International Journal of Basic & Clinical Pharmacology
Priyadharshini R et al. Int J Basic Clin Pharmacol. 2025 May;14(3):418-422
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20251070

Review Article

The role of probiotics in managing premenstrual syndrome: insights into beneficial bacterial strains

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Received: 06 November 2024
Accepted: 05 December 2024

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ABSTRACT

Premenstrual disorders (PMDs), encompassing premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD), affect a significant number of women globally. Despite various hypothesized causes like hormonal shifts, serotonin imbalances, and lifestyle factors, the precise etiology remains unclear. Recent research emphasizes the crucial role of the gut microbiota in influencing mental and physical health, particularly through the gut-brain axis, which facilitates neuroendocrine communication. The gut microbiome's impact on endocrine, metabolic, and immune systems is significant, linking variations in gut microbiota diversity to conditions such as major depressive disorder (MDD) and metabolic disorders. Probiotics, known for modulating gut microbiota, show promise in managing PMDs and primary dysmenorrhea by influencing microbial diversity, metabolite profiles, and inflammatory pathways. Studies indicate that certain probiotic strains regulate cytokine production, enhance immunological tolerance, and may alleviate symptoms of hormone-related disorders. Traditional treatments for primary dysmenorrhea, including NSAIDs and hormonal therapy, often have adverse effects and limited efficacy, making probiotics a safer and potentially more effective alternative. Further research is essential to fully understand the molecular mechanisms of probiotics. However, current evidence suggests they could significantly improve women's reproductive health, reduce premenstrual symptoms, and offer a novel approach to managing primary dysmenorrhea, thereby enhancing the quality of life for affected women.

Keywords: Premenstrual disorders, Gut microbiota, Gut-brain axis, Probiotics, Cytokine production, Immune modulation, Hormone-related disorders

INTRODUCTION

Premenstrual disorders (PMDs) are the aggregate term for premenstrual symptoms, which impact a significant proportion of women worldwide. Previously, PMS and PMDD were the two categories into which premenstrual symptoms fell. The precise cause is still unknown despite a number of hypothesized causes, including hormonal shifts, serotonin imbalances, and lifestyle elements including stress and sleep habits.[1] However, current studies highlight the important role that the gut microbiota plays in impacting mental and physical health. The gut microbiome, also referred to as the "second brain," has a significant impact on endocrine, metabolic, and immune system processes.[2] Variations in the diversity of gut microbiota have been linked to a number of illnesses, including mental health disorders like MDD and metabolic problems.[3] The gut-brain axis, which promotes neuroendocrine communication between the gut and the brain emphasizes the complex relationship between gut health and psychological well-being through neuroimmune pathways. Research reveals a connection between MDD and low-grade inflammation, which may be impacted by microbiota-related processes such as bacterial translocation and the ensuing activation of inflammatory pathways. Recognizing these connections provides women with potential ways to improve their menstrual health generally and reduce premenstrual symptoms, such as probiotic therapies.[4]

PROBIOTICS: HARMONIZING AGENTS

Female reproductive health is initiated and maintained in large part by sex hormones. It has been demonstrated that three key physiological processes in the human body are regulated by total testosterone (TT), estradiol (E2), and sex hormone-binding globulin (SHBG, a protein that binds to sex hormones).[5] While testosterone acts as a precursor to the production of estradiol and has androgenic effects, estrogen has an impact on a variety of biological systems, including the skeletal, circulatory, and neurological systems. Furthermore, sex hormone-binding globulin plays a crucial part in the cyclical dynamics of male and female sex hormone dynamics by transporting androgens and estrogens.[6] To put it succinctly, it regulates endocrine balance. Sex hormone imbalances can cause a variety of negative health effects, including osteoporosis, cardiovascular disease, and menopausal symptoms in postmenopausal women as well as conditions like infertility and polycystic ovary syndrome (PCOS) in premenopausal women.[7] Above and beyond these direct consequences, there is growing evidence that abnormalities connected to sex hormones have a wider influence on a variety of illnesses, such as neuropsychiatric conditions and different kinds of cancer.[8] As such, these illnesses have the capacity to worsen disease loads among women. The human gut is a reservoir filled with billions of bacteria known as the gut microbiota, which work in symbiosis with their human host to form a dynamic ecosystem.[9] This complex microbiota has developed alongside the human counterpart, playing vital roles in protecting, metabolizing, and providing structural support for the host.[10] According to a prior review, women's sex hormone-related disorders like PCOS, postmenopausal osteoporosis, and ovarian cancer may be influenced by the gut flora.[11]

