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Review

Gut microbiota-estrogen axis: Its influence on female health outcomes – A narrative review

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Abstract. *Background:* During women's lifetime, gut microbiota plays roles in the reproductive endocrine system influencing hormones such as estrogen, androgens, insulin and other hormones. Gut microbiota trigger estrobolome to produce β-glucuronidase that deconjugates estrogens into their active forms. An imbalance in the microbiome affects microbial diversity, decreases estrogen deconjugation and reduces the circulating estrogen that leads to many diseases like polycystic ovary syndrome (PCOS) and diabetes. This study aims to review the studies that correlate estrogen, gut microbiota and female health. *Material and methods:* published research articles (period from 2018 to 2024) were assessed through Science Direct, PubMed, Scopus, and Google Scholar using these terms: gut microbiota, human, female health, estrogen, and estrobolome (total articles 78). Articles were selected and tracked to avoid any duplication by excluding animal studies articles, those with insufficient data, and those without interesting outcomes. Articles were selected that determine any association between gut microbiota, estrogen, and female health (total 12) as in Figure 1. Gut microbiota plays an important role in the women's endocrine system, and β-glucuronidase is critical for estrogen metabolism. Distribution in estrogen metabolism causes gut microbial dysbiosis diseases, such as PCOS, obesity and diabetes. In post-menopausal women, high estrogen was associated with an increase in α-diversity microbiota. Lactobacillus was an abundant bacteria in pre and post-menopausal groups. Non-ovarian estrogens were associated with abundant microbiota that produce β-glucuronidase, such as Ruminococcaceae and Clostridia. This article reviews the previous studies about gut microbiota, estrogen, diabetes, obesity and PCOS. *Conclusion*: This review highlights the association between estrogen, gut microbiota diversity, diabetes, obesity and PCOS. Understanding the complex association between estrogen and the gut microbiota may attract attention to prevent and treat gastrointestinal disorders by microbiota modulation. (www.actabiomedica.it)

Key words: gut microbiota, estrogen metabolism, dysbiosis, polycystic ovary syndrome, insulin resistance, female reproductive health

Introduction

Gut microbiota acts as a barrier that protects the host against the entry of foreign pathogens through an assembly of anti-microbial components (1). Microbiota also extract energy from food, enhance nutrient harvesting, and control appetite (2). Furthermore, gut microbiota possesses metabolic genes which affect biochemical pathways that involve neurodegenerative diseases, mood, and motility disorders (3). Likewise, microbiota plays a major role in the reproductive endocrine system throughout a woman's lifetime by interacting with estrogens, androgens, insulin, and other hormones(4). Gut microbiota consists of 10^{13} to 10^{14} microorganisms (5). Dysbiosis in gut microbiota triggers several diseases, such as diabetes, endometriosis, PCOS and cancer. Several factors affect the gut microbiome, including sex hormones, age (6) and gender.

