REVIEW ARTICLE

Natural Products in Women's Health Across the Lifespan: Hormones, Microbiome, and Preventive Therapeutics

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Abstract

Women experience profound physiological transitions across early, mid-, and late life that fundamentally reshape reproductive, metabolic, skin, and psychosocial health. Hormonal fluctuations - from the first menstrual cycle through post-menopause - do not act in isolation. They interact dynamically with the gut, vaginal, and skin microbiomes, driving a growing burden of chronic symptoms, metabolic dysfunction, and disease risk. Natural products, including botanicals, biotics, antioxidants, and functional nutrients, offer compelling preventive and therapeutic promise because they engage multiple biological pathways simultaneously: hormonal signaling, microbial ecology, inflammatory tone, and oxidative stress. This mini-review synthesizes current evidence linking women's health challenges across the lifespan to hormonal and microbiome dynamics, surveys key natural product categories and their mechanisms, and highlights critical knowledge gaps that urgent, rigorously designed clinical trials must close. The convergence of aging demographics, unmet clinical need, and rising consumer demand makes this one of the most important - and most underserved - frontiers in preventive medicine.

Keywords: Women's health; menopause; hormones; microbiome; natural products; Aging; preventive medicine

1. Introduction

Women's health is one of the most complex and persistently under-addressed areas in modern medicine. Across the lifespan, women experience biological transitions unlike anything men encounter - driven by cyclical and age-related hormonal shifts that touch nearly every physiological system. We are talking about reproductive function, metabolic health, immune regulation, brain health, skin integrity, and emotional well-being. These are not isolated domains. They are interconnected, and when hormones shift, everything shifts with them.

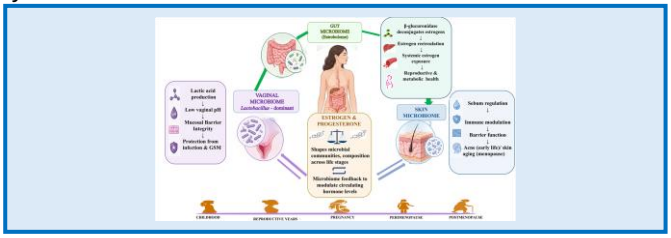

Figure 1. Bidirectional crosstalk between the gut, vaginal, and skin microbiomes and sex hormones across women's life stages. Each microbial niche plays distinct but interconnected roles in estrogen metabolism, mucosal homeostasis, and systemic inflammatory regulation

Consider the numbers: globally, over 60 million American women are currently peri- or post-menopausal, and nearly 80% report at least one moderate-to-severe menopausal symptom - hot flashes, sleep disruption, mood changes, vaginal dryness, and accelerated skin aging among the most common [1], [2]. The economic cost of unmanaged menopausal symptoms in the United States alone exceeds $25–30 billion annually, and the global menopause therapeutics and women's wellness market is on track to surpass $60–70 billion within this decade. These numbers reflect both massive unmet need and massive commercial opportunity. But beyond menopause, younger women face rising rates of polycystic ovary syndrome (PCOS), which affects 6–10% of reproductive-age women worldwide, along with irregular menstruation, infertility, anxiety, acne, and metabolic dysregulation [3]. This is not a niche problem. It is a population-level crisis. What makes women's health so challenging - and so fascinating - is that hormonal change does not happen in a biological vacuum. Estrogens, progesterone, androgens, and adrenal hormones operate within a web that includes the gut microbiome, the vaginal microbiome, the skin microbiome, immune signaling, and metabolic pathways. Disruption at any node ripples through the entire network. This is why a simple symptom like bloating or brain fog after menopause is rarely

just one thing. It is the result of estrogen deficiency intersecting with gut dysbiosis, systemic inflammation, and impaired mucosal barriers - all happening simultaneously.

This mini-review synthesizes what we currently know about the interplay between hormones, the microbiome, and women's health across three key life stages - early life, mid-life, and late life - and explores the emerging evidence for natural products as integrative, preventive, and therapeutic tools. The potential is real. But so is the gap between compelling preclinical data and the rigorous clinical evidence women deserve.

