4 Variation in Secondary Metabolic Traits and Influencing Factors

4.1 Metabolic differences among germplasms and varieties

Leonurus japonicus exhibits substantial intraspecific variation in secondary-metabolite traits that is closely tied to its genetic diversity across populations. Phylogenetic work based on concatenated plastid and nuclear markers has divided Chinese germplasm into four deeply divergent clades, with divergence events linked to geological uplift and Quaternary climate shifts (Wang et al., 2023a). This population structure provides a genomic framework for chemotype formation, because nucleotide diversity “hotspots” and clade differentiation are expected to underlie differences in biosynthetic capacity and regulatory networks influencing alkaloids, flavonoids, and terpenoids. At the same time, comparative genomics within the genus shows that leonurine accumulation is species-specific, driven by duplication and neofunctionalization of a UGT-SCPL gene cluster in *L. japonicus* but not in the low-leonurine species L. sibiricus, emphasizing how relatively recent gene-level changes can create marked metabolic contrasts between otherwise related lineages (Li et al., 2023).

Chemotaxonomic analysis of accessions from multiple provenances confirms that germplasms differ not only in overall metabolite content but also in the relative proportions of leonurine and other active markers important for gynecological efficacy (Han et al., 2023). High-performance liquid chromatography combined with multivariate statistics has resolved origin-specific clusters, in which some populations consistently show higher levels of key uterotonic and cardioprotective constituents than others, even under similar analytical conditions. These chemotype differences likely translate into variable clinical potency for indications such as regulating menstruation or promoting postpartum uterine involution, and they underscore the need to match germplasm to pharmacopoeial standards when developing standardized modern preparations. Integrating genome information with metabolite profiling-linking specific clades or alleles to leonurine and phenolic contents-offers a path toward breeding elite lines with optimized secondary-metabolite profiles for gynecological applications.

4.2 Regulation of metabolism by environmental factors

Environmental conditions strongly modulate secondary-metabolite accumulation in medicinal plants, and *L. japonicus* is no exception. A multi-origin study combining phylogenetics and chemical analysis showed that differences in active-ingredient profiles among regions could not be explained by genetics alone, implying a major contribution of local climate and edaphic conditions to observed metabolic variation (Han et al., 2023). In parallel, ecological modeling at the species level has identified precipitation patterns and temperature regimes-especially precipitation of the warmest quarter and minimum temperature of the coldest month-as key determinants of ecological suitability, with highly suitable habitats tending to support plants with higher expression of medicinal markers (Chen et al., 2024a). These findings suggest that water availability and thermal stress shape secondary metabolism in the field, for example by influencing pathways for alkaloids and phenylpropanoids that underpin gynecological indications such as hemostasis and uterine activation.

More broadly, reviews on plant secondary metabolism under abiotic stress demonstrate that light intensity and spectrum, temperature, soil moisture, nutrient status, and salinity can all shift both the quantity and profile of secondary metabolites, often through transcriptional regulation of biosynthetic genes (Jan et al., 2021). Even modest variation in a single factor-such as soil water or fertility-can significantly alter the levels of phenolics, terpenes, or alkaloids while other factors remain constant, indicating that cultivation practices for *L. japonicus* must carefully manage irrigation, fertilization, and shading to maintain consistent chemical quality (Yang et al., 2018). Climate-change-oriented syntheses further highlight that elevated temperature, drought, and changing CO_2 can either enhance or suppress specific metabolite classes, implying that future field production of motherwort may drift in chemotype unless adaptive agronomic strategies are implemented to stabilize uterotonic and anti-inflammatory components critical for gynecological efficacy (Qaderi et al., 2023).

4.3 Effects of developmental stages and harvesting time

Ontogeny exerts a powerful influence on secondary metabolism, and developmental regulation needs to be considered when defining optimal harvest windows for gynecological use of *L. japonicus*. General analyses of medicinal plants show that biosynthesis and storage of key secondary metabolites are tightly linked to organ