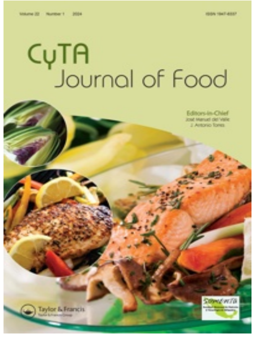

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Effects of nutraceuticals on antibiotic efficacy: a scoping review

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ABSTRACT
Interaction between nutraceuticals and antibiotics has attracted increasing interest as a potential approach to improve antibiotic efficacy. This scoping review aims to provide a comprehensive overview of the existing literature on the effects of nutraceuticals on antibiotic efficacy. An information specialist executed a multi-database search following the PRISMA-2020 guidelines to find articles published between 1 January 2013, and 1 April 2023. The addition of nutraceuticals to antibiotic treatments has shown promising results, for urinary tract infections, the supplementation of vitamin E alongside antibiotics significantly reduced the frequency of fever and urinary symptoms. In patients with hidradenitis suppurativa, the combination of MI, folic acid, and liposomal magnesium improved the efficacy of concurrent therapies and metabolic profiles. Immune manipulation with a nutraceutical alongside antibiotics proved effective and safe in reducing symptoms over time. These findings highlight the potential of nutraceutical addition to antibiotics in improving patient outcomes.

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KEYWORDS
Nutraceuticals; antibiotic; efficacy; interaction; nutrition

Introduction

Antibiotics play a crucial role in treating bacterial infections by inhibiting bacterial growth or killing bacteria. However, the overuse and misuse of antibiotics have led to the emergence of antibiotic-resistant bacteria, which has become a significant public health concern (Amann et al., 2019; Ventola, 2015). Antibiotic resistance occurs when bacteria evolve to become resistant to antibiotics, making it difficult to treat bacterial infections (Moghadam et al., 2020). The development of multidrug-resistant (MDR), extensively drug-resistant (XDR), and pan drug-resistant (PDR) bacteria have emerged, posing difficulties in treating infections with existing antibiotics (Magiorakos et al., 2012; Moghadam et al., 2020).

The rise of antibiotic-resistant bacteria has led to higher rates of morbidity, mortality, and healthcare costs, particularly among vulnerable populations such as geriatric and pediatric patients (Galistiani et al., 2022; Kusuma, Matuz, et al., 2022). It is estimated that antibiotic-resistant infections cause at least 700,000 deaths globally each year, and this number is expected to rise to 10 million by 2050 if appropriate measures are not taken (World Health Organization, 2014). The emergence of antibiotic-resistant bacteria poses a severe threat to public health, necessitating responsible antibiotic use and the development of novel strategies to combat antibiotic resistance (Begum et al., 2021; O'Neill, 2016). One promising area of investigation is the role of nutraceuticals in antibiotic efficacy.

Nutraceuticals are coined from "nutrition" and "pharmaceutical", bioactive compounds derived from food sources that, have gained recognition for their potential health benefits (Awuchi & Okpala, 2022; Karan et al., 2019). Nutraceuticals possess various therapeutic properties, such as anti-cholesterol, antioxidant, anti-inflammatory, and immune-modulating effects (Asif & Mohd, 2019; Marazzi et al., 2011). In the context of antibiotic therapies, nutraceuticals may offer a safer and more cost-effective alternative to conventional drugs, with potential benefits in modulating the immune response and maintaining gut health (Catinean et al., 2018; Larussa et al., 2017). The interaction between nutraceuticals and antibiotics has attracted increasing interest as a potential approach to augment antibiotic efficacy. The combined use of nutraceuticals and antibiotics may lead to synergistic effects, such as enhanced antimicrobial activity, reduced adverse effects, and the potential restoration of antibiotic sensitivity in resistant strains. Furthermore, nutraceuticals may play a role in promoting therapeutic success in challenging-to-treat infections or when used in conjunction with conventional antibiotic therapy. This interest is reflected in several studies that have investigated the effects of nutraceuticals on the intestinal microbiota and broiler meat production (Tolnai et al., 2021). Additionally, the use of medicinal plants and probiotics as nutraceuticals has gained attention as a potential avenue for biocompatible drug discovery and alternative food therapy (Anand et al., 2019; Bhandary et al., 2022). However, limited information exists regarding the relationship between nutraceutical use and antibiotic resistance, particularly in the context of increasing herbal remedy use among patients (Ward et al., 2002). Despite the potential benefits of nutraceuticals,

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further scientific studies are needed to prove their efficacy and reduce their side effects (Kalra, 2003).

This scoping review provided a comprehensive overview of the existing literature on the effects of nutraceuticals on antibiotic efficacy. This review established the current state of knowledge, identified the research gaps, and guided future research directions. The findings are relevant to healthcare professionals, researchers, and individuals seeking alternative or complementary treatment options.

