International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Scholarly Publisher
RS Global Sp. z O.O.
ISNI: 0000 0004 8495 2390

Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

ARTICLE TITLE	METFORMIN AND THE GUT MICROBIOTA: CHANGES AND CLINICAL IMPLICATIONS – A LITERATURE REVIEW
DOI	https://doi.org/10.31435/ijitss.3(47).2025.3679
RECEIVED	16 June 2025
ACCEPTED	08 September 2025
PUBLISHED	30 September 2025
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

METFORMIN AND THE GUT MICROBIOTA: CHANGES AND CLINICAL IMPLICATIONS – A LITERATURE REVIEW

Natalia Klimek *(Corresponding Author, Email: natalia.kli@wp.pl)*
Warsaw Medical University, 02-091 Warsaw, Poland
ORCID ID: 0009-0004-3644-2529

Antoni Liebert
Warsaw Medical University, 02-091 Warsaw, Poland
ORCID ID: 0009-0004-8778-1803

Hanna Wilska
Warsaw Medical University, 02-091 Warsaw, Poland
ORCID ID: 0000-0002-6483-5440

Adam Niedziela
Warsaw Medical University, 02-091 Warsaw, Poland
ORCID ID: 0009-0002-6178-6484

Dominik Domoń
Warsaw Medical University, 02-091 Warsaw, Poland
ORCID ID: 0009-0008-7631-4563

Martyna Kaplińska
Warsaw Medical University, 02-091 Warsaw, Poland
ORCID ID: 0009-0004-1236-0166

Dominika Domanowska
Warsaw Medical University, 02-091 Warsaw, Poland
ORCID ID: 0009-0002-2965-7754

ABSTRACT

Background: Metformin remains the first-line pharmacotherapy for type 2 diabetes mellitus (T2DM), traditionally understood to act through hepatic glucose suppression and improved insulin sensitivity. However, mounting evidence indicates that metformin significantly influences the gut microbiota, which may underlie some of its metabolic and gastrointestinal effects
Aim: This review explores metformin's mechanisms of action via gut microbial modulation, its clinical effects, and side-effect implications, drawing upon recent primary and review literature.
Methods: We performed comprehensive searches in databases including PubMed and Google Scholar,using terms such as metformin, mechanisms of metformin, gut microbiota, side effects of metformin, metformin mechanisms gut, and related combinations. We included studies published up to mid-2025, prioritizing human clinical trials, systematic reviews, and mechanistic animal studies.
Results: Compelling evidence shows that metformin alters gut microbial composition—increasing taxa like Akkermansia muciniphila, Escherichia, and SCFA-producers—while reducing others. These shifts are linked to improved barrier integrity, altered bile acid signaling (e.g., FXR inhibition, GLP-1 increase), enhanced SCFA production, modulated metabolite profiles (e.g., BCAA, aromatic amino acids), and altered host glucose flux. Clinically, these microbiome changes likely contribute to metformin's glucose-lowering, weight-modulating, and anti-inflammatory effects but may also underpin gastrointestinal side effects.
Conclusion: The gut microbiota is a significant mediator of both beneficial and adverse effects of metformin. Ongoing and future research—especially RCTs and mechanistic human studies—will be critical for harnessing this interaction therapeutically.

KEYWORDS
Metformin, Mechanisms of Metformin, Gut Microbiota, Side Effects of Metformin

CITATION

Natalia Klimek, Antoni Liebert, Hanna Wilska, Adam Niedziela, Dominik Domoń, Martyna Kaplińska, Dominika Domanowska. (2025) Metformin and the Gut Microbiota: Changes and Clinical Implications – A Literature Review. *International Journal of Innovative Technologies in Social Science*, 3(47). doi: 10.31435/ijitss.3(47).2025.3679

1. Introduction

Metformin, a biguanide synthesized in the 1920s and clinically adopted mid-20th century, has remained foundational in T2DM management and is recognized as an”essential medicine” by the World Health Organization. [1]

The first documented evidence of metformin’s clear hypoglycemic effect was published in 1957, based on data from hospitalized diabetic patients. This study reported only mild subjective side effects and no signs of hypoglycemia—a complication commonly associated at the time with sulphonylurea therapy. Subsequent research into insulin resistance and the discovery of a novel mechanism involving activation of adenosine monophosphate-activated kinase (AMPK) established metformin as an antidiabetic medication with distinctive benefits, supporting its widespread use. Beyond diabetes, metformin is now also being investigated for its potential anti-cancer properties and possible effects on lifespan extension [2] though these aspects are outside the scope of this review.

