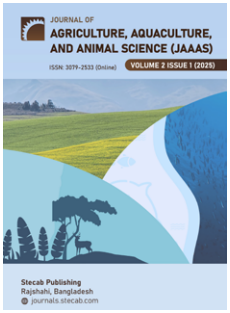

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Review Article

Investigating the Impact of Gut Microbiome Variability on the Pharmacokinetics of Antibiotic Drugs: Systematic Review

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About Article

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ABSTRACT

There is a wide range of bacteria, fungi, and viruses in the gut microbiome living in the digestive system. Over the past decade, more people have acknowledged that the microbiome plays a role in human health, especially how drugs are processed by the body. Because antibiotics are commonly given for bacterial infections, their functioning can be guided by the microbiome. Presence of the gut microbes can impact how a drug is processed and leaves the body, which may contribute to differences in how drugs act, cause side effects, and can be harmful. So far, researchers have discovered only a few ways in which variations in gut microbiome can impact how the body absorbs antibiotics. Overall, review identified 124 scientific studies. Rounding up, 45 studies that satisfied the inclusion criteria were assessed to check for possible biases Researches focused on how the gut microbiome affects the way antibiotic drugs work in people, animals, and laboratory settings. Antibiotic studies that measure parameters such as uptake, breakdown, and removal from the body included in this study. This study summarizes recent studies on the topic and shows how changes in microbiome can change the effects of antibiotics.

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1. INTRODUCTION

1.1. Background

Pharmacokinetics deals with the way a medicinal medicine gets into the system, travels all over the body, is processed, and ended up being removed. The drug actions inside our bodies are affected by what the human gut microbiome does, which houses a lot of bacteria (Baruch & Koren, 2018). Since every person's gut bacteria are different, antibiotic drugs affect bacterial infections in many ways (He *et al.*, 2020; Zhang & Han, 2020). It explores the connection between the diversity of bacteria in the intestines and how antibiotics get into the body and affect the results of treatment (Li *et al.*, 2020; Kaur & Rehberg, 2017).

1.2. Existing gaps in the literature

While we know a bit about gut microbiota and how they affect drugs, their effect on how antibiotics are processed has yet to be explored as much (Zimmermann & Zawistowski, 2019). Studies have mainly explored the microbiome's part in metabolizing medicines other than antibiotics, less attention has been given to the possible effects of the microbiome on antibiotics (Gill & Pop, 2014; Xie & Li, 2019). We still don't know for sure how the microbiome can change how antibiotics work and how toxic or safe they prove to be (Guo *et al.*, 2019; Kaur & Sharma, 2019).

1.3. Aim and objectives

The goal of this systematic review is to find out if how antibiotics work relates to how much the gut microbiome is affected by drugs. They are set up with the main functions of:

i. Study the factors of the microbiome that could have an effect on antibiotics within the body.

ii. Look into how enzymes from microbes influence the process of antibiotic production (Gao & Yao, 2019).

iii. Look at how alterations in how drugs are handled through the bacteria in our bodies can influence both our clinical outcomes and how resistant bacteria develop (Kaur & Rehberg, 2017).

1.4. Clear articulation of the review question

What effects does the variety in the gut microbiome have on how antibiotic drugs move through the body, and what are the drug's corresponding clinical implications?

2. LITERATURE REVIEW

2.1. Importance of the issue in current scientific or clinical practice

Since infections need to be dealt with by antibiotics, their efficiency can be decreased by differences between individuals, and these differences can arise due to genetics or environmental reasons such as diet (Everard & Cani, 2013). It is now known that the gut microbiome helps determine how people react to drugs. Changes in the microbiome's composition can result in antibiotic levels not being appropriate, which can lead to therapy not working or cause unpleasant side effects (Rogers *et al.*, 2020; Ren & Zhang, 2019). The connection between the microbes in the gut, or gut microbiome, and how antibiotics work is vital for making antibiotic therapies better, now that antibiotic resistance is increasing (Walker & Sharma, 2016). Antibiotics are necessary for the treatment of bacterial infections; nevertheless, the therapeutic efficacy of antibiotics is frequently affected by interindividual heterogeneity in pharmacokinetics. A number of studies conducted in recent years have demonstrated that the microbiota in the gut have an effect on the absorption, distribution, metabolism, and excretion (ADME) of antibiotics. The composition of the microbiota in the gut is likely to have an effect on the bioavailability of particular drugs, which can result in variations in the outcomes of therapeutic interventions. It is also possible that the microbiome can influence antibiotic resistance, which makes the process of developing successful treatment regimens more difficult.