2. Women's Health, Hormonal Changes, and Associated Challenges

Hormonal regulation is the cornerstone of women's physiology. But unlike the relatively stable hormonal milieu in adult males, women's endocrine environment is in constant flux. Three distinct life stages each carry their own hormonal signature and their own clinical burden.

2.1. Early Life and the Reproductive Years

Activation of the hypothalamic–pituitary–gonadal (HPG) axis during puberty initiates menstrual cyclicity; however, this transition is often marked by neuroendocrine instability[4]. Immature feedback regulation between gonadotropin-releasing hormone (GnRH), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) frequently results in anovulatory cycles driven by estrogen–progesterone imbalance[5]. Concurrently, hyperandrogenism contributes to clinical manifestations such as acne and hirsutism, while luteal phase insufficiency can compromise endometrial receptivity and fertility. Psychosocial stress further exacerbates this dysregulation through elevated cortisol levels, which suppress GnRH pulsatility and disrupt downstream hormonal signaling. Polycystic Ovary Syndrome exemplifies the long-term consequences of early endocrine dysfunction, extending beyond reproductive abnormalities to include metabolic disturbances, mood disorders, and increased cardiovascular risk later in life.

2.2. Mid-life and Peri-menopause

As women move into their late 30s and 40s, ovarian hormone production becomes erratic. Progesterone declines first, creating a state of relative estrogen dominance, followed by widening fluctuations in estradiol that destabilize the entire hormonal feedback system. Vasomotor symptoms emerge - hot flashes, night sweats - alongside sleep disruption, anxiety, cognitive fog, weight gain concentrated in the abdomen, insulin resistance, declining libido, and the early signs of vaginal atrophy and skin aging[6]. These are not cosmetic inconveniences. They represent real physiological vulnerability that, unaddressed, increases long-term risks for cardiometabolic disease, osteoporosis, and cognitive decline. For example, a meta-analysis of 11 studies showed that vasomotor symptoms are associated with a higher risk of cardiovascular events in women under 60 years (RR 1.12), but not in older women, suggesting vasomotor symptoms as an early marker of cardiometabolic risk during menopause [7].

2.3. Late life and Post-Menopause

The estrogen metabolite ratio (EMR), specifically the ratio of 2-hydroxyestrone (2OHE1) to 16α-hydroxyestrone (16αOHE1), is considered an important biomarker in women’s health because it reflects the balance between two major estrogen metabolic pathways. 2OHE1 estrogen metabolite is considered a protective metabolite and has been associated with normal cellular functions, whereas 16αOHE1 promotes sustained cellular proliferation, which increases the risk of breast cancer[8]. Moreover, in the postmenopausal state, estrogen levels decline, with systemic consequences. In this state, the bone mineral density declines, sarcopenia accelerates, cardiovascular risk climbs, and the brain becomes increasingly vulnerable. Genitourinary syndrome of menopause (GSM) affects up to 70% of post-menopausal women, with vaginal dryness, dyspareunia, and recurrent infections arising from the collapse of the *Lactobacillus*-dominated vaginal microbiome. Skin thins and loses elasticity as collagen synthesis falls with declining estrogen, slowly mounting systemic inflammatory burden - what we call inflammaging - amplifies every one of these processes.

A critical limitation in managing these challenges has been the diagnostic framework itself. Standard hormonal testing - serum estradiol, FSH, LH - provides static snapshots of a highly dynamic system. Particularly during perimenopause, when daily hormonal variability can be enormous, a single blood draw offers limited clinical utility. Many women experience significant symptom burden with hormone values that appear normal on paper, reflecting the reality that tissue-level sensitivity to estrogen varies enormously between individuals. Better integrative diagnostic approaches, such as longitudinal profiling, symptom-biomarker correlation, and microbiome assessment, are urgently needed.

