and functional divergence within these pathways provide a mechanistic explanation for the high accumulation of leonurine in *L. japonicus*, thereby directly linking genetic architecture with pharmacologically relevant alkaloid traits.

At the functional level, the diverse metabolite profile of *L. japonicus* underpins its multi-target pharmacological activities, particularly in gynecological contexts. Total alkaloid fractions and enriched extracts have been shown to promote angiogenesis, accelerate tissue repair, and facilitate endometrial recovery through signaling pathways such as SRC/MEK/ERK and PI3K/AKT/NF-κB, supporting its traditional application in postpartum rehabilitation and inflammatory uterine conditions. Systems pharmacology approaches further demonstrate that multiple metabolite classes collectively modulate endocrine, vascular, and inflammatory networks, with hub targets including AKT1, ESR1, and PTGS2 serving as key regulatory nodes. Flavonoids such as luteolin and luteolin-7-methylether provide an additional layer of endocrine regulation by suppressing aromatase-mediated estrogen biosynthesis via pathways such as p38 MAPK/AKT and TPL2-p38-CREB, suggesting therapeutic potential in estrogen-related disorders including polycystic ovary syndrome. Meanwhile, labdane diterpenoids, particularly those localized in glandular trichomes, exhibit anti-inflammatory, antithrombotic, and anti-proliferative activities, expanding the spectrum of bioactive constituents involved in regulating uterine blood flow, thrombosis, and pelvic inflammation. Together, these findings support a multi-component, multi-target mode of action that bridges traditional concepts with modern molecular pharmacology.

Despite significant progress, important challenges remain in fully elucidating the relationship between metabolite diversity and gynecological efficacy. Existing studies are often fragmented across different extract types, plant tissues, developmental stages, and geographical origins, with relatively few investigations systematically linking natural variation in metabolite profiles to standardized clinical outcomes. Although genetic and environmental factors have been shown to influence metabolite composition, the specific ecological drivers and agronomic strategies for optimizing key bioactive compounds remain insufficiently defined. Furthermore, while network pharmacology and *in vitro* or animal studies provide valuable mechanistic insights, rigorously designed clinical trials that incorporate chemical quality and genetic background are still lacking. The expansion of genomic resources, including chromosome-level assemblies and organelle genomes, offers new opportunities for integrative research; however, comprehensive genotype-metabolite-phenotype association studies remain in their early stages. Future research should prioritize multi-omics integration across diverse germplasm to develop predictive models linking genome, environment, and metabolite traits to gynecological functions. Such efforts, combined with precision breeding strategies and improved quality control frameworks that incorporate multi-component fingerprints and pharmacokinetic data, will be essential for advancing the standardized, safe, and evidence-based application of *L. japonicus* in modern obstetrics and gynecology.

Acknowledgements

The authors appreciate the editorial assistance and constructive feedback received during the preparation and revision of this manuscript.

Conflict of Interest Disclosure

The authors affirm that this research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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