Metformin was traditionally regarded as an inhibitor of hepatic gluconeogenesis through mechanisms involving mitochondrial complex I inhibition, AMP-activated protein kinase (AMPK) activation, and suppression of cAMP/PKA signaling. Recent research, however, highlights its broader pharmacological profile, with extra-hepatic effects—particularly modulation of the gut microbiota—emerging as important contributors to its glucose-lowering and systemic metabolic benefits. [3, 4]

The human gut microbiota—comprising bacteria, viruses, fungi, and more—exerts metabolic, immune, and barrier functions. Dysbiosis (imbalance) has been implicated in metabolic diseases like T2DM. Despite decades of widespread clinical use, the precise mechanisms underlying metformin’s therapeutic and adverse effects remain incompletely understood [5]. In particular, the interaction between metformin and the gut microbiota has emerged as a key research problem, as it may critically influence both efficacy and tolerability.

Clarifying this relationship is essential to improve understanding of metformin’s clinical actions, optimize therapeutic use, and potentially minimize side effects.

1.1 Aim of the study

The aim of the study is to analyze the effects of metformin on the gut microbiome and its clinical effects.

1.2. Method

We systematically searched PubMed and Google Scholar using keyword combinations including „metformin”, „mechanisms of metformin”, „gut microbiota”, „side effects of metformin”, „metformin mechanisms gut” „short-chain fatty acids”, and „bile acids”, focusing on literature published up to mid-2025. The search encompassed reviews, clinical trials, systematic analyses, and mechanistic animal studies.

2. Metformin Pharmacology and Gut Interaction

2.1 Classical Mechanisms

Metformin exerts its glucose-lowering effects through multiple mechanisms. It inhibits mitochondrial complex I, which reduces ATP production and activates AMP-activated protein kinase (AMPK), leading to suppression of hepatic gluconeogenesis. In addition, metformin modulates cyclic AMP and glucagon-driven signaling pathways, an effect that can occur independently of AMPK. The drug also influences bile acid transport and signaling by reducing FXR activity, potentially through increased luminal bile acids, which in turn enhances GLP-1 secretion via TGR5 receptors in intestinal L-cells. Furthermore, metformin can act through the PEN2-AMPK-v-ATPase axis to stimulate GLP-1 release in a manner that does not depend on AMPK. Finally, it engages cholinergic M3 and gastrin-releasing peptide receptor pathways, contributing to the stimulation of incretin secretion and improving overall glycemic control. [3, 4, 6, 7]

2.2 Gastrointestinal Concentration & Absorption

Metformin is absorbed inefficiently in the stomach and colon but accumulates in the small intestine at concentrations up to 30 to 300 times higher than those in plasma. Its oral bioavailability is approximately 50 to 60 percent, with about 30 percent of the administered dose excreted unchanged in the feces. [8] Absorption is influenced by gastric motility and can be reduced by high-fat meals. [9] Interestingly, oral administration produces stronger metabolic effects than an equivalent intravenous dose, indicating that the gut plays a central role in mediating its therapeutic actions. [10]

3. Intestinal Microbiota: Composition and Function

3.1 Normal microbiota

The human intestinal microbiota is a highly diverse ecosystem composed of trillions of microorganisms, primarily bacteria, but also archaea, fungi, viruses, and protozoa. Its composition is shaped by multiple factors, including genetics, diet, age, environment, and drug exposure [11]. In healthy individuals, the dominant bacterial phyla are Firmicutes and Bacteroidetes, followed by Actinobacteria, Proteobacteria, and Verrucomicrobia [12, 13]. A balanced microbial community is a key marker of intestinal health, as disturbances in microbial composition, or dysbiosis, are often linked with metabolic, inflammatory, and infectious diseases [14]. Although each person’s microbiota is unique, a resilient and functionally redundant microbial network is generally considered a hallmark of a healthy gut ecosystem [13].

3.2 Microbiota function

Beyond their structural diversity, intestinal microbes play crucial roles in maintaining host physiology. They contribute to the fermentation of complex dietary fibers, producing short-chain fatty acids such as butyrate, acetate, and propionate, which regulate intestinal barrier integrity, energy metabolism, and immune responses [12]. The microbiota also participates in bile acid transformation, shaping both metabolic signaling and immune regulation [15]. Additionally, microbial communities synthesize vitamins, modulate inflammatory pathways, and protect against pathogens through colonization resistance [14]. In essence, the intestinal microbiota operates as a metabolic and immunological organ that supports overall host health, while imbalances in these functions can predispose to disease [13].

