes, tannins, phenols, flavonoids, and alkaloids classes, who proven in different studies mentioned in the table below (Table 1) to have the capacity to disrupt the cell membrane, the cell wall, to prevent protein, DNA and ribonucleic acid (RNA) synthesis and to inhibit the efflux pump of the bacterial cell. The organisms inhibited are represented by gram positive (e.g. *Staphylococcus aureus, Staphylococcus saprophyticus, Streptococcus pneumoniae, Clostridium difficile,* and *Bifidobacterium longum)* and gram negative bacteria (e.g. *Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Escherichia coli*) (Riaz et al., 2023).

The effect of the associations on the antibacterial activity was reported as the FIC index. FIC index is a lab metric used in microbiology to quantify the interaction between two antimicrobial drugs, showing if they are synergistic, antagonistic, or additive, calculated by dividing the MIC of each drug in combination by its MIC alone, then summing these fractions. A lower FIC index generally suggests stronger synergy, with values around equal to 0.5 indicating strong synergy, 0.5-1.0 meaning partial synergy/additive effect, 1.0-4.0 indicating indifference, and more than 4.0 meaning antagonism.

Due to the extra protection afforded by the outer membrane, Gram (-) bacteria allow to be more resistant to antimicrobial agents than Gram (+) bacteria. Due to porin proteins, which facilitate the permeation of small molecules with a mass below 500 Da, the outer membrane is more permeable than the cell membrane. The passage of larger molecules through the cell membrane becomes easier if the outer membrane is damaged or loosened by Mg^{2+} removal, which leads to bacterial toxicity (Tao et al., 2016).

Probably, the different degrees of synergy between antibiotics and extracts used in the studies described below may have been due to the physicochemical interactions of molecules, as well as the different degrees of sensitivity of bacteria to the components of the herbal products (Khaliullina et al., 2024).

Table 1.

Herbal products and the antimicrobial activity of their bioactive compounds

Plant Name	Part Used	Main bioactive compounds	Organism inhibited	Mechanism	Refs.
Angelica archangelica	Root	Terpenes: α-pinene, δ-3-carene, β- phellandrene, limonene	*Bifidobacterium longum* *Bifidobacterium bifidum* *Clostridium difficile*	Disruption of the cell membrane	(Abass et al., 2022), (Fraternale et al., 2014)
			Escherichia coli *Bacteroides fragilis*		
			Candida albicans		
	Bark		*Listeria innocua*		