Methods

Study design

A systematic literature search was conducted, and articles published between 1 January 2013, and 1 April 2023 were included in this scoping review. This scoping review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines used to guide this review (Page et al., 2021). The PICOS items, i.e. population, intervention, comparator, outcomes, and study design followed the previous scoping review (Kusuma, Pratiwi, et al., 2022). All curated studies were then imported into Zotero to identify and to remove duplicate records.

Search strategy

The systematic literature search was performed using PubMed, Cochrane, EBSCO, EMBASE, OVID, ProQuest, and Web of Science databases. The search strategy included both controlled vocabulary (e.g. MeSH terms) and relevant keywords related to nutraceuticals and antibiotics. The search strategy included a combination of keywords (nutraceuticals) AND (antibiotics) to conduct a scoping review following the PRISMA.

Eligibility criteria

The eligibility criteria for this scoping review were designed to identify relevant studies on the impact of nutraceuticals on antibiotic effectiveness while ensuring a focused and comprehensive approach. The inclusion criteria encompassed a variety of study types, including clinical trials in patients, case studies, observational studies, in vivo experiments, and surveys. This broad range of study designs allows for a comprehensive exploration of the topic from different angles and sources of evidence. On the other hand, the exclusion criteria were employed to exclude review articles, meta-analyses, in vitro studies, and in silico studies. By focusing on primary research and excluding these types of studies, the scoping review maintains a primary emphasis on original research and avoids duplication or summaries of existing literature.

Study selection

Two independent reviewers (IYK, MIB) screened the titles and abstracts of all identified articles for eligibility using the predefined inclusion and exclusion criteria using Rayyan AI software (Ouzzani et al., 2016). The data extraction screening included information on study design, participant characteristics, intervention details, outcomes, and limitations. Any disagreements were resolved through discussion and consensus. The full text of potentially eligible articles was then reviewed by the same two reviewers (IYK, MIB) using the same criteria. A third round of screening was also conducted to identify additional studies that met the inclusion criteria based on the full-text review of the reference lists. Two reviewers (IYK, MIB) separately extracted data, then cross-checked and compiled it by IYK. The synthesis involved a descriptive summary of the study characteristics and a thematic analysis of the reported outcomes in Microsoft Office Excel 2019 using a standardized template. The data included the author, year, country, title, study design, population/participants, intervention, duration of intervention, comparison/control group, and outcome provided (Table 1).

Results

Flow chart diagram

Based on the data presented in the flowchart diagram (Figure 1), a total of 536 records were identified from databases, including PubMed ($n = 49$), Cochrane ($n = 2$), EBSCO ($n = 2$), EMBASE ($n = 264$), OVID ($n = 60$), ProQuest ($n = 39$) and Web of Science ($n = 120$) databases. After removing duplicates by Zotero, 461 articles were assessed based on established inclusion and exclusion criteria. A total of 461 articles were excluded from the review that did not meet the established criteria. These exclusions were mainly due to inappropriate information such as population, study design, publication type, or outcome. The eligibility of the remaining 16 reports was assessed in the first screening.

Afterward, those 16 articles were subjected to a second screening performed through a face-to-face discussion and full-text analysis. After the second screening, we excluded 10 articles that did not meet the established criteria. Finally, 6 studies were selected (Alnour et al., 2022; Angka, 2015; Fabbrocini et al., 2016; Hu et al., 2021; La Manna et al., 2022; Yousefichaijan et al., 2015). The scoping review identified 6 studies that met the inclusion criteria, providing valuable insights into the application of nutraceuticals to antibiotics effectivity in patients. These findings can inform further research and practice in this area.

Characteristics of included studies

The included studies encompassed various study designs, including randomized controlled trials, laboratory-based in vitro studies, cross-sectional studies, and clinical trials. These studies were conducted in different countries, namely Iran, Italy, Canada, and China (see Table 1). The target groups of the studies ranged from patients with specific conditions (e.g. pyelonephritis, hidradenitis suppurativa, acute myeloid leukemia) to healthy individuals, researchers, healthcare professionals, and cancer patients undergoing chemotherapy.

Regarding our findings, based on studies published from 2013 to 2023, the addition of nutraceuticals to antibiotic treatments has shown promising results in various medical conditions. For urinary tract infections, the supplementation of vitamin E alongside antibiotics significantly reduced the frequency of fever and urinary symptoms (Yousefichaijan et al., 2015). In patients with hidradenitis suppurativa, the combination of MI, folic acid, and liposomal magnesium improved the efficacy of concurrent therapies and metabolic

Table 1. Summary findings of effects of nutraceuticals on antibiotics efficacy.