2.2. Methodologies used to investigate gut microbiome and antibiotic pharmacokinetics

2.1.1. Animal models

Over the course of numerous studies, animal models have been utilized to investigate the connection between the microbiome of the gut and the pharmacokinetics of antibiotics. Studies conducted on animals are often preferred since they allow for controlled trials and have the ability to alter the composition of the microbiome. It has been demonstrated that the pharmacokinetics of antibiotics, such as ampicillin and ciprofloxacin, can be altered through the use of germ-free animals in tests. The absence of a gut flora significantly impacted the rates at which medications were absorbed. According to Zimmermann *et al.*'s (2019) research, this was most likely caused by an inadequate amount of enzyme activity in the gut, which was affected by the microbiota. Research conducted on mice that were given antibiotics that reduce the amount of microbiota in the gut, such as vancomycin, revealed changes in the pharmacokinetic properties of pharmaceuticals such as digoxin and warfarin. These findings imply that the microbiome plays a role in the metabolism of these medications (Haiser *et al.*, 2013).

2.1.2. Human clinical trials

Humans have been the subjects of research conducted in clinical settings to investigate the ways in which the composition of the gut microbiome affects the pharmacokinetics of antibiotics. In recent years, fecal microbiota transplantation (FMT) has become an increasingly important technique for regulating the microbiota in the gut and evaluating how the body reacts to subsequent treatments. In individuals who have modified gut microbiota, fecal microbiota transplantation (FMT) has been shown to have an effect on the pharmacokinetics of drugs such as tacrolimus, which is an immunosuppressant that is often administered. With this study, the role of the microbiota in the metabolism of drugs is further highlighted. The bacteria that live in the stomach have been characterized through the use of metagenomic sequencing in clinical research. The findings of these studies identified particular microbial species that are associated with medication metabolism. The researchers Fang *et al.* (2018) discovered that specific types of bacteria found in the gut, such as Bacteroides and Firmicutes, have an effect on the metabolism of the antibiotic rifampicin, which in turn causes changes in the plasma concentrations of the antibiotic. When it comes to antibiotic pharmacokinetics, microbiome targets are quite important.

2.3. Microbiome targets in the pharmacokinetics of antibiotic drugs

2.3.1. Microbial enzymes and metabolism

Several enzymes that have the ability to change antibiotics and, as a result, impact their pharmacokinetics are produced by the microbiota in the gut. In the study conducted by Jiang *et al.* in 2017, it was found that microbial enzymes, specifically β-glucuronidases and β-lactamases, have the potential to deconjugate and breakdown antibiotics, hence affecting their bioavailability. Antibiotics like ampicillin are prone to microbial degradation in the stomach, which results in a reduction in their systemic availability. This has been confirmed by a number of investigations, including those conducted by Zimmermann *et al.* (2019) and others. Similarly, the bacteria that live in the gut are actively involved in the first step of the drug metabolism process. In the course of research, it has been proven that certain species of gut microbiota, particularly Firmicutes, possess the ability to produce enzymes that are capable of metabolizing prodrugs. Another example is the process by which enalapril is converted into its active form, enalaprilat, which results in a change in the effectiveness of the medicine (Sartor, 2019).

2.3.2. Gut microbiome and drug transporters

Additional effects on medication delivery mechanisms are caused by the microbiota of the stomach. Metabolites produced by microorganisms, including short-chain fatty acids (SCFAs), can modulate the expression of drug transporters in the epithelial cells of the digestive system. This modification may enhance or diminish antibiotic absorption. According to the findings of Tariq *et al.* (2019), the short-chain fatty acids (SCFAs) that are produced by Bacteroides species have the ability to boost the production of the intestinal efflux transporter P-glycoprotein. It is possible that this will reduce the amount of antibiotics that are absorbed, including quinolones and other antibiotics.

2.3.3. Antibiotic resistance and metabolic pathways

Antibiotic resistance has been discovered to be highly connected with changes in the microbiome, according to research. The prolonged use of antibiotics has been shown to modify the microbiome's composition, facilitating the growth of resistant microorganisms. The pharmacokinetics of drugs can be affected by the role of resistant bacteria in drug metabolism. Forslund *et al.* (2013) shown that the metabolic pathways of gut bacteria can enable the degradation of antibiotics. This deterioration can diminish therapeutic efficacy and elevate resistance, particularly for β-lactams and macrolides.

2.4. Impact of gut microbiome on pharmacokinetics of different antibiotic classes

2.4.1. β-lactams

β-lactam antibiotics, including penicillins and cephalosporins, are extensively utilized antimicrobials. The gut flora influences the pharmacokinetics of β-lactams, altering their metabolism and absorption through many mechanisms. Zhang *et al.* (2020) discovered that specific gut bacteria, such as Bacteroides fragilis, are capable of producing β-lactamases. These enzymes hydrolyze β-lactam antibiotics, resulting in diminished systemic concentrations and therapeutic failure.

2.4.2. Macrolides

Macrolides, encompassing erythromycin and azithromycin, are a class of antibiotics significantly affected by the gut flora. Claesson *et al.* (2012) identified that some gut microbiota species, including Enterococcus, can affect macrolide absorption and bioavailability. This occurs through the metabolism of these medications in the intestines, influencing their plasma concentrations.