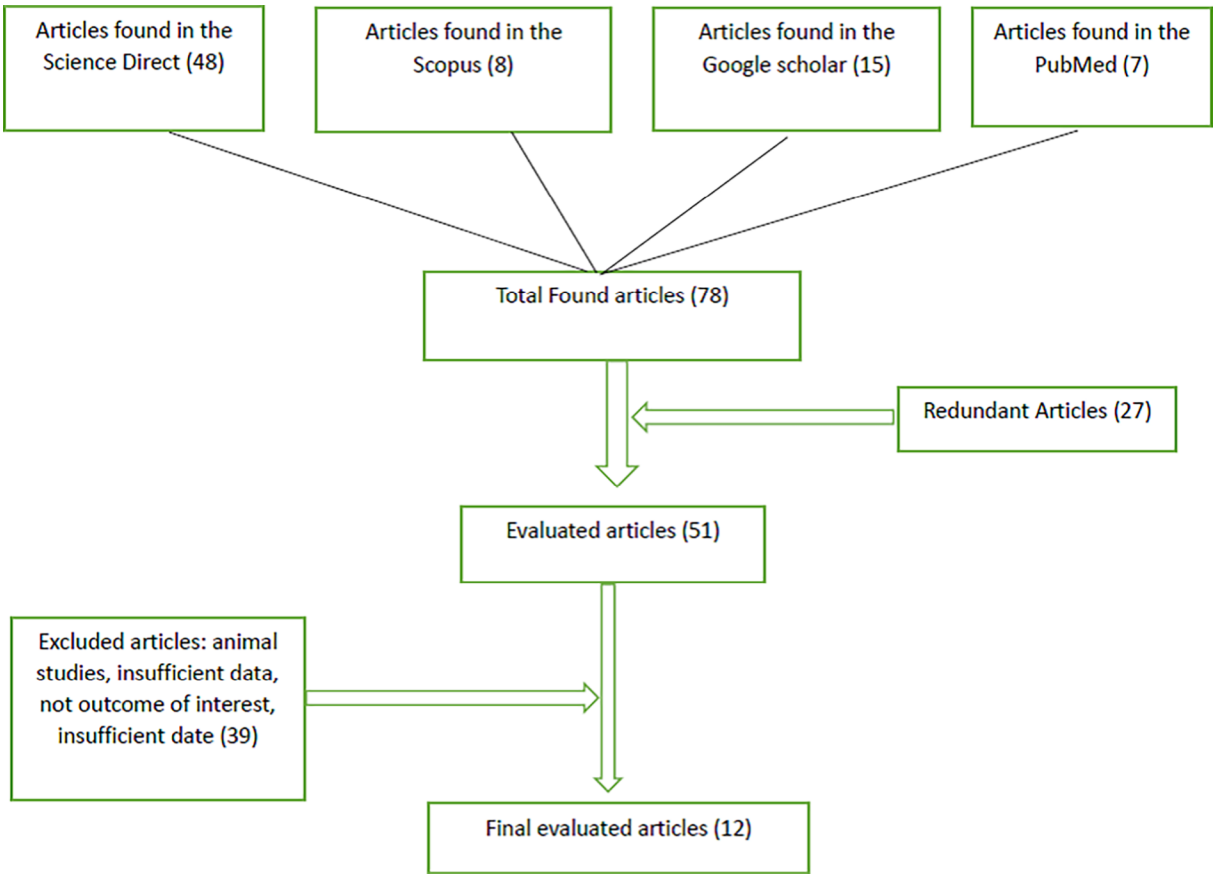

Figure 1. The flowchart for the selection process of the articles

Bacteria-to-human cell ratio is higher among women than men. The interaction between the gut microbiome and the sex hormones refers to the microgenderome. Sex hormones play a role in the interaction between the microbiome and the gastrointestine. Estrogen influences the gut microbiome, which in turn influences the metabolism of estrogen (7). This narrative review will discuss the interaction between microbiota, estrogen, diabetes, obesity and PCOS.

Data collection

Published articles and reviews from 2018 through 2024 were interrogated using the keywords combinations: gut microbiota, human, female health, estrogen, and estrobolome. The following databases were utilized: PubMed, Science Direct, Scopus and Google Scholar (Figure 1).

Gut microbiota and short-chain fatty acids

Gut microbiota encompasses a wide variety of commensal microbes containing trillions of bacteria, viruses, and fungi. Gut microbiota breaks down non-digestible substrates, such as dietary fibres and endogenous intestinal mucus, to generate chain fatty acids (SCFAs) that have a key role in microbiota-gut-brain crosstalk (8). The main SCFAs created are acetate, butyrate and propionate. The chief energy source for human colonocytes is butyrate, which initiates colon cancer cell apoptosis and triggers intestinal gluconeogenesis, which has a critical role in glucose metabolism

