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EXPLORING THE HEALTH EFFECTS OF DRUG INDUCED GUT MICROBIAL CHANGES: IMPLICATIONS FOR PERSONALISED MEDICINE

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ABSTRACT

The human gut microbiome, comprising over 100 trillion microorganisms, plays a crucial role in maintaining health by influencing immunity, nutrient absorption, and defence against pathogens. Growing evidence highlights how various medications, both antibiotic and non-antibiotic, can significantly alter the microbiome's composition and function, leading to diverse health outcomes. This review investigates the microbiome-modifying effects of widely-used drugs, including proton pump inhibitors (PPIs): non-steroidal anti-inflammatory drugs (NSAIDs): metformin, antidepressants, and immunosuppressants-has been shown to notably rearrange the composition and function of the gut microbiome. These disruptions manifest as alter microbial diversity, increased colonization by pathogenic bacteria, and alter metabolic function leading to serious health implications including infection susceptibility, gastrointestinal disorders, and metabolic imbalance. This review emphasizes the censorious need for personalized medicine approaches to reduce these adverse effects. Recognizing these effects can illuminate the development of personalized medicine approaches, such as microbiome profiling, to optimize drug efficacy and reduce adverse outcomes. This emerging field of research not only highlights the complicated relationship between pharmaceuticals and bacteria, but it also lays the foundation for future microbiome-informed precision medicine

KEYWORDS: Gut microbiome, Drug - induced microbial changes, Personalized medicine, Dysbiosis, probiotics & prebiotics.

1. INTRODUCTION

The human gastrointestinal (GI) tract contains an abundant and diverse microbial community that gathers more than 100 trillion microorganisms.[1]The microbiota offers many benefits to the host, through a range of physiological functions such as strengthening gut integrity or shaping the intestinal epithelium, harvesting energy, protecting against pathogens and regulating host immunity.[2] The gut microbiome plays a crucial role in preventing the proliferation of pathogenic microorganisms, a phenomenon known as colonization resistance.[3] Disruption of this resistance can lead to overgrowth of MultiDrug Resistant Organism (MDROs) such as Clostridium difficile, vancomycin-resistant enterococci, and antibiotic-resistant Enterobacteriaceae in the gut.[3] Understanding drug processes and the medications and the composition of gut microbes.[4] Some research article suggest that Antibiotic induced changes in microbial composition can have a negative impact on host health including reduced microbial diversity, changes in functional attributes of the microbiota, formation, and selection of antibiotic-resistant strains making hosts more susceptible to infection with pathogens such as Clostridium difficile.[5] In addition to antibiotics, many human-targeted non-antibiotic drugs were associated with changes in microbial composition.[6] One very important recent finding is that many commonly used non-antibiotic drugs—such as proton pump inhibitors (PPIs), metformin, NSAID, Immunosuppressants, Antidepressants—change microbiome composition and function. These changes can influence health outcomes or reduce drug efficacy.[7] The physiological gut microbiota variations have huge implications in intestinal and extra-intestinal disorders.[8] This study intends to explore the impact of a variety of medications on the

composition and functioning of the gut microbiome. These medications include antibiotics and non-antibiotic drugs such as metformin, NSAIDs, PPIs, immunosuppressants, and antidepressants. We will also look at how these drug-induced alterations can impact health outcomes.[7]

