

VALORIZATION OF AGRO-INDUSTRIAL WASTE: BIOTECHNOLOGICAL
POTENTIAL OF FERMENTED APPLE PEEL IN THE MODULATION OF DYSBIOSIS
AND WOMEN'S HEALTH IN THE CONTEXT OF SUSKarine Valverde Da Costa Gomes^{1*}, Cláudia Cristina Hastenreiter Da Costa Nascimento²,
Gláucio Diré Feliciano³¹Master's Student in Environmental Science and Technology at the State University of Rio de Janeiro (UERJ).²Master in Environmental Science and Technology from UERJ. Collaborating Researcher at the Laboratory of Chemical and Biological Analysis (LAQB/UERJ).³PhD in Biology (Nuclear Biosciences) from UERJ. Associate Professor of the Department of Pharmacy and Permanent Professor of the Graduate Program in Environmental Science and Technology at UERJ.

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(UERJ).<https://doi.org/10.5281/zenodo.18440783>**How to cite this Article:** Karine Valverde Da Costa Gomes^{1*}, Cláudia Cristina Hastenreiter Da Costa Nascimento², (2026). Valorization Of Agro-Industrial Waste: Biotechnological Potential Of Fermented Apple Peel In The Modulation Of Dysbiosis And Women's Health In The Context Of Sus. International Journal of Modern Pharmaceutical**ABSTRACT**

Recognized as a critical public health challenge, endometriosis transcends its definition as a mere gynecological condition, manifesting as a systemic inflammatory syndrome that burdens the Unified Health System (SUS) and impairs women's overall functionality. Emerging etiological perspectives locate the disease's aggressiveness within the gut-uterus axis, identifying dysbiosis and "estrobolome" dysregulation, specifically bacterial β -glucuronidase hyperactivity, as mechanisms that sustain hormonal recycling and chronic inflammation. This integrative review (2015–2025) investigated the biotechnological feasibility of repurposing apple (*Malus domestica*) waste into therapeutic inputs. Screening across PubMed, SciELO, and ScienceDirect databases revealed that agro-industrial fruit by-products act as reservoirs of pectin and ursolic acid. When subjected to solid-state fermentation by *Lactobacillus plantarum*, these compounds undergo bioconversion, yielding metabolites that inhibit the NF- κ B inflammatory pathway and restore the intestinal barrier. We conclude that formulating a symbiotic from this environmental liability aligns with Bioeconomy and One Health principles, offering the SUS a cost-effective, highly scalable prophylactic tool for complementary endometriosis management in Primary Care.

KEYWORDS Endometriosis, Gut Dysbiosis, *Malus domestica*, Estrobolome, Public Health.**1. INTRODUCTION**

Defining endometriosis solely by the ectopic presence of endometrial tissue is an obsolete, reductionist view, given the condition's true complexity. Modern science has reclassified the pathology as a systemic, chronic, inflammatory, and intrinsically estrogen-dependent condition. There is a warning that this shift in perspective is vital because the damage to a woman's life extends far beyond the reproductive sphere, severely impacting her finances and mental health. Furthermore, there is a social aggravation in the management of pain and infertility, as vulnerable patients face a veritable abyss when trying to access complex exams, such as magnetic resonance imaging, which perpetuates an unacceptable diagnostic delay for effective intervention.^[1]

In Brazil, public health indicators raise a warning flag. Upon analyzing DATASUS data, a concerning increase in hospitalizations was identified, with an average annual growth of 24.99% between 2020 and 2024.^[2] This growing demand strains the SUS budget, resulting in annual direct costs of around 8 million reais. Castro *et al.* expose the cruelty of this scenario, as revealed by the time elapsed between the first symptom of the disease and the final diagnosis, a gap that often exceeds 7 years. Such delay, combined with the lack of specialized clinics, severely punishes those who depend exclusively on the public network, aggravating endometriosis foci and harming women's health in multiple aspects.^[3]

This rising incidence of endometriosis cases is no mere coincidence. This epidemiological picture mirrors contemporary lifestyles. According to Castro *et al.*, the

disease is born from the clash between genetics and the "exposome," the sum of chronic stress and environmental contaminants.^[3] Consequently, diet is a decisive factor, as the routine intake of ultra-processed foods drives systemic inflammation, creating fertile ground for endometriosis lesions to thrive.^[4]

To understand the disease in depth, one must look at the gut. Recent meta-analyses confirm that these patients harbor an imbalanced microbiota with reduced bacterial diversity.^[5] This imbalance disrupts the "estrobolome," the cluster of bacterial genes that should regulate estrogen. Salliss *et al.* explain the chemistry of the problem by noting that, in dysbiosis, bacteria produce excess β -glucuronidase. This enzyme prevents estrogen from being eliminated in the stool, recirculating it back into the bloodstream. The result is a vicious cycle of hormonal recycling that fuels inflammation and endometriosis foci.^[6]