3. Women's Health and the Microbiome

The microbiome is not a passive passenger in women's health. It is an active biological regulator of endocrine and immune homeostasis - and it is highly sensitive to the hormonal transitions that define women's lives. Throughout a woman's lifespan, fluctuations in ovarian steroid hormones, specifically estrogen and progesterone, from puberty through the reproductive years, pregnancy, and menopause, continuously shape the composition and function of microbial communities residing in the gut, vagina, urinary tract, and skin. For example, rising estrogen at puberty promotes *Lactobacillus* dominance in the vagina, while cyclical hormonal changes during the reproductive years lead to transient shifts in the vaginal microbiota[9]. Pregnancy is associated with a stable, *Lactobacillus*-rich vaginal microbiome and alterations in the gut microbiome, whereas declines in menopausal estrogen result in reduced *Lactobacillus* abundance and increased microbial diversity, predisposing to dysbiosis. Similarly, hormonal regulation of sebum production influences the skin microbiota, with increased *Cutibacterium acnes* (*C. acnes*) during puberty and altered microbial composition with age. Hormone-driven alterations govern the transition between eubiotic and dysbiotic microbial states, thereby shaping host susceptibility to infection and inflammatory conditions [10]. Estrogen, in particular, functions as a pivotal integrative signal at the interface of microbial activity, immune modulation, and reproductive physiology, mediating epithelial integrity, mucosal immunity, and nutrient availability within these niches. Conversely, commensal and symbiotic microbiota actively contribute to the regulation of systemic hormone levels through enzymatic processes, including deconjugation and biotransformation of steroid hormones, thus establishing a dynamic and reciprocal hormone–microbiome axis. Disruption of this tightly regulated crosstalk has been increasingly implicated in adverse reproductive and metabolic outcomes, including infertility, impaired reproductive tract function, and the pathogenesis of hormone-responsive disorders.

3.1. The Gut Microbiome and the Estrobolome

The estrobolome is perhaps the most important concept in this space, yet most clinicians have never heard of. It is an important interface between the gut microbiome and the endocrine system, with a deep influence on women's health. Estrobolome represents a collection of microbial genes, specifically those encoding β-glucuronidase enzymes and related enzymes. These enzymes regulate the metabolism, deconjugation, and recirculation of estrogens within the gastrointestinal tract[11]. Through these enzymatic activities, the estrobolome controls the balance between estrogen excretion and reabsorption, thereby influencing circulating hormone levels and systemic endocrine function. However, disruption of gut microbial homeostasis can significantly alter β-glucuronidase activity, thereby disturbing the tightly regulated balance of estrogen metabolism. Such dysregulation may lead either to enhanced deconjugation and excessive enterohepatic recirculation of estrogens, contributing to endometriosis and breast cancer, or to increased estrogen excretion and diminished systemic availability, which may exacerbate menopausal symptoms and bone loss [12], [13]. Collectively, these observations highlight that the estrobolome functions as a critical regulator of endocrine homeostasis, underscoring the concept that the gut microbiome operates as an extension of the host's hormonal system.

3.2. The Vaginal Microbiome

In healthy, premenopausal women, the vaginal microbiome is typically characterized by low-diversity, *Lactobacillus*-dominated community state types (CSTs), particularly CST I, II, III, and V, enriched with species such as *Lactobacillus crispatus*, *L. iners*, *L. gasseri*, and L. *jensenii* [14]. These bacteria contribute to mucosal homeostasis through multiple mechanisms, including the production of D- and L-lactic acid isomers, hydrogen peroxide, and bacteriocins, which collectively maintain a vaginal pH below 4.5, inhibit pathogen colonization, and support immune tolerance. Estrogen is the primary driver of this *Lactobacillus* dominant state, as it promotes glycogen deposition in vaginal epithelial cells, providing substrates that are metabolized by Lactobacilli to generate lactic acid. In addition to metabolic functions, Lactobacilli actively modulate host immune responses by influencing epithelial barrier integrity, tight junction proteins, and cytokine signaling pathways.

However, during perimenopause and post menopause, the estrogen levels decline, which disrupts this tightly regulated system. This leads to reduced glycogen availability, thinning of the vaginal epithelium, and a shift toward more diverse, anaerobe-rich communities (CST IV), including *Gardnerella*, *Atopobium*, and *Prevotella*[15], [16]. The transition is associated with elevated vaginal pH, increased local inflammation, compromised mucosal defenses, recurrent urinary tract infections (UTIs), and genitourinary syndrome of menopause[17]. These changes represent a hormonally driven ecological transition rather than a passive consequence of aging. Therefore, targeted microbiome-modulating interventions, including *Lactobacillus*-based probiotics, prebiotics, and postbiotic formulations, are emerging as promising strategies to restore vaginal eubiosis and improve urogenital health in estrogen-deficient states.