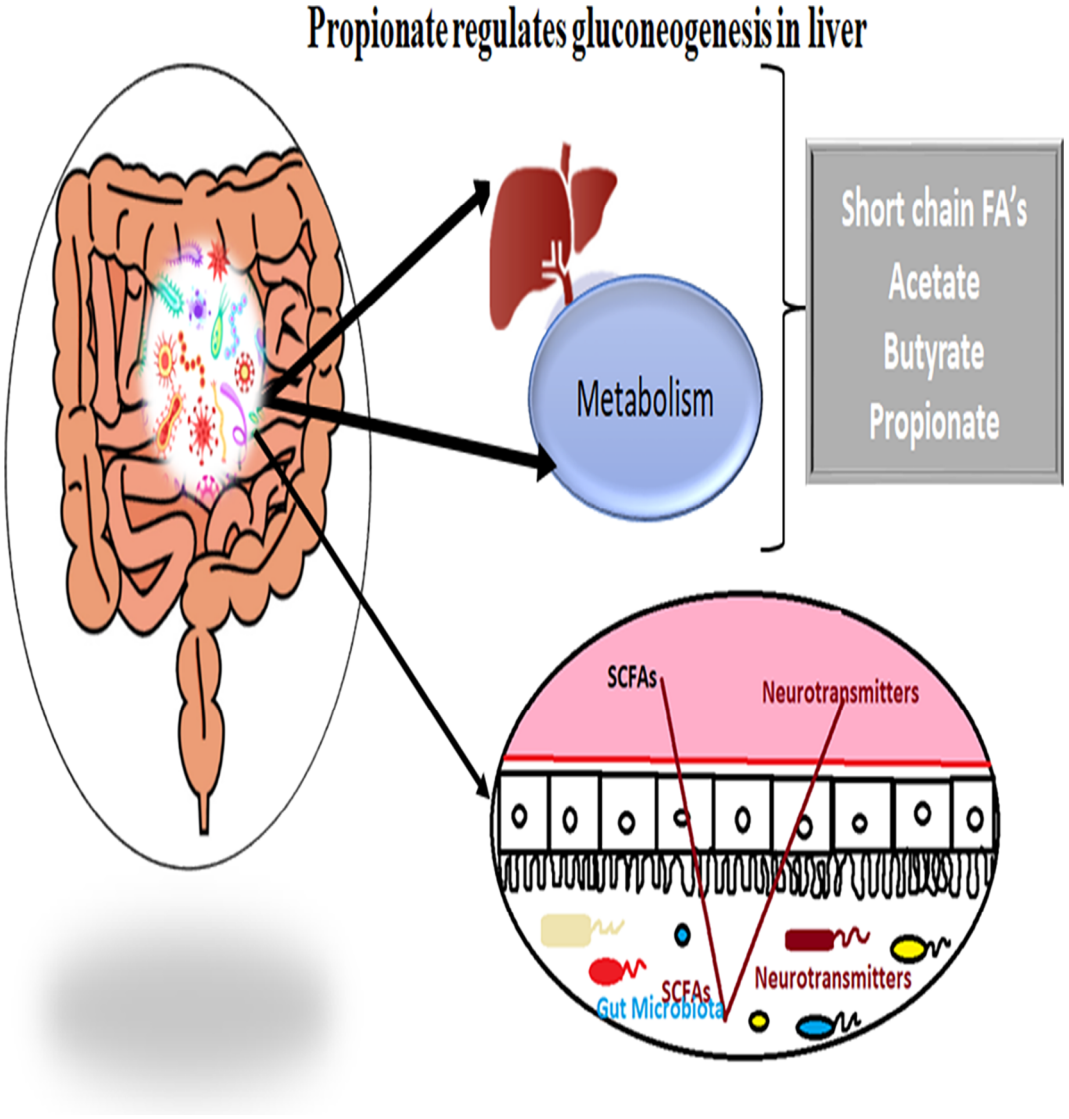

Figure 2. The gut microbiota regulates complex endocrine networks (Drawn by Authors). Propionate regulates fatty acids in the liver. SCFAs are short fatty acids.

and energy homeostasis (9). However, SCFA's butyrate is considered vital for epithelial cells to guzzle high amounts of oxygen through β oxidation, creating a hypoxia condition that sustains oxygen balance in the gut and further inhibits gut microbiota dysbiosis (10). Another SCFA is Propionate, which regulates gluconeogenesis in the liver and replete signalling through the gut fatty acid receptors (Figure 2). Acetate microbiota is promoted in the peripheral tissues and affects cholesterol metabolism as well as lipogenesis. The microbial enzymes present in the gut activate bile acids metabolism, creating unconjugated secondary bile acids, which act as signalling molecules in host pathways (11). Gut microbiota produces numerous hormones which travel through endocrine cells, regulate the complex endocrine network and target the enteric nervous system and the brain area. Gut microbiota and their metabolites influence human health through interconnection with the gut-brain axis. Gut microbiota-brain effects include neurotransmitter regulation,

direct vagus nerve activation, immune modulation of bacterial metabolite production, and endocrine response modification with sex hormones (12).