Author Name	Country	Study Design	Target Group	Nutraceuticals vs Antibiotics Name	Outcome Measure	Summary of Findings
Yousefichaijan et al., 2015	Iran	Randomized Controlled Trial	152 girls aged 5 to 12 years	Supplements of vitamin E in addition to the antibiotics (vitamin E, fat-soluble vitamin that functions as an antioxidant vs Antibiotic, Intravenous Ceftriaxone and Oral Cefixime)	The results of DMSA (Dimercaptosuccinic Acid) scan	The mean frequency of fever, urinary frequency, urgency, dribbling, and urinary incontinence were significantly lower in the intervention group (14-day treatment with supplements of vitamin E + Antibiotic) compared to the control group (Antibiotic only). There was no significant difference in the results of urine culture 3 to 4 days after the start of treatment and 7 to 10 days after its termination. There was also no significant difference between the results of DMSA scan 4 to 6 months after the start of treatment. Vitamin E supplementation has a significant effect in ameliorating sign and symptoms of UTI (Urinary Tract Infection).
Fabbrocini et al., 2016	Italy	Randomized Controlled Trial	30 young male patients with acne resistant and an altered metabolic profile hidradenitis suppurativa (HS) Group A: 15 subjects (myo-inositol) 2000 mg, liposomal magnesium (56.25 mg) and folic acid associated to topical antibiotics and normocaloric diet Group B: 10 subject only topical antibiotic and normocaloric diet	Liposomal Magnesium and folic acid vs clindamycin and rifampicin	Sarturius score, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)	Supplementation of MI, folic acid and liposomal magnesium in hidradenitis suppurativa (HS) can improve the efficacy of concomitant therapies (clindamycin 300 mg b.i.d. and rifampicin 600 mg daily for 6 weeks) and the metabolic profile.
Angka, 2015	Canada	Laboratory-Based In Vitro Study Conducted on Three acute myeloid leukemia (AML) Cell Lines (OCI-AML2, KG1a And U937)	Cancer patients who are undergoing chemotherapy	Drug nutraceutical (zinc) vs cytarabine and daunorubicin	Identification of zinc as a nutraceutical that enhanced acute myeloid leukemia (AML) chemotherapy efficacy and echinacea as a nutraceutical that hindered AML chemotherapy efficacy	Zinc enhanced AML chemotherapy efficacy while echinacea hindered it. Patients undergoing chemotherapy must consult with their oncologist before consuming over-the-counter supplements due to the positive and negative effects of nutraceuticals.
Hu et al., 2021	China	Randomized, Double-Blind Exploratory Clinical Trial.	1295 Adults with acute uncomplicated diarrhoea aged 18 to 70 Group A: loperamide Group B: loperamide and berberine Group C: loperamide and turmeric Gruop D: loperamide, berberine and turmeric	Loperamide, berberine and turmeric vs ciprofloxacin	Primary feasibility outcomes, Secondary patient-centred outcomes, use of antibiotics, Severity of symptoms, Incidence of side-effects	Only a small percentage of patients were eligible for the study, with mild symptoms, and good follow-up. Re-consultation rates were low, and there were no serious treatment-related adverse events. Most participants recovered quickly without antibiotics. Patients with mild diarrhea accepted trying an alternative to antibiotics. The three-nutraceuticals therapy requires further evaluation in a fully powered, randomized controlled trial among a broader sample.

(*Continued*)

Table 1. (Continued).

Author Name	Country	Study Design	Target Group	Nutraceuticals vs Antibiotics Name	Outcome Measure	Summary of Findings
La Manna et al., 2022	Italy	Randomized Controlled Trial, Clinical Trial	Group A was treated with an oral antibiotic for 7–10 days associated with a 2-week Group B was treated with antibiotics and a 2-week course of Abincol® alone	Abincol vs antibiotic (treatment of acute pharyngotonsillitis)	Wilcoxon test to compare severities and the McNemar test to compare proportions	922 outpatients with acute pharyngotonsillitis were enrolled and well-matched in two groups. At T1, there was no significant difference in symptom frequency and severity between groups. At T2, Group A had a lower frequency of symptoms, but no significant difference in severity. At T3, there was no intergroup difference in symptom frequency and severity, but both progressively diminished. Immune manipulation with the nutraceutical was found to be effective and safe as a therapeutic option for managing patients with acute pharyngotonsillitis and treated with antibiotics.
Alnour et al., 2022	Italy	Cross-Sectional Study, In Vitro Protocol	Researchers, healthcare professionals, and individuals	Flavonoids rutin and quercetin vs antibiotics gentamicin (an aminoglycoside) and ceftriaxone (a third-generation cephalosporin)	MIC (Minimum Inhibitory Concentration) and checkerboard assay	Rutin and quercetin showed no response when tested against resistant clinical isolates. However, combinations of these compounds with gentamicin or ceftriaxone exhibited a synergistic effect against MDR and XDR isolates. The synergism effect occurred within the standard MIC level of gentamicin and ceftriaxone. Rutin and quercetin, which are commonly found in human diets, have the potential to restore the efficacy of antibiotics against drug-resistant clinical isolates. Their use as nutraceuticals in adjuvant therapies in combination with antibiotics is a promising therapeutic strategy against superbug infections.

