Journal of Cell and Tissue Research Vol. 24(2): 7529-7531 (2024)
(Available online at www.tcrjournals.com)
ISSN: 0973-0028; E-ISSN: 0974-0910

Review Article

RELATIONSHIP BETWEEN ESTROGENS AND GUT MICROBIOTA

GUPTA, P. D.

Former Director Grade Scientist, Centre for Cellular and Molecular Biology, Hyderabad
E. mail: pdg2000@hotmail.com, Cell: 080728 91356

Received: December 1, 2024: Accepted: December 22, 2024

Abstract: ***Lately it was established that female sex steroid hormones- estrogens, in addition to traditionally defined functions, play a very important in cooperation with the human gut microbiota. It seems it is two-way system, regulate each other to provide health benefits to the host. By maintaining estrogen levels in the circulating blood stream, microbiota, prevents harmful effects of the high estrogen levels, on the other hand by limiting population of harmful bacteria in the gut microbiota content, estrogens prevent infectious diseases.***

Keywords: Estrogens levels, Gut microbiota

Female sex hormone, estrogens make a woman a woman because it plays an important role throughout a woman's lifetime. It not only has the physiological effect of promoting reproductive organs and maintaining female secondary sexual characteristics, but also has obvious effects on the metabolic process, cardiovascular system and bone growth and maturation. Circulating estrogen levels mainly depend on (a) production of estrogens, and (b) estrogen metabolism.

Estrogen metabolism can lead to disruption of estrogen levels in the body and estrogen-related diseases are produced [1,2]. The gut microbiota plays a vital role in the reproductive endocrine system throughout a woman's whole life, and gut microbial β-glucuronidase (gmGUS) is a key factor in regulating host estrogen metabolism [3]. Moreover, the human gut microbiota is considered an endocrine organ because it produces hormones and metabolites that influence the body beyond the gastrointestinal tract [4].

The gut microbiota also produces metabolites that regulate hormone release. For example, the metabolism of tryptophan by gut microbes produces indoles, which can act as endocrine molecules [5].

In addition to hormones and their metabolites the gut microbiota also produces neurotransmitters like GABA, dopamine, and serotonin. GABA is the main inhibitory transmitter in the brain, while dopamine and serotonin are monoamines [6]. The gut microbiota is larger and more biochemically complex than other endocrine organs. The gut contains trillions of bacteria, which outnumber the body's host cells. These bacteria convert environmental cues into hormone-like signals that impact the body's

physiology and chronic diseases. The gut microbiota produces a wide variety of hormones, including ghrelin, PYY, GLP-1, and CCK. These hormones are released after eating and affect the central nervous system (CNS).

The estrogen levels also influence the composition as well as the diversity of gut microbiota. The human gut microbiota is a mature endocrine organ that can play both local and long-distance roles involving metabolites, immunologic messengers, and hormonal intermediates as mentioned above.

Estrogen metabolism: The gut microbiome contains bacteria that metabolize estrogens, and the gut microbiota can also metabolize estrogen-like compounds in food. Estrogen produced by the ovaries, adrenal glands, and adipose tissue is metabolized in the liver within two phases to form a biologically inactive conjugated form, and the conjugated estrogen is deconjugated by β-glucuronidase [7] encoded by gut microbiota and changes to a deconjugated form with biological activity,

Estrogen-mediated diseases: Changes to the estrobolome can lead to estrogen-mediated pathologies, such as breast cancer, endometrial cancer, and polycystic ovarian syndrome (PCOS). The estrobolome is a collection of bacterial genes that regulate estrogen metabolism. When the estrobolome is altered, it can affect the levels of circulating estrogen, which can lead to estrogen-related diseases [8-11]. It is carried out by the ways that the estrobolome can be altered such as presented in figure 1.

* **Increased abundance of β--glucuronidase-producing bacteria:** This can lead to higher levels of circulating estrogens, which can drive diseases like endometriosis and cancer (12).

* **Endocrine disruptors:** Prolonged exposure to low levels of endocrine disruptors can increase the

