The integrated analysis indicates that metabolite divergence cannot be explained by genetics alone, and that ecological variables-particularly climate and edaphic conditions-shape local chemotypes, likely through modulation of stress-responsive and specialized-metabolism gene networks. Broad-scale ecological modeling further supports this view: areas with higher climatic suitability for *L. japonicus* tend to harbor plants with more favorable profiles of medicinal marker compounds, linking habitat quality to metabolite accumulation (Chen et al., 2024a).

High-resolution metabolomics has revealed that beyond a few alkaloid markers, the *L. japonicus* metabolome encompasses extensive diversity in flavonoids, phenylethanoid glycosides, terpenoids, and fatty-acid esters, with many of these constituents varying quantitatively among origins (Garran et al., 2019). Comparative surveys suggest that some regions produce material enriched in alkaloids and flavonoids, whereas others are relatively richer in terpenoid scaffolds, implying origin-specific pharmacological tendencies within the same species. Large-scale distribution modeling predicts a future poleward expansion and reshaping of suitable areas under climate change, raising the prospect that both the geographic supply and typical metabolite profiles of medicinal *L. japonicus* will shift over time (Chen et al., 2024b). Together, these data underscore that "origin" encodes a complex combination of genetic background, local environment, and resulting metabolite pattern, with direct relevance to quality evaluation.

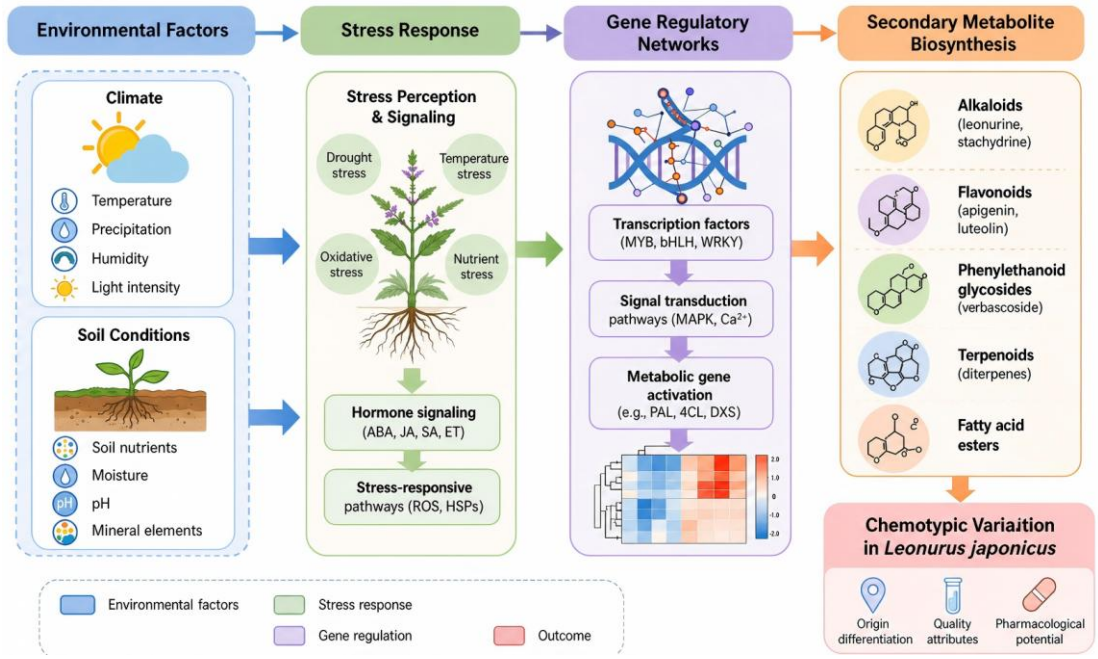

Figure 3 Conceptual model illustrating how environmental factors (climate and soil conditions) influence stress-responsive pathways and specialized metabolism gene networks, ultimately shaping chemotypic variation in *Leonurus japonicus* (Adopted from Han et al., 2023)

8.2 Pharmacodynamic evaluation (*in vitro* and *in vivo* models)

Pharmacodynamic studies integrating chemical profiling with bioassays have begun to clarify how origin-linked metabolite differences translate into gynecologically relevant activities. Total alkaloid fractions, dominated by leonurine-type and related bases, promote angiogenesis, endothelial migration, and collagen deposition via SRC-MEK-ERK signaling, supporting tissue repair after uterine or perineal injury (Shi et al., 2022). Parallel work in trauma-induced blood-stasis models demonstrates that whole-plant extracts rich in alkaloids and flavonoids improve hemodynamics, decrease platelet aggregation, and modulate vasoactive mediators, providing mechanistic support for traditional indications of "activating blood circulation" in dysmenorrhea and postpartum conditions (Zhang et al., 2023). Because the abundance of these bioactive constituents is origin-dependent, extracts from alkaloid-rich regions are expected to exert stronger pro-angiogenic and hemorheologic effects at equivalent doses (Han et al., 2023).