profiles (Fabbrocini et al., 2016). However, caution is advised for patients undergoing chemotherapy, as zinc enhanced chemotherapy efficacy while echinacea hindered it, highlighting the importance of consulting oncologists before using over-the-counter supplements (Angka, 2015). In the case of acute uncomplicated diarrhea, a three-nutraceutical combination demonstrated potential as an alternative to antibiotics, with low re-consultation rates and quick recovery observed (Hu et al., 2021). Furthermore, in the management of acute pharyngotonsillitis, immune manipulation with a nutraceutical alongside antibiotics proved effective and safe in reducing symptoms over time. Lastly, rutin and quercetin, when combined with certain antibiotics, exhibited a synergistic effect against drug-resistant clinical isolates, suggesting their potential use as adjuvant therapies to restore antibiotic efficacy against superbugs (La Manna et al., 2022). Overall, these findings highlight the potential of nutraceutical addition to antibiotics in improving patient outcomes (Table 1).

Discussion

The findings of this scoping review shed light on the effects of nutraceuticals on antibiotic efficacy in various clinical contexts. Several key themes and patterns emerged from the reviewed studies, which provide valuable insights and implications for healthcare professionals, researchers, and individuals seeking alternative or complementary treatment options.

The studies highlight the complex interplay between nutraceutical supplements and traditional treatments across various medical conditions. They emphasize the importance of consulting healthcare professionals before incorporating supplements into treatment regimens. Findings suggest promising adjunctive therapies, such as vitamin E for urinary tract infections (UTIs) and flavonoids with antibiotics for drug-resistant infections. The mechanism of flavonoids in infection therapy can be seen in Figure 2. Integrating nutraceuticals with conventional treatments shows potential in optimizing outcomes and managing symptoms effectively. Further research is needed to validate these findings and establish evidence-based guidelines for their use. Overall, these insights underscore the evolving landscape of healthcare and the potential benefits of personalized, integrated treatment approaches.

In addition to human health, the use of antibiotics in animal production has raised concerns due to the emergence of antibiotic resistance. Researchers are exploring alternative antimicrobial options such as nutraceuticals. Nutraceuticals like polyphenols, essential oils, and probiotics are being investigated for their potential to replace antibiotics in livestock farming (Xia et al., 2021). Studies have shown that nutraceuticals, including anthocyanidins and anthocyanins, possess antimicrobial properties and can contribute to improving animal health and productivity (Khoo et al., 2017). Additionally, the use of optimal combinations of alternatives, along with good management practices, is crucial for maximizing animal performance while reducing antibiotic use in the animal industry (Gadde et al., 2017). Furthermore, nutraceuticals derived from sources like mushrooms, grape flavonoids, and Bambara groundnut are being studied for their potential health benefits and antimicrobial properties (Barros et al., 2008; Georgiev et al., 2014). These natural compounds offer promising alternatives to antibiotics in animal feed. For instance, botanical products are being used as nutraceutical feed additives in livestock farms to enhance animal health and productivity (El-Sabrout et al., 2023). Moreover, the bioactive peptides found in sources like octopus skin mucus are being explored for their antimicrobial properties, presenting a natural alternative to synthetic antibiotics (Pérez-Polo et al., 2023).

