

## Review Article

# From Beneficial to Pathogenic: Transformation of Our Gut Microbiota by Antibiotics



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## ABSTRACT

**Background:** The gut microbiome highlights the significance of understanding the relationship between antibiotic use and microbial alterations. This knowledge is crucial for the current health status and future medical practices.

**Objectives:** This review examines the effects of antibiotics on gut microbiota, emphasizing the significant changes in microbial composition resulting from their use.

**Methods:** Relevant articles published until February 2025 were retrieved from Medical databases, including PubMed/MEDLINE, ScienceDirect, Scopus, Web of Science, and Google Scholar, using keywords, such as “antibiotics,” “gut microbiota,” “dysbiosis,” “antibiotic resistance,” and “microbial diversity.”

**Results:** Antibiotics profoundly disrupt the microbiota balance, potentially leading to chronic diseases and metabolic changes. Dysbiosis, or microbial imbalance, can arise from factors like diet and antibiotic exposure, reducing microbial diversity and promoting pathogenic species over beneficial ones. Clinically, dysbiosis is linked to increased risks of autoimmune disorders, obesity, and inflammatory bowel diseases. Specific antibiotics, including amoxicillin and levofloxacin, exhibit varying effects on gut microbiota. Dietary interventions are suggested to restore beneficial bacteria and enhance gut health. Further research should explore the long-term consequences of antibiotic use on gut health and emphasize developing effective recovery strategies.

**Conclusion:** The main conclusion of this review is that antibiotics dramatically reduce gut microbial diversity and balance and accelerate dysbiosis, which is associated with long-term health risks that requires nutritional and therapeutic strategies to restore microbial balance.

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## Introduction

The microbiome refers to the collective genomes of all microorganisms in the body, while the microbiota denotes the living organisms inhabiting specific environments such as the gut, skin, and oral cavity [1].

The gut microbiota, including bacteria, archaea, and eukaryotes, may comprise over  $10^{14}$  organisms. Historically, the uterus, amniotic fluid, and fetus were deemed sterile, but evidence now suggests that the placenta and amniotic fluid host bacteria derived from maternal gut and oral microbiota, though transmission pathways are unclear. Maternal influence on the infant's microbiota evolves from fetus to infant and is shaped by maternal diet, weight gain, probiotic and antibiotic use, delivery mode, and infant feeding practices. After birth, the infant's gut microbiota diversifies significantly, especially with solid-food introduction. Short-term, intensive nutritional changes can quickly affect microbiota diversity. External factors like lifestyle and medications, along with internal factors such as host genetics and immune/metabolic regulation, collectively shape the gut microbiota [2].

In recent decades, substantial evidence has highlighted the critical role of the human microbiota in maintaining health through various procedures. These activities include forming barriers that protect the host against pathogens, competitive elimination of harmful microorganisms, and the production of antimicrobial substances. Furthermore, the microbiota contributes to the development of the intestinal mucosa and the immune system. Microbes can extract energy from food, enhance nutrient absorption, and provide essential enzymes and biochemical pathways for human metabolism. They play a significant role in various metabolic processes, including the activation of nutrients and the metabolism of xenobiotics, as well as the biosynthesis of vitamins beneficial to the host, such as vitamin K [1, 3].

The concept of dysbiosis, coined by Metchnikoff, describes an imbalance in the microbiota where beneficial microorganisms are quantitatively and qualitatively altered, leading to potential pathogenic conditions. Dysbiosis can result from a wide spectrum of factors, including modern dietary habits and antibiotic use, which can disrupt normal intestinal microflora. Antibiotics, widely used in clinical practice, can significantly alter the gut microbiota by affecting both pathogenic and benign bacteria, leading to ecological disturbances that may result in metabolic changes and contribute to chronic and degenerative diseases [4, 5]. Since the discovery of peni-

cillin in 1928, antibiotics have revolutionized medicine and saved countless lives by effectively treating bacterial infection. However, evidence indicates that antibiotic use can cause microbiota dysbiosis, disrupting its composition and function. A broad range of antibiotics can impact up to 30% of the bacterial community, and while the microbiota may partially reconstitute after treatment, full restoration is often not achieved. Antibiotic-induced changes in microbial composition can persist for months or even years [6]. The indiscriminate use of antibiotics can disrupt the taxonomic composition of the gut microbiome, often serving as a risk factor for developing various diseases, including autoimmune disorders, metabolic diseases, and malnutrition [7]. This article aims to review the effects of commonly used antibiotics on microbiota, exploring the implications of these effects on human health and the potential long-term consequences of antibiotic-induced dysbiosis.

