whereas LjTPS6 produces a mixture of labdane products; mutational analysis of a single active-site residue in LjTPS6 can shift product specificity toward a single 9,13-epoxy-labdane epimer, underscoring how subtle protein changes reprogram diterpenoid profiles.

5.2 Regulatory networks of related genes and transcription factors

Genome-level analyses of *L. japonicus* identify expanded gene families in specialized metabolism, particularly diterpenoid biosynthesis, suggesting that duplication and diversification of pathway genes provides a genomic substrate for regulatory rewiring of secondary metabolite output (Wang et al., 2024). In Leonurus WRKY transcription factor (TF) families, drought-responsive members (e.g., LjWRKY1, 4, 23, 44) show strong induction or repression under stress, and differentially expressed genes under drought are enriched in plant hormone signaling, MAPK cascades and secondary metabolite biosynthesis, implying a coordinated TF-centered network that links environmental cues to metabolite pathways (Guo et al., 2025).

Across plant species, transcription factors from WRKY, MYB, AP2/ERF, bHLH, bZIP and NAC families act as master regulators of secondary metabolism by binding cis-elements in promoters of biosynthetic genes and modulating their transcription in response to biotic and abiotic stimuli (Jan et al., 2021; Rabeh et al., 2025). Stress-inducible TFs often converge on precursor-producing steps such as the shikimate and phenylpropanoid pathways, creating regulatory nodes where environmental signals can adjust flux toward flavonoids, alkaloids or terpenoids; these principles are likely conserved in *L. japonicus* and underpin stress- and tissue-dependent variability in leonurine and labdane diterpenoids (Zhan et al., 2022).

5.3 Advances in molecular markers and metabolic regulation

The chromosome-level genome of *L. japonicus*, with over 22,000 annotated genes and clear expansion of specialized-metabolism families, provides a foundational resource for designing molecular markers targeting loci involved in diterpenoid and alkaloid biosynthesis and for associating allelic variation with chemotype differences among germplasm (Wang et al., 2024). Population-level work correlating ITS and plastid markers with inter-origin variation in active components already shows that genetic divergence only partially explains metabolite differences, emphasizing the need for pathway-anchored markers that can directly track biosynthetic capacity in breeding for stable gynecological quality traits (Han et al., 2023).

Multi-omics approaches in related medicinal species illustrate how integrating transcriptomics, metabolomics and co-expression network analysis can reveal key control points and candidate regulators for flavonoid and other secondary-metabolite pathways, offering a template for similar systems-level dissection in *L. japonicus* (Yang et al., 2019; Chen et al., 2024b). In such frameworks, hub TFs (including WRKYs) and tailoring enzymes like UGTs emerge as central levers of metabolic regulation; manipulating these nodes by marker-assisted selection, transgenic or genome-editing strategies could rationally enhance leonurine and labdane-diterpenoid profiles that contribute to uterotonic, hemostatic and anti-inflammatory effects in gynecological applications (Li et al., 2023; Guo et al., 2025).

6 Pharmacological Effects of *Leonurus japonicus* in Gynecological Disorders

Leonurus japonicus, known as a “sacred medicine of gynecology,” has long been used to treat menstrual disorders and postpartum conditions. Its major secondary metabolites, including alkaloids, flavonoids, and terpenoids, exert multi-target effects on circulation, inflammation, and endocrine regulation, supporting its therapeutic role (Shang et al., 2014; Li et al., 2019). Modern studies indicate that these compounds act synergistically through multiple pathways, providing a mechanistic basis for its traditional functions such as promoting blood circulation and alleviating gynecological disorders.

6.1 Mechanisms of promoting blood circulation and regulating menstruation

Animal models of trauma-induced blood stasis demonstrate that *L. japonicus* extracts significantly reduce plasma viscosity, platelet aggregation, fibrinogen, thromboxane B_2, and plasminogen activator inhibitor-1, while increasing antithrombin III and tissue-type plasminogen activator, indicating coordinated antithrombotic and profibrinolytic effects that improve microcirculation (Zhang et al., 2023). In the same model, extract treatment