2. METHODS AND MATERIALS

This study focus on investigating drug-induced changes in the gut microbiome and their implications for health. The primary sources of data include peer-reviewed research articles, journals, and meta-analyses retrieved from databases like PubMed, Nature Communications, and Gut Microbes. The study involves the analysis of commonly used drugs, including proton pump inhibitors (PPIs) such as pantoprazole and esomeprazole, non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen and aspirin, metformin for type 2 diabetes, selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, and immunosuppressants like tacrolimus and corticosteroids. Biological samples such as fecal material are collected to assess gut microbiome composition and diversity, along with blood or plasma samples to measure metabolic biomarkers. DNA sequencing methods, including 16S rRNA or whole-genome sequencing, are employed for microbiome profiling, while metabolomic techniques like gas chromatography-mass spectrometry (GC-MS) are used to quantify short-chain fatty acids (SCFAs) and other microbial metabolites. Changes in microbial diversity are assessed using indices like Shannon or Simpson diversity indices, and statistical tools such as R or SPSS are utilized for multivariate data analysis. The study adopts an experimental approach, administering drugs in controlled doses to test subjects and monitoring physiological and metabolic parameters, including inflammation markers and intestinal permeability. Furthermore, interventions such as probiotics, prebiotics, or fecal microbiota transplantation (FMT) are explored as potential methods to mitigate adverse effects of microbial dysbiosis. This comprehensive approach ensures a robust analysis of the impact of drugs on the gut microbiome, facilitating the development of microbiome-informed therapeutic strategies.

3. GUT MICROBIOME STRUCTURE AND FUNCTION

The human gut microbiome is one of the most complex and dynamic microbial ecosystems and it consists of three phyla: Firmicutes, Bacteroidetes, and Actinobacteria. This vast microbial population amounts to about 10^{13}-10^{14} microbial cells and, in turn, exists at a roughly 1:1 ratio with human cells. The colon has the highest density at 3.8×10^{13} bacteria.[9] It acts as a functional expansion of host genomes, holding 50-100 times more genes than the human genome, enabling it to perform crucial functions through enzymatic proteins not expressed by the human host. These microbes contribute significantly to host metabolism. They ferment unavailable starch and soluble diet fiber to short-chain fatty acids including butyrate, propionate, and acetate, supplying an extra 10% of the day's diet energy and produce 70% of colon ATP. This micro flora not only produces critical nutrients as vitamin K2 and B-complex vitamins but also takes the part in bile acid metabolism, and Treg/TH17 ratio for regulation of proper balance of the immune response. Moreover, such colonisation of pathogens is restricted due to directly competing for resources as well as host defense mechanisms enhancement by direct competitions. Diet, the use of antibiotics, and environmental toxicants as well as host genetic variants affect gut microbiome composition and diversity, which can significantly affect its functionality. This thus means that any disruption to its fragile balance, that is known as dysbiosis, has the potential to cause health issues, making it essential to maintain a healthy, diverse gut microbiome.[9]

4. DRUG - INDUCED MODIFICATIONS TO THE GUT MICROBIOTA

4.1 PROTON PUMP INHIBITOR

Standard treatment of a vast array of medical conditions Proton pump inhibitors (PPIs) including pantoprazole, esomeprazole and omeprazole.[10] PPIs are weak bases and can inhibit the H+/K+ ATPase proton pump in an irreversible manner at parietal cells of gastric lining decreasing acid secretion, increasing with time the pH of stomach contrarily effect on gut microbiota or parasite colonization.[10]

4.2 Mechanism of alteration

Researchers speculate that lower gastric acid levels induced by PPI therapies directly influence the gut microbiota. Thus, PPIs alter stomach acid which in turn changes the gut microbiome and lets more bacteria cross the barrier into your intestines to make a home there.[10] This acidity is one of the main defences against bacteria invasions with food consumption and also during oral mucus formation. PPIs lower the acidity of the stomach, and hence more bacteria can penetrate beyond the protective barrier. We have shown that the gut microbiome in PPI users is indeed enriched for oral taxa. The long-term use of PPIs has a profound effect on the microbiota in the small intestine, leading to Small intestine bacterial overgrowth (SIBO); it is known that gastric acid acts as one effective barrier against bacteria. Allowing for distribution of pathogens and bacterial metabolites (e.g., nitrogenous substances, toxin).[11]