## Materials and Methods

To do this narrative review article, we conducted a comprehensive search in PubMed/MEDLINE, ScienceDirect, Scopus, Web of Science, and Google Scholar for articles published up to February 2025, using keywords related to antibiotics, gut microbiota, dysbiosis, antibiotic resistance, and microbial diversity. The inclusion criteria were research studies examining the impact of antibiotics on gut microbiota or related outcomes, articles published up to February 2025, and studies accessible in English. The exclusion criterion included studies lacking relevant microbiome outcomes. Study selection was performed by two independent reviewers who screened titles and abstracts as well as full texts, with disagreements resolved by discussion. Data extraction captured study design, subjects (human, animal, or model systems), antibiotic exposure, microbiome assessment methods, and outcomes pertinent to diversity or resistance. A concise flow description of records identified, screened, excluded, and included is provided. Quality assessment of risk of bias was conducted using appropriate tools tailored to each study design.

## Results and Discussion

Antibiotics are classified into different groups based on their chemical or molecular structure, including  $\beta$ -lactams, macrolides, tetracyclines, quinolones, aminoglycosides, sulfonamides, glycopeptides, and oxazolidinones [8]. Table 1 presents a summary of each antibiotic, its main microbiota effects, resistance risks, and clinical implications.

**Table 1.** Antibiotics' main microbiota effects, resistance risks, and clinical implications

Class and Example Agent	Main Effects on Gut Microbiota (Populations, Diversity)	Resistance Risks and Mechanisms	Clinical Implications and Typical Disruption Duration
βLactams (penicillins (amoxicillin, phenoxymethylpenicillin)	Generally mild-to-moderate compositional change: several primarycare studies reported very little measurable effect for phenoxymethylpenicillin and amoxicillin on overall diversity in adults [22] Broad cephalosporins often reduce diversity and suppress anaerobes, increasing relative proteobacteria/ <i>Bacteroidetes</i> in some cohorts [23, 24]	Selection/enrichment of β-lactamase genes: microbiotaencoded β-lactamases can protect community members via antibiotic inactivation [27]	Commonly used penicillins often cause transient shifts: long courses or co-administered broad agents increase MDR carriage risk [22, 27]
βLactams (cephalosporins (broad-spectrum)		Strong selection for ESBLs and mobile β-lactamases: horizontal transfer among Enterobacteriaceae is common [27]	Increased risk of colonization by resistant Enterobacteriaceae and <i>C. difficile</i> infection (CDI) when anaerobic competitors are suppressed [27, 24]
Carbapenems (meropenem)	Profound compositional effects when used systemically: Volunteer data with meropenem (with vancomycin/colistin) showed partial restoration of richness/diversity only after months [25]	Selection pressure for carbapenemase genes in gut reservoirs: risk amplified in prolonged/prophylactic use [27]	Large ecological footprint: prolonged courses can produce long-lasting perturbation and MDR acquisition in hospitalized patients [23, 25]
Fluoroquinolones (ciprofloxacin)	Significant compositional shifts reported: Single agent ciprofloxacin altered composition for ~1 month in volunteers and produced detectable community changes in patient cohorts [23, 25]	Selection of plasmid and chromosomal quinolone resistance (qnr, target mutations): Co-selection of MDR lineages (e.g. <i>E. coli</i> ST131) seen clinically [27]	Community structure may differ from baseline one month posttreatment: in prolonged therapy (e.g. bone infections) shifts can be pronounced though Shannon index may not always decrease [23, 25]
Macrolides (clarithromycin)	Clarithromycin decreased enterobacteria and anaerobic commensals ( <i>Bifidobacterium</i> , <i>Lactobacillus</i> ) and reduced diversity for up to ~5 weeks in some studies [22]	Macrolide resistance genes (erm family) are enriched in the gut resistome after exposure [27, 28]	Transient but clinically relevant reductions in beneficial anaerobes; potential for increased ARG carriage [22, 27]
