Gynecological inflammation models offer additional insight into how metabolite patterns shape efficacy. Motherwort total alkaloids significantly ameliorate bacteria-induced endometritis in rats, reducing inflammatory mediator overproduction and promoting endometrial repair through regulation of PI3K-AKT-NF-κB signaling (Ou et al., 2025). In parallel, combination formulas containing *L. japonicus* with other herbs show robust efficacy against bovine and rodent endometritis, lowering uterine bacterial load and inflammatory scores while improving oxidative status, consistent with a multi-component, multi-target anti-inflammatory mode of action (Tan et al., 2025). In endocrine-related disorders, *L. japonicus*-derived flavonoids such as luteolin and luteolin-7-methylether inhibit aromatase-mediated estrogen biosynthesis in granulosa cells and alleviate polycystic ovary syndrome (PCOS) phenotypes in mice, implicating origin-dependent flavonoid content in modulation of ovarian steroidogenesis (Du et al., 2020; Shi et al., 2024). Collectively, these *in vitro* and *in vivo* data indicate that variation in alkaloid and flavonoid levels across origins is likely to produce distinct profiles of uterotonic, anti-inflammatory, vascular, and endocrine activities.

8.3 Validation of correlations between metabolic profiles and clinical efficacy

Establishing robust links between origin-specific metabolite signatures and clinical gynecological outcomes requires coordinated chemical, pharmacokinetic, and clinical data. Multi-marker quality control work has identified leonurine, stachydrine, and trigonelline as quantitative "Q-markers" that are both pharmacodynamically relevant and sufficiently stable for routine measurement, enabling standardized comparison of materials from different regions and plant parts (Zhao et al., 2022). Broad metabolomic and genomic analyses demonstrate that *L. japonicus* accessions with higher expression of leonurine-biosynthesis genes accumulate more leonurine in aerial tissues, whereas closely related Leonurus species lacking these pathway innovations are essentially leonurine-free, highlighting a genetic basis for inter- and intra-specific differences in clinically important alkaloids. Integrating such markers with origin information allows retrospective correlation of clinical preparations-long valued for treating menoxenia, dysmenorrhea, amenorrhea, postpartum hemorrhage, and lochial disorders-with defined ranges of bioactive constituents (Shang et al., 2014; Miao et al., 2019).

Translational studies in gynecologically relevant models provide a bridge between chemistry and real-world therapeutic outcomes. Leonurine isolated from *L. japonicus* exhibits potent antimycobacterial activity against Mycobacterium tuberculosis and reduces mycobacterial load in a rat model of genital tuberculosis, directly linking an origin- and pathway-dependent alkaloid to improved uterine infection control (Gan et al., 2019). Similarly, motherwort-based formulations and extracts rich in leonurine and related secondary metabolites alleviate obstetric and gynecologic conditions such as postpartum hemorrhage, irregular menstruation, and dysmenorrhea in clinical and preclinical settings, in line with their vascular, uterotonic, anti-inflammatory, and endocrine-modulating activities (Wen et al., 2019). As ecological modeling now connects climatic suitability and gene expression with medicinal compound accumulation, origin-informed cultivation strategies can be used prospectively to produce chemotypes optimized for specific gynecologic indications, creating a feedback loop in which metabolic profiling, pharmacodynamics, and clinical efficacy mutually refine quality standards for *L. japonicus*-based therapies.

9 Conclusion and Future Perspectives

Research on *Leonurus japonicus* has firmly established it as a key medicinal plant in gynecology, with its therapeutic efficacy closely linked to a chemically diverse and dynamic secondary metabolite system. The plant contains abundant alkaloids, diterpenoids, and flavonoids, among which leonurine, stachydrine, and trigonelline are considered core bioactive compounds. These metabolites not only contribute to traditional indications such as regulating menstruation and promoting blood circulation but also serve as important quality markers connecting phytochemical variation with clinical consistency. Advances in chromatographic and metabolomic analyses have revealed substantial intra- and interspecific variation in these compounds, highlighting leonurine as a species-specific chemical signature distinguishing *L. japonicus* from related taxa such as L. sibiricus. More importantly, the integration of genomics, transcriptomics, metabolomics, and enzymology has enabled reconstruction of the leonurine biosynthetic pathway, identifying key enzymes such as arginine decarboxylase (ADC), UDP-glycosyltransferases (UGTs), and serine carboxypeptidase-like proteins (SCPLs). Gene duplication