One notable finding is the significant reduction in symptoms associated with urinary tract infections (UTIs) through the supplementation of vitamin E in combination with antibiotics (Hemilä, 2016; Nazıroğlu et al., 2012). Vitamin E addition with antibiotics significantly reduces fever, urinary frequency, urgency, dribbling, and urinary incontinence in UTI patients, with no significant difference in urine culture results and DMSA scan after treatment (Yousefichaijan et al., 2015). This effect may be attributed to the antioxidant properties of vitamin E, which can help alleviate inflammation and oxidative stress in the urinary tract, contributing to the pathogenesis of UTIs (Figure 3). Furthermore, the combination of vitamin E and antibiotics may enhance both antimicrobial activity and the immune response necessary for a complete recovery from UTIs (Hemilä, 2016; Nazıroğlu et al., 2012). The effect of vitamin E on antibiotics has been investigated in several studies, revealing its potential as an adjuvant and immune-modulatory agent (Liu et al., 2014). Vitamin E has shown synergistic antimicrobial effects when used in combination with distinct antibiotic compounds, making it a promising adjunct treatment option against infectious diseases caused by multidrug-resistant bacteria such as *Pseudomonas aeruginosa, Burkholderia cenocepacia*, and Methicillin-resistant staphylococcus aureus (MRSA) (Hartman, 2020). Additionally, vitamin E has been found to inhibit bacterial lipocalin antibiotic binding, increasing the sensitivity of bacteria to antibiotics and enhancing their killing efficacy in vitro and in vivo (Naguib et al., 2018). Furthermore, studies have demonstrated that vitamins, including vitamin E, exhibit synergistic antimicrobial effects with antibiotics against resistant bacterial strains, suggesting their potential use as tools to treat multidrug-resistant superbugs (Shahzad et al., 2018). Moreover, vitamin E has shown to modulate neutrophil responses and enhance their ability to kill *Streptococcus pneumoniae*, suggesting its potential as a nutritional intervention to combat pneumococcal infections (Bou Ghanem et al., 2017). These findings highlight the promising role of vitamin E in enhancing the efficacy of antibiotics, combating multidrug-resistant bacteria, and modulating host immune responses against bacterial challenges.

In the context of hidradenitis suppurativa (HS), the supplementation of Myo-inositol, folic acid, and liposomal magnesium has shown promising results in improving the effectiveness of concomitant therapies and enhancing the metabolic profile (Fabbrocini et al., 2016). A recent study also found that these supplementations have enhanced the effectiveness of concomitant therapies and have improved the metabolic profile in individuals with HS (Kim et al., 2022). Myo-inositol, in particular, has demonstrated its safety and efficacy in restoring ovarian activity and fertility in patients with polycystic ovary syndrome (PCOS) (Yasmin et al., 2019). The combined supplementation of myo-inositol and folic acid has also shown effectiveness in reducing the risk of neural tube defect (NTD) pregnancies (Cavalli et al., 2011).