3.3. The Skin Microbiome and Aging

The skin microbiome occupies a less prominent but equally important position. The skin microbiome comprises a diverse community of bacteria, fungi, and viruses that inhabit distinct ecological niches shaped by factors such as sebum production, moisture, pH, and host immunity. The dominant genera, including *Cutibacterium, Staphylococcus*, and *Corynebacterium*, contribute to skin homeostasis by maintaining barrier integrity, modulating immune responses, and preventing pathogen colonization through competitive exclusion and antimicrobial activity[18].

Skin dysbiosis results from disruption of the balanced microbial ecosystem, often characterized by the overgrowth of opportunistic taxa such as *C. acnes*, driven in part by hormone-regulated changes in sebum production and immune activity. During adolescence, androgen-induced sebum excess promotes *C. acnes* proliferation and acne-associated inflammation. In contrast, aging, particularly menopause-related estrogen decline, leads to reduced collagen synthesis, impaired barrier function, and increased oxidative stress, creating conditions that favor microbial imbalance. These changes underscore a bidirectional relationship between hormonal regulation, skin physiology, and microbiome dynamics.

Given the multifactorial nature of skin dysbiosis and aging, emerging therapeutic strategies are increasingly focused on multi-targeted approaches. Botanical antioxidants, postbiotics, and bioactive compounds that support collagen integrity and barrier function offer the potential to modulate oxidative stress, inflammation, and microbial composition simultaneously. Unlike single-target pharmaceutical interventions, these approaches may provide a more holistic means of restoring skin homeostasis by addressing the interconnected pathways linking hormones, host physiology, and the skin microbiome.

4. Natural Products: Multi-Targeted Mechanisms for Women's Health

The appeal of natural products in women's health is not just cultural or commercial - it is scientific. Unlike single-target pharmacologic agents, botanical extracts, biotics, and functional nutrients typically engage multiple biological pathways in a coordinated fashion. This biological multiplicity makes them particularly well-suited to the complex, interconnected pathology of hormonal aging and microbiome dysbiosis.

4.1. Botanicals

Shatavari (*Asparagus racemosus*) stands out as a women-centered adaptogenic botanical with plausible multi-pathway mechanisms. Unlike classical phytoestrogens, Shatavari does not operate primarily through direct estrogen receptor agonism. Instead, it engages the HPA (hypothalamic-pituitary-adrenal) axis to reduce cortisol-mediated disruption of hormonal signaling, attenuates neuroinflammatory pathways that amplify vasomotor symptoms, and exerts adaptogenic effects that improve resilience to hormonal variability. Randomized, double-blind, placebo-controlled trials have reported meaningful improvements in menopausal rating scale scores - including vasomotor, psychological, and urogenital subscales - with an excellent safety profile[19]. For women who cannot or do not wish to use menopausal hormone therapy, Shatavari represents a scientifically credible, non-hormonal alternative.

Soy isoflavones and whole-soy dietary patterns act through selective estrogen receptor modulation (SERM-like activity) rather than full agonism, which is an important distinction from exogenous hormones. Recent landmark randomized trial data demonstrate that a low-fat, plant-based dietary pattern including whole soy substantially reduces moderate-to-severe hot flash frequency - by as much as 84% in some cohorts - alongside improvements in sexual function and quality of life[20]. Critically, the heterogeneity in individual responses appears to be substantially mediated by gut microbiome composition, specifically by the capacity to produce equol - a bioactive isoflavone metabolite generated by specific bacterial taxa. This finding has profound implications: it means that microbiome profiling could predict which women will respond to phytoestrogen-based interventions, enabling genuinely personalized preventive strategies.

