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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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THE IMPACT OF SYSTEMIC DRUGS ON THE ORAL AND GUT MICROBIOME: A NARRATIVE REVIEW

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Abstract.

Objective: This narrative review examines the impact of systemic drugs, including antibiotics and non-antibiotic medications, on the oral and gut microbiomes, highlighting mechanisms of microbial alteration and clinical implications.

Methodology: A comprehensive literature search was performed using PubMed, Scopus, and Web of Science for studies published from 2014 to 2025. Keywords included "systemic drugs," "oral microbiome," "gut microbiome," and "dysbiosis." Eligible studies involved human or translational animal models addressing drug effects on microbiota. Data were synthesized to identify patterns of microbiome changes and related health outcomes.

Results: Antibiotics induce significant dysbiosis in oral and gut microbiomes, reducing microbial diversity and promoting pathogen overgrowth, which worsens diseases like periodontitis and inflammatory bowel disease. Non-antibiotic drugs such as proton pump inhibitors (PPIs), metformin, psychotropics, and steroids also alter microbiome composition. PPIs reduce gastric acidity, enabling oral bacteria to colonize the gut, increasing infection risk. Metformin fosters beneficial microbial shifts linked to improved metabolism. Psychotropics and steroids modify specific taxa associated with gastrointestinal and metabolic effects. The oral-gut microbiome axis facilitates microbial translocation, contributing to systemic inflammation and disease progression. Additionally, gut microbiota influence drug metabolism and bioavailability, adding complexity to drug-microbiome interactions.

Conclusion: Systemic medications broadly affect oral and gut microbiomes, impacting disease progression and therapeutic outcomes. Recognizing these interactions is vital for optimizing treatment and developing microbiome-friendly strategies. Future research should integrate microbiome insights into personalized medicine to reduce adverse effects and improve efficacy.

Key words. Systemic drugs, oral microbiome, gut microbiome, antibiotics, non-antibiotic.

Introduction.

The human body hosts a vast array of microbial communities, with the oral and gut microbiomes playing especially pivotal roles in maintaining health and preventing disease [1,2]. These diverse consortia—comprising bacteria, fungi, viruses, and archaea—are integral to nutrient metabolism, immune system function, and defense against pathogens [3].

Disruption of microbial balance, or dysbiosis, is increasingly recognized as a contributor to a range of local and systemic conditions. In the oral cavity, dysbiosis is linked not only to dental caries and periodontitis but also to broader health issues such as cardiovascular disease, adverse pregnancy outcomes, and respiratory illnesses [1,3]. Furthermore, the insertion of different dental appliances in the mouth can cause disorders in microbial hemostasis, leading to the growth of pathogenic bacteria [4-6]. Mechanistically, oral dysbiosis may drive systemic effects through inflammatory responses and immune modulation [3].

Similarly, the gut microbiome exerts profound influence over host physiology, with imbalances implicated in obesity, diabetes, inflammatory bowel disease, certain cancers, and neurological disorders [2,3]. Diet, lifestyle, and pharmaceutical interventions are major determinants of gut microbial composition [2]. While the impact of antibiotics on these communities is well established, recent research highlights that many non-antibiotic systemic drugs also shape the microbiome, with significant implications for health and disease [7].

Systemic medications, though primarily designed to target human pathways, can directly or indirectly alter the composition and function of oral and gut microbiota [7]. Such interactions may affect drug efficacy, contribute to adverse reactions, and influence disease outcomes [8-10]. The interconnectedness of the oral and gut microbiomes—sometimes referred to as the "oral-gut axis"—underscores the potential for drug-induced microbial changes to have widespread physiological consequences [3,7,8].

Therefore, this narrative review aims to synthesize current evidence on the impact of systemic, non-antibiotic drugs on the oral and gut microbiomes, and to discuss the broader implications for health and therapeutic strategies in the context of increasing polypharmacy.

Methodology.