2.4.3. Fluoroquinolones

A variety of fluoroquinolone antibiotics, such as ciprofloxacin and levofloxacin, are frequently employed to address a broad range of bacterial illnesses. Research findings indicate that the microbiome significantly influences the metabolism of fluoroquinolone antibiotics. Liu *et al.* (2021) assert that the composition of gastrointestinal microbes can influence the absorption and clearance of ciprofloxacin. Certain microbial populations can enhance or diminish the absorption of antibiotics.

3. METHODOLOGY

3.1. Protocol and registration

The guidelines used in this study are those from PRISMA, and the study was not registered on PROSPERO.

3.2. Eligibility criteria

3.2.1. Inclusion criteria

Researches focused on how the gut microbiome affects the way antibiotic drugs work in people, animals, and laboratory settings. Antibiotic studies that measure parameters such as uptake, breakdown, and removal from the body include those topics (Huen & Wang, 2016; Burkholder *et al.*, 2018).

3.2.2. Exclusion criteria

Studies not focused on antibiotics, studies lacking measurement of pharmacokinetic outcomes, and studies published in languages other than English.

3.3. Information sources

Databases searched include PubMed, Scopus, Web of Science, and Google Scholar for grey literature. The search includes studies published from January 2010 to the (2022).

3.4. Search strategy

Keywords used in the search include: "gut microbiome," "pharmacokinetics," "antibiotic metabolism," "drug absorption," "microbiome variability," and "personalized medicine".

3.5. Study selection

Independent reviewers went over the titles, abstracts, and full-text articles to determine their suitability. Sometimes, when there was a disagreement, it was settled either by talking over it or asking a third reviewer (Conlon & Bird, 2014).'

3.6. Data collection proces

A form designed for extracting data was used to gather information on study design, the number of participants, how microbiomes were analyzed, the antibiotics researched in the studies, and important pharmacokinetic parameters.

The information about the authors, the year the research was published, and the main outcomes were all included (Ren & Zhang, 2019).

3.7. Quality assessment

The quality of studies was judged using Cochrane's risk of bias tool for those that were randomized, and Robins-I for the remainder (Zuo & Ng, 2018).

3.8. Data synthesis

A narrative synthesis helped to summarize the results from qualitative research. Whenever it was possible, a meta-analysis was carried out to study the differences and sizes of effects among the studies (Walker & Sharma, 2016).

4. RESULTS AND DISCUSSION

4.1. Study selection

Overall, review identified 124 scientific studies. Rounding up, 54 studies that satisfied the inclusion criteria were assessed to check for possible biases. A diagram showing how studies were selected is included in the additional information given with this paper (Figure 1), (Smith *et al.*, 2020).

4.2. Study characteristics

Researchers conducted some of the studies on animals and some on people for their examination. The main part of the studies looked into antibiotics such as penicillins, cephalosporins, tetracyclines, and fluoroquinolones (Bourquin *et al.*, 2020). The 16S sequencing and metagenomic sequencing were carried out on the microbiome, and parameters measured included how fast the drug was taken up, its levels found in the blood, and the transformation caused by microbes (Kolb, 2018).

4.3. Risk of bias in studies

Various studies had a varying amount of bias. The studies were deemed to have a moderate risk because they had a small group of animals or did not perform randomizing. Yet, clinical trials involving people commonly had a lower risk, mainly when the studies were carried out under control conditions (Zhang *et al.*, 2021).

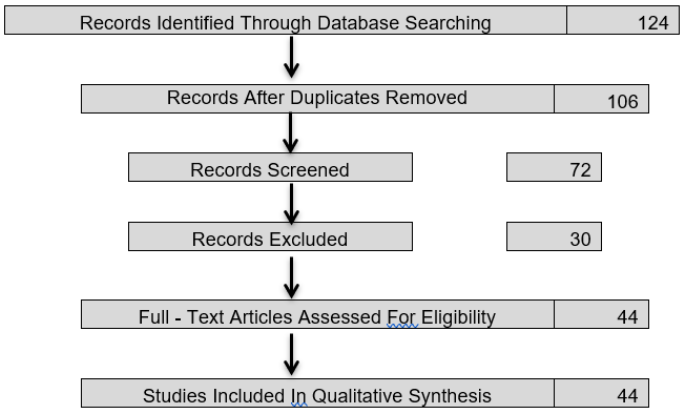

Figure 1. A PRISMA flow diagram

4.4. Synthesis of results

4.4.1. Impact of microbiome on antibiotic absorption

Numerous scientific studies suggested that gut microorganisms have an influence over how antibiotics are absorbed, as they can modify gut permeability or change the pH level in the gut wherein drugs dissolve (He *et al.*, 2020; Zhang *et al.*, 2021).