THE ASSOCIATION REGARDING PMS SYMPTOMS WITH THE GUT-BRAIN AXIS

The gut-brain axis facilitates bidirectional communication and is essential for maintaining intestinal homeostasis and brain function. Through immunological, endocrine, and neuronal processes, the gut microbiome alters this communication system. There is evidence to support multiple theories that the gut microbiota affects mood, behavior, and recognition, among other aspects of brain function. The gut-brain axis has been shown to be significantly mediated by the gut microbiome, which has led to the development of the "microbiota-gut-brain axis" hypothesis.[12] Physiological and psychological discomfort can be experienced by healthy women of reproductive age in the weeks preceding their periods. Four days after the beginning of the menstrual cycle, these symptoms usually go away. With symptoms that vary greatly from person to person, about 90% of young women experience premenstrual symptoms to some extent. A condition known as clinically significant PMS is identified when at least one symptom linked to social or economic dysfunction prior to menstruation persists for at least three menstrual cycles. The reproductive hormones estradiol (E2) and progesterone (P4), pituitary hormones (gonadotropins), prostaglandins, and neurotransmitters in the brain all fluctuate periodically, and these variations are linked to physiological or psychological symptoms that are depending on the menstrual cycle. PMS or PMS pathophysiology may be influenced by psychological stress, including depression, as it can alter E2 and P4 levels via the hypothalamus-pituitary-gonadal (HPG) axis.[13] Many different regions of the brain are home to glutamatergic acidrgic (GABA) neurons. This includes the hypothalamus, where the generation of E2 and P4 is regulated by the HPG axis, and the hypothalamic-pituitary-adrenal (HPA) axis, both of which are influenced by GABAergic signaling. These axes' mutual influence could account for the recent sex-dependence of stress susceptibility. There is mounting evidence that the gut microbiota may impact the metabolism of estrogen, which could have knock-on effects including cancer, metabolic syndrome, and malfunctions in the gut-brain axis.[14]

RESEARCH FINDINGS AND CLINICAL EVIDENCE

The immune system is greatly impacted by the secretion of anti-inflammatory cytokines by probiotic bacteria in the stomach. Numerous immune cell types, such as dendritic cells, monocytes, macrophages, lymphocytes, natural killer (NK) cells, and epithelial cells, can be influenced by these cytokines. The activation of pattern recognition receptors (PRRs) on immune and non-immune cells is a crucial mechanism. To completely understand the precise molecular interactions that probiotics have with the host, more research is necessary. While some *Lactobacillus* species have been shown to influence cytokine production, some Bifidobacterium species are linked to improved immunological tolerance.[15] Probiotic strains such *Lactobacillus plantarum*, *Lactobacillus acidophilus*, *Lactobacillus breve*, and *Lactobacillus lactis* can be taken orally to control proinflammatory cytokine release. These probiotic strains' structural traits, the mediators they release, and the variety of their numerous regulatory roles are facilitated by the activation of the immune pathways.[16]

WORKING PRINCIPLES: THE MANNER IN WHICH PROBIOTICS REDUCE THE PMS SYMPTOMS

The gut microbiota's influence on disorders linked to sex hormones is explained by a variety of intricate interactions and modulations. Probiotics have the ability to affect the makeup and functionality of the gut microbiota, according to recent research that have explored these pathways. These relationships, which include complex microbial-host interactions, the synthesis of metabolites, and the regulation of inflammatory pathways, add to the possibility that probiotics can lessen related illnesses.[17] Microbial diversity, metabolite profiles, and the ratio of pathogenic to helpful microbes all play a role in forming the complex web of effects that probiotics mediate.