4.3 Increase bacteria due to PPI use

Research has identified significant changes in the gastrointestinal microbiome of proton pump inhibitor (PPI) users, with notable increases in commensals typically found in the oral and upper GI tract. Streptococcus from the family Streptococcaceae shows marked elevation in abundance among PPI users.[12] [13] alongside significantly higher levels of Enterococcus (study 13). Studies have also documented increased presence of Staphylococcus and potentially pathogenic Escherichia coli in the gut microbiota of individuals on

PPI therapy (study 14). Additionally, the genus Rothia appears over-represented in the fecal microbiome of PPI users (study 13): while elevated levels of Fusobacteria and Firmicutes have been particularly noted in gastric mucosal samples from those using PPIs (study 15). These shifts in microbial composition may have important implications for gastrointestinal health and function in patients receiving PPI treatment.[13][14][15]

4.4 Decrease bacteria due to PPI use

Gut Commensals: Ruminococcaceae and Lachnospiraceae: Families crucial for short-chain fatty acid production are significantly depleted in PPI users.[15] Overall, there is a marked decrease in bacterial diversity, with Shannon's diversity index showing significant reductions among PPI users compared to non-users.[12] [15]

General Microbial Diversity: Studies indicate that about 20% of bacterial taxa show significant changes, leaning towards a less healthy gut microbiome composition due to PPI use.[14] [15]

4.5 Health Implications

1. **Increased Risk of Enteric Infections:** PPI use is linked to a 65% increase in the incidence of *Clostridium difficile* infections. This is attributed to changes in the gut microbiome that reduce its ability to resist pathogenic colonization.[12] an increased susceptibility to other enteric infections, such as *Salmonella* and *Campylobacter*. The alteration in gut flora allows for easier colonization by these pathogens.[14] [13]
2. **Gut Dysbiosis:** PPI users exhibit significantly lower microbial diversity, which is associated with a less healthy gut microbiome. This dysbiosis can impair the gut's protective functions and increase vulnerability to infections.[12] [15] The composition of the gut microbiota shifts, with an increase in oral bacteria such as *Streptococcus*, *Enterococcus*, and *Staphylococcus*. These changes suggest a migration of bacteria from the oral cavity to the gut, which can lead to opportunistic infections.[10]
3. **Gastrointestinal Disorders:** Long-term PPI use may contribute to Intestinal Bacterial Overgrowth (SIBO): which can cause symptoms like bloating, diarrhoea, and malabsorption of nutrients.[10] There is evidence linking PPI use to microscopic colitis, a condition characterized by chronic diarrhoea and inflammation of the colon, which is also associated with dysbiosis.[10]
4. **Nutritional Deficiencies:** Dysbiosis caused by PPIs can lead to deficiencies in essential nutrients, including vitamin B12 and magnesium, due to impaired absorption mechanisms linked to altered gut flora.[15]
5. **Immune System Implications:** Changes in gut microbiota may affect immune responses, potentially increasing susceptibility to infections and inflammatory conditions. The gut microbiome plays a crucial role in modulating immune function; thus, its disruption can have far-reaching effects on health.[13]

5. NON-STEROIDAL ANTI-INFLAMMATORY DRUG

Non-steroidal anti-inflammatory drugs (NSAIDs) in particular because of their antipyretic, analgesic and anti-inflammatory properties; NSAIDs exert a therapeutic action by preventing cyclooxygenase and thereby reducing prostaglandin synthesis.[16]

5.1 Mechanism of alteration

Direct effect: By preventing or promoting microbial growth, causing microbial cell death, and/or affecting microbial metabolism, NSAID use can directly affect the composition of the gut microbiota and its metabolic activity.