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Plant Name	Part Used	Main bioactive compounds	Organism inhibited	Mechanism	Refs.
Cinnamon zeylanicum		Terpenes: cinnamaldehyde, L-linalool, β- caryophyllene, eucalyptol, eugenol	*Staphylococcus aureus* *Bacillus cereus* *Escherichia coli* *Pseudomonas aeruginosa*	Disruption of the cell membrane	(Abass et al., 2022), (Alizadeh Behbahani et al., 2020)
Woodfordia fructicosa	Flower	Tannins	*Bacillus subtilis* *Micrococcus flavus* *Proteus mirabilis*	Disruption of the cell membrane	(Abass et al., 2022; Parekh & Chanda, 2007)
Hedychium spicatum	Rhizomes	Ethyl cinnamate Eucalyptol	*Bacillus subtilis* *Staphylococcus aureus* *Escherichia coli* *Pseudomonas aeruginosa* *Candida albicans*	Disruption of the cell wall	(Abass et al., 2022; Armugan, 2021)
Triumfetta welwitschii	Leaves	Phenols, flavonoids	*Bacillus cereus* *Escherichia coli*	Disruption of the cell membrane	(Abass et al., 2022; Moyo & Mukanganyama, 2015)
Cissus welwitschii	Leaves	Phenols, flavonoids	*Bacillus cereus* *Escherichia coli*	Disruption of the cell membrane Disruption of the cell membrane	(Abass et al., 2022; Moyo & Mukanganyama, 2015)
Dioscorea deltoidea	Tuber	Glycosides, alkaloids, tannins	*Staphylococcus aureus* *Escherichia coli*	Disruption of the cell wall	(Abass et al., 2022; Mierza et al., 2020)
Ginkgo biloba	Leaves	Flavonoids, terpenes, Ginkgolic acids, lipid (polyprenol)	*Staphylococcus saprophyticus*	Disruption of the cell membrane	(Abass et al., 2022; Zhang et al., 2018)
Humulus lupulus	Female cones	Rutin, bitter acids	*Staphylococcus aureus* *Staphylococcus epidermidis* *Cutibacterium acnes*	Cell wall damage	(Abass et al., 2022; Di Lodovico et al., 2020)
Aegle marmelos	Leave, fruits, barks	Cuminaldehyde, marmelosin (coumarin)	*Escherichia coli* *Salmonella typhimurium* *Staphylococcus aureus* *Streptococcus pneumoniae* *Klebsiella pneumonia* *Pseudomonas aeruginosa*	Prevents protein synthesis	(Abass et al., 2022)
Berberis aristata	Leaves	Berberine	*Bacillus cereus,* *Staphylococcus aureus* *Escherichia coli,* *Klebsiella pneumoniae*	Prevents protein and DNA synthesis	(Abass et al., 2022; Peng et al., 2015)
Phyllanthus emblica	Fruits	Alkaloids, tannins, saponins, flavonoids	*Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa*	RNA synthesis inhibition	(Abass et al., 2022; Dhale & Mogle, 2011; Kumari & Khatkar, 2016)
Rosa x damascena	Flower	Terpenes: β-linalool, citronellyl-formate	*Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa*	Inhibition of DNA gyrase	(Eman, 2014)

Plant Name	Part Used	Main bioactive compounds	Organism inhibited	Mechanism	Refs.
Urtica dioica	Leaves	Alkaloids, flavonoids, tannins, saponins, phenols	*Bacillus subtilis* *Staphylococcus aureus* *Pseudomonas aeruginosa*	Prevention of DNA synthesis	(Abass et al., 2022; Salih, 2014)
Silybum marianum	Fruits	Silybin Silymarin II	*Bacillus subtilis* *Staphylococcus epidermidis*	Inhibition of RNA synthesis and protein synthesis	(Lee et al., 2003)
Callistemon citrinus	Leaves	Alkaloids	*Escherichia coli* *Salmonella typhimurium* *Pseudomonas aeruginosa*	Inhibition of the efflux pump	(Abass et al., 2022; Mabhiza et al., 2016)
			Staphylococcus aureus, *Pseudomonas aeruginosa*		

DNA: deoxyribonucleic acid; RNA: ribonucleic acid.

Nevertheless, the analysed studies emphasize the synergistic effect between herbal products and antibiotics on both Gram (-) and Gram (+) bacteria. Among the associations that attracted attention, according to table 2, are: terpenes from *Salvia officinalis* + Ampicillin (FIC = 0.25)/ + Gentamicin (FIC = 0.25), *Thymus vulgaris*, *Origanum vulgare* + Imipenem against Carbapenem resistant *Acinetobacter baumanii*, + Trimethoprim against MRSA (FIC= 0.039), terpenes from *Zataria multiflora* + Vancomycin against *S. aureus* (FIC = 0.185), polyphenols from *Arctostahyllos uva-ursi* + Oxacilin + cefmetazole against MRSA, from *Senna macranthera* + Gentamicin (FIC = 0.32), Epigallocatechin-gallate from *Camellia sinensis* + Erythromycin, ampicilin/sulbactam, penicilin against MRSA, and alkalois from *Berberidaceae spp* (berberine) + Azythromycin (FIC = 0.375), from *Botryodiscia tetrandra* (*Stephania tetrandra*) + Cefazolin against MRSA.

Table 2.