Despite all accumulated knowledge, standard treatment insists on surgical interventions and hormonal blockade. Moreira *et al.* reviewed these therapies, and their verdict is clear; they are costly for the SUS and carry long-term sequelae, such as bone density loss. It is necessary to develop affordable, sustainable, and functional options for women.^[7]

This is where the opportunity to utilize what the industry discards arises. The apple supply chain (*Malus domestica*) wastes nearly 30% of the fruit.^[8] What is currently environmental waste can become a public health solution. Research shows that fermenting these peels with *Lactobacillus plantarum* produces a potent immunomodulator that repairs the intestinal barrier.^[9,10] This study aims to investigate the feasibility of this eco-friendly symbiotic approach as a new weapon in the fight against endometriosis.

2. MATERIALS AND METHODS

This study was designed as an integrative literature review, a method chosen for its ability to synthesize evidence and apply it to health biotechnology. The methodological path followed six rigorous phases: defining the guiding question, establishing eligibility criteria, conducting a database search, conducting a critical analysis, and interpreting and synthesizing the knowledge.

The research was guided by the following question: "How can the biotechnological use of fermented apple residues (*Malus domestica*) act in the modulation of intestinal dysbiosis and in the complementary treatment of endometriosis?"

The bibliographic survey took place between November and December 2025, consulting the PubMed/MEDLINE, SciELO, and ScienceDirect databases. The search strategy combined the descriptors "Endometriosis", "Dysbiosis", "Intestinal Microbiota", "*Malus domestica*",

"*Lactobacillus*", and "Fermentation", using the Boolean operator "AND".

Original articles and reviews, preferably published between 2015 and 2025, in Portuguese and English, that linked the pathophysiology of endometriosis to nutritional interventions or food biotechnology were selected. Opinion texts and literature without peer review were excluded. The analysis focused on extracting molecular mechanisms, such as the NF- κ B pathway, and phytochemical data, which were later organized into thematic axes.

3. DEVELOPMENT

3.1. Pathophysiological bases: dysbiosis as a trigger of endometriosis

The perspective of endometriosis as a purely pelvic condition is no longer sustainable. Science has broken with this anatomical paradigm, and today, the disease is understood as a systemic pathology whose worsening is intrinsically linked to the intestinal microenvironment. Notably, literature from 2025 reinforces the existence of a bidirectional axis in which gut health dictates the pace of gynecological progression.

The role of estrobolome in hormonal homeostasis

If estrogen is the fuel of the disease, hormonal control is the priority. Yet, the ovaries do not work alone. The concept of the "estrobolome" has been highlighted: a set of bacterial genes that determines the fate of this hormone. In a healthy body, the liver performs its role: it conjugates estrogen with glucuronic acid so that it is invariably expelled via stool.^[6]

Crucially, a pathological scenario arises during dysbiosis. A recent meta-analysis confirms that patients with endometriosis exhibit a distinct microbial signature, characterized by an overpopulation of phyla such as *Firmicutes* and *Bacteroidetes*. These microorganisms secrete high levels of β -glucuronidase, an enzyme that reverses hepatic conjugation. As previously elucidated, this "deconjugation" reaction reactivates estrogen while it remains in the intestinal lumen, allowing its reabsorption into the systemic circulation. This biochemical recycling keeps the body in a state of constant hyperestrogenism, which feeds ectopic endometrial foci.^[5,6]

Intestinal Permeability and Inflammatory Cascade

Beyond hormonal dysregulation, dysbiosis fundamentally undermines the intestine's physical barrier. Evidence details that a decline in bacterial diversity, particularly the depletion of *Lactobacillus*, triggers the release of zonulin, a protein that destabilizes tight junctions between enterocytes. This compromised state, known as Leaky Gut, facilitates the translocation of lipopolysaccharides (LPS) directly into the peritoneal cavity. Once present, these endotoxins activate TLR-4 receptors, triggering a chronic immune response that

intensifies pain sensitivity and promotes the formation of new lesions.^[11]

Clinical implications and comorbidities

Mucosal inflammation manifests clinically. Reports indicate that women with endometriosis bear a threefold higher risk of developing irritable bowel syndrome (IBS), pointing to a shared inflammatory etiology.^[12] Furthermore, warnings exist that standard hormonal therapies may exacerbate pre-existing intestinal inflammation, underscoring the imperative for non-pharmacological strategies to restore eubiosis.^[13]

3.2. Apple peel (*Malus domestica*): Bioactive potential and sustainability

Selecting the apple (*Malus domestica*) as a matrix for therapeutic development is grounded in a dual rationale: economic feasibility and phytochemical specificity. Frequently overlooked as refuse, the fruit's peel represents a concentrated reservoir of essential compounds for managing pelvic inflammation.