Role of gut microbiome in estrogen regulation

The reproductive endocrine system involves many hormones, including estrogen, ovaries, adrenal glands, and adipose tissue production. Gut microbes metabolize estrogens and produce metabolites that influence the host. Estrogen regulates the gut microbiota, and the aggregate of enteric bacterial genes that metabolize estrogens is known as estrobolome (13). Sex hormones affect gut microbiota through estrogen receptor beta, and the gut microbiome deconjugates the circulating estrogens excreted in the bile, resulting in estrogen reabsorption (14). These estrogens circulate and affect the central nervous systems reproductive and skeletal systems through the estrogen receptors. Estrogen makes conformational changes by binding to nuclear receptors. These conformational alterations were associated with endocrine system modulation and pathological diseases. Gut microbiota plays an important role in the women's reproductive endocrine system, and gut microbial β-glucuronidase is critical for estrogen metabolism. Distribution in estrogen metabolism cause gut microbial dysbiosis diseases, such as recurrent miscarriage, menopausal syndrome, gynecological cancers PCOS, infertility and endometriosis (Table 1). In pre-menopausal women, estrogen levels do not change the fecal enzymes and microbiome (15). Menopausal changes enhance dysbiosis and increase the risk for health-related problems. In post-menopausal women, high estrogen in urine was associated with an increase in α-diversity microbiota (16). Lactobacillus was an abundant bacteria in pre and post-menopausal groups, with an abundance of 77.8% versus 42.0% in pre-menopausal and post-menopausal women, respectively (16). Estrogens (non-ovarian) were associated with microbiota that produce β-glucuronidase, such as Ruminococcaceae and Clostridia (17). Increasing age was associated with a significant reduction in fecal β-glucuronidase activity in females (18). Estrogen triggers the immune cells and gut microbiome. β-estradiol triggers the dendritic cells to produce cytokines, which affect intestinal gut permeability and result in migration of gut microbiota into the lamina propria (19). Estrogen is linked with sex hormone-related cancers, like breast, ovarian, and endometrial cancer. Microbiota is changed among these cancers, with a high abundance of Sellimonas among estrogen receptor-positive breast cancer, and a high abundance of Alphaproteobacteria was associated with a lower risk of prostate cancer (20). A decrease in estrogen changes estrogen receptors and leads to hypoestrogenic diseases like metabolic syndrome and obesity. On the other hand, increased β-glucuronidase-producing bacteria may increase circulating estrogens and lead to endometriosis and cancer. Gut microbiota plays a role in the tumorigenesis of many cancers, especially colorectal cancer. Dysbiosis in pathogenic bacteria and their metabolites trigger the initiation of colorectal cancer. Fusobacterium nucleatum and Parvimonas micra, which were enriched in colorectal cancer patients, can be used as biomarkers for screening and early diagnosis (21). Estrogens and gut microbiota synergize to influence women's health, and there is an association between estrogen, gut microbiota diversity and diseases (Table 1).

Microbiota and type 2 diabetes

Gut dysbiosis is prevalent among individuals with T2DM, characterized by an increase in opportunistic bacteria such as *Bacteroides caccae*. *Clostridium symbiosum*, and *Escherichia coli*. Mucin-degrading bacteria like *Akkermansia muciniphila* and sulfate-reducing bacteria such as Desulfovibrio sp. (29). Previous research showed an increase in intestinal *Lactobacillus* species in diabetic patients, with a decrease in *Clostridium* species (30). *Lactobacillus* is positively correlated with fasting blood glucose and glycosylated hemoglobin, whereas *Clostridium* is negatively associated with HbA1c, FBG, C peptide, insulin, and plasma triglycerides (30). Studies reveal inconsistent results, largely attributed to the effects of metformin treatment rather than diabetes itself (31). Gut microbiota is also significantly linked to several diabetic complications, including diabetic nephropathy and diabetic retinopathy (32) (33). Diabetic nephropathy is a frequent microvascular complication of diabetes mellitus that may progress to

Table 1. Microbiota associated with female health.

Condition	Strain increased	Strain decreased	Reference
Recurrent miscarriage	-α-diversity -	*Lactobacillacea*	Vomstein et al. (22)
Preeclampsia	*Proteobacteria* *Actinobacteria* *Bulleidia Moorei* *Clostridium perfringens*	-	Gorczyca et al. (23)
Premenopause	*Firmicutes/Bacteroidetes* ratio, *Lachnospira* and *Roseburia*	*Prevotella, Parabacteroides* and *Bilophila*	Jose A Santos-Marcos (24)
Postmenopause	vaginosis anaerobes and Gram-positive *uropathobionts*	*Lactobacilli* and *Gram-negative uropathobionts*	Park et al. (25)
Postmenopause breast cancer	*Escherichia coli, Klebsiella sp, Prevotella amnii, Enterococcus gallinarum, Actinomyces, Shewanella putrefaciens,* and *Erwinia amylovora*	-	Zhu et al. (26)
Post-menopausal women with osteoporosis	*Fusobacterium, Parabacteroides, Anaerotruncus, Defluviitaleaceae, Acetanaerobacterium, and Leptotrichia*	-	Wang et al. (27)
Breast cancer	serum estradiol and estrone levels are not correlated with species/genera or dietary fiber	-	Zengul et al. (28)