Black cohosh (*Actaea racemosa*) has accumulated the broadest evidence base among menopausal botanicals, with meta-analyses across more than 16 randomized controlled trials demonstrating moderate but consistent reductions in vasomotor symptom frequency and severity without measurable estrogenic effects on the endometrium (Hedaoo et al., 2024). Its mechanism appears to involve serotonergic and dopaminergic pathway modulation - targeting the central neurological drivers of hot flashes - rather than hormonal activity. This makes it particularly relevant for women with hormone-sensitive conditions for whom estrogen exposure is contraindicated.

4.2. Biotics: Probiotics, Prebiotics, and Postbiotics

The case for biotics in women's health begins with the estrobolome and extends to every microbiome niche touched by hormonal change. Probiotic interventions with well-characterized *Lactobacillus* strains, including *L. crispatus, L. rhamnosus* GR-1, and *L. reuteri* RC-14, have demonstrated the capacity to restore vaginal pH, reduce pathogen

colonization, and alleviate vaginal dryness and dyspareunia in peri- and post-menopausal women - through mechanisms that directly address the microbiological consequences of estrogen deficiency [21]. In the gut, specific *Lactobacillus* and *Bifidobacterium* species modulate β-glucuronidase activity, influencing circulating estrogen levels in ways that may be clinically meaningful.

Emerging clinical evidence in PCOS further highlights the therapeutic potential of microbiome modulation, where synbiotic interventions have been shown to improve androgen profiles, normalize LH/FSH ratios, enhance insulin sensitivity, and reduce systemic inflammation. Postbiotics, including short-chain fatty acids, exopolysaccharides, and cell wall-derived bioactives, are gaining attention as next-generation therapeutics, offering defined mechanisms of action, improved stability, and enhanced safety profiles. Collectively, these findings position the microbiome as a modifiable and clinically actionable target in women's endocrine and reproductive health.