Indirect effect: By inhibiting COX-1 and COX-2 enzymes, NSAIDs reduce inflammation as well as suppress the synthesis of defensive prostaglandins in the gut. Mucosally absorbed prostaglandins are important for both mucous membrane proliferation and secretion as well as immunity regulation, if their levels are insufficient there will be a drop in natural barrier function leading to increased permeability of the intestine along with changes in what comprises its microorganisms.[17] The prostaglandin inhibition leads to an unstable intestinal barrier. As a result, once bacteria and their products (such as lipopolysaccharides [LPS]) enter the mucosal layer, it's all over. At times, this movement provides stimuli for inflammation, changing the composition of bacteria still farther.[18] [19]

5.2 Increased Bacteria due to NSAIDs use

Research has demonstrated that non-steroidal anti-inflammatory drug (NSAID) use significantly alters gut microbiota composition, with particular effects on specific bacterial populations. Studies reveal that NSAID consumption increases Firmicutes abundance in the gut; while this phylum contains many beneficial bacteria, dysbiosis conditions can promote the development of harmful strains.[20] [18] Additionally, NSAIDs have been shown to boost levels of gram-negative bacteria, particularly Escherichia coli, which can intensify inflammation and gastrointestinal damage through lipopolysaccharide (LPS) release.[17] [18] This overall increase in potentially pathogenic species creates microbial imbalance that may worsen NSAID-induced enteropathy. These findings highlight the complex relationship between NSAIDs, gut microbiota alterations, and gastrointestinal health outcomes, suggesting a need for therapeutic strategies that address both inflammation control and microbiome preservation.[18]

5.3 Decreased Bacteria due to NSAIDs use

NSAIDs have been shown to decrease the abundance of Bacteroidetes, a phylum generally containing beneficial bacteria crucial for digestion and metabolism. Alongside

this reduction, NSAID use diminishes beneficial commensals from the Lachnospiraceae and Ruminococcaceae families, which play vital roles in maintaining gut health and supporting metabolic functions. Chronic NSAID consumption is associated with an overall decrease in microbial diversity, a condition frequently linked to poorer health outcomes and heightened susceptibility to various gastrointestinal disorders. This significant disruption of the gut microbiome balance highlights the potential for NSAIDs to negatively impact digestive health beyond their well-known direct effects on the gastrointestinal mucosa, suggesting that microbiome alterations may represent an important mechanism underlying NSAID-associated digestive complications.[18] [20] [21]

5.4 Health implications

1. **NSAID-Induced Enteropathy**: The role of the gut microbiota in NSAID enteropathy has attracted much attention. Large-scale studies have shown that the administration of NSAIDs may disturb this fine-tuned balance and result in a relative increase in Gram-negative taxa and decrease in many fundamental health-promoting species such as different Firmicutes. And when bacteria adhere to a host, they release inflammatory molecules and go through Toll-Like Receptor 4 which leads them down the inflammation pathway. Overall, a dysbiosis microbiota augments NSAID enteropathy and promotes gall bile toxicity.[16]
2. **Gastrointestinal Symptoms**: Patients using NSAIDs may experience symptoms such as nausea, diarrhoea, constipation, and abdominal pain due to changes in gut flora and the resultant inflammation.[21]
3. **Increased Risk of Infections**: Dysbiosis can increase susceptibility to infections, including those caused by opportunistic pathogens that exploit the altered gut environment.[22]
4. **Potential for Colorectal Disease**: There is emerging evidence suggesting that dysbiosis related to NSAID use may contribute to conditions like inflammatory bowel disease (IBD) and colorectal cancer due to chronic inflammation and impaired mucosal barrier function.[18]

6. METFORMIN

Metformin is the first-line medication for type 2 diabetes control. It decreases blood glucose levels by improving insulin sensitivity and reducing hepatic glucose production. Findings in recent studies have suggested a significant role of metformin-induced changes on the gut flora that may partially explain its therapeutic effects.[23]