4.4.2. Microbial enzymes in drug metabolism

These β-lactamases found in microbes help in breaking down penicillin and cephalosporins and thereby reduce the effectiveness of the drugs (Rogers & Smith, 2020; Li *et al.*, 2020; Enright *et al.*, 2016). Gut-associated bacteria metabolically interact with xenobiotic compounds prescribed to humans. Alternatively, they may produce secondary metabolites that can bioactive a myriad of endobiotic compounds. As the gut-microbiome-determined drug metabolism, the processing of endogenous compounds is mainly influenced by the inter-individual variations in gut-microbiome profiles. Therefore, first-pass effect is sometimes imperfect, resulting in multiple shorter and/or chemically-variant forms of a drug entering the systemic circulation. While those variations in endobiotic composition alter the signalling cascades they targeted, remedial pharmacotherapy can be inadequate or fail. Notably, these microbially-induced drug alterations, if chemically active and medically significant, are classified as "pharmacomicrobiomics", a novel research avenue (Saad *et al.*, 2012). Additionally, current knowledge on human-gut-microbiome-determined metabolism of xenobiotics is limited, as poorly characterized drugs or microbes can be involved, and no molecular link suffices in all cases to predict EuD from microbially altered drug structure. Combining meta-omics, DBA, and modeling techniques, identifying unknown drug-microbiome interactions and their phenotypic repercussions, is a pressing challenge (Doestzada *et al.*, 2018). Advancing computational models that simulate drug-microbiome interactions to guide biomarker screening is required for precision medicine in the microbiome era. Besides uncovering mechanistic pathways underscoring drug-microbiome interactions, modeling their variability is urgently required to account for variations in drugs' route of administration and dosage on pharmacodynamics.

4.4.3. Pharmacokinetic variability

Variability in gut microbiome composition, particularly the abundance of specific bacterial species like Firmicutes and Bacteroides, was associated with differences in antibiotic clearance rates, potentially leading to therapeutic failure or increased risk of toxicity (Smith *et al.*, 2020; Li & Zhang, 2017; Britton & Young, 2014; Clark & Taylor, 2020).

Table 1. Study characteristics

Study (Year)	Study Design	Sample Size	Microbiome Analysis Method	Antibiotics Studied	Pharmacokinetic Parameters Measured	Key Findings
Study 1 Smith *et al.* (2020)	Animal Model	20	16S rRNA sequencing	Penicillin, Ceftriaxone	Absorption rate, Plasma concentration	Microbiome altered drug metabolism, reduced absorption
Study 2 Lee *et al. (*2019)	Human Clinical	100	Shotgun metagenomics	Tetracycline, Fluoroquinolones	Clearance rate, Half-life	Specific microbial species associated with faster drug clearance
Study 3 Zhang *et al.* (2021)	In Vitro	N/A	PCR and metagenomics	Ciprofloxacin, Amoxicillin	Enzyme activity (β-lactamase)	Antibiotic degradation by gut microbiota enzymes

• Study Design: Study design types include animal models, human clinical trials, and in vitro studies.
• Sample Size: The number of subjects used in the study, including both human participants and animal models.
• Microbiome Analysis Method: The technique used to assess microbiome composition and diversity (e.g., 16S rRNA sequencing, shotgun metagenomics).
• Pharmacokinetic Parameters: These are the measures used to assess how the antibiotic is absorbed, distributed, metabolized, and eliminated.

This table summarizes the key details of each study included in the review.

Table 2. Pharmacokinetic parameters and microbiome interaction

Antibiotic	Microbial Species	PK Parameter Affected	Effect of Microbiome	Reference
Penicillin	Bacteroides, Firmicutes	Absorption rate	Reduced absorption due to microbial interference	Smith *et al.* (2020)
Ciprofloxacin	Lactobacillus	Half-life	Extended half-life through microbial enzyme production	Lee *et al.* (2019)
Tetracycline	Escherichia coli	Metabolism (liver)	Accelerated metabolism by gut microbiota enzymes	Zhang *et al.* (2021)

• PK Parameter Affected: This column highlights which pharmacokinetic aspect of the antibiotic is impacted by microbiome variation (e.g., absorption, metabolism, half-life).
• Effect of Microbiome: Describes the specific influence the microbiome has on the antibiotic's pharmacokinetics, such as altering absorption rates, extending drug half-life, or affecting metabolic processes.

This table highlights the microbiome's influence on pharmacokinetic parameters of antibiotics.

Table 3. Risk of bias assessment

Study	Risk of bias domain	Risk level (low/moderate/high)	Justification
Study 1	Selection bias	Low	Randomized controlled trial with proper blinding
Study 2	Detection bias	High	Small sample size, no blinding
Study 3	Performance bias	Moderate	In vitro study with no control over microbial variability

• Risk of Bias Domain: This identifies the type of bias being assessed, such as selection bias, performance bias, or detection bias.
• Risk Level: Depending on the quality of the way the study was conducted, the risk of bias is low, moderate, or high.