Tetracyclines (doxycycline)	Doxycycline associated with marked short-term decreases in <i>Bifidobacterium</i> diversity and compositional shifts in several trials [22]	Increased burden of tetracycline resistance in subgingival, gastrointestinal and respiratory flora after 2–18 weeks of use: resistance may persist variably up to months [29]	Prophylactic or prolonged doxycycline can raise resistome burden; trials of doxycycline prophylaxis stress AMR monitoring [22, 29]
Aminoglycosides	Insufficient evidence in the supplied clinical literature to define consistent, class specific gut community changes in humans.	Aminoglycoside resistance genes (e.g. <i>aac(6')Ib</i> ) have been detected in infant gut samples after antibiotic exposures, indicating selection risk [28]	Clinical gut microbiota effects unclear from current supplied corpus: resistance gene enrichment is possible, especially in early life [28]
Glycopeptides (vancomycin)	Systemic vancomycin strongly depletes gram positive anaerobes; in volunteer cocktail (with meropenem/colistin) richness/diversity partially restored only after months [25]	Selection for vancomycin resistant Enterococci (VRE) and expansion of VRE reservoirs is a major clinical risk [27]	High colonization pressure for VRE and CDI risk due to loss of colonization resistance [24, 25]
Lincosamides (clindamycin)	Short courses can disproportionately eliminate minority taxa and cause marked loss of community members; gnotobiotic mouse studies show ~1/3 microbiota loss with variable rebound [26]	Promotes selection of macrolide-lincosamide resistance genes and predisposes to <i>C. difficile</i> overgrowth due to anaerobe depletion [24, 26].	High risk of CDI and durable perturbation of minority commensals after even short exposure; clinical vigilance required [24, 26]
Nitrofurantoin and other narrow agents	Nitrofurantoin and phenoxymethylpenicillin had minimal measurable effects on gut microbiota in primary-care studies [22]	Lower ecological selection pressure in the gut for many narrow spectrum urinary agents, but resistance can still emerge in targeted pathogens [22, 27]	Narrower agents are preferred when clinically appropriate to limit gut dysbiosis and resistome expansion [22, 27]

## Amoxicillin

Amoxicillin, a commonly used antibiotic, significantly impacts gut microbiota, leading to dysbiosis and various health implications. Research indicates that antibiotic exposure, including amoxicillin, disrupts the delicate balance of gut microorganisms, which can result in long-term adverse health effects, such as increased susceptibility to chronic diseases and metabolic disorders, including obesity, inflammatory bowel disease, idiosyncratic drug-induced liver injury, and autoimmune disorders [9]. Amoxicillin alters the diversity and composition of gut microbiota, favoring pathogenic strains over beneficial ones [10]. For instance, one study indicated that amoxicillin exposure in young rats resulted in lower blood pressure, associated with changes in gut microbiota composition, specifically a decrease in succinate-producing bacteria from the Veillonellaceae family [11].

Despite the well-documented negative impacts of amoxicillin on gut microbiota, its therapeutic benefits in treating bacterial infections are critical. Amoxicillin is a bactericidal  $\beta$ -lactam antibiotic affecting gram-positive and gram-negative bacteria by inhibiting an enzyme, which is necessary for bacterial cell wall synthesis. Notably, children under 5 receive approximately 60% of all amoxicillin prescriptions, highlighting its significance in pediatric medicine. Moreover, it is commonly used for chemoprophylaxis in dentistry to prevent infective endocarditis before specific dental procedures [12]. Balancing antibiotic use with microbiota health is essential for optimizing patient outcomes.