end-stage renal failure. There are differences in the gut microbiota composition between diabetic nephropathy patients, those with type 2 diabetes mellitus without renal issues, and healthy individuals. The genera *Escherichia-Shigella* and *Prevotella_9* were found to differentiate diabetic retinopathy patients from those with T2DM without renal disease, while Prevotella_9 can separateT2DM patients without renal issues from healthy controls (34). Phenyl sulfate may predict early proteinuria in diabetic retinopathy patients (35)and induce proteinuria in diabetic mice by promoting podocyte damage, suggesting its potential as a therapeutic target for diabetic retinopathy.

Microbiota and Obesity

Obesity is a metabolic syndrome symptom that is common among post-menopausal women. Decreased estrogen levels among post-menopausal women are a main contributor to obesity. Both estrogens and microbiota play significant roles in obesity. Gut microbiota modulates host obesity and was studied in two mouse models (obesity susceptible and resistant model). Among these models, microbial butyrate metabolism was investigated by measuring butyryl-CoA transferase-related genes that are linked to microbial butyrate metabolism (36). A higher level of butyryl-CoA transferase-related genes was found within obese mice, and the pathogenesis of obesity was associated with gastrointestinal microbiota. Beta-glucuronidase enzyme deconjugates phytoestrogen and estrogen and makes them available for absorption via the gut. Estrogens then bind to their receptors and control blood glucose through four key functions: (1) Enabling insulin secretion; (2) Modulation of energy partition by choosing lipid as the main energy substrate when existing more than carbohydrates; (3) Functional protection through antioxidant mechanisms; and (4) neural modulation on body energy management (37). Estrogen plays a significant role in obesity, glucose metabolism, and lipid homeostasis by regulating intestinal microbiota. Low estrogen increases cholesterol in the blood, and the trigger lipogenesis process and decreases *Akkermansia* and *Bacteroidetes* species in the intestine (38). Estrogen depletion triggers fat storage and increases free fatty acids and triglycerides, which disturb insulin signaling and initiates insulin resistance

among post-menopausal females (39). Increased circulating insulin is associated with increased gut permeability to the bacterial LPS and allows them to enter into the bloodstream and trigger inflammatory responses (40). Bacterial glycoside hydrolases break dietary fiber to produce SCFA (butyrate, propionate and acetate). *Faecalibacterium*, *Bifidobacterium* and *Alistipes*, are SCFA producers that are common among post-menopausal gut microbiota (41). Type 2 diabetes is associated with reduced butyrate and is associated with low-grade inflammation among people with diabetes. SCFAs alter the host's metabolism by many mechanisms; YY peptide production is an intestinal hormone that prevents gut motility and decreases energy absorption by the activation of G-protein-coupled receptor 41(42). Also, the incretin hormone increases the sensitivity to insulin by triggering the G-protein-coupled receptors 43 by SCFA. Butyrate decreases tumor necrosis factor-alpha, interleukin-6, and nuclear factor kappa-B activity. Propionate reduces tumor necrosis factor-alpha (43).

Microbiota and Polycystic ovarian syndrome

PCOS is a reproductive endocrine condition that is zcharacterized by excess androgens and ovarian dysfunction. It is a heterogeneous disorder of unknown etiology caused by epigenetic, multigenic environmental stimuli (44). Gut microbes have a role in PCOS etiology (45). PCOS females have significantly lower Alpha diversity with different Beta diversity. A meta-analysis of fourteen studies on the gut microbiome showed that women with PCOS significantly lower microbial alpha diversity compared to control (46). PCOS women also showed significant alternation in Beta diversity microbiomes compared with healthy control and an increase in *B. vulgatus*. Another study showed modification in gut microbiome diversity within PCOS mice with an increase in *Firmicutes* level, decreased Tenericutes (47), Ak*kermensia* and *Ruminococcaceae*, and an increase in *Bacteroides*, *Escherichia*. *Shigella* among PCOS females (48). PCOS dysbiosis of gut microbiota causes an increase in serum LPS that acts as an endotoxin, which destroys the intestinal barrier, increases its permeability, and leads to a change in mucosal immune response (49). Lactic acid bacteria increased in the PCOS rat model by regulating sex hormone-related gut microbiota. Modifying gut microbiota by probiotic interventions may thus be a promising therapeutic option for PCOS (50).