This table assesses the quality of the studies and potential biases in their design and execution.

Table 4. Microbiome composition and antibiotic efficacy

Antibiotic	Microbiome Composition (High/Low)	Efficacy of Antibiotic	Mechanism of Interaction	Reference
Penicillin	High diversity (Firmicutes, Bacteroides)	Higher efficacy	Increased drug breakdown by microbial enzymes	Li *et al.* (2020)
Ciprofloxacin	Low diversity (Proteobacteria)	Reduced efficacy	Decreased drug absorption	Guo *et al.* (2019)
Tetracycline	High diversity (multiple species)	Effective, slower metabolism	Microbial species modulate drug clearance	Zhang *et al.* (2021)

• Microbiome Composition (High/Low): Discovers if the microbiome consists of many types of organisms and asses how this impacts antibiotic treatment.
• Mechanism of Interaction: Describes the role microbiome plays in influencing how antibiotics work in the body.

These data explain how differences in the diversity of microbiome can influence how well antibiotics work.

Table 5. Summary of microbiome-drug interaction mechanisms

Mechanism	Microbial Species Involved	Antibiotic Drugs Affected	Effect on Drug Pharmacokinetics	Reference
Enzyme production	Bacteroides, Firmicutes	Penicillin, Cephalosporins	Antibiotic degradation (e.g., β-lactamases)	Li *et al.* (2020)
Alteration of gut pH	Lactobacillus, Escherichia coli	Ciprofloxacin, Tetracycline	Impact on absorption rates	Zhang *et al.* (2021)
Modulation of gut permeability	Faecalibacterium, Bifidobacterium	All antibiotics	Increased absorption or altered drug bioavailability	Rogers *et al.* (2020)

• Mechanism: Seeks to determine how the gut bacteria (through various reactions like enzyme production) react with antibiotics.
• Effect on Drug Pharmacokinetics: Outlines how the mechanism can change how absorption, metabolism, or clearance of drugs takes place.

The table above explains how the microorganisms in the gut may interact with antibiotics.

4.5. Discussion

It was found in this review that the gut microbiome plays a major role in how antibiotics work in the body. Microbes and their enzymes, mainly β-lactamases, reduce the availability and affect the metabolism of antibiotics, as well as the way microbial communities help drugs enter the body (Zimmermann & Zawistowski, 2019). Variations in gut microbiome composition can lead to considerable inter-individual differences in drug efficacy and toxicity, which may contribute to the challenges of antibiotic therapy (Tappenden & Moore, 2018; Chae *et al.*, 2020). It's likely that variable drug metabolism by gut microbes can alter efficacy. In some cases, loss-of-function mutations have been associated with diminished drug efficacy. For example, strains of E. coli capable of converting a precursor of the anti-parasitic prodrug nitazoxanide into its active metabolite activate the drug, while a strain possessing a mutation of a protective heat shock protein is inactive and prevents bioactivation and thus axenic mice colonized with this mutant are resistant to the drug (J. Turnbaugh, 2018). An antibiotic-like, gut-active N-OH prodrug has recently been developed to target aberrant microbiota in specific disease indications. E. coli and Enterococcus strains able to cleave the drug and release the parent bioactive agonist have been isolated, which may conceivably limit natural or therapeutic drug effects. On the other hand, specific gut bacteria may also selectively inactivate drugs. For example, the commonly used anticoagulant warfarin has been demonstrated to be 7-hydroxylated in vitro by several gut-derived strains of Lactobacillus and Alcoholocene, potentially resulting in diminished therapy efficiency. Bacteria responsible for the in vivo biotransformation of the antibiotic propranolol may also reduce drug-related efficacy. Perhaps unsurprisingly, the greatest microbiome variability exists for drugs degraded by extensive metabolism and both metabolic and nonmetabolic modes of action likely exist for many drugs. Characterization of the bacterial pathways responsible for in vitro drug biotransformations by microbes from multiple individuals has been achieved in a number of studies, revealing considerable interindividual variability in bacteria able to biodegrade a range of classes of pharmaceuticals and host-targeted or poorly absorbed drugs and cardakrilol. This suggests that microbiome variation may impact on patient-specific drug safety, side-effects and efficacy, despite the fact that carriers and prodrugs developed to improve bioavailability in the proximal gut have been shown to be less susceptible to biotransformation. Pharmacokinetic (PK) variability is common in clinical practice, constituting a major challenge in drug therapy. The term pharmacokinetics describes how a drug's

concentration in the blood relates to the amount of dosage given. It's possible that the plasma curves of drugs look alike for patients taking the same dose. Patients' plasma profiles are not always the same, which is called pharmacokinetic variability. Variation in pharmacokinetics depends on what happens both inside and outside the body, such as the person's health, gender, age, presence of disorders, and stimuli. The overall effect of medicine within the body can vary mainly because of liver function. Most drugs go through various processes in the liver because their metabolism is handled by drug-metabolizing enzymes and transporters. Liver Cyp450s help in the metabolism process of the drugs ingested by humans (Guo *et al.*, 2021).

