Ecologically, *L. japonicus* prefers moist environments and is commonly found along field margins, riverbanks, disturbed ground, and grasslands from sea level up to about 3400 m (Rojas-Sandoval and Acevedo-Rodríguez, 2022). The species tolerates semi-shade but grows best in full sun and on a wide range of soils with pH 4-8, highlighting broad edaphic adaptability. Niche-modeling studies further reveal that precipitation in the warmest quarter and temperature in the coldest quarter are key climatic factors shaping its distribution, and future climate scenarios predict a northward and upward shift in suitable ranges, with expansion at higher latitudes (Wang et al., 2023a).

2.3 Genetic diversity and germplasm resources

Genetic studies based on complete chloroplast genomes and plastome hotspot regions have shown that *L. japonicus* in China possesses relatively low average nucleotide diversity ($\pi \approx 0.00029$) but is structured into four well-supported clades, reflecting historical divergence influenced by geological events such as the uplift of the Hengduan Mountains and Quaternary climate oscillations. Sliding-window analyses identified variable intergenic spacers (petN-psbM and rpl32-trnL) that serve as cost-effective markers for genotype discrimination and provide useful tools for monitoring population structure in germplasm collections (Wang et al., 2023b). AFLP and ISSR marker analyses across multiple accessions and provenances have also revealed rich polymorphism and clear clustering, confirming that substantial genetic variation persists despite localized bottlenecks (Chen et al., 2009; Wang, 2009).

At a broader phylogenetic scale, ITS-based analyses within Leonurus and comparative genomic work with L. sibiricus indicate that *L. japonicus* forms distinct genetic lineages, with chromosome-level genome assemblies now available to support fine-scale exploration of biosynthetic and adaptive traits (Yang et al., 2022; Arabova et al., 2025). Recent work combining DNA barcoding (ITS + plastid loci) with HPLC profiling has further shown that genetic groupings among different geographic origins correlate with variation in active ingredient content, although environmental factors also contribute significantly to metabolite differences (Figure 2) (Han et al., 2023; Hu et al., 2025). These findings highlight the importance of conserving diverse wild populations and developing genotype-informed germplasm banks to secure both genetic diversity and the spectrum of secondary metabolite phenotypes relevant to gynecological applications.

3 Types and Composition of Secondary Metabolites in *Leonurus japonicus*

Leonurus japonicus exhibits a chemically diverse profile with over one hundred secondary metabolites, including alkaloids, flavonoids, phenolic acids, and terpenoids, which collectively contribute to its gynecological effects such as uterotonic, anti-inflammatory, and antioxidant activities. Although pharmacopoeial standards often rely on single markers like leonurine, modern analyses reveal complex multi-component interactions influenced by plant origin and processing (Zhao et al., 2022; Han et al., 2023). Advanced chromatographic and metabolomic studies have further identified over 130 compounds, highlighting key groups such as alkaloids, flavonoids, and terpenoids as central to its therapeutic functions.

3.1 Alkaloids

Alkaloids are widely regarded as the primary signature metabolites of Leonurus, distinguishing *L. japonicus* from many other Lamiaceae that are dominated by terpenoids alone (Zhang et al., 2018; Li et al., 2023). Leonurine, a guanidine-type pseudoalkaloid, together with betaine-type alkaloids such as stachydrine and trigonelline, represents the major nitrogen-containing constituents quantified in pharmacopeial materials and in pharmacokinetic studies. Targeted LC-MS/MS analysis across different plant parts has confirmed these three molecules as the principal activity-related substances, with measurable stability and reproducible content suitable for use as quality markers (Zhao et al., 2022). Multi-omics comparison between *L. japonicus* (high-leonurine) and L. sibiricus (trace-leonurine) further shows that leonurine accumulation is species-specific and controlled by a specialized biosynthetic pathway, explaining why Chinese motherwort is particularly rich in this gynecological alkaloid.

Functionally, leonurine and stachydrine are strongly implicated in the uterine and cardiovascular actions that justify traditional indications such as regulation of menstruation, treatment of dysmenorrhea, and promotion of