Bioeconomy and application in the SUS

The core objective of applying bioeconomy principles here is to convert potential waste into a health-promoting agent. It is estimated that nearly 30% of apples constitute industrial refuse, comprising peels, seeds, and pomace.^[8] Yet, biotechnology transforms this environmental liability into an asset. Evidence demonstrates that the highest nutrient density is concealed precisely within these by-products. Reintegrating this biomass through *upcycling* (functional flours) provides the SUS with a solution of negligible cost and massive scalability.^[14]

Mineral and prebiotic mechanisms

Nutritionally, the peel surpasses the pulp. Comparative analysis revealed that the epidermis harbors significantly higher levels of Magnesium (Mg) and Potassium (K). This composition offers direct functional benefits: magnesium facilitates uterine muscle relaxation, mitigating dysmenorrhea, while potassium aids in electrolyte regulation, counteracting bloating.^[15]

Simultaneously, this residue has been validated as a dense prebiotic matrix containing up to 27.71% total dietary fiber, primarily pectin. This fiber serves as a selective substrate for *Lactobacillus*, and colonic fermentation yields short-chain fatty acids that are essential for repairing the intestinal barrier.^[16]

Safety and phytochemical profile

The therapeutic distinctiveness lies in the presence of Ursolic Acid, the predominant triterpene in the peel's cuticular wax, particularly in red cultivars such as 'Royal Gala'. This compound displays potent anti-proliferative activity against endometrial lesions.^[17] Furthermore, emphasis is placed on the pivotal role of organic management. Beyond ensuring the absence of synthetic fungicides (thereby supporting probiotic survival), this cultivation method stimulates higher anthocyanin

synthesis, thereby elevating the material's antioxidant potential.^[18,19]

3.3. Biotechnological innovation: Fermentation and bioavailability

Merely consuming the residue *in natura* fails to guarantee maximum therapeutic efficacy. Solid-state fermentation stands as the requisite biotechnological lever to unlock and amplify the matrix's properties.

Microbial growth and viability

For any symbiotic strain, survival is non-negotiable. Data indicate that apple pomace provides the precise carbohydrate and micronutrient profile needed for *Lactobacillus plantarum* to thrive, achieving counts exceeding 3.8×10^8 CFU/mL (Colony Forming Units). This confirms the residue not merely as a carrier, but as a robust, cost-effective vehicle, eliminating the need for expensive synthetic culture media.^[9]

Biotransformation and anti-inflammatory action

The actual value of fermentation lies in its role as a chemical unlocking system. It has been reported that bacteria such as *L. plantarum* employ enzymatic tools, specifically β -glucosidase, to cleave complex bonds. The result of this cutting is the conversion of trapped compounds (glycosides) into free, potent forms (aglycones), such as Quercetin. The clinical implications were evident *in vitro*: this fermented extract effectively halted the NF- κ B pathway, the master switch of inflammation, by blocking the production of cytokines that drive pelvic pain and root adhesions.^[10]

Stable and affordable product

For viable distribution within the SUS, physicochemical stability is paramount. A production protocol for a stable lyophilized powder was validated, capable of maintaining bacterial viability above 10^6 CFU/g without requiring a rigorous cold chain. Such a pharmaceutical presentation streamlines logistics and democratizes access, ensuring treatment adherence across diverse socioeconomic demographics.^[20]

4. CONCLUSION

Synthesizing the gathered evidence suggests that endometriosis management necessitates a paradigm transition, moving beyond a strictly surgical focus toward a systemic, integrative approach. As corroborated by current analyses, the disease's multidimensional impact demands interventions that neutralize its root causes: chronic inflammation and gut dysbiosis.^[1]

Within this framework, formulating a symbiotic from fermented apple peel emerges as an innovative strategy, anchored in the One Health and Bioeconomy pillars. Transforming this environmental liability, which accounts for roughly 30% of the fruit, into a health asset enables a low-cost therapy devoid of the typical side effects associated with hormonal suppression.^[8] For the SUS, particularly against the backdrop of a 24.99%

annual surge in hospitalizations^[2], integrating this technology into Primary Care could be an effective mechanism for long-term harm reduction and cost control.

Finally, in line with established nutritional guidelines, a distinct scientific gap persists: the need for clinical trials to validate this bioproduct in the Brazilian population.^[4] Consequently, fostering future research that quantifies improvements in patient quality of life is recommended, thereby establishing this biotechnological innovation as an accessible, sustainable Integrative Practice in women's healthcare.

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