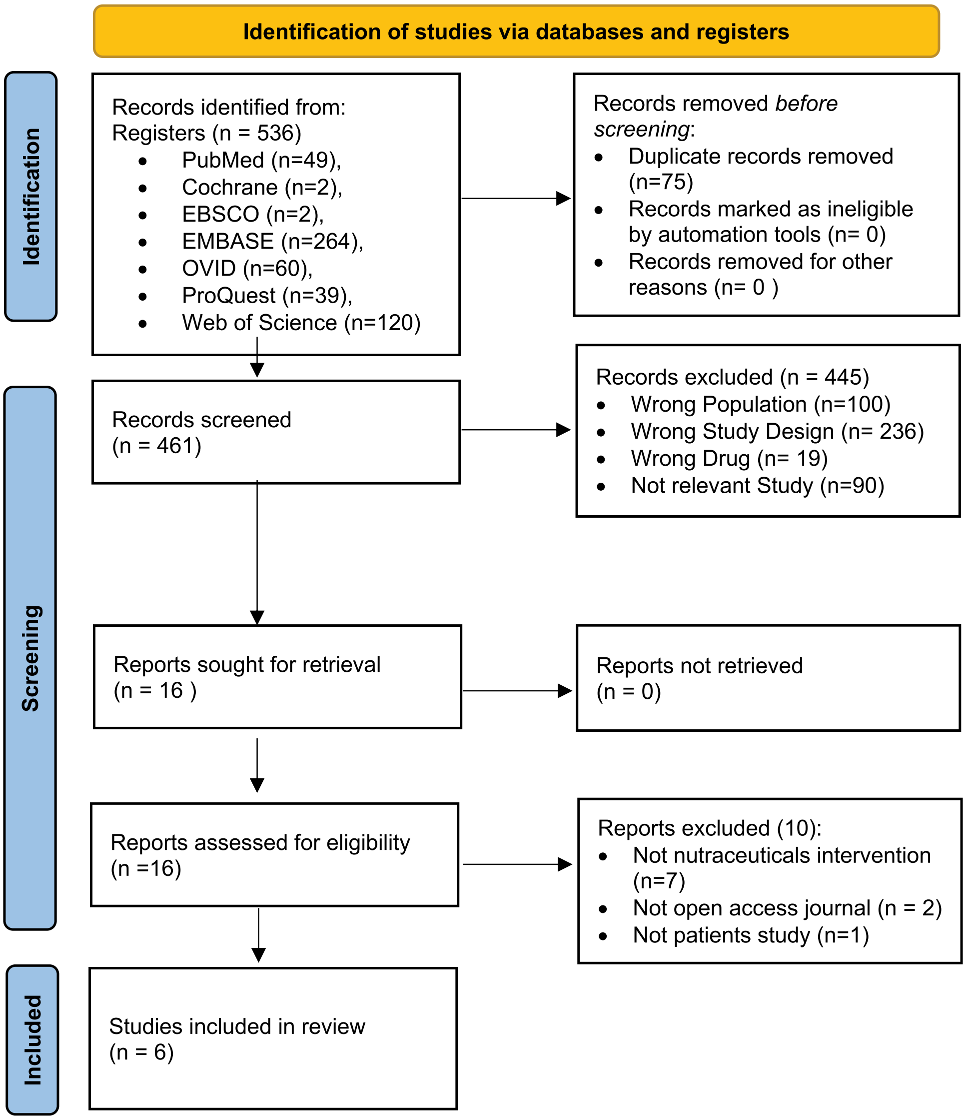

Figure 1. Flowchart diagram a scoping review of effects of nutraceuticals on antibiotics efficacy.

The effect of myo-inositol on antibiotics has been investigated in several studies. One study conducted on common carp infected with Aeromonas hydrophila found that the co-administration of myo-inositol and florfenicol, an antibiotic, significantly increased the bactericidal efficacy of florfenicol and reduced the bacterial load in infected fish tissues, suggesting that myo-inositol enhances the antimicrobial activity of antibiotics against A. hydrophila infection. Additionally, myo-inositol exhibited synergistic action with other antibiotics, such as neomycin sulfate, ceftriaxone, and enrofloxacin (Liang et al., 2018). Another study focusing on *Escherichia coli* infection revealed that exogenous myo-inositol improved the ability of macrophages to eliminate balofloxacin-resistant *E. coli*. Myo-inositol depolarized macrophages, enhancing their adherence to both balofloxacin-sensitive and balofloxacin-resistant strains, thereby promoting phagocytosis of the resistant strain. These findings suggest that myo-inositol can modulate host responses and aid in eliminating antibiotic-resistant bacteria (Hai et al., 2015). Furthermore, a study on *Lactobacillus plantarum*, a lactic acid bacterium, showed that an inositol-producing strain exhibited antibacterial activity against *Pseudomonas fluorescens* and *Listeria monocytogenes* (Fu et al., 2022). Collectively, these studies highlight the potential of myo-inositol as an adjuvant to antibiotics, enhancing their efficacy against bacterial infections and potentially reducing the occurrence of antibiotic resistance. Chen, et.al. also reported that myo-inositol-1-phosphate synthase played a critical role in oxidative stress resistance in *Corynebacterium glutamicum* (Chen et al., 2019). Our findings highlight the potential of myo-inositol as an adjuvant to antibiotics, enhancing their efficacy against bacterial infections and potentially reducing the occurrence of antibiotic resistance.

Chemotherapy patients should exercise caution when considering nutraceutical supplementation. In Addition, zinc improved the effectiveness of AML chemotherapy. At the same time, echinacea had a negative impact, highlighting the importance for chemotherapy patients to consult with their oncologist regarding the use of nutraceuticals. In contrast, echinacea has been shown to have a negative impact (Angka, 2015). Therefore, chemotherapy patients need to consult with their oncologist regarding the use of nutraceuticals. Previous research also supports these findings, as a randomized, blinded, controlled clinical trial found that Echinacea reduced antibiotic usage in children by preventing respiratory tract infections (Ogal et al., 2021).