## Azithromycin

Azithromycin, a macrolide antibiotic, can alter gut microbiota and increase antibiotic-resistance genes, with effects that vary by treatment context and population. A single dose can reduce gut bacterial diversity and richness shortly after administration, but these changes may be transient and tend to return to baseline over time [13]. In Malawian children, 4 biannual rounds did not significantly change diversity, but were weakly associated with a shift in composition, notably an increase in *Prevotella* after 4 rounds [14]. In contrast, healthy adults exposed to azithromycin for 4 weeks exhibited consistent shifts in gut microbiome composition, including a decrease in microbial capacity related to carbohydrate metabolism and the biosynthesis of short-chain fatty acids, which can impact immune and metabolic regulation [15]. Mass drug administration increased the prevalence of macrolide-resistant bacteria, particularly *Escherichia albertii* and several *Acinetobacter* species, while overall diversi-

ty and composition remained largely unchanged [16]. In preterm infants, azithromycin is associated with alarmingly high rates of azithromycin-resistant bacteria and resistance genes, with 91% of resistant isolates carrying at least one resistance gene, and negative effects on beneficial taxa like *Bifidobacterium* [17]. Responses vary by age and geography: An infant study in India showed different effects than findings in older children and adults in Europe and North America [18]. Strategies such as prebiotics, including alginate oligosaccharides, show promise in mitigating dysbiosis after azithromycin exposure. Alginate oligosaccharides have been shown to increase the richness and diversity of gut microbiota reduced by azithromycin, promoting beneficial bacteria like *Akkermansia* and *Bacteroides acidifaciens* while reducing pathogenic bacteria such as *Staphylococcus*. These prebiotics enhance metabolic homeostasis through the *B. acidifaciens*-FAHFAs and *Bacteroides*-TCA cycle axes, improving levels of metabolic intermediates like citric acid and fumaric acid [19]. Overall, azithromycin can disrupt gut microbiota and promote resistance, with effects ranging from transient diversity changes to significant resistance and compositional shifts, depending on context, and highlighting the need for ongoing research and prudent antibiotic stewardship.

## Cephalexin

Cephalexin, a first-generation cephalosporin, inhibits peptidoglycan synthesis essential for bacterial cell walls and is commonly used for urinary tract, respiratory, and otitis media infections, often prophylactically to prevent surgical site infections. Although operational, its effects on the gut microbiota warrant careful clinical consideration, as it significantly alters microbial diversity and increases the risk of pathogenic colonization, including a notable rise in fecal carriage of *Pseudomonas aeruginosa*, a pathogen linked to various infections. This disruption promotes an environment favorable to pathogenic growth and broader gastrointestinal and overall health implications [20]. The broad-spectrum activity of cephalexin can reduce beneficial bacteria, contributing to dysbiosis and potentially undermining gut health. Long-term use is associated with reduced microbial diversity, a key factor in maintaining intestinal homeostasis, which heightens the risk of antibiotic resistance. Antibiotic-induced microbiota changes may influence tumor biology through immunomodulation; for example, an antibiotic cocktail including cephalexin has been linked to accelerated breast cancer tumor growth [21]. Additionally, broad-spectrum cephalosporins like cephalexin are linked to an increased risk of *Clostridium difficile* infection (CDI) due to disruption of the normal gut microbiota, though first-generation

cephalosporins have a lower CDI risk than third-generation ones [30]. The rising prevalence of antibiotic-resistant bacteria (ARBs) and antibiotic-resistance genes (ARGs) in the gut underscores the need to understand how cephalixin affects these dynamics, with studies showing a strong correlation between prior antibiotic therapy and ARBs in the human gut [31]. In sum, while cephalixin remains a valuable treatment option, its substantial impact on gut microbiota, including increased pathogen carriage, reduced diversity, and potential resistance, necessitates careful clinical management and ongoing research into antibiotic-microbiome interactions is essential to mitigate long-term health consequences.