6.1 Mechanism of alteration

Metformin is significantly more concentrated in the gastrointestinal tract (30-300 times higher than in plasma): which allows it to exert direct effects on gut microbiota. Approximately 30-50% of the drug reaches the colon and is excreted in feces, indicating its strong local effects.[24][25] Metformin was observed to mediate the modulation of an intestinal microbiota through inflammatory cytokines, TLR4 signalling defects and glycolysis regulation increasing number SCFA-producing bacteria.[26] Metformin can alter the gut microbiota profile through a modulation that increases Escherichia sp, Akkermansia muciniphila and Subdoligranuum variable but reduces Intestinibacter bartletti; increasing concentration of short chain fatty acids like butyrate and propionate. It suggests that metformin may have anti-obesity properties by changing the gut microbiome and metabolites. Nevertheless, the specific mechanisms by which it works are unknown.[27]

6.2 Increased Bacteria due to metformin use

Akkermansia muciniphila is often increased with metformin treatment and is associated with enhanced gut barrier function and metabolic benefits[25][28] The abundance of Escherichia species tends to increase, which may enhance SCFA production and influence glucose metabolism positively[29] [30] Metformin has been linked to an increase in members of the Bacteroidetes phylum, which are important for carbohydrate metabolism.[24]

6.3 Decreased Bacteria due to metformin use

The abundance of Intestinibacter bartlettii generally decreases with metformin treatment, which is associated with negative metabolic outcomes.[29] Metformin may reduce the abundance of bacteria associated with dysbiosis, contributing to improved gut health and metabolic function.[24] [28]

6.4 Health Implications

1. **Improved Metabolic Health**: Changes in microbial composition can enhance SCFA production, particularly butyrate and propionate, which are known to improve insulin sensitivity and glucose metabolism.[24] [30]
2. **Enhanced Intestinal Barrier Function**: The increase in beneficial microbes like Akkermansia muciniphila may help maintain the integrity of the intestinal barrier, reducing inflammation and metabolic dysregulation.[25]
3. **Weight Loss Support**: By improving gut health and metabolic profiles, metformin may aid in weight management efforts for individuals with obesity or those at risk for type 2 diabetes.The modulation of gut microbiota can support dietary changes by enhancing the metabolic effects of food intake.[29]

7. ANTIDEPRESSANTS

Antidepressants, specifically selective serotonin reuptake inhibitors (SSRIs): are a common treatment for depression and anxiety disorders. These drugs affect the gut microbiome and it is suggested that this could be a factor for both their intended therapeutic effects as well as side effects.[31]

7.1 Mechanism of alteration

SSRIs such as fluoxetine and sertraline led to changes in the gut microbiome, with an increase perhaps in species like Lactobacillus or Bifidobacterium reported so far (two bacteria that may be responsible for healthy gut status and mood regulation).[31] The microbiome there operates the gut-brain axis, contributing to Behavioural health through synthesizing neurotransmitters like serotonin and GABA. Consequently, antidepressant-induced alterations of the gut microbiome might be associated to their mood and anxiolytic events.[32]

7.2 Increased Bacteria due to antidepressants use

Ruminococcus flavefaciens bacterium has been implicated in alleviating depressive-like behaviours, suggesting a potential role in mediating the effects of antidepressants.[33] Some studies indicate that antidepressant treatment may lead to an increase in beneficial bacterial strains that could positively impact metabolic and psychological health.[34]

7.3 Decreased Bacteria due to Antidepressant use

Research indicates reductions in genera such as Ruminococcus and Adlercreutzia, which are important for maintaining gut health and metabolic functions.[35] [36]

7.4 Health Implications

1. **Impact on Mental Health**: The alterations in gut microbiota may play a role in the efficacy of antidepressant treatments by influencing mood and behaviour through the gut-brain axis.[33] [34]
2. **Potential for Side Effects**: Changes in gut microbiota can lead to gastrointestinal side effects, including nausea and diarrhoea, which are common among individuals taking antidepressants.[34]
3. **Long-term Health Outcomes:** Dysbiosis resulting from antidepressant use could have long-term implications for metabolic health, immune function, and overall well-being, emphasizing the need for careful consideration of these effects in clinical practice.[36] [17]