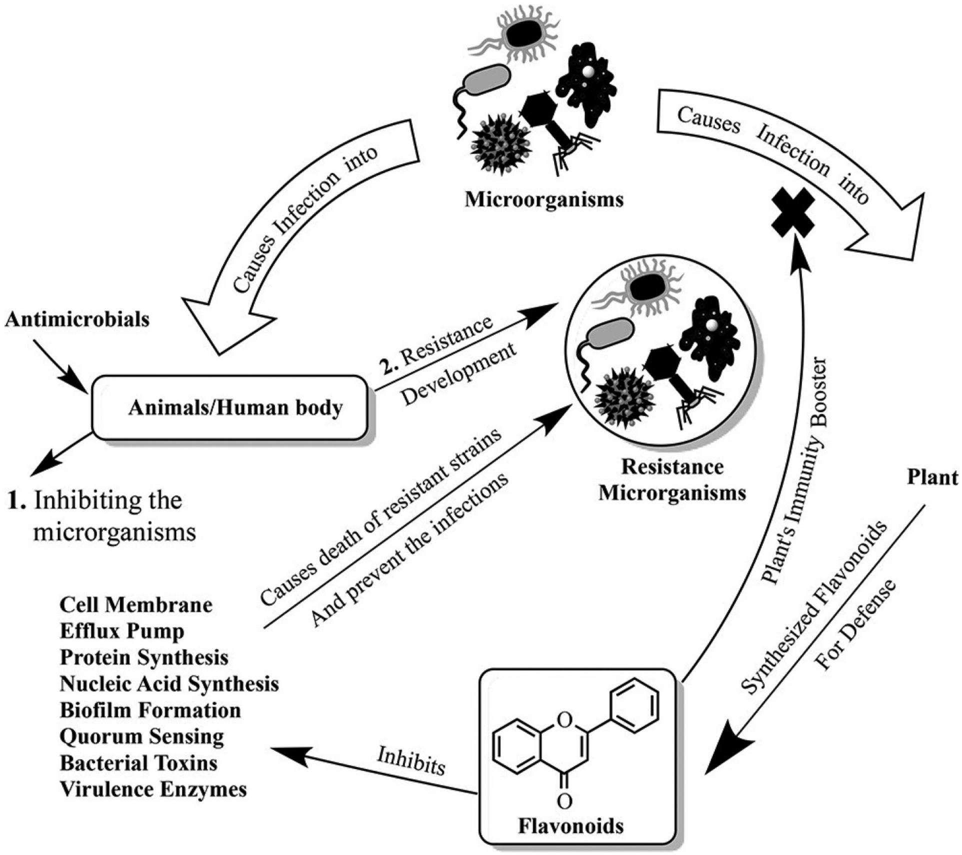

Figure 2. Mechanism of flavonoids with antibiotics for drug-resistant infections.

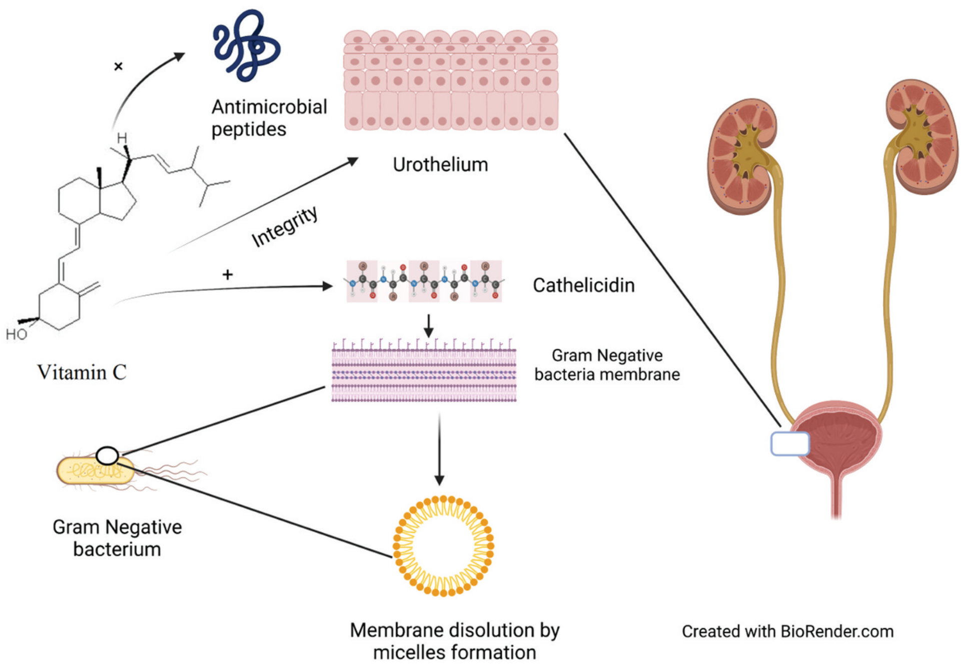

Figure 3. Effect of vitamin E on urinary tract infections (UTIs).

For patients experiencing diarrhea, it is advisable to reconsider the use of antibiotics and explore safe nutraceutical alternatives. In China, physicians successfully avoided prescribing antibiotics to patients with mild diarrhea by utilizing loperamide, berberine, and turmeric as alternative treatments (Hu et al., 2021). However, further research is needed to evaluate the efficacy of these alternative therapies. It is important to note that berberine can bind to human serum albumin, potentially influencing its distribution and metabolism within the body (Hu et al., 2009). Additionally, berberine has the ability to reduce the oral bioavailability of the antibiotic ciprofloxacin (Hwang et al., 2012). Therefore, caution should be exercised when combining loperamide, berberine, and turmeric with other medications, and close monitoring of potential drug interactions is recommended.