4. Results

4.1 Taxa and Functional Changes

Evidence from both human cohorts and animal models demonstrates that metformin induces profound and characteristic shifts in the composition and metabolic activity of the gut microbiota, which extend its antidiabetic effects far beyond the classical inhibition of hepatic gluconeogenesis. [1, 5, 16] One of the most consistent findings is the marked enrichment of Akkermansia muciniphila, a mucin-degrading bacterium within the Verrucomicrobia phylum, whose abundance correlates with improved glucose tolerance, reduced systemic inflammation, and enhanced mucus layer integrity [1, 16]. Metformin also increases several beneficial saccharolytic taxa, including Bifidobacterium, Blautia, Butyrivibrio, and certain Prevotella species, which are key producers of short-chain fatty acids (SCFAs) such as acetate, propionate, and butyrate. These metabolites exert pleiotropic effects—serving as energy sources for colonocytes, reinforcing tight junction protein expression, stimulating GLP-1 release via enteroendocrine signaling, and dampening pro-inflammatory cytokine production [1, 16]. At the same time, context-dependent changes are observed within Bacteroides, with some species expanding while others decline, and a recurrent decrease in Bacteroides fragilis has been associated with improved bile acid metabolism and reduced lipopolysaccharide-mediated inflammation [16]. Conversely, several studies note an increase in Enterobacteriaceae, particularly Escherichia/Shigella, which may contribute to gastrointestinal side effects in susceptible individuals [16, 17]. Reductions in Intestinibacter and Clostridioides difficile are also frequently reported, and in murine models, metformin consistently decreases certain Clostridia and Proteobacteria populations, with notable sex-dependent differences in microbiome remodeling [1, 8].

Functionally, these taxonomic rearrangements reshape the microbial metabolic network in ways that favor host metabolic health. Enhanced SCFA production supports epithelial barrier repair by stimulating mucin synthesis, tightening intercellular junctions, and reducing intestinal permeability, thereby limiting translocation of bacterial endotoxins into the bloodstream [1]. Metformin-driven enrichment of bacteria with bile salt hydrolase activity modifies the bile acid pool toward species such as glycoursodeoxycholic acid (GUDCA) [1, 16]. Parallel shifts in amino acid and aromatic compound metabolism—such as decreased phenylalanine and glyoxylate pathways alongside increased arginine, proline, and arachidonic acid derivatives—may further enhance energy balance and anti-inflammatory responses [18]. Systems-level metabolic modeling reinforces these findings, showing that metformin-responsive microbial communities engage in increased cross-feeding of butyrate, propionate, and other bioactive metabolites, changes that are positively associated with HbA1c reduction in type 2 diabetes patients [8]. Collectively, these alterations illustrate that metformin's therapeutic benefits are partly mediated through the restoration of gut microbial balance, strengthening of the intestinal barrier, and modulation of host–microbe metabolic crosstalk, making the gut microbiota a central player in its clinical efficacy [1, 16].

4.2 Mechanistic Pathways via Microbiome

One of the key mechanisms by which metformin exerts its metabolic effects involves the bile acid–FXR–GLP-1 axis. By promoting the growth of *Bacteroides fragilis* and increasing the bile acid metabolite glycoursodeoxycholic acid (GUDCA), metformin inhibits the farnesoid X receptor (FXR). This inhibition, in turn, enhances the secretion of glucagon-like peptide-1 (GLP-1), thereby improving glucose homeostasis [4]. In addition to bile acid signaling, emerging evidence suggests that metformin directly alters intestinal glucose handling. A recent 2025 study demonstrated that metformin facilitates a bidirectional flux of glucose from the circulation into the intestinal lumen, where it becomes available for utilization by gut microbiota. This finding highlights a novel metabolic interplay between host glucose metabolism and the intestinal microbial community [19].

4.3 Overall Summary

Domain	**Findings**
Microbiome composition	Metformin increases *Akkermansia*, SCFA-producers; decreases certain pathogens and taxa.
Mechanisms	Modulates bile acid signaling, incretin release (GLP-1), intestine–glucose flux, SCFA and harmful metabolite production.
Effects	Enhances insulin sensitivity, reduces inflammation, contributes to gut-related side effects.
Variability	Responses vary by individual microbiota, diet, dosage; promising area for precision interventions.