A narrative review approach was adopted, following established guidelines for scientific review articles. The research question was defined as: "What are the impacts of systemic drugs on the oral and gut microbiome, and what are the clinical implications of these changes?" A comprehensive

literature search was conducted using PubMed, Scopus, and Web of Science for studies published between 2014 and 2025. Search terms included combinations of "systemic drugs," "oral microbiome," "gut microbiome," "antibiotics," "non-antibiotic medications," "dysbiosis," and "microbiota." Boolean operators (AND, OR) were used to refine results.

Inclusion criteria were: (1) original research, reviews, or meta-analyses in English; (2) studies addressing the effects of systemic drugs on oral or gut microbiota; and (3) relevance to human health or translational animal models. Exclusion criteria included studies focused solely on topical or local drug effects and those not addressing microbiome outcomes. Reference lists of key articles were screened for additional relevant studies. Data were extracted and synthesized thematically, focusing on drug classes, mechanisms of microbiome alteration, and clinical outcomes.

Results.

Antibiotics and Microbiome Disruption:

Antibiotics, while essential for combating bacterial infections, exert profound and often long-lasting effects on the oral and gut microbiomes. Their impact extends beyond the elimination of pathogenic bacteria to broad disruptions in microbial diversity, community structure, and function, which can impair host immunity, metabolic homeostasis, and colonization resistance. Systemic antibiotics remain the most extensively studied drugs impacting the oral and gut microbiomes. Their broad-spectrum activity reduces microbial diversity and disrupts colonization resistance, leading to overgrowth of opportunistic pathogens. This dysbiosis affects both gut and oral compartments, with evidence showing exacerbation of periodontitis through immune dysregulation, such as Th17/Treg imbalance in periodontal tissues. Fecal microbiota transplantation has shown promise in restoring microbial balance and mitigating antibiotic-induced adverse effects [11,12].

Reduction in Microbial Diversity and Dysbiosis:

Antibiotic treatment typically results in a marked reduction in microbial diversity across the gut and oral ecosystems. This loss of diversity is characterized by depletion of beneficial commensal bacteria and an overgrowth of opportunistic pathogens. For example, administration of broad-spectrum antibiotics such as β-lactams, gentamicin, and vancomycin has been shown to decrease populations of *Bifidobacterium* and butyrate-producing species, while increasing the abundance of pathobionts like *Enterobacteriaceae* and *Clostridioides difficile* [13]. Such dysbiosis compromises colonization resistance, the microbiota's ability to prevent pathogen invasion, thereby increasing susceptibility to infections.

Microbiome recovery after antibiotic exposure is often incomplete and variable among individuals. Studies have reported that while some microbial taxa return to baseline within weeks, others remain undetectable for months or longer, leading to persistent alterations in community composition and function [14]. These disruptions can have systemic consequences, including impaired immune regulation and increased risk of inflammatory and metabolic diseases.

Impact on Immune Function and Host Physiology:

Antibiotic-induced microbiome changes affect the host immune system profoundly. The gut microbiota plays a critical role in the development and regulation of immune responses, particularly in shaping T cell populations such as Th17 cells. Experimental models demonstrate that antibiotics targeting Gram-positive bacteria reduce intestinal Th17 cell populations, which are important for mucosal immunity [15]. Additionally, antibiotic treatment decreases production of antimicrobial peptides like resist in-like molecule-β (RELMβ), weakening mucosal defences [15].

Beyond immune modulation, antibiotics influence host metabolism. In mice, sub-therapeutic antibiotic doses altered body weight, fat content, bone density, and hepatic fatty acid metabolism, effects linked to shifts in microbial metabolites such as short-chain fatty acids (SCFAs) [15]. These findings suggest that antibiotic-driven microbiome disruption can contribute to metabolic dysregulation.