A new multi-component food supplement called Abincol Immuno® has been proven to aid in the recovery from acute pharyngotonsillitis. The supplement contains a probiotic mixture consisting of *L. plantarum, Lacticaseibacillus rhamnosus*, and *Lactobacillus delbrueckii subsp. bulgaricus*, as well as zinc, inulin, and vitamin D. Several studies have provided support for the effectiveness of this supplement. For example, La Mantia et al. discovered that a probiotic mixture containing *L. plantarum LP01, Lactobacillus lactis* subspecies cremoris LLC02, and *Lactobacillus delbrueckii* reduced symptoms and potential relapse in patients with both acute and chronic pharyngotonsillitis (La Mantia et al., 2020). However, supplementing probiotic treatment with *Streptococcus salivarius* in patients with acute pharyngotonsillitis treated with penicillin was found to be ineffective according to a study by Gilbey et al (Gilbey et al., 2015). Another study by Salvatore et al. found that zinc supplements significantly reduced stool output and the duration, persistency, and severity of diarrhea in acute gastroenteritis (Salvatore et al., 2007). Further research is needed to determine the overall efficacy of this treatment in the management of pharyngotonsillitis due to the there have been no trials conducted with zinc in developed countries.

In the context of rutin and quercetin, their application can alter the resistance mechanism of antimicrobial agents, shifting them towards susceptibility and thereby reinstating the efficacy of the drugs (Alnour et al., 2022). Ghanbari-Movahed et al. study demonstrated that nano-formulations of rutin and quercetin exhibit anticancer activities and molecular mechanisms that enhance the treatment of various malignancies (Ghanbari-Movahed et al., 2022).

To optimize antibiotic use, addressing antimicrobial resistance, understanding the role of the microbiome, improving diagnostic tools, and addressing socioeconomic factors are crucial. Strategies like antibiotic stewardship programs, microbiome-targeted therapies, and enhanced healthcare access can help mitigate these challenges and ensure effective antibiotic treatment while minimizing resistance and improving patient outcomes.

This review has several limitations to consider. Firstly, publication bias may exist as only published studies were included, potentially excluding studies with non-significant or negative findings. Secondly, the heterogeneity of study designs, methodologies, sample sizes, and populations studied may limit direct comparisons and data synthesis. Thirdly, a formal quality assessment of the included studies was not conducted, which may impact the overall reliability and quality of the evidence. This is because a review is more than just a review and integration of existing literature; extensive critical analysis and conceptual innovation are the most important foundations of this type of review. Emphasis is on the conceptual contribution of the included studies, rather than on formal quality assessment. Fourthly, the search strategy focused on specific databases and was limited to English language publications, potentially overlooking relevant studies and introducing a language bias. Furthermore, the lack of standardized terminology for nutraceuticals may lead to inconsistencies in reporting and categorization. Additionally, the review did not perform a meta-analysis due to the heterogeneity of the studies, limiting the ability to provide quantitative summaries. Lastly, the review's findings are based on literature up until April 2023, and more recent evidence may not be captured. Despite these limitations, this scoping review offers a comprehensive overview, identifies key themes, and serves as a valuable resource for healthcare professionals and individuals seeking alternative treatment options.

Conclusion

This scoping review highlights the potential of nutraceuticals in enhancing antibiotic efficacy across various clinical contexts. Vitamin E supplementation shows promise in alleviating symptoms of urinary tract infections (UTIs) and boosting immune response. Myo-inositol supplementation may enhance the effectiveness of concomitant therapies and combat antibiotic resistance in conditions like hidradenitis suppurativa (HS). Caution is advised for chemotherapy patients considering nutraceutical supplementation. Safe alternatives such as loperamide, berberine, and turmeric should be explored for managing diarrhea. The multi-component food supplement Abincol Immuno® aids in the recovery from acute pharyngotonsillitis. Rutin and quercetin have the potential to reinstate antimicrobial efficacy. Future research should focus on well-designed trials to validate these findings, explore mechanisms of action, optimize treatment protocols, and address limitations. This will enhance our understanding of nutraceuticals' role in enhancing antibiotic efficacy and guide evidence-based treatment strategies in infectious diseases, including the possibility of conducting meta-analyses for more robust conclusions.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Authors contributions

IYK and MI drafted the initial version of the report, designed, and implemented the literature search. EAW contributed to the review of abstracts and full texts. IYK, NH, and MI were responsible for analyses. All authors contributed to the interpretation of findings and revision of drafts and approved the final version of the manuscript.

Data availability statement

The data supporting this study findings are available from the corresponding author upon reasonable request.

Abbreviations

MDR: Multidrug-resistant; XDR: Extensively drug-resistant; PDR: Pan drug-resistant; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PICOS: Population, intervention, comparator, outcomes, and study design; UTIs: Urinary tract infections; DMSA: Dimercaptosuccinic acid; MRSA: Methicillin-resistant staphylococcus aureus; HS: Hidradenitis suppurativa; PCOS: Polycystic ovary syndrome; NTD: Neural tube defect; AML: Acute myeloid leukemia.

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