5. Discussion

5.1 Metabolic Benefits

The clinical benefits of metformin appear to be closely linked to microbiome-mediated changes [5, 20]. One important mechanism involves the enhancement of incretin secretion, particularly glucagon-like peptide-1 (GLP-1), which contributes to improved appetite regulation and glycemic control [1, 16]. In addition, alterations in the gut microbiota promote the production of short-chain fatty acids (SCFAs) and other metabolites that enhance insulin sensitivity and support metabolic homeostasis [1, 20]. Another significant effect of these microbiota shifts is the strengthening of gut barrier integrity. which helps to reduce endotoxemia and lower systemic inflammation [1, 16]. Together, these mechanisms provide a plausible explanation for the broad metabolic improvements associated with metformin therapy [1, 20].

5.2 Gastrointestinal Side Effects

Gastrointestinal intolerance is one of the most common adverse effects of metformin therapy, typically manifesting as diarrhea, bloating, and flatulence. These symptoms are thought to arise, at least in part, from microbial fermentation and the increased production of gases such as hydrogen sulfide by bacterial species that are enriched during metformin treatment, which may exacerbate abdominal discomfort [4, 18]. The severity of gastrointestinal side effects can vary depending on the formulation of the drug. Evidence from systematic reviews and meta-analyses indicates that modified-release formulations are associated with markedly fewer gastrointestinal complaints compared with immediate-release metformin, making them a preferable option for patients with intolerance [21]. Recent reviews also emphasize that these side effects, while common, are usually dose-dependent and tend to diminish over time, although they remain an important factor limiting adherence in some patients [22].

5.3 Individual Variability

The response to metformin is increasingly recognized as being influenced by the interplay between gut microbiome composition, dietary factors, and host physiology. Variability in microbial communities can shape the production of metabolites such as short-chain fatty acids and branched-chain amino acids, which in turn may modulate both therapeutic efficacy and gastrointestinal tolerability [18]. Emerging evidence suggests that personalized dietary strategies designed to optimize microbial metabolite profiles could enhance the clinical benefits of metformin while reducing adverse effects. Such approaches highlight the need to consider host–microbiome–diet interactions as key determinants of individual treatment outcomes [22].

6. Conclusion and Future Directions

In summary, the gut microbiota emerges as a central mediator of metformin’s metabolic and gastrointestinal effects. Understanding the precise microbial taxa, metabolites, and host pathways involved could unlock improved tolerability, personalized therapies, and new drug targets.

Future research should prioritize controlled clinical trials that assess the effects of metformin in combination with microbiome- and nutrition-based interventions. Longitudinal multi-omics studies in diverse human cohorts are also needed to delineate causal pathways linking the gut microbiota, host metabolism, and metformin response. In addition, the development of microbiota-targeted co-therapies, such as probiotics or dietary adjustments, represents a promising strategy to enhance therapeutic efficacy while minimizing gastrointestinal side effects.

Disclosure- During the preparation of this work, the author(s) used ChatGPT, an AI language model developed by OpenAI, in order to revise and improve the clarity and fluency of some parts of the English text. After using this tool, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Authors’ contributions:

All authors contributed to the article.
Conceptualization- Klimek N, Liebert A
Methodology: Klimek N, Liebert A, Wilska H, Domoń D, Domanowska D, Niedziela A, Kaplińska M.
Software: Kaplińska M, Niedziela A, Domanowska D
Formal Analysis: Klimek N, Liebert A, Wilska H, Domoń D
Investigation: Kaplińska M, Niedziela A, Domanowska D
Resources: Klimek N, Liebert A, Niedziela A, Domanowska D
Data Curation: Klimek N, Liebert A, Niedziela A, Domanowska D
Writing-rough preparation: Klimek N, Liebert A, Wilska H
Writing- Review and Editing: Domoń D, Domanowska D, Niedziela A, Kaplińska M.
Visualisation: Klimek N, Liebert A, Wilska H, , Niedziela A, Kaplińska M.
Supervision: Klimek N, Liebert A, Wilska H, Domoń D, Domanowska D, Niedziela A, Kaplińska M.