8. IMMUNOSUPPRESSANTS

For preventing transplant rejection and treating autoimmune diseases, lifelong immunosuppression is necessary for organ transplantation to be successful, otherwise the transplanted organs will very quickly be rejected. Its justification, at least in part, is based on the use of a wide range of drugs potentially affecting gut homeostasis and promoting harmful metabolic changes such as post-transplant diabetes mellitus (PTDM).[37]

8.1 Mechanism of alteration

Immunosuppressive drugs: These can disrupt the equilibrium of symbiotic and fluorogenic commensal bacteria in the colon as well alter colonization resistance by increasing opportunistic pathogens.For example, corticosteroids and mycophenolic acid are confirmed to reduce gut microbiota diversity; calcineurin inhibitors such as tacrolimus can also result in an overgrowth of specific bacterial strains within the gut. These changes can importantly alter drug metabolism and efficacy leading to metabolic disorders such as PTDM.[37]

8.2 Increased Gut Bacteria

Lactobacillus johnsonii and Lactobacillus acidophilus have been found to be more abundant in the gut microbiome of patients receiving immunosuppressants. These bacteria are known for their butyrate production, which is beneficial for intestinal health and may contribute to metabolic changes associated with immunosuppression.[38] Akkermansia muciniphila bacterium is often increased in immunosuppressed states and is associated with metabolic health, particularly in obese and diabetic patients. Its presence may indicate changes in gut permeability and metabolic function.[38] Enterobacter and Klebsiella genera may also see increased levels due to the disruption of normal gut flora, particularly when antibiotics are used alongside immunosuppressants.[39]

8.3 Decreased Gut Bacteria

Faecalibacterium prausnitzii;This beneficial bacterium, known for its anti-inflammatory properties and butyrate production, tends to decrease with immunosuppressant use.[52] Its reduction is concerning as it plays a crucial role in maintaining gut health and modulating immune responses.[40] Eubacterium plexicaudatum associated with starch degradation and butyrate production, this bacterium is less prevalent in immunosuppressed individuals, depriving the gut of its positive effects.[38] Immunosuppressant therapy, particularly with agents like tacrolimus and mycophenolate mofetil, has been shown to reduce overall microbial diversity in the gut. This loss of diversity is linked to increased risks of infections and other complications.[39] [41]

8.4 Health Implications

1. **Increased Risk of Infections**: The shift toward pathogenic bacteria raises the risk of infections, which is a significant concern in immunocompromised patients.[41]
2. **Metabolic Disorders**: Dysbiosis has been linked to metabolic issues such as post-transplant diabetes mellitus (PTDM): where changes in microbial composition may influence insulin resistance and glucose metabolism.[37] [41]

9. PERSONALISED MEDICINE AND MICROBIOME PROFILING

Medical treatments are tailored to each patient's unique traits through personalised medicine. The collection of all bacteria that reside in our body, known as the microbiome, is essential to this.[42] When creating individualised treatments, it is crucial to take into account how changes in the microbiome may impact our response to drugs.

9.1The Role of Microbiome Profiling in Predicting Drug Responses:

Microbiome profiling is examining the makeup of the body's microorganisms. This can assist in forecasting a person's reaction to specific medications.[43] Drug metabolism, efficacy, and toxicity can all be impacted by variations in gut flora, which can be important for maximising individualised treatment.[44] One example of a microbiome-informed treatment for a Clostridium difficile infection is faecal microbiota transplantation (FMT).[45] Another involves modifying the gut microbiota to boost the efficacy of particular cancer immunotherapies.[46]