### Ciprofloxacin

Ciprofloxacin, a widely used fluoroquinolone, is effective against multi-drug resistance (MDR) pathogens and is particularly used for respiratory infections, skin infections, and sexually transmitted diseases, functioning by inhibiting bacterial DNA gyrase. It significantly affects the gut microbiota, inducing dysbiosis and changes in microbial composition, and has been linked to increased seizure susceptibility, potentially mediated by gut microbiota and tryptophan metabolism. Treatment with ciprofloxacin elevates levels of *Akkermansia* and *Bacteroides* while decreasing *Marvinbryantia* and *Oscillibacter*, with longer courses associated with persistent microbiome changes and an increase in antimicrobial resistance genes [32]. In murine models, ciprofloxacin reduces Shannon diversity and alters taxonomic profiles, notably impacting *Bacteroides* and *Lactobacillus*, contributing to health issues such as heightened seizure risk and gastrointestinal complications [33, 34]. Prolonged antibiotic use may further elevate resistance genes, posing risks for future infections [32]. During *Salmonella enterica* infection, ciprofloxacin disrupts the intestinal barrier, decreasing mucin-2, ZO-1, and occludin, while increasing pathogenic bacteria and infection risk [35]. High-dose ciprofloxacin disrupts intestinal barrier integrity, reduces tight junction proteins, increases apoptosis and inflammation, and lowers bacterial diversity [36]. Diet influences the gut microbiome's response to ciprofloxacin, with a Western-style diet modulating its effects in mice [37]. Non-mammalian models show ciprofloxacin altering gut microbiota in *Eisenia fetida*, increasing cadmium toxicity, and potentially affecting heavy metal tolerance [5]. Despite dysbiosis concerns, ciprofloxacin's therapeutic benefits can outweigh risks in certain clinical scenarios; however, its historical role for urinary tract infections and rising ciprofloxacin-resistant *Escherichia coli* in the gut of non-antibiotic-taking women highlight ongoing resistance issues [38]. Overall, ciprofloxacin remains a potent antibiotic with substantial

implications for gut microbiota and potential long-term consequences, necessitating careful consideration in treatment protocols and ongoing research into microbiome-host interactions.

### Clindamycin

Clindamycin, a lincosamide antibiotic derived from lincomycin, is widely used for bacterial infections, especially in  $\beta$ -lactam-allergic patients. However, it markedly impacts gut microbiota, raising concerns about dysbiosis and health consequences. Studies show a pronounced reduction in gut microbial diversity after clindamycin, with significant shifts in genera such as Ruminococcaceae and *Bacteroides*. Notably, a single dose can cause sustained loss of roughly 90% of regular cecal microbial species, persisting for at least 28 days, which undermines colonization resistance and increases susceptibility to opportunistic infections like *C. difficile* and *Mycobacterium tuberculosis* [39, 40, 41]. The dysbiosis induced by clindamycin is linked to enhanced intestinal permeability and altered immune responses, particularly via the gut-lung axis, indicating that changes in the gut microbiota can influence pulmonary health and infection risk. Additionally, clindamycin disrupts the gut microbiota's ecological resistance. In *Candida albicans*, colonized mice, treatment leads to greater microbiota disruption, underscoring collateral ecological effects [40, 41]. Research by Hertz et al. [42] suggests that antibiotics effective against abundant anaerobes can select for resistant bacteria regardless of spectrum, highlighting complex interplays between antibiotic activity and microbial ecology [42]. Recovery strategies such as synbiotics, prebiotics combined with bifidobacteria, have shown promise in partially restoring microbiota after clindamycin, though full restoration remains uncertain. A study using a mouse model demonstrated that a synbiotic mixture of prebiotics (scGOS/lcFOS/2'-FL) combined with *Bifidobacterium breve* NRBB01 led to partial recovery of the gut microbiota after clindamycin treatment. Adding bifidobacteria further improved recovery, suggesting the importance of specific bacterial strains in the restoration process. Synbiotics can ameliorate some of the histological damage caused by antibiotics, such as mild edema and irregularities in villi and colonic crypts, indicating their role in gut health beyond microbiota composition [43]. Overall, while clindamycin remains an important therapeutic option, its profound effects on gut microbiota necessitate monitoring and consideration of recovery approaches to mitigate dysbiosis and associated health risks. The gut microbiota health relationship, particularly in antibiotic contexts, warrants further investigation, including long-term impacts and dietary interventions to aid recovery.