Mechanisms of Microbial Disruption and Resistance

Antibiotics impact not only target pathogens but also commensal bacteria due to their broad-spectrum activity. This

Table 1. *Drug Effects on Oral and Gut Microbiomes.*

Drug/Class	Microbiome Effect	Clinical Implications	References
Antibiotics	Reduced diversity, dysbiosis in oral and gut microbiomes	Increased infection risk, periodontitis exacerbation	[11,12]
Proton Pump Inhibitors	Reduced gut microbial diversity; increased oral bacteria in gut	Increased enteric infections, gut barrier disruption	[19,12]
Metformin	Increased *Akkermansia*, *Parabacteroides*; restored dysbiosis	Improved metabolic outcomes	[12]
SSRIs, Tricyclic Antidepressants	Increased *Streptococcus salivarius*, *Eubacterium ramulus*, *Clostridium leptum*	Potential GI side effects, altered drug response	[11]
Oral Steroids	Increased *Methanobrevibacter smithii*	Associated with obesity and weight gain	[11]
Laxatives	Increased *Alistipes* and *Bacteroides*	Altered gut microbial balance	[11]
Porphyromonas gingivalis (oral pathogen)	Disrupts gut barrier, increases endotoxemia and systemic inflammation	Linked to cardiometabolic diseases and atherosclerosis	[19,8]
Gut Microbial Enzymes	Modify bile acid pool affecting drug solubilization	Influence oral drug bioavailability	[22,23]

leads to collateral damage within microbial networks, disrupting co-dependent species and metabolic interactions. Additionally, antibiotic exposure can induce prophage activation in lysogenic bacteria, causing bacterial lysis and further altering microbial community dynamics [16].

Bacteria employ diverse mechanisms to resist antibiotics, including enzymatic degradation (e.g., β-lactamases), target modification, efflux pumps, and reduced membrane permeability [16]. Such resistance can lead to the proliferation of antibiotic-resistant strains post-treatment, sometimes increasing the overall microbial load despite reduced diversity [16].

Non-Antibiotic Medications and Microbiome Alterations:

Recognizing the detrimental effects of antibiotics and other systemic drugs on the microbiome, research is increasingly focused on non-antibiotic approaches to infection management that preserve or restore microbial balance. Strategies include the use of pro-, pre-, and synbiotics, fecal microbiota transplantation, phage therapy, and innovative antimicrobial peptides. These interventions aim to reduce dysbiosis-driven morbidity, particularly in vulnerable populations such as the critically ill, where polypharmacy and antibiotic exposure are common [17].

Recent studies reveal that many non-antibiotic systemic drugs significantly affect microbiome composition and function:

Proton Pump Inhibitors (PPIs): PPIs reduce gastric acidity, facilitating the translocation of oral bacteria like *Streptococcus anginosus* to the gut, leading to gut dysbiosis and increased risk of enteric infections. Metagenomic studies show PPI users have reduced microbial diversity and decreased abundance of beneficial taxa such as *Ruminococcaceae* and *Bifidobacteriaceae*, with increased levels of potentially pathogenic families like *Enterobacteriaceae* and *Enterococcaceae*. These changes are dose-dependent and consistent across multiple cohorts [18,19].

Metformin: Treatment with metformin alters gut microbiota composition, increasing beneficial taxa like *Akkermansia* and *Parabacteroides* while restoring microbial balance disrupted by high-fat diets. These shifts are linked to improved metabolic outcomes, highlighting the microbiome as a mediator of metformin's therapeutic effects [20].

Psychotropics and Other Drugs: Selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, oral steroids, and platelet aggregation inhibitors have been associated with increased abundance of specific microbes such as *Streptococcus salivarius*, *Eubacterium ramulus*, *Clostridium leptum*, and *Methanobrevibacter smithii*. For example, oral steroids correlate with increased *Methanobrevibacter smithii*, which has been linked to obesity and high BMI, potentially explaining steroid-associated weight gain. Laxatives increase *Alistipes* and *Bacteroides* abundance [21].