Interactions between plant extracts/bioactive compounds and antibiotics on microbial strains

Herbal product/ bioactive compound	Bioactive compounds	Antibiotic	Bacteria treated	∑FIC	MIC	Interaction (SE-synergistic effect AE-additive effect)	Ref.
Salvia officinalis	Terpene and phenolic compounds: caryophyllen, eugenol, thymol	**Ampicillin** **Kanamycin** **Chloramphenicol** **Gentamicin** **Tetracycline**		0.25 0.37 1.5 0.25 0.375		SE SE indifference SE SE	(Silva et al., 2019)
Senna macranthera	Phenolic compounds: emodin, physcione, chrysophanol	**Ampicillin** **Kanamycin** **Chloramphenicol** **Gentamicin** **Tetracycline**		0.5 0.37 0.62 0.32 0.32		SE SE AE SE SE	(Silva et al., 2019)
Berberis sp.	Alkaloid: berberine	**Azithromycin**	**MRSA**	0.375		SE	(Hemaiswarya et al., 2008)
		Methicillin	**MRSA**			SE	
Stephania tetranda	Alkaloid: tetrandrine	**Cefazolin**	**MRSA**	0.250		SE	(Zuo et al., 2011)
Broussonetia papyrifera	Terpenes: carvacrol, borneol	**Pristinamycin**	*Klebsiella pneumonia*	0.500		SE	(Romo-Castillo et al., 2023)
Thymus maroccanus	Terpenes: carvacrol, thymol	**Ciprofloxacin**	***Vibrio cholerae***	0.140		SE	(Aelenei et al., 2016)
			Klebsiella pneumonia	0.370		SE	
			Staphylococcus aureus	0.260		SE	
			Pseudomonasaeruginosa	0.150		SE	
Zataria multiflora	Terpenes: thymol, carvacrol	**Vancomycin**	*Staphylococcus aureus*	0.185		SE	(Mahboubi & Ghazian Bidgoli, 2010)
		Vancomycin	**MRSA**	0.320		SE	
Arctostaphylos uva-ursi	Polyphenol: corilagin	**Oxacilin, Cefmetazole**	**MRSA**			SE	(Hemaiswarya et al.,

Herbal product/ bioactive compound	Bioactive compounds	Antibiotic	Bacteria treated	∑FIC	MIC	Interaction (SE-synergistic effect AE-additive effect)	Ref.
							2008; Shimizu et al., 2001)
Lycopus europaeus	Diterpenes	**Tetracycline**	*Staphylococcus aureus*			SE	(Gibbons et al., 2003; Hemaiswarya et al., 2008)
Hypericum perforatum	Polyphenol: Novoimanin	**Ampicillin, kanamycin, fusidic acid, rifocin**	*Staphylococcus aureus*			SE	(Hemaiswarya et al., 2008)
Punica granatum		**Ciprofloxacin, chloramphenicol, gentamicin, ampicillin, tetracycline, oxacillin**	**MRSA**			SE	(Braga et al., 2005)
Erythrina variegata	Isoflavone	**Mupirocin**	**MRSA**			SE	(Hemaiswarya et al., 2008; Sato et al., 2004)
Camellia sinensis	Epigallocatechin-gallate	**Erythromycin, ampicillin/sulbactam, ampicillin, penicillin**	**MRSA**			SE	(Reygaert, 2018)
Thymus vulgaris, Origanum vulgare, Lepidium flavum, Citrus bergamia	Essential oil: terpene: carvacrol	**Imipenem**	**Carbapenem-resistant** *Acinetobacter baumannii*			SE	(Al-Tawalbeh et al., 2024)
Carvacrol		**Sulfamethoxazole, Linezolid, Minocycline, Trimethoprim**	**MRSA**	0.039	4.000 15.6 62.5 7.8	SE, AE SE	(Al-Tawalbeh et al., 2024)
Thymus willdenowii	Essential oil	**Ticarcillin**	***Escherichia coli, Pseudomonas putida, Salmonella enteritidis, Enterobacter aerogenes, Pseudomonas aeruginosa***			SE	(Moussaoui & Alaoui, 2016)
Origanum compactum	Essential oil	**Tobramycin**	***Pseudomonasaeruginosa, Proteusmirabilis***			SE	(Moussaoui & Alaoui, 2016)
		Ticarcillin	***Staphylococcus aureus, Proteusmirabilis, Pseudomonas putida, Escherichia coli***				
Origanum majorana	Essential oil	**Tobramycin**	***Klebsiella pneumoniae, Pseudomonas putida***			SE	(Moussaoui & Alaoui, 2016)
		Imipenem	***Escherichia coli, Pseudomonas aeruginosa, Salmonella enteritidis, Pseudomonas putida, Klebsiella pneumoniae***				
		Gentamicin	***Klebsiella pneumoniae***				
		Ticarcillin	***Escherichia coli***				
Origanum vulgare		**Oxacilin**	***Staphylococcus aureus***		61.7 µg/mL	SE	(Rosato et al., 2020)