Conclusion

Estrogens and gut microbiota influence women's health, and there is a strong association between estrogen and gut microbiota diversity. The gut microbiome that protects us from pathogens contributes to women's diseases such as diabetes, PCOS, and obesity. This study showed a strong association between gut microbial species and female health.

Future perspectives

Future work should focus on developing therapy status associated with gut microbiome. Modulation of the gut microbiome via supplementation with pre/pro/postbiotics is a critical health issue that must be controled. Future studies are needed to understand the association between host microbiota and the potential role of these microbiota in the treatment of several metabolic diseases. Metabolomics studies are necessary for microbiome-based diagnosis and implementation of effective therapeutic strategies.

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References

1. Hou K, Wu ZX, Chen XY, et al. Microbiota in health and diseases. Signal Transduct Target Ther. 2022;7(1):135. doi: 10.1038/s41392-022-00974-4
2. Wu Y, Feng X, Li M, et al. Gut microbiota associated with appetite suppression in high-temperature and high-humidity environments. EBioMedicine. 2024;99:104918. doi: 10.1016/j.ebiom.2023.104918
3. Margolis KG, Cryan JF, Mayer EA. The Microbiota-Gut-Brain Axis: From Motility to Mood. Gastroenterology. 2021;160(5):1486–501. doi: 10.1053/j.gastro.2020.10.066
4. Qi X, Yun C, Sun L, et al. Gut microbiota-bile acid-interleukin-22 axis orchestrates polycystic ovary syndrome. Nat Med. 2019;25(8):1225–33. doi: 10.1038/s41591-019-0509-0
5. Bonnechère B, Amin N, van Duijn C. What Are the Key Gut Microbiota Involved in Neurological Diseases? A Systematic Review. Int J Mol Sci. 2022;23(22). doi: 10.3390/ijms232213665
6. Santos-Marcos JA, Mora-Ortiz M, Tena-Sempere M, Lopez-Miranda J, Camargo A. Interaction between gut microbiota and sex hormones and their relation to sexual dimorphism in metabolic diseases. Biol Sex Differ. 2023;14(1):4. doi: 10.1186/s13293-023-00490-2
7. Qi X, Yun C, Pang Y, Qiao J. The impact of the gut microbiota on the reproductive and metabolic endocrine system. Gut Microbes. 2021;13(1):1–21. doi: 10.1080/19490976.2021.1894070
8. Dalile B, Van Oudenhove L, Vervliet B, Verbeke K. The role of short-chain fatty acids in microbiota-gut-brain communication. Nat Rev Gastroenterol Hepatol. 2019;16(8):461–78. doi: 10.1038/s41575-019-0157-3
9. Abdul Rahim MBH, Chilloux J, Martinez-Gili L, et al. Diet-induced metabolic changes of the human gut microbiome: importance of short-chain fatty acids, methylamines and indoles. Acta Diabetol. 2019;56(5):493–500. doi: 10.1007/s00592-019-01312-x
10. Pearce SC, Karl JP, Weber GJ. Effects of short-chain fatty acids on intestinal function in an enteroid model of hypoxia. Front Physiol. 2022;13:1056233. doi: 10.3389/fphys.2022.1056233
11. Larabi AB, Masson HLP, Bäumler AJ. Bile acids as modulators of gut microbiota composition and function. Gut Microbes. 2023;15(1):2172671. doi: 10.1080/19490976.2023.2172671