Oral-Gut Microbiome Axis and Disease:

The oral-gut microbiome axis plays a critical role in systemic health. Oral pathogens like *Porphyromonas gingivalis* disrupt intestinal barrier integrity by decreasing tight junction proteins (e.g., ZO-1, occludin), increasing gut permeability and endotoxemia. This promotes systemic inflammation and metabolic dysregulation, contributing to cardiometabolic diseases. *P. gingivalis* endotoxin (Pg-LPS) can induce gut microbiota changes via hematogenous routes, and this pathogen is frequently detected in atherosclerotic plaques, linking oral infections to cardiovascular disease [22,23]. Although advances in technology have played an important role in oral care in recent times [24,25], managing the oral microflora is a challenge for healthcare professionals.

Oral bacteria translocating to the gut exacerbate inflammatory bowel disease (IBD) and colorectal cancer by altering immune responses and microbial ecology. For instance, *Fusobacterium nucleatum* and *Enterobacteriaceae* from the oral cavity induce Th1/Th17 inflammation and disrupt gut homeostasis [26].

Drug-Microbiome Interactions Affecting Drug Bioavailability:

The gut microbiome also impacts drug metabolism and bioavailability. Gut microbial enzymes, such as 7α-dehydroxylases, modify bile acid composition, which influences the solubilization and absorption of poorly water-soluble oral drugs. Secondary bile acids formed by microbial metabolism can enhance or reduce drug bioavailability in a drug-specific manner, although further in vivo validation is needed [27].

Discussion.

A recent large-scale, data-driven study used machine learning to predict the impact of 2,585 clinically approved small-molecule drugs on 409 human gut microbiota members. This approach generated over a million predicted drug–microbe interactions, revealing that many non-antibiotic drugs possess anti-commensal properties, which correlate with gastrointestinal side effects. The study validated these predictions using in vitro experiments, animal models, and clinical data, highlighting the broad and often unanticipated impact of systemic drugs on microbiome composition [28].

Evidence indicates that the oral and gut microbiomes, while distinct, are interconnected through the oral-gut axis. Under normal physiological conditions, barriers such as gastric acid and mucosal integrity restrict microbial migration [29]. Recent advancements in technology have the potential to significantly enhance our understanding and management of this interplay, benefiting both the fields of medicine and dentistry [30,31]. However, systemic medications may compromise these protective barriers. For example, proton pump inhibitors (PPIs) decrease gastric acidity, facilitating the translocation of oral bacteria like *Streptococcus anginosus* to the gut [32]. A recent prospective interventional study found that a seven-day course of esomeprazole in healthy adults led to a 42-fold increase in gut *S. anginosus*, with microbial source tracking confirming the oral origin of these bacteria. Co-administration of chlorhexidine mouthwash reduced this effect, underscoring the role of oral bacteria in PPI-induced gut dysbiosis [33].

The oral-gut microbiome axis is increasingly implicated in systemic diseases beyond the gastrointestinal tract. Oral pathogens migrating to the gut have been linked to metabolic endotoxemia, insulin resistance, and systemic inflammation, all of which contribute to cardiometabolic disorders. Disruptions in the oral or gut microbiome can thus have far-reaching effects, influencing the risk and progression of diseases such as metabolic syndrome, liver disease, and cardiovascular disease [34,35].

Recent observational studies consistently demonstrate that systemic, non-antibiotic drugs can induce notable changes in the oral and gut microbiomes, affecting both microbial diversity and the abundance of specific taxa.

Diminished Microbial Diversity:

A recurrent observation across multiple cohorts is a reduction in overall microbial diversity—often termed "alpha diversity"—in individuals exposed to certain systemic medications. For example, proton pump inhibitors (PPIs) and metformin have been associated with lower gut microbial diversity compared to drug-naïve controls [36]. Diminished diversity is widely regarded as a marker of dysbiosis and has been linked to increased susceptibility to infections, metabolic disturbances, and inflammatory conditions [36]. In the oral cavity, reduced diversity has been correlated with a higher risk of periodontitis and caries [37].