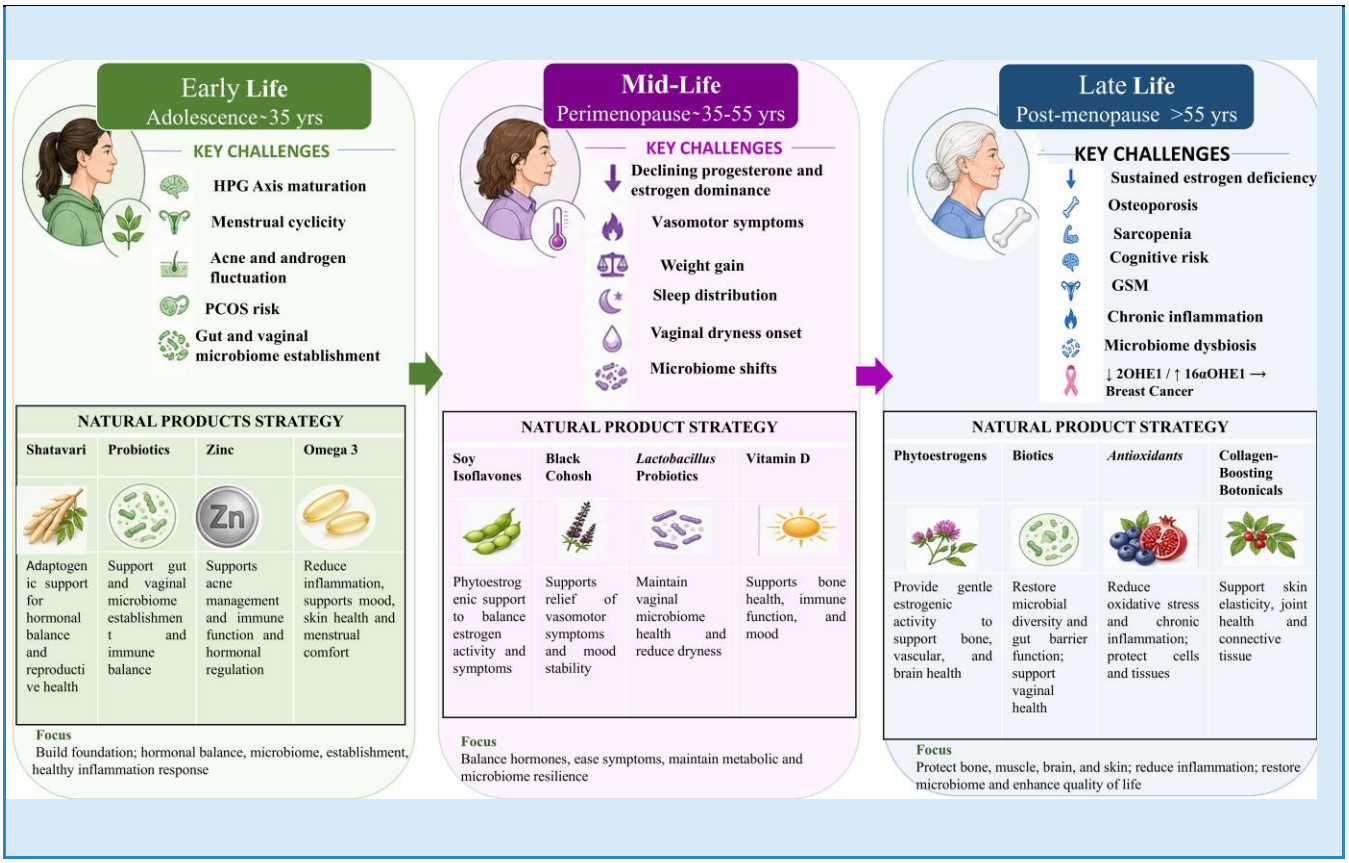

Figure 2. Stage-specific hormonal challenges and corresponding natural product strategies across the women's health lifespan. Effective prevention requires matching intervention type, mechanism, and timing to each distinct biological phase.

5. Summary of Clinical and Preclinical Evidence

The following table summarizes key studies evaluating natural product interventions across women's health domains, spanning randomized clinical trials, meta-analyses, and preclinical models (Table 1).

Table 1. Summary of selected clinical and preclinical studies evaluating natural products for women's health outcomes.

Product / Ingredient	Study Design	Key Outcomes	Duration	Conclusions	References
Shatavari (*Asparagus racemosus*)	RCT, double-blind, placebo-controlled, n=117 peri/postmenopausal women	Improvements in MRS (menopause rating scale) total and subscale scores; reduced hot flashes, improved sleep, and mood	12 weeks	Shatavari shows promise as a non-hormonal intervention for menopausal symptoms; favorable safety profile	[22]

Shatavari (*Asparagus racemosus*) and Ashwagandha root	RCT, double-blind, placebo-controlled, n=135 peri/postmenopausal women	Improved profile of Mood States (POMS) score, hot flashes, and mood.	8 weeks	Shatavari root extract demonstrated a promising option in managing menopausal symptoms and enhancing overall health.	[23]
Soy isoflavones / whole soy (low-fat plant-based diet)	RCT, n=84 postmenopausal women; low-fat plant-based diet with soy	~84% reduction in moderate-to-severe hot flashes; improvements in sexual function and quality of life	12 weeks	Dietary phytoestrogens significantly reduce vasomotor symptoms; gut microbiome (equol production) may mediate the benefit	[24]
L. rhamnosus + *L. reuteri* (probiotics)	RCT, n=70, peri/postmenopausal; oral probiotic supplementation	Improved vaginal pH, *Lactobacillus* abundance, reduced vaginal dryness, and discomfort	12 weeks	Probiotics effectively restore the vaginal microbiome during hormonal decline, promising for GSM management	[25]–[27]
Rosmarinic acid / polyphenol-rich extract	Preclinical (*C. elegans* + in vitro); mechanistic study	Activated DAF-16/FOXO, extended lifespan, improved collagen gene expression, reduced ROS	3–6 months (preclinical)	Strong mechanistic evidence for anti-aging and collagen-preserving effects; supports clinical translation	[28]
Vitamin D3 + Omega-3 fatty acids (combined)	RCT, n=70, postmenopausal women with low bone density	Improved bone mineral density, reduced inflammatory markers (IL-6, CRP), improved mood scores	24 weeks	Combined micronutrient approach addresses osteoporosis and inflammatory burden; effective in deficient women	[29]
Black cohosh (Actaea racemosa)	Meta-analysis, 16 RCTs, n>2,000 peri/postmenopausal women	Moderate reduction in vasomotor symptom frequency and severity vs placebo; no estrogenic effect on endometrium	8–24 weeks	Effective for hot flashes without hormonal risk; the mechanism involves serotonergic and dopaminergic pathways	[30]
Lactobacillus acidophilus + prebiotic FOS (synbiotic)	RCT, n=60, women with PCOS, double-blind	Reduced testosterone and LH/FSH ratio, improved insulin sensitivity, and menstrual regularity was restored in 67%	12 weeks	Gut microbiome modulation through synbiotics shows metabolic and hormonal benefits in PCOS; large trials needed	[31]