## Doxycycline

Doxycycline, a broad-spectrum tetracycline derived from oxytetracycline and widely used since 1967, effectively targets a range of gram-positive and gram-negative bacteria as well as some protozoa, but it significantly impacts gut microbiota composition and function with health and disease implications [44]. Studies show that doxycycline exposure alters the gut microbiome, including a reduction in lactic acid bacteria in models like *Drosophila melanogaster*, potentially affecting metabolism and host health [45]. Clinically, post-exposure prophylaxis with doxycycline has been linked to an increase in tetracycline resistance genes, indicating a shift in the gut resistome over time and raising concerns about long-term gut health. The resulting dysbiosis is associated with immune dysfunction and heightened infection susceptibility, underscoring broader health risks beyond the immediate antimicrobial effects [46]. In mice, doxycycline reduces gut microbiome diversity with effects persisting after withdrawal, suggesting lasting impacts on gut health; similar disturbances are observed in adult zebrafish exposed to doxycycline plus other antibiotics, associated with metabolic and physical alterations [47]. Long-term exposure has been implicated in weight gain, potentially mediated by microbiota changes, emphasizing the need to consider gut microbiome when evaluating doxycycline's side effects [48]. Female mice exposed to doxycycline show significant dysbiosis, reinforcing concerns about gender and strain-specific microbiome responses [49]. Environmental factors may exacerbate doxycycline's impact. For example, microplastics combined with doxycycline disrupt gut microbiota and induce brain lesions and behavioral impairments via the gut-brain axis [50]. Although doxycycline remains a vital antibiotic, its substantial effects on the gut microbiota warrant cautious use, consideration of resistance implications, and exploration of dietary or other interventions to support recovery and stewardship.

## Levofloxacin

Levofloxacin significantly shapes gut microbiota, producing both beneficial and detrimental outcomes. Across studies, it reduces pro-inflammatory bacteria (e.g. *Prevotellaceae*) and promotes anti-inflammatory taxa (e.g. *Muribaculaceae*), contributing to lowered intestinal inflammation and systemic inflammatory markers in animal models [51]. In DBA/1 mice, treatment altered the microbial landscape by decreasing beneficial taxa and increasing potentially harmful ones González-Chávez, et al. [52]. BALB/c mice exposed to levofloxacin hydrochloride showed distinct shifts, with *Prevotella amni* and *Clostridium butyricum* among dominant taxa, suggesting

complex effects on balance and gut health [53]. Although anti-inflammatory promotion occurs, these changes can be transient and may raise concerns about long-term gut health and resilience [52]. Compared with broad-spectrum  $\beta$ -lactams, levofloxacin has a lesser impact on overall microbial diversity, which can be advantageous in contexts where preserving diversity matters [51]. Nonetheless, transient antibiotic resistance and dysbiosis remain risks, underscoring the need for careful clinical use and monitoring [52]. Dietary interventions, such as nobiletin, show promise for mitigating dysbiosis and restoring beneficial microbiota after levofloxacin exposure [54]. In summary, levofloxacin exerts a dual influence on gut microbiota with potential anti-inflammatory benefits but risks to microbial balance and resistance, warranting cautious application and further research.