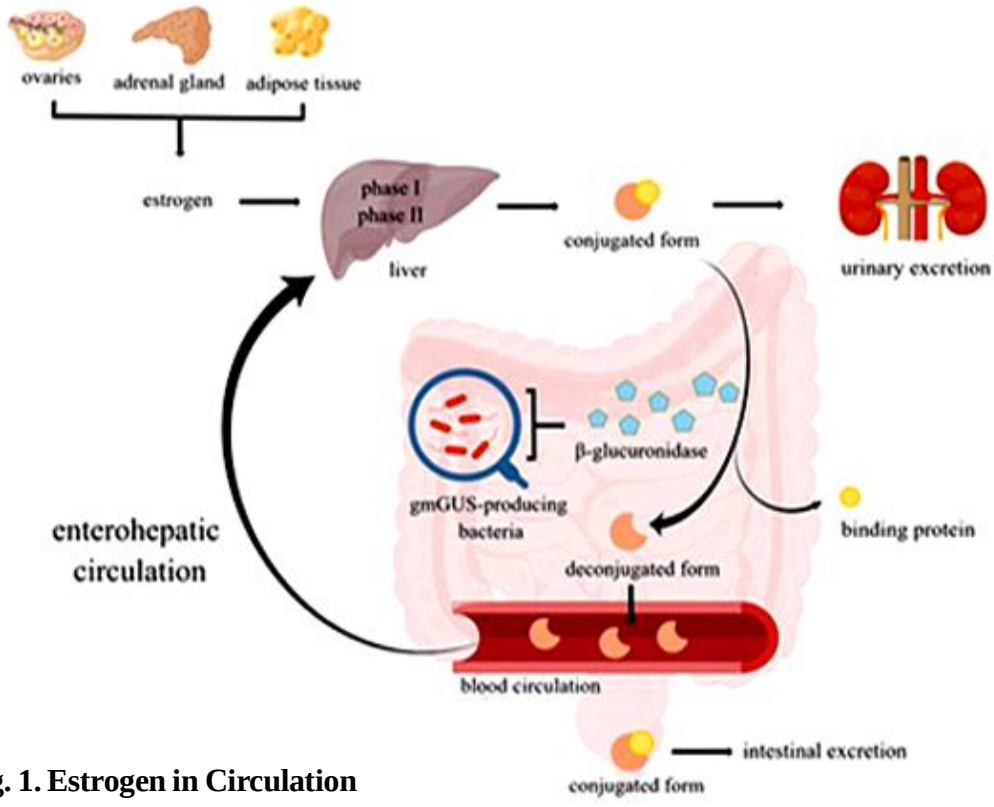

Fig. 1. Estrogen in Circulation

risk of developing cancer. Some pesticides and heavy metals have been linked to an increased risk of breast cancer. Endocrine disruptors (EDCs) can alter the composition and diversity of the gut microbiome, which can lead to dysbiosis. Dysbiosis can contribute to several disorders [13]. Interventions that can alter the gut microbiome composition and impact estrogen-mediated disease include: Bariatric surgery, Faecal-microbiome transplant, and Metformin.

* **Breast cancer:** The potential role of microbiota in breast cancer by next-generation sequencing using breast tumor tissue and paired normal adjacent tissue from the same patient. In a qualitative survey of the breast microbiota DNA, we found that the bacterium *Methylobacterium radiotolerans* is relatively enriched in tumor tissue, while the bacterium *Sphingomonas yanoikuyae* is relatively enriched in paired normal tissue. The relative abundances of these two bacterial species were inversely correlated in paired normal breast tissue but not in tumour tissue, indicating that dysbiosis is associated with breast cancer [14].

* **Mental health:** Sex hormones like estrogen and testosterone can directly affect the gut microbiome and immune cells that like anxiety and post-traumatic stress disorder (PTSD). An imbalanced gut microbiota, or dysbiosis, can contribute to mental health issues like anxiety, depression, and schizophrenia. Gut microbiota differ between sexes and can be linked to neuropsychiatric disorders. For example, autism spectrum disorder (ASD) is more prevalent in males, and schizophrenia and major depressive disorder (MDD) have sex-specific gut microbiota modifications [15].

REFERENCES

[1] Gupta P D. Natural and Synthetic Estrogens Regulate Human Health. J Chem Appl. 2: 21-24. 2020.

[2] Gupta P.D. Hormone Imbalance: The Serious Health Hazard for Woman. J. Gyn Obst. 3(1): 03-08. 2020.

[3] Hu, S., el al. Gut microbial beta-glucuronidase: a vital regulator in female estrogen metabolism. Gut Microbes, 15(1). 2023.

[4] Brown, JM, and Hazen, SL.: The gut microbial endocrine organ: bacterially derived signals driving cardiometabolic diseases. Annu Rev Med. 66:343-59. 2015

[5] Marialetizia R et al.: The Gut Microbiome Influences Host Endocrine Functions, Endocrine Reviews. 40 (5), 1271–1284, 2019

[6] Pires, L. et al.: Gut Microbiota as an Endocrine Organ: Unveiling Its Role in Human Physiology and Health. Appl. Sci. , 14, 9383. 2024

[7] Randall, B. et al.:PharmacologyofEstrogens in Treatment of the Postmenopausal Woman in Estrogen Metabolism (Third Edition), 2007 ttps://www.sciencedirect.com/topics/immunology-and-microbiology/estrogen-metabolism#chapters-articles

[8] Xuan C, et al.: Microbial dysbiosis is associated with human breast cancer. PLoS One. 9(1):e83744) 2014.

[9] Gupta, P.D.: Disturbed Steroid Hormonal Milieu is a Potential Cause of Cancer Acta Scientific Cancer biology. 5 (46).

[10] Gupta PD, and Pushkala K Parabens: The love - hatemolecule. Clin J Obstet Gynecol.; 3: 037-0384. 2020.

[11] Bonnie J Deroo and Kenneth S Korach Estrogen receptors and human disease J. Clin Invest .116(3):561–570 2006

[12] Dashnyam, P., et al. â-Glucuronidases of opportunistic bacteria are the major contributors to xenobiotic-induced toxicity in the gut. Sci Rep 8, 16372. 2018.

[13] Hampl R, Stárka L. Endocrine disruptors and gut microbiome interactions. Physiol Res. 69 (Suppl 2):S211-S223. 2020.

[14] Gupta. P.D.:"Potential Cause of Cancer Breast Cancer: Xenoestrogens", J. Oncology and Cancer Screening, 3(4); 2021.

[15] Shobeiri, P. et al. Shedding light on biological sex differences and microbiota–gut–brain axis: a comprehensive review of its roles in neuropsychiatric disorders. Biol Sex Differ 13, (12) 2022.