Because of their known capacity to alter the gut microbiota, probiotics are a viable treatment option for related illnesses. But despite growing interest, there is no proof that consuming probiotics in postmenopausal and premenopausal women is still restricted when it comes to sex hormones.[18] The intricate relationships that exist between sex hormone-related illnesses and the gut microbiota are illustrated in this flowchart, along with the possible impact of probiotics on these relationships. There is yet little data to draw firm conclusions about, probiotics affect women's sex hormones, despite the intriguing paths and mechanisms.

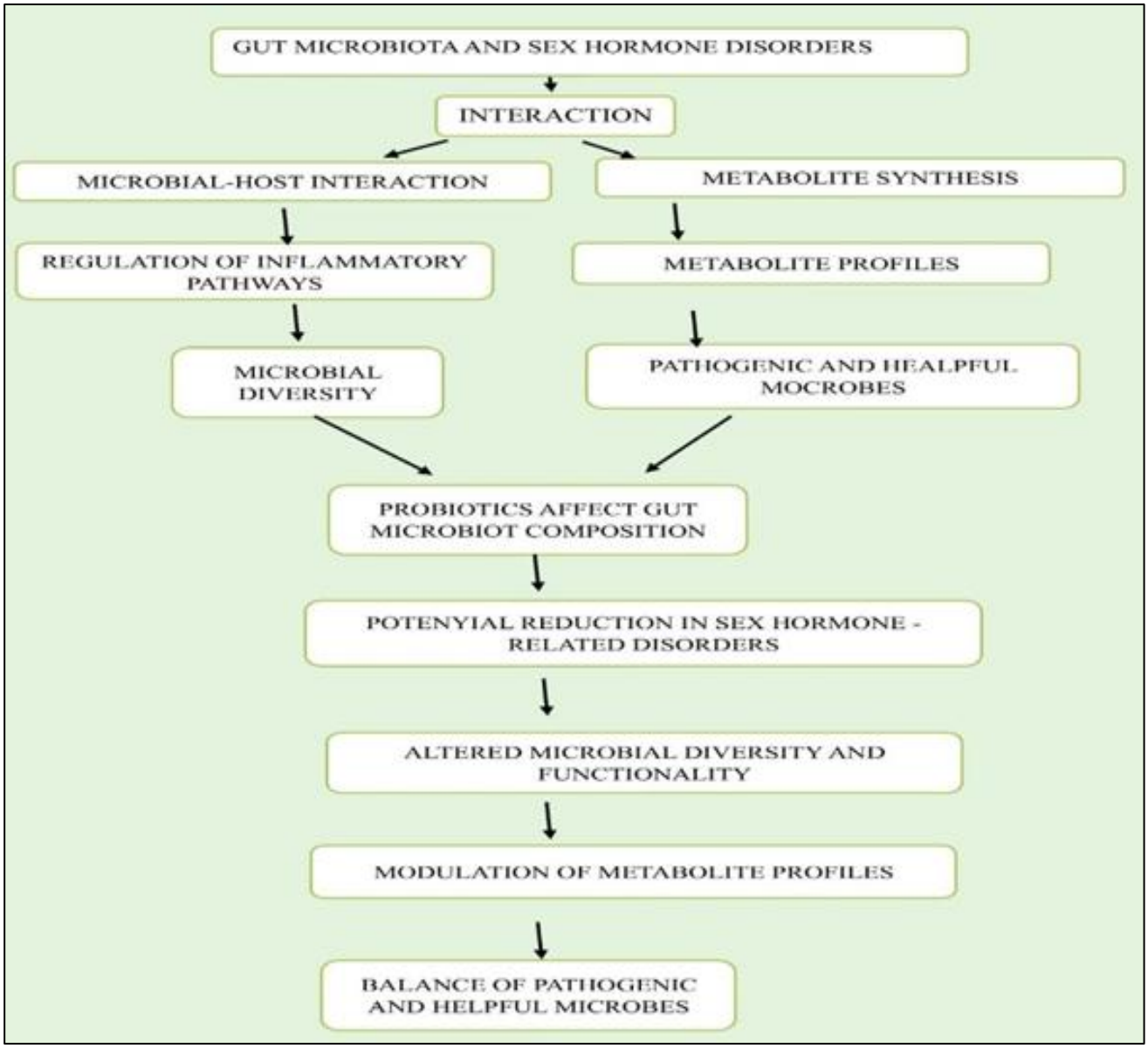

Figure 1: Study criteria.