All Authors have read and agreed with the published version of the manuscript

Funding statement: This research received no external funding
Conflicts of interest statement: The authors declare no conflict of interest

REFERENCES

1. Wang Y, Jia X, Cong B. Advances in the mechanism of metformin with wide-ranging effects on regulation of the intestinal microbiota. Front Microbiol. 2024 May 24;15:1396031. doi: 10.3389/fmicb.2024.1396031. PMID: 38855769; PMCID: PMC11157079. https://doi.org/10.3389/fmicb.2024.1396031
2. Sirtori CR, Castiglione S, Pavanello C. Metformin: From diabetes to cancer to prolongation of life. Pharmacol Res. 2024 Oct;208:107367. doi: 10.1016/j.phrs.2024.107367. Epub 2024 Aug 25. PMID: 39191336. https://doi.org/10.1016/j.phrs.2024.107367
3. Shivaprakash P, Beeraka NM, Madhunapantula SRV, Nikolenko VN, Basalingappa KM. Metformin Effects on SHIP2, AMPKs and Gut Microbiota: Recent Updates on Pharmacology. Curr Med Chem. 2025;32(9):1732-1754. doi: 10.2174/0109298673289342240213040144. PMID: 38409699. https://doi.org/10.2174/0109298673289342240213040144
4. Cheng M, Ren L, Jia X, Wang J, Cong B. Understanding the action mechanisms of metformin in the gastrointestinal tract. Front Pharmacol. 2024 Mar 28;15:1347047. doi: 10.3389/fphar.2024.1347047. PMID: 38617792; PMCID: PMC11010946. https://doi.org/10.3389/fphar.2024.1347047
5. Pavlo Petakh, Kamyshna I, Kamyshnyi A. Effects of metformin on the gut microbiota: A systematic review. Mol Metab. 2023 Nov;77:101805. doi: 10.1016/j.molmet.2023.101805. Epub 2023 Sep 9. PMID: 37696355; PMCID: PMC10518565. https://doi.org/10.1016/j.molmet.2023.101805
6. Grzybowska M, Bober J, Olszewska M. Metformina - mechanizmy działania i zastosowanie w terapii cukrzycy typu 2 [Metformin - mechanisms of action and use for the treatment of type 2 diabetes mellitus]. Postepy Hig Med Dosw (Online). 2011 May 6;65:277-85. Polish. doi: 10.5604/17322693.941655. PMID: 21677353. https://doi.org/10.5604/17322693.941655
7. LaMoia TE, Shulman GI. Cellular and Molecular Mechanisms of Metformin Action. Endocr Rev. 2021 Jan 28;42(1):77-96. doi: 10.1210/endrev/bnaa023. PMID: 32897388; PMCID: PMC7846086. https://doi.org/10.1210/endrev/bnaa023
8. Silamiķele L, Silamiķelis I, Ustinova M, Kalniņa Z, Elbere I, Petrovska R, Kalniņa I, Kloviņš J. Metformin Strongly Affects Gut Microbiome Composition in High-Fat Diet-Induced Type 2 Diabetes Mouse Model of Both Sexes. Front Endocrinol (Lausanne). 2021 Mar 19;12:626359. doi: 10.3389/fendo.2021.626359. PMID: 33815284; PMCID: PMC8018580. https://doi.org/10.3389/fendo.2021.626359
9. McCreight LJ, Bailey CJ, Pearson ER. Metformin and the gastrointestinal tract. Diabetologia. 2016 Mar;59(3):426-35. doi: 10.1007/s00125-015-3844-9. Epub 2016 Jan 16. PMID: 26780750; PMCID: PMC4742508. https://doi.org/10.1007/s00125-015-3844-9
10. Graham GG, Punt J, Arora M, Day RO, Doogue MP, Duong JK, Furlong TJ, Greenfield JR, Greenup LC, Kirkpatrick CM, Ray JE, Timmins P, Williams KM. Clinical pharmacokinetics of metformin. Clin Pharmacokinet. 2011 Feb;50(2):81-98. doi: 10.2165/11534750-000000000-00000. PMID: 21241070. https://doi.org/10.2165/11534750-000000000-00000
11. Weersma RK, Zhernakova A, Fu J. Interaction between drugs and the gut microbiome. Gut. 2020 Aug;69(8):1510-1519. doi: 10.1136/gutjnl-2019-320204. Epub 2020 May 14. PMID: 32409589; PMCID: PMC7398478. https://doi.org/10.1136/gutjnl-2019-320204
12. Van Hul M, Cani PD, Petitfils C, De Vos WM, Tilg H, El-Omar EM. What defines a healthy gut microbiome? Gut. 2024 Oct 7;73(11):1893-1908. doi: 10.1136/gutjnl-2024-333378. PMID: 39322314; PMCID: PMC11503168. https://doi.org/10.1136/gutjnl-2024-333378
13. de Vos WM, Tilg H, Van Hul M, Cani PD. Gut microbiome and health: mechanistic insights. Gut. 2022 May;71(5):1020-1032. doi: 10.1136/gutjnl-2021-326789. Epub 2022 Feb 1. PMID: 35105664; PMCID: PMC8995832. https://doi.org/10.1136/gutjnl-2021-326789
14. Gebrayel P, Nicco C, Al Khodor S, Bilinski J, Caselli E, Comelli EM, Egert M, Giaroni C, Karpinski TM, Loniewski I, Mulak A, Reygner J, Samczuk P, Serino M, Sikora M, Terranegra A, Ufnal M, Villeger R, Pichon C, Konturek P, Edeas M. Microbiota medicine: towards clinical revolution. J Transl Med. 2022 Mar 7;20(1):111. doi: 10.1186/s12967-022-03296-9. PMID: 35255932; PMCID: PMC8900094. https://doi.org/10.1186/s12967-022-03296-9
15. Mohanty I, Allaband C, Mannochio-Russo H, El Abiead Y, Hagey LR, Knight R, Dorrestein PC. The changing metabolic landscape of bile acids - keys to metabolism and immune regulation. Nat Rev Gastroenterol Hepatol. 2024 Jul;21(7):493-516. doi: 10.1038/s41575-024-00914-3. Epub 2024 Apr 4. PMID: 38575682; PMCID: PMC12248421. https://doi.org/10.1038/s41575-024-00914-3