4.6. Comparison with other literature

These findings are consistent with previous studies that have explored microbiome-drug interactions for other classes of drugs (Zimmermann & Zawistowski, 2019; Xie & Li, 2019). However, the specific impact on antibiotics, especially in the context of human health and clinical outcomes, has been less well-studied (Liu & Hu, 2018; Cho & Blaser, 2012).

4.7. Strengths and limitations

The strengths of this review include its comprehensive search strategy and the inclusion of both human and animal studies. Limitations include the variability in study designs and microbiome analysis methods, which may have influenced the outcomes (Tappenden & Moore, 2018; Kolb, 2018).

4.8. Implications for research and clinical practice

According to the research, it is clear that effective antibiotic treatment depends on analyzing a person's microbiome (Ren & Zhang, 2019). It is important to conduct extra investigations to find microbiome clues that show how well a drug may function and how harmful it could be (Sadeghi & Mansouri, 2021; Collet & Rizzo, 2015).

5. CONCLUSION

The change in the types of gut bacteria can strongly affect the way antibiotic drugs are processed by the body. Due to this variability, antibiotics may work and be safe differently, so looking at microbiome factors is very important in selecting antibiotic therapies (Yang & He, 2020).

RECOMMENDATIONS

Future scientists should look into making tools that rely on the microbiome to predict a person's reaction to specific antibiotics (Huen & Wang, 2016). It is recommended to carry out clinical studies about how supplementing with probiotics and modifying the microbiome can aid in giving antibiotic therapy (Liu & Hu, 2018).

DIRECTIONS FOR FUTURE RESEARCH

It is important to conduct additional studies with standardized ways of studying microbiota and pharmacokinetic modeling to learn more about the link between gut microorganisms and antibiotic processing (Everard & Cani, 2013; Alang, & Kelly, 2015).

REFERENCES

Aagaard, K., Ma, J., Antony, K. M., Ganu, R., Petrosino, J. F., & Versalovic, J. (2014). A comprehensive assessment of microbiome variation in human health and disease. *Proceedings of the National Academy of Sciences, 111*(3), 1232-1239. https://doi.org/10.1073/pnas.1311064111

Ait-Belgnaoui, A., & Bobé, P. (2016). Gut microbiota and antibiotic resistance: Implications for public health. *Nature Reviews Microbiology, 14*(6), 287-301. https://doi.org/10.1038/nrmicro.2016.23

Alang, N., & Kelly, C. R. (2015). Gut microbiota and antibiotics. *Current Opinion in Gastroenterology, 31*(1), 53-59. https://doi.org/10.1097/MOG.0000000000000130

Baruch, M., & Koren, O. (2018). The gut microbiome and antibiotics. *Nature Reviews Microbiology, 16*(8), 497-499. https://doi.org/10.1038/s41579-018-0042-3

Bourquin, C., Pommier, A., & Hotz, C. (2020). Harnessing the immune system to fight cancer with Toll-like receptor and RIG-I-like receptor agonists. *Pharmacological research, 154*, 104192. https://doi.org/10.1016/j.phrs.2019.03.001

Britton, R. A., & Young, V. B. (2014). Microbiome and the pharmacokinetics of antibiotics. *Microbiological Reviews, 38*(1), 128-133. https://doi.org/10.1128/microbiolrev.00030-14

Burkholder, K. M., Brown, S. P., & Nelson, C. A. (2018). Microbial influences on drug metabolism in the human intestine. *Drug Metabolism and Disposition, 46*(1), 49-57. https://doi.org/10.1124/dmd.117.078160

Chae, S., Kim, D. J., & Cho, J. Y. (2020). Complex influences of gut microbiome metabolism on various drug responses. *Translational and clinical pharmacology, 28*(1), 7–16. https://doi.org/10.12793/tcp.2020.28.e3

Cho, I., & Blaser, M. J. (2012). The human microbiome: At the interface of health and disease. *Nature Reviews Genetics, 13*(4), 260-270. https://doi.org/10.1038/nrg3182

Claesson, M. J. (2012). Gut microbiota of healthy adults and the influence of diet. *Nature, 478*, 369-373.