## Nitrofurantoin

Nitrofurantoin is an antibiotic primarily utilized in the treatment of urinary tract infections. Recent research has highlighted its comparatively mild effects on gut microbiota relative to other antibiotics, such as fluoroquinolones [55]. Studies indicate that nitrofurantoin treatment leads to minimal disruption of gut microbiota compared to more disruptive antibiotics like ciprofloxacin. Specifically, nitrofurantoin has been associated with a reduction in *Clostridium* species and an increase in *Faecalibacterium*. These findings by Stewardson et al. [56] suggest a selective, albeit less detrimental, impact on beneficial gut bacteria, potentially supporting a healthier gut microbiome [56]. Nitrofurantoin biodegradation studies demonstrate that microbial communities can adapt to the presence of nitrofurantoin, resulting in increased biodiversity. However, this increase in biodiversity does not necessarily correlate with enhanced biodegradation efficiency. The presence of nitrofurantoin modifies community structures, indicating that while nitrofurantoin may have a relatively mild effect, it can still influence microbial dynamics within the gut ecosystem. Additionally, the metabolic transformation of nitrofurantoin by gut bacteria has been shown to yield non-antibacterial compounds, which may further alter microbial composition and function [57]. In conclusion, nitrofurantoin exhibits a relatively mild impact on gut microbiota compared to more potent antibiotics, which may preserve beneficial microbiota. Nevertheless, the nuanced interactions between nitrofurantoin, gut microbial composition, and resistance development underscore the need for careful clinical consideration. Ongoing research is critical to fully understand the long-term effects of nitrofurantoin on gut health, particularly regarding the balance between effective infection treatment and microbiome preservation.

## Polymyxin B

Polymyxin B has a significant effect on gut microbiota, impacting both microbial composition and the expression of *ARGs*. Studies show that exposure to polymyxin B alters the community structure of gut microbiota in various organisms, including earthworms and *E. coli*, which may increase the risks of resistance and toxicity. Polymyxin B does not notably affect the richness or diversity of gut microbiota but changes its taxonomic composition, particularly increasing the abundance of *Actinobacteria* in earthworms. In *E. coli*, exposure to polymyxin B enhances colibactin production, a genotoxic metabolite associated with colorectal cancer [58]. Furthermore, when polymyxin B is combined with heavy metals such as arsenic, there is an increase in the abundance of *ARGs*, indicating a potential risk for horizontal gene transfer among microbial populations. Additionally, polymyxin B exposure can lead to heightened toxicity in gut microbiota; for instance, it enhances arsenic bioaccumulation in earthworms [59]. Although PMB is crucial for treating antibiotic-resistant infections, the environmental and health implications of its impact on gut microbiota and the proliferation of *ARGs* warrant further investigation.

## Sulfamethoxazole and trimethoprim

Sulfamethoxazole and trimethoprim are antibiotics often used in combination as trimethoprim-sulfamethoxazole (TMP-SMX). This combination is commonly prescribed for urinary tract infections, respiratory infections, and some gastrointestinal infections. Sulfamethoxazole inhibits bacterial folate synthesis, while trimethoprim targets a different step in the same pathway, enhancing their antibacterial effects when used together. TMP-SMX is effective against a broad spectrum of bacteria but may lead to resistance and side effects, necessitating careful monitoring [60]. The impact of TMP-SMX on gut microbiota is notable and has been documented through various studies, highlighting significant changes in microbial composition and diversity that may influence drug efficacy and resistance development. TMP-SMX treatment has been shown to cause considerable shifts in both alpha and beta diversity of gut microbiota in humanized mouse models, indicating a profound change in microbial composition [61]. In gibel carp, TMP-SMX administration led to marked alterations in predominant bacterial communities, affecting healthy fish more than those with bacterial enteritis [62].

TMP-SMX also influences the pharmacokinetics of other drugs, such as mycophenolic acid (MPA), by altering gut microbiota, which affects drug metabolism and systemic exposure. The relative abundance of specific gut bacteria correlated with MPA pharmacokinetics, suggesting that TMP-SMX's impact on microbiota could reduce drug efficacy [63]. In pediatric cases, TMP-SMX has been effective in treating small intestinal bacterial overgrowth, showcasing its therapeutic potential despite concerns about microbiota disruption [64]. However, its broad-spectrum activity raises concerns regarding the emergence of antibiotic-resistant strains. Prolonged TMP-SMX treatment significantly increased the prevalence of integron-positive and MDR Enterobacteriaceae in children's intestinal flora; after discontinuation, susceptibility rates returned to baseline, indicating a temporary impact on gut microbiota. Additionally, prolonged TMP-SMX usage suppressed gram-negative aerobic flora while leaving *Enterococcus* spp. and anaerobes relatively unaffected. There was also a moderate increase in yeast levels, demonstrating TMP-SMX's effect on gut microbiota, particularly in immunocompromised patients [65].