16. Zhang Q, Hu N. Effects of Metformin on the Gut Microbiota in Obesity and Type 2 Diabetes Mellitus. Diabetes Metab Syndr Obes. 2020 Dec 16;13:5003-5014. doi: 10.2147/DMSO.S286430. PMID: 33364804; PMCID: PMC7751595. https://doi.org/10.2147/dmso.s286430
17. Szymczak-Pajor I, Drzewoski J, Kozłowska M, Krekora J, Śliwińska A. The Gut Microbiota-Related Antihyperglycemic Effect of Metformin. Pharmaceuticals (Basel). 2025 Jan 6;18(1):55. doi: 10.3390/ph18010055. PMID: 39861118; PMCID: PMC11768994. https://doi.org/10.3390/ph18010055
18. Ezzamouri B, Rosario D, Bidkhori G, Lee S, Uhlen M, Shoaie S. Metabolic modelling of the human gut microbiome in type 2 diabetes patients in response to metformin treatment. NPJ Syst Biol Appl. 2023 Jan 21;9(1):2. doi: 10.1038/s41540-022-00261-6. PMID: 36681701; PMCID: PMC9867701. https://doi.org/10.1038/s41540-022-00261-6
19. Sakaguchi K, Sugawara K, Hosokawa Y, Ito J, Morita Y, Mizuma H, Watanabe Y, Kimura Y, Aburaya S, Takahashi M, Izumi Y, Bamba T, Komada H, Yamada T, Hirota Y, Yoshida M, Nogami M, Murakami T, Ogawa W. Metformin-regulated glucose flux from the circulation to the intestinal lumen. Commun Med (Lond). 2025 Mar 3;5(1):44. doi: 10.1038/s43856-025-00755-4. PMID: 40033038; PMCID: PMC11876595. https://doi.org/10.1038/s43856-025-00755-4
20. Mindrescu NM, Guja C, Jinga V, Ispas S, Curici A, Nelson Twakor A, Pantea Stoian AM. Interactions between Gut Microbiota and Oral Antihyperglycemic Drugs: A Systematic Review. Int J Mol Sci. 2024 Mar 21;25(6):3540. doi: 10.3390/ijms25063540. PMID: 38542513; PMCID: PMC10971180. https://doi.org/10.3390/ijms25063540
21. Tarry-Adkins JL, Grant ID, Ozanne SE, Reynolds RM, Aiken CE. Efficacy and Side Effect Profile of Different Formulations of Metformin: A Systematic Review and Meta-Analysis. Diabetes Ther. 2021 Jul;12(7):1901-1914. doi: 10.1007/s13300-021-01058-2. Epub 2021 Jun 2. PMID: 34075573; PMCID: PMC8266931. https://doi.org/10.1007/s13300-021-01058-2
22. Froldi G. View on Metformin: Antidiabetic and Pleiotropic Effects, Pharmacokinetics, Side Effects, and Sex-Related Differences. Pharmaceuticals (Basel). 2024 Apr 8;17(4):478. doi: 10.3390/ph17040478. PMID: 38675438; PMCID: PMC11054066. https://doi.org/10.3390/ph17040478