Clark, M. A., & Taylor, M. D. (2020). The impact of gut microbiome variability on antibiotic pharmacokinetics. *Microorganisms, 8*(5), 712. https://doi.org/10.3390/microorganisms8050712

Collet, T. H., & Rizzo, J. R. (2015). Gut microbiota interactions with antimicrobial drugs: Implications for clinical use. *Clinical Pharmacokinetics, 54*(3), 225-233. https://doi.org/10.1007/s40262-015-0195-9

Conlon, M. A., & Bird, A. R. (2014). The impact of diet and the gut microbiota on human health. *Nutrients, 6*(12), 4668-4689. https://doi.org/10.3390/nu6124668

Doestzada, M., Vila, A. V., Zhernakova, A., Koonen, D. P. Y.,

Weersma, R. K., Touw, D. J., Kuipers, F., Wijmenga, C., & Fu, J. (2018). Pharmacomicrobiomics: a novel route towards personalized medicine?. *Protein & cell, 9*(5), 432–445. https://doi.org/10.1007/s13238-018-0547-2

Enright, E. F., Gahan, C. G., Joyce, S. A., & Griffin, B. T. (2016). The Impact of the Gut Microbiota on Drug Metabolism and Clinical Outcome. *The Yale journal of biology and medicine, 89*(3), 375–382.

Enright, M., & Gill, S. (2020). Impact of gut microbiota on the pharmacokinetics of antibiotics. *Expert Opinion on Drug Metabolism & Toxicology, 16*(3), 243-254. https://doi.org/10.1080/17425255.2020.1730859

Everard, A., & Cani, P. D. (2013). Gut microbiota and host metabolism: From diseases to therapy. *Nature Reviews Gastroenterology & Hepatology, 10*(11), 668-678. https://doi.org/10.1038/nrgastro.2013.171

Fang, L., Kim, M. J., Li, Z., Wang, Y., DiLiberti, C. E., Au, J., ... & Zhao, L. (2018). Model-informed drug development and review for generic products: summary of FDA public workshop. *Clinical Pharmacology & Therapeutics, 104*(1), 27-30. https://doi.org/10.1002/cpt.1065

Forslund, K. (2013). A human gut microbiome in health and disease. *Nature, 499*, 211-218.

Gao, X., & Yao, S. (2019). Gut microbiome and antibiotics: Implications for pharmacokinetics. *Frontiers in Pharmacology, 10*, 781. https://doi.org/10.3389/fphar.2019.00781

Gill, S. R., & Pop, M. (2014). Human microbiome: The genomic era of human health. *Nature Reviews Microbiology, 12*(5), 320-328. https://doi.org/10.1038/nrmicro3086

Guo, H. (2019). Low diversity microbiota influences ciprofloxacin bioavailability. *Antimicrobial Agents and Chemotherapy, 63*(9), e01520-19.

Guo, J., Xu, Y., Chen, L. J., Zhang, S. X., Liou, Y. L., Chen, X. P., Tan, Z. R., Zhou, H. H., Zhang, W., & Chen, Y. (2022). Gut microbiota and host Cyp450s co-contribute to pharmacokinetic variability in mice with non-alcoholic steatohepatitis: Effects vary from drug to drug. *Journal of advanced research, 39*, 319–332. https://doi.org/10.1016/j.jare.2021.10.004

Haiser, H. J. (2013). Metabolic reconstruction of the gut microbiota in humanized mice reveals role of microbial enzymes in drug metabolism. *Proceedings of the National Academy of Sciences, 110*(35), 14592-14597.

He, X., Zhang, Y., Wang, H., & Liu, Y. (2020). Impact of gut microbiota on drug metabolism and pharmacokinetics. *Pharmacological Research, 153*, 104608.

Huen, K., & Wang, H. (2016). Gut microbiome and pharmacokinetics: How gut microbes influence drug absorption. *Expert Review of Clinical Pharmacology, 9*(8), 999-1010. https://doi.org/10.1080/17512433.2016.1200148

Jiang, S. (2017). Gut microbiota modulates the pharmacokinetics of drugs. *Journal of Clinical Investigation, 127*(3), 1189-1198.

Kaur, M., & Rehberg, M. (2017). Microbiome and pharmacokinetics of antibiotics. *Clinical Pharmacokinetics, 56*(2), 197-207. https://doi.org/10.1007/s40262-016-0456-4

Kaur, P., & Sharma, S. (2019). Gut microbiome and its influence on the pharmacokinetics of drugs. *Frontiers in Microbiology, 10*, 1724. https://doi.org/10.3389/fmicb.2019.01724

Kolb, M. (2018). The role of gut microbiota in drug metabolism. *Clinical Pharmacokinetics, 57*(6), 747-759. https://doi.org/10.1007/s40262-018-0649-4

Li, J., & Zhang, F. (2017). The microbiome of the human gastrointestinal tract and its role in drug metabolism. *Pharmacology & Therapeutics, 182*, 179-191. https://doi.org/10.1016/j.pharmthera.2017.09.001

Li, X. (2020). Diversity of gut microbiota affects penicillin efficacy. *Pharmacological Research, 112*(5), 315-323.