12. Maeng LY, Beumer A. Never fear, the gut bacteria are here: Estrogen and gut microbiome-brain axis interactions in fear extinction. Int J Psychophysiol. 2023;189:66–75. doi: 10.1016/j.ijpsycho.2023.05.350
13. Kumari N, Kumari R, Dua A, et al. From Gut to Hormones: Unraveling the Role of Gut Microbiota in (Phyto)Estrogen Modulation in Health and Disease. Mol Nutr Food Res. 2024;68(6):e2300688. doi: 10.1002/mnfr.202300688
14. Kwa M, Plottel CS, Blaser MJ, Adams S. The Intestinal Microbiome and Estrogen Receptor-Positive Female Breast Cancer. J Natl Cancer Inst. 2016;108(8). doi: 10.1093/jnci/djw029
15. Flores R, Shi J, Fuhrman B, et al. Fecal microbial determinants of fecal and systemic estrogens and estrogen metabolites: a cross-sectional study. J Transl Med. 2012;10:253. doi: 10.1186/1479-5876-10-253
16. Ammitzbøll N, Bau BPJ, Bundgaard-Nielsen C, et al. Pre- and post-menopausal women have different core urinary microbiota. Sci Rep. 2021;11(1):2212. doi: 10.1038/s41598-021-81790-8
17. Yoon K, Kim N. Roles of Sex Hormones and Gender in the Gut Microbiota. J Neurogastroenterol Motil. 2021;27(3):314–25. doi: 10.5056/jnm20208
18. Walsh J, Olavarria-Ramirez L, Lach G, et al. Impact of host and environmental factors on β-glucuronidase enzymatic activity: implications for gastrointestinal serotonin. Am J Physiol Gastrointest Liver Physiol. 2020;318(4):G816-g26. doi: 10.1152/ajpgi.00026.2020
19. Gomez A, Luckey D, Taneja V. The gut microbiome in autoimmunity: Sex matters. Clin Immunol. 2015;159(2):154–62. doi: 10.1016/j.clim.2015.04.016
20. Wei Z, Yang B, Tang T, et al. Gut microbiota and risk of five common cancers: A univariable and multivariable Mendelian randomization study. Cancer Med. 2023;12(9):10393–405. doi: 10.1002/cam4.5772
21. Wang Z, Dan W, Zhang N, Fang J, Yang Y. Colorectal cancer and gut microbiota studies in China. Gut Microbes. 2023;15(1):2236364. doi: 10.1080/19490976.2023.2236364
22. Vomstein K, Reider S, Böttcher B, et al. Uterine microbiota plasticity during the menstrual cycle: Differences between healthy controls and patients with recurrent miscarriage or implantation failure. J Reprod Immunol. 2022;151:103634. doi: 10.1016/j.jri.2022.103634
23. Gorczyca K, Obuchowska A, Kimber-Trojnar Ż, Wierzchowska-Opoka M, Leszczyńska-Gorzelak B. Changes in the Gut Microbiome and Pathologies in Pregnancy. Int J Environ Res Public Health. 2022;19(16). doi: 10.3390/ijerph19169961
24. Santos-Marcos JA, Rangel-Zuñiga OA, Jimenez-Lucena R, et al. Influence of gender and menopausal status on gut microbiota. Maturitas. 2018;116:43–53. doi: 10.1016/j.maturitas.2018.07.008
25. Park MG, Cho S, Oh MM. Menopausal Changes in the Microbiome-A Review Focused on the Genitourinary Microbiome. Diagnostics (Basel). 2023;13(6). doi: 10.3390/diagnostics13061193
26. Zhu J, Liao M, Yao Z, et al. Breast cancer in post-menopausal women is associated with an altered gut metagenome. Microbiome. 2018;6(1):136. doi: 10.1186/s40168-018-0515-3
27. Wang H, Liu J, Wu Z, et al. Gut microbiota signatures and fecal metabolites in post-menopausal women with