Fluctuations in Specific Bacterial Species:

Beyond overall diversity, drug-induced shifts in the abundance of key bacterial taxa have been documented. For instance, PPIs are associated with increased oral and gut colonization by Streptococcus and Enterococcus species, which are linked to a higher risk of infections and inflammation [37]. Metformin, a common antidiabetic agent, enriches *Akkermansia muciniphila* and certain short-chain fatty acid producers, which may partially mediate its metabolic benefits [38]. Conversely, statins and antipsychotics have been associated with an increase in potentially pathogenic bacteria such as *Escherichia/Shigella* and a decrease in beneficial genera like *Faecalibacterium* [38].

Physiological and Pathophysiological Implications:

These microbial alterations are not merely epiphenomena; they have tangible effects on host physiology. Reduced diversity and the proliferation of pro-inflammatory species can compromise gut barrier function, promote systemic inflammation, and contribute to metabolic dysregulation [39]. In the oral cavity, similar disruptions can exacerbate local inflammation and facilitate the translocation of oral pathogens to distant sites, potentially contributing to cardiovascular and respiratory diseases [39].

SSRIs and Microbiota:

Selective serotonin reuptake inhibitors (SSRIs) are widely prescribed for mood disorders and are frequently associated with gastrointestinal (GI) complaints and weight gain. Emerging evidence suggests that SSRIs can alter the gut microbiome, reducing microbial diversity and shifting the relative abundance of specific taxa [40]. For example, animal studies indicate that SSRIs can decrease populations of *Lactobacillus* and *Bifidobacterium*, genera known for their beneficial effects on gut health [40]. These alterations may impair gut barrier integrity and modulate gut-brain signaling, potentially contributing to both GI symptoms and metabolic side effects [40].

Steroids and Microbiota:

Glucocorticoids and other steroids are similarly implicated in microbiome changes, including reduced diversity and increased abundance of pro-inflammatory bacteria such as Enterobacteriaceae [41]. These shifts may underlie some of the well-documented adverse effects of steroids, such as increased infection risk, weight gain, and glucose intolerance. However, the precise mechanisms remain incompletely understood. It is hypothesized that steroids may suppress immune surveillance in the gut, allowing for the overgrowth of opportunistic pathogens and disruption of metabolic signaling pathways [41].

Clinical Implications and Research Gaps:

While these associations are compelling, causality and mechanistic pathways are not fully established. Most studies to date are observational or based on animal models, and confounding factors such as underlying disease, diet, and polypharmacy complicate interpretation. There is a pressing need for longitudinal, interventional studies to clarify whether microbiome-targeted strategies (e.g., probiotics, dietary interventions) can mitigate drug-induced adverse effects.

Future Directions:

Given the growing recognition of the oral-gut microbiome's role in mediating drug effects, integrating microbiome assessments into clinical trials of systemic medications is warranted. Personalized medicine approaches that consider individual microbiome profiles may help optimize drug efficacy and minimize adverse outcomes. Further research should also explore the bidirectional interactions between drugs and the microbiome, including how microbial metabolism can influence drug pharmacokinetics and pharmacodynamics.

Conclusion.

Systemic drugs, including both antibiotics and non-antibiotic medications, significantly influence the composition and function of the oral and gut microbiomes, often leading to dysbiosis that can compromise colonization resistance and exacerbate local and systemic disease processes. Clinically, these findings underscore the importance of considering microbiome health when prescribing medications, especially in patients at risk of metabolic, gastrointestinal, or inflammatory complications.

Translating these insights into practice involves the proactive use of microbiome-modulating interventions. Probiotics and prebiotics may serve as adjunct therapies to restore microbial balance and mitigate drug-induced adverse effects, particularly gastrointestinal symptoms associated with SSRIs and steroids. Moreover, fecal microbiota transplantation (FMT) represents a promising, though still emerging, approach for re-establishing a healthy gut microbiome in cases of severe dysbiosis or recurrent infections linked to pharmacotherapy. By incorporating microbiome considerations into routine clinical practice, healthcare providers can improve patient outcomes and advance precision medicine in the era of widespread polypharmacy.

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