Herbal product/ bioactive compound	Bioactive compounds	Antibiotic	Bacteria treated	∑FIC	MIC	Interaction (SE-synergistic effect AE-additive effect)	Ref.
			Staphylococcus epidermidis Enterococcus faecalis		53.3 µg/mL 51.9 µg/mL		
		Gentamicin	***Staphylococcus aureus Staphylococcus epidermidis Enterococcus faecalis***		63.4 µg/mL 50.3 µg/mL 53.2 µg/mL	SE	
		Norfloxacin	***Staphylococcus aureus*** ***Staphylococcus epidermidis Enterococcus faecalis***		55.6 µg/mL 59.4 µg/mL 53.2 µg/mL	SE	
Melissa officinalis	Essential oil	**Tobramycin**	***Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas putida***			SE	(Moussaoui & Alaoui, 2016)
		Ticarcillin	***Escherichia coli, Klebsiella pneumoniae***				
		Imipenem	***Salmonella enteridis***				
		Gentamicin	***Proteus mirabilis***				
Glebionis coronaria (Chrysanthemum coronarium)		**Tobramycin**	***Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes, Staphylococcus aureus, Proteus mirabilis, Pseudomonas putida***			SE	(Moussaoui & Alaoui, 2016)
		Ticarcillin	***Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Pseudomonas mirabilis, Salmonella enteritidis***				
		Imipenem	***Escherichia coli, Staphylococcus aureus, Pseudomonas putida, Pseudomonas aeruginosa, Salmonella enteritidis***				
		Gentamicin	***Escherichia coli, Enetrobacter aerogenes***				
Cinnamaldehyde		**Cefotaxime**	***Escherichia coli,*** ***Klebsiella pneumoniae***	0.07-0.3/ 0.07-0.5	7.34 µg/mL/ 0.91 g/mL	SE	(Dhara & Tripathi, 2020)
		Ciprofloxacin	***Escherichia coli,*** ***Klebsiella pneumoniae***	0.07-0.5/0.1-0.5			
Cinnamomum zeylanicum	Cinnamaldehyde	**Gentamicin**	***Staphylococcus aureus*** ***Staphylococcus epidermidis Enterococcus faecalis***		64.8 µg/mL 63.2 µg/mL 55.9 µg/mL	SE	(Rosato et al., 2020)