PROSPECTIVE ROUTES: INCREASING THE APPLICATION OF PROBIOTIC TREATMENT

Regarding women of reproductive age, primary dysmenorrhea is a common problem that is frequently overlooked. Their capacity to work and attend school is severely impacted, which results in high absenteeism rates and a lower standard of living.[19] Additionally, because of central sensitization, young women with dysmenorrhea may be more susceptible to chronic pain in the future. This disorder affects women with normal menstrual cycles and does not have any underlying organic disease causes, such as ovarian or uterine disorders, endometriosis, uterine fibroids, or adenomyosis.[20] Many studies have connected prostaglandins (PGs) to the discomfort, uterine contractions, and inflammation associated with primary dysmenorrhea, even though the exact origin of the condition is still unknown.[7] Menstrual cramp severity and associated dysmenorrhea symptoms are directly correlated with the quantity of PGF2α released.8Proinflammatory cytokines like interleukins (IL)-6 and IL-8 have been shown to upregulate the synthesis of PGF2α

(prostaglandin F 2 alpha), whereas anti-inflammatory markers like IL-11 have been shown to downregulate it.[9] Nonsteroidal anti-inflammatory medications (NSAIDs) have no effect on leukotrienes, another lipoxygenase enzyme pathway byproduct that intensifies uterine contractions.[21] This could clarify why NSAIDs don't work for some patients who have primary dysmenorrhea. Some researchers have also looked at the role of other mediators, including progesterone, vasopressin, and calcium channels; however, there is currently insufficient data to determine if these mediators can be usefully used as therapeutic agents.[22] Traditionally, oral NSAIDs and hormonal tablets are used to inhibit ovulation and reduce inflammation in the treatment of primary dysmenorrhea. But it has been discovered that these therapies have negative impacts on health and cancer risk, especially when used over an extended period of time. Oral contraceptive pill users have an increased risk of breast cancer, according to new literature, and NSAIDs can cause organ damage by building up oxidative stress species.[23] Limited therapeutic alternatives are available because some patients do not react to NSAIDs, and hormonal therapy is inappropriate in certain situations. Finding a different medication with minimal adverse effects is always a goal, especially for long-term usage. Probiotics are an additional therapy option for primary dysmenorrhea. Probiotic supplements have been demonstrated to colonize the human gut and offer a host of health advantages, especially for disorders involving inflammation and immunomodulation.[24] Live bacteria known as probiotics can improve health in a variety of illness situations. Different human microbiomes govern specific metabolic processes by fostering favorable conditions in the gut environment of the host *Lactobacillus gasseri* GG has been shown to enhance verbal rating scores and visual analog scale (VAS) ratings for dysmenorrhea in endometriosis patients by suppressing the development of ectopic endometriotic lesions in a mouse model. After using oral *Lactobacillus* supplements, individuals with endometriosis reported lower pain scores.[25]

CONCLUSION

The complex interplay between the gut microbiota and the immune, endocrine, and nervous systems highlights the potential of probiotics in managing PMDs and primary dysmenorrhea. The gut-brain axis is crucial for neuroendocrine communication, affecting mental and physical well-being. Probiotics can modulate microbial diversity, metabolite profiles, and inflammatory pathways, offering promising therapeutic benefits. Research indicates that certain probiotic strains regulate cytokine production, enhance immunological tolerance, and may alleviate symptoms of hormone-related disorders. Traditional treatments for primary dysmenorrhea, such as NSAIDs and hormonal therapy, often have adverse effects and limited efficacy, making probiotics a safer and potentially more effective alternative. While further research is needed to fully understand the molecular mechanisms of probiotics, current evidence suggests they could play a pivotal role in improving women's reproductive health, reducing premenstrual symptoms, and providing a novel approach to managing primary dysmenorrhea, thus enhancing the overall quality of life for women suffering from these conditions.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Priyadharshini R, Subhashini R. The role of probiotics in managing premenstrual syndrome: insights into beneficial bacterial strains. J Basic Clin Pharmacol 2025;14:418-22.