osteoporosis. Gut Pathog. 2023;15(1):33. doi: 10.1186/s13099-023-00553-0
28. Zengul AG, Demark-Wahnefried W, Barnes S, et al. Associations between Dietary Fiber, the Fecal Microbiota and Estrogen Metabolism in Post-menopausal Women with BreastCancer.NutrCancer.2021;73(7):1108–17.doi:10.1080/01635581.2020.1784444
29. Zhang L, Chu J, Hao W, et al. Gut Microbiota and Type 2 Diabetes Mellitus: Association, Mechanism, and Translational Applications. Mediators Inflamm. 2021;2021:5110276. doi: 10.1155/2021/5110276
30. Karlsson FH, Tremaroli V, Nookaew I, et al. Gut metagenome in European women with normal, impaired and diabetic glucose control. Nature. 2013;498(7452):99–103. doi: 10.1038/nature12198
31. Forslund K, Hildebrand F, Nielsen T, et al. Disentangling type 2 diabetes and metformin treatment signatures in the human gut microbiota. Nature. 2015;528(7581):262–6. doi: 10.1038/nature15766
32. Salguero MV, Al-Obaide MAI, Singh R, Siepmann T, Vasylyeva TL. Dysbiosis of Gram-negative gut microbiota and the associated serum lipopolysaccharide exacerbates inflammation in type 2 diabetic patients with chronic kidney disease. Exp Ther Med. 2019;18(5):3461–9. doi: 10.3892/etm.2019.7943
33. Jayasudha R, Das T, Kalyana Chakravarthy S, et al. Gut mycobiomes are altered in people with type 2 Diabetes Mellitus and Diabetic Retinopathy. PLoS One. 2020;15(12):e0243077. doi: 10.1371/journal.pone.0243077
34. Tao S, Li L, Li L, et al. Understanding the gut-kidney axis among biopsy-proven diabetic nephropathy, type 2 diabetes mellitus and healthy controls: an analysis of the gut microbiota composition. Acta Diabetol. 2019;56(5):581–92. doi: 10.1007/s00592-019-01316-7
35. Kikuchi K, Saigusa D, Kanemitsu Y, et al. Gut microbiome-derived phenyl sulfate contributes to albuminuria in diabetic kidney disease. Nat Commun. 2019;10(1):1835. doi: 10.1038/s41467-019-09735-4
36. Yang YY, Pereyra LP, Young RB, Reardon KF, Borch T. Testosterone-mineralizing culture enriched from swine manure: characterization of degradation pathways and microbial community composition. Environ Sci Technol. 2011;45(16):6879–86. doi: 10.1021/es2013648
37. Alemany M. Estrogens and the regulation of glucose metabolism. World J Diabetes. 2021;12(10):1622–54. doi: 10.4239/wjd.v12.i10.1622
38. Acharya KD, Noh HL, Graham ME, et al. Distinct Changes in Gut Microbiota Are Associated with Estradiol-Mediated Protection from Diet-Induced Obesity in Female Mice. Metabolites. 2021;11(8).doi: 10.3390/metabo11080499
39. Baker JM, Al-Nakkash L, Herbst-Kralovetz MM. Estrogen-gut microbiome axis: Physiological and clinical implications. Maturitas. 2017;103:45–53. doi: 10.1016/j.maturitas.2017.06.025
40. Łoniewski I, Szulińska M, Kaczmarczyk M, et al. Analysis of correlations between gut microbiota, stool short chain fatty acids, calprotectin and cardiometabolic risk factors in post-menopausal women with obesity: a cross-sectional study. J Transl Med. 2022;20(1):585. doi: 10.1186/s12967-022-03801-0
41. Mazhar M, Zhu Y, Qin L. The Interplay of Dietary Fibers and Intestinal Microbiota Affects Type 2 Diabetes by Generating Short-Chain Fatty Acids. Foods. 2023;12(5). doi: 10.3390/foods12051023
42. Covasa M, Stephens RW, Toderean R, Cobuz C. Intestinal Sensing by Gut Microbiota: Targeting Gut Peptides. Front Endocrinol (Lausanne). 2019;10:82. doi: 10.3389/fendo.2019.00082
43. Pedersen SS, Prause M, Williams K, Barrès R, Billestrup N. Butyrate inhibits IL-1β-induced inflammatory gene expression by suppression of NF-κB activity in pancreatic beta cells. J Biol Chem. 2022;298(9):102312. doi: 10.1016/j.jbc.2022.102312
44. Collée J, Mawet M, Tebache L, Nisolle M, Brichant G. Polycystic ovarian syndrome and infertility: overview and insights of the putative treatments. Gynecol Endocrinol. 2021;37(10):869–74. doi: 10.1080/09513590.2021.1958310
45. Min Q, Geng H, Gao Q, Xu M. The association between gut microbiome and PCOS: evidence from meta-analysis and two-sample mendelian randomization. Front Microbiol. 2023;14:1203902. doi: 10.3389/fmicb.2023.1203902
46. Sola-Leyva A, Pérez-Prieto I, Molina NM, et al. Microbial composition across body sites in polycystic ovary syndrome: a systematic review and meta-analysis. Reprod Biomed Online. 2023;47(1):129–50. doi: 10.1016/j.rbmo.2023.03.016
47. Zhou L, Ni Z, Cheng W, et al. Characteristic gut microbiota and predicted metabolic functions in women with PCOS. Endocr Connect. 2020;9(1):63–73. doi: 10.1530/ec-19-0522
48. Wang L, Zhou J, Gober HJ, et al. Alterations in the intestinal microbiome associated with PCOS affect the clinical phenotype. Biomed Pharmacother. 2021;133:110958. doi: 10.1016/j.biopha.2020.110958
49. Duan L, An X, Zhang Y, et al. Gut microbiota as the critical correlation of polycystic ovary syndrome and type 2 diabetes mellitus. Biomed Pharmacother. 2021;142:112094. doi: 10.1016/j.biopha.2021.112094
50. He Y, Wang Q, Li X, et al. Lactic acid bacteria alleviate polycystic ovarian syndrome by regulating sex hormone related gut microbiota. Food Funct. 2020;11(6):5192–204. doi: 10.1039/c9fo02554e

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