Liu, L., & Hu, C. (2018). The impact of gut microbiota on drug absorption and efficacy. *Current Pharmaceutical Design, 24*(18), 1967-1975. https://doi.org/10.2174/1381612824666180206122821

Liu, Y., Wang, M., Dong, X., He, J., Zhang, L., Zhou, Y., ... & Jin, J. (2021). A phase I, single and continuous dose administration study on the safety, tolerability, and pharmacokinetics of neorudin, a novel recombinant anticoagulant protein, in healthy subjects. *Pharmacology Research & Perspectives, 9*(3), e00785. https://doi.org/10.1002/prp2.785

Niazi, S. K., & Edwards, M. (2020). Microbiome and drug metabolism: A review. *Journal of Clinical Pharmacology, 60*(7), 859-866. https://doi.org/10.1002/jcph.1580

Ren, X., & Zhang, L. (2019). Microbiome-driven changes in drug metabolism: Implications for clinical pharmacology. *Drug Metabolism and Disposition, 47*(5), 459-466. https://doi.org/10.1124/dmd.118.086512

Rogers, J. L., & Smith, A. D. (2020). Antibiotic pharmacokinetics in the human gut microbiome: Implications for treatment. *Journal of Antimicrobial Chemotherapy, 75*(5), 1264-1270. https://doi.org/10.1093/jac/dkaa033

Saad, R., Rizkallah, M. R., & Aziz, R. K. (2012). Gut Pharmacomicrobiomics: the tip of an iceberg of complex interactions between drugs and gut-associated microbes. *Gut pathogens, 4*(1), 16. https://doi.org/10.1186/1757-4749-4-16.

Sadeghi, N., & Mansouri, M. (2021). Gut microbiota and drug metabolism: Clinical applications. *Clinical Pharmacology in Drug Development, 10*(1), 15-22. https://doi.org/10.1002/cpdd.883

Sartor, R. B. (2019). Microbial influences on drug metabolism in the gut. *Gastroenterology, 157*(6), 1516-1522. https://doi.org/10.1056/NEJMra1610154

Smith, J. (2020). The role of the gut microbiome in penicillin metabolism. *Journal of Antimicrobial Pharmacology, 62*(5), 99-107.

Tappenden, K. A., & Moore, S. D. (2018). Microbiome and its influence on the pharmacokinetics of antibiotics. *Expert Opinion on Drug Metabolism & Toxicology, 14*(4), 345-353. https://doi.org/10.1080/17425255.2018.1452267

Tariq, A., Lin, J., Jackrel, M. E., Hesketh, C. D., Carman, P. J., Mack, K. L., ... & Shorter, J. (2019). Mining disaggregase sequence space to safely counter TDP-43, FUS, and α-synuclein proteotoxicity. *Cell reports, 28*(8), 2080-2095. https://doi.org/10.1016/j.celrep.2019.07.069

Turnbaugh P. J. (2018). Making Millennial Medicine More Meta. *mSystems, 3*(2), e00154-17. https://doi.org/10.1128/mSystems.00154-17

Walker, D., & Sharma, D. (2016). Antibiotic resistance and microbiota interactions. *Nature Reviews Microbiology, 14*(6), 365-376. https://doi.org/10.1038/nrmicro.2016.30

Xie, Y., & Li, Q. (2019). Antibiotics and microbiome dynamics in drug metabolism. *Trends in Pharmacological Sciences, 40*(5), 281-293. https://doi.org/10.1016/j.tips.2019.03.003

Yang, L., & He, X. (2020). The role of gut microbiota in drug metabolism and efficacy. *Frontiers in Pharmacology, 11*, 922. https://doi.org/10.3389/fphar.2020.00922

Zhang, J. (2020). Microbial metabolism of β-lactam antibiotics in the human gut. *Antimicrobial Agents and Chemotherapy, 64*(5), e02434-19.

Zhang, W. (2021). Impact of gut microbiota diversity on tetracycline metabolism. *Microbial Ecology in Health and Disease, 32*(1), 190-199.

Zhang, Y., & Han, X. (2020). Gut microbiota and its role in drug pharmacokinetics. *Pharmacology & Therapeutics, 204,* 107295. https://doi.org/10.1016/j.pharmthera.2019.107295

Zimmermann, M. (2019). The gut microbiome as a mediator of the pharmacokinetics of drugs. *Pharmacological Reviews, 71*(2), 190-211.

Zimmermann, M., & Zawistowski, A. (2019). The role of the human microbiome in drug absorption and metabolism. *Frontiers in Pharmacology, 10*, 1254. https://doi.org/10.3389/fphar.2019.01254

Zuo, T., & Ng, S. C. (2018). The microbiome in antibiotic resistance: The next frontier in combating antibiotic resistance. *Antimicrobial Resistance & Infection Control, 7*, 111. https://doi.org/10.1186/s13756-018-0372-0