6. Conclusion and Future Perspectives

Women's health across the lifespan is shaped by intricate, bidirectional interactions among hormones, the microbiome, immune function, and lifestyle factors. Early-life reproductive challenges, mid-life perimenopausal turbulence, and late-life estrogen deficiency contribute to a substantial and growing global burden of symptoms, chronic disease, and diminished quality of life. Conventional pharmacologic approaches - hormone replacement therapy foremost among them - remain valuable for selected women but are limited by safety concerns, contraindications, and an orientation toward treatment rather than prevention.

Natural products - botanicals such as Shatavari, black cohosh, and polyphenol-rich extracts; biotics targeting gut and vaginal microbiome composition; antioxidant nutrients supporting the Nrf2 pathway and collagen homeostasis - offer a scientifically compelling, multi-targeted alternative [32]. Their mechanisms align with the complex, systems-level biology of hormonal aging: they engage the estrobolome, support mucosal barriers, reduce oxidative and inflammatory burden, and modulate the neuroendocrine drivers of menopausal symptoms simultaneously. This biological multiplicity is not a limitation - it is a strength, particularly for conditions as multifactorial as perimenopause and post-menopause.

But the evidence base is uneven, and intellectual honesty demands that we acknowledge this. For some interventions - soy isoflavones, black cohosh, specific *Lactobacillus* strains - randomized trial data are reasonably robust. For others, mechanistic plausibility outpaces clinical substantiation. The path forward requires:

- Rigorous clinical trial design: Well-powered, randomized, placebo-controlled trials with pre-specified primary endpoints, validated symptom instruments, and mechanistic biomarkers - including microbiome profiling - are the standard we must hold ourselves to.
- Microbiome-informed personalization: Equol-producer status, estrobolome composition, and vaginal microbiome profiling offer the possibility of identifying, in advance, which women will respond to specific natural product interventions. This is precision medicine for women's preventive health.
- Lifespan-based prevention models: Women's health strategies must shift from reactive symptom management to proactive, stage-specific prevention beginning in adolescence. The biological groundwork for menopausal health is laid decades before menopause begins.
- Translational research pipelines: Investments in mechanistic preclinical science - including cellular aging models and *C. elegans* studies - must be coupled with disciplined clinical translation, creating evidence packages that satisfy both regulatory standards and clinical credibility.

The convergence of aging demographics, unmet clinical needs, advancing microbiome science, and rising consumer demand for safer, long-term wellness solutions creates a rare opportunity. Advancing women's health through natural products is not about rejecting evidence-based medicine - it is about expanding what evidence-based medicine looks like for the half of the population that has been underserved by it for too long.

Author Contributions

Conceptualization, A.B. and C.D.; methodology, A.B.; software, E.F.; validation, A.B., C.D. and E.F.; formal analysis, A.B.; investigation, A.B.; resources, C.D.; data curation, A.B.; writing—original draft, A.B.; writing—review and editing, C.D. and E.F.; visualization, A.B.; supervision, C.D.; project administration, C.D.; funding acquisition, C.D. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of [Institution Name] (Protocol No. XXXX, approved DD Month YYYY).

Conflicts of Interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analysis, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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Abbreviations

GnRH	Gonadotropin-releasing hormone

LH	Luteinizing hormone
FSH	Follicle-stimulating hormone
GSM	Genitourinary syndrome of menopause
UTI	Urinary tract infections
SERM	Selective estrogen receptor modulation
CSTs	Community state types
PCOS	Polycystic Ovary Syndrome

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