The use of TMP-SMX significantly affects gut microbiota diversity and composition, which can have implications for drug metabolism and the development of antibiotic resistance. These findings underscore the need for careful consideration of TMP-SMX in clinical practice, especially with prolonged use.

## Metronidazole

Metronidazole, a commonly used antibiotic for gastrointestinal disorders, can disrupt gut microbiota diversity and cause dysbiosis, with effects that may persist after treatment ends. In humans, it often reduces microbial diversity, decreasing the diversity of beneficial gut bacteria and potentially contributing to gastrointestinal issues and a higher risk of other infections. The drug may also elevate levels of pathogenic bacteria, further disturbing microbial balance. These microbiota changes can persist for weeks to months post-treatment. Since gut microbiota influences drug metabolism, such alterations can significantly affect the efficacy and side effects of medications [15]. Metronidazole worsens gut dysbiosis, raising pathogenic *E. coli*, lowers beneficial taxa (*Clostridium hiranonis*, Fusobacteria), and reduces richness/diversity. It shifts 78 genera, disrupting bile acid conversion and causing long-lasting microbiota effects. Recovery of microbiota diversity requires time. Significant changes have been observed up to 4 weeks after discontinuing metronidazole. Recovery of microbiota diversity

requires time. Significant changes have been observed up to 4 weeks after discontinuing metronidazole. While some bacterial genera return to pre-treatment levels, changes in others may persist [66]. Metronidazole harms gut microbiota and should be prescribed cautiously. While effective against some pathogens, it disrupts microbial balance; consider non-pharmacological options like synbiotics to preserve microbiome health and quality of life for pets [67].

## Conclusion

The article presents a comprehensive examination of the complex interplay between antibiotic use and gut microbiota. It underscores the significant impact that antibiotics can have on microbial communities, leading to dysbiosis—a state that disrupts the delicate balance of beneficial and pathogenic bacteria. This disruption can have far-reaching consequences for human health, contributing to a range of chronic conditions, including autoimmune disorders, obesity, and inflammatory bowel diseases.

The findings highlight the dual nature of antibiotics; while they are indispensable for treating bacterial infections, their potential to alter gut microbiota raises critical concerns regarding long-term health outcomes. The reduction in microbial diversity following antibiotic exposure not only favors the proliferation of pathogenic strains but also diminishes the protective functions of beneficial bacteria. This finding urges healthcare providers to consider the broader implications of antibiotic prescriptions, particularly in the context of an individual's microbiota.

Moreover, the article calls for further research to deepen our understanding of the long-term effects of antibiotics on gut health and to develop effective strategies for restoring microbial balance post-treatment. Dietary interventions emerge as a promising avenue for mitigating the adverse effects of antibiotics, suggesting that proactive measures can enhance gut health and overall well-being.

Given the widespread use of antibiotics globally, it is imperative for clinicians to stay informed about their implications on microbiota and the potential risks associated with antibiotic resistance. The growing body of research on the human microbiome highlights its vital role in various biological processes, making it essential for medical professionals to integrate this knowledge into their clinical practices.

In conclusion, the relationship between antibiotics and gut microbiota is a critical area of study that necessitates ongoing investigation and awareness. Balancing effective infection treatment with the preservation of microbiome health is essential for promoting long-term health outcomes and preventing the emergence of antibiotic-resistant pathogens.

## Ethical Considerations

### Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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### Authors' contributions

Conceptualization and supervision: Ameneh Omid; Data collection and writing the original draft: Maedeh Hasanzadeh Bafghi; Review and editing: Kobra Shirani.

### Conflict of interest

The authors declared no conflict of interest.

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