9.2 Individualized Approaches to Mitigate Adverse Microbiome Effects

Probiotics, prebiotics and faecal microbiota transplants are examples of targeted interventions that are currently being investigated as to whether they can help reduce the negative impacts of shifts in the microbiome. These therapies aim at recovering the structure and function of a healthy microbiome in order to reduce inflammation and improve the overall health[47], The gut microbiota (GM) significantly influences drug metabolism, efficacy, and toxicity by enzymatically modifying drug structures, bioavailability, and activity. For instance, Eggerthella lenta inactivates digoxin, and microbial tyrosine decarboxylase reduces the therapeutic efficacy of levodopa in Parkinson's patients. Probiotics like Lactobacillus and Bifidobacterium promote beneficial bacterial growth, while prebiotics stimulate microbial populations to enhance drug efficacy and mitigate side effects. FMT has shown promise in restoring GM balance in conditions like chemotherapy-induced dysbiosis. Advances in multi-omics, synthetic microbial communities(SynComs): and engineered microbes provide further precision in manipulating GM to enhance therapeutic outcomes. These approaches have improved responses to cancer immunotherapies, diabetes treatments like metformin, and rheumatoid arthritis therapies such as methotrexate, underscoring their potential in personalized medicine to minimize adverse effects and optimize health outcomes.[55]

9.3Advances in Tailoring Drug Therapies to an Individual's Microbiome

It has been made possible by the advancement in the technological aspect especially in microbiome profiling thus enabling the development of tailored medication. Some of the strategies that can be used to achieve this include the use of probiotics, prebiotics and the small chemical microbiome modulators. New research is also being conducted in order to develop synthetic microbiome therapeutics with an aim of improving the treatment outcomes.[47]

10. FUTURE DIRECTIONS AND RESEARCH OPPORTUNITIES

The complete understanding of drug-microbiome interactions must be the main emphasis of future personalised medicine research.[48] To personalise medical treatment, individualised antibiotic medication and the development of microbiome-based biomarkers are required.[49][50] Mechanistic studies would clarify how antibiotics and non-antibiotic medications affect the gut microbiota, emphasising the changes they go through and the consequences they have on general health.[51] Advanced analytical tools like metagenomics and metabolomics will make it possible to thoroughly examine these complex interactions.[52] Longitudinal studies will be required to monitor the long-term impacts of pharmaceutical interventions on microbial communities.[48] [53] Computer frameworks could be developed to predict drug-microbiome interactions by combining genetic and chemical data.[50] Researchers should create simultaneous plans to use faecal microbiota transplantation, probiotics, and prebiotics to repair the microbiome.[54] By comprehending the complex interaction between medications and the gut microbiota, the objective is to create personalised medical treatments that minimise negative side effects and optimise outcomes for each patient.

11. RESULTS AND DISCUSSION

Research indicates that both antibiotic and non-antibiotic medications profoundly alter the gut microbiome's composition, leading to a shift from a healthy, diverse state to dysbiosis, characterized by reduced microbial diversity and the proliferation of opportunistic pathogens. Commonly used drugs such as PPIs, NSAIDs, and antidepressants have been shown to rearrange microbial function, resulting in clinical implications like increased susceptibility to Clostridium difficile infections, gastrointestinal inflammation, and metabolic imbalances. For instance, while PPIs promote the migration of oral bacteria into the gut, metformin can enhance beneficial taxa like Akkermansia muciniphila, illustrating the bidirectional nature of drug-microbiome interactions. These findings highlight a critical need for personalized medicine, where microbiome profiling and targeted interventions—such as probiotics, prebiotics, and fecal microbiota transplantation—can be used to tailor treatments, optimize drug efficacy, and minimize adverse health outcomes for individual patients.

12. CONCLUSION

This review reveals that various commonly used drugs, beyond antibiotics, induce significant changes in gut microbiome composition, with effects ranging from decreased microbial diversity to enhanced colonization by pathogenic bacteria. Such alterations can compromise gut health, leading to risks like infections, dysbiosis, gastrointestinal disorders, and even metabolic issues. Personalized medicine approaches, including microbiome profiling, offer promising pathways to tailor treatments by considering individual microbial responses. The adoption of prebiotics, probiotics, and microbiome-informed therapies represents a critical advance for optimizing drug efficacy and minimizing side effects. Moving forward, incorporating microbiome-

based insights into routine medical practice can enhance therapeutic outcomes and improve patient care.

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