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Herbal product/ bioactive compound	Bioactive compounds	Antibiotic	Bacteria treated	∑FIC	MIC	Interaction (SE-synergistic effect AE-additive effect)	Ref.
		Oxacilin	***Staphylococcus aureus*** ***Staphylococcus epidermidis*** ***Enterococcus faecalis***		52.2 µg/mL 64.3 µg/mL 45.2 µg/mL		
		Norfloxacin	***Staphylococcus aureus*** ***Staphylococcus epidermidis*** ***Enterococcus faecalis***		53.2 µg/mL 64.5 µg/mL 53.5 µg/mL		
Ginkgo biloba	Lipid (polyprenol)	**Gentamicin**	***Staphylococcus aureus*** ***Escherichia coli***		33.0 µg/mL 3.0 µg/mL	SE AE	(Tao et al., 2016)
Humulus lupulus		**Amikacin**	***Methicillin-resistant Staphylococcus*** ***Streptococcus sobrinus***		32 µg/mL 64 µg/mL 16 µg/mL	SE	(Khaliullina et al., 2024)
		Ciprofloxacin	***Methicillin-resistant Staphylococcus (MRSA)*** ***Streptococcus sobrinus*** ***Streptococcus salivarius***		16 µg/mL 16 µg/mL 16 µg/mL	SE	
		Ceftriaxone	***Methicillin-resistant Staphylococcus (MRSA)*** ***Streptococcusmutans*** ***Streptococcus sobrinus***		4 µg/mL 0.5 µg/mL 16 µg/mL 16 µg/mL	SE	
Cuminum cyminum	Essential oil: cuminaldehyde	**Ciprofloxacin**	***Escherichia coli*** ***Staphylococcus aureus***			SE	(Monteiro-Neto et al., 2020)
Tannic acid			***Acinetobacter baumannii*** ***Streptococcus agalactiae*** ***Pasteurella aerogenes***		>187.50 µg/mL >320 µg/mL 162.50 µg/mL	SE	(Lorca et al., 2024)
Silybum marianum	Silymarin, silibin	**Amikacin** **Gentamicin** **Amikacin** **Gentamicin**	***Escherichia coli***		156.25µg/mL 39.06 µg/mL 39.06 µg/mL 39.06 µg/mL	SE	(Rakelly de Oliveira et al., 2015)
Eucalyptus camaldulensis	Essential oil: eucalyptol	**Gentamycin, ciprofloxacin, polymixin**	***Acinetobacter baumannii***	<0.5	0.0005-0.002 mg/mL	SE	(Knezevic et al., 2016)
Mentha x piperita	Menthol, 1-menthone	**Oxacilin**	***Staphylococcus aureus*** ***Staphylococcus epidermidis*** ***Enterococcus faecalis***		59.0 µg/mL 67.6 µg/mL 45.2 µg/mL	SE	(Rosato et al., 2020)
		Gentamicin	***Staphylococcus aureus*** ***Staphylococcus epidermidis***		68.7 µg/mL 51.9 µg/mL	SE	

Herbal product/ bioactive compound	Bioactive compounds	Antibiotic	Bacteria treated	∑FIC	MIC	Interaction (SE-synergistic effect AE-additive effect)	Ref.
			Enterococcus faecalis		55.9 µg/mL		
		Norfloxacin	***Staphylococcus aureus***		47.7 µg/mL	SE	
			Staphylococcus epidermidis		58.9 µg/mL		
			Enterococcus faecalis		53.5 µg/mL		

SE: synergistic effect; AE: additive effect.

Validating the synergistic effect is crucial for safety in therapy, and there are still many combinations that lack clinical and toxicological studies. Thus, taking into account the benefits of combinations of plant products with antibiotics in fighting bacterial resistance, focusing on such studies is crucial for their use in the therapy of infections.

CONCLUSIONS

The prevalence of antibiotic resistance is a global clinical issue that is increasing every year.

Due to the limited development of new antimicrobial drugs or the reduced in vivo effectiveness of developed ones, combinative therapy, which involves combining substances from different chemical classes, but also from different sources in the case of natural preparations, is a forward-looking strategy for combating multi-resistant pathogens.

Antibacterial combinations can improve the effectiveness of antibiotics and suppress antibacterial resistance through synergistic activities.

Although the association of natural products with antibiotics is a promising area of research, their use in clinical practice is limited by the lack of solid scientific evidence, the risk of interactions and toxicity, and the difficulty of standardisation. Any such association must be made under strict medical supervision.

AUTHORS CONTRIBUTIONS

Conceptualization, M.L.M.; methodology, A.M.; data collection M.L.M.,E.C., F.G.G; data validation, M.L.M., L.I.V. and G.C.; data processing M.L.M.; writing—original draft preparation, M.L.M.; writing—review and editing, M.L.M.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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