

Feature Review

Open Access

Breeding Strategies for Enhancing Medicinal Properties of Lonicera japonica Jianmin Zheng¹, Xiaocheng Wang²

1 Institute of Life Sciences, Jiyang Colloge of Zhejiang A&F University, Zhuji, 311800, Zhejiang, China

2 Traditional Chinese Medicine Research Center, Cuixi Academy of Biotechnology, Zhuji, 311800, Zhejiang, China

Corresponding author: <u>xiaocheng.wang@cuixi.org</u>

Medicinal Plant Research, 2024, Vol.14, No.2 doi: 10.5376/mpr.2024.14.0008

Received: 20 Feb., 2024

Accepted: 25 Mar., 2024

Published: 12 Apr., 2024

Copyright © 2024 Zheng and Wang, This is an open access article published under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Preferred citation for this article:

Zheng J.M. and Wang X.C., 2024, Breeding strategies for enhancing medicinal properties of *Lonicera japonica*, Medicinal Plant Research, 14(2): 97-106 (doi: 10.5376/mpr.2024.14.0008)

Abstract *Lonicera japonica* is widely recognized for its medicinal properties, especially in traditional medicine, where it is known for its anti-inflammatory, antiviral and antioxidant effects. In this study, the methods of improving the medicinal quality of honeysuckle by breeding strategies were discussed, focusing on increasing the yield of flavonoid and other key active compounds. The study analyzed genetic diversity and molecular markers associated with medicinal traits in wild populations to support the development of good genotypes, and evaluated the effectiveness of traditional crossbreeding, marker-assisted selection (MAS), and modern genomic tools such as CRISPR-Cas9 in improving these medicinal traits. The production of active compounds has been optimized through traditional breeding methods such as genotype selection and hybridization, combined with advanced technologies such as genome selection and CRISPR/Cas9 gene editing. Despite breeding and regulatory challenges, the study concludes that breeding programs that combine traditional and modern techniques hold great promise in enhancing the medicinal value of honeysuckle.

Keywords Lonicera japonica; Medicinal properties; Genome sequencing; Carotenoid metabolism; Molecular breeding

1 Introduction

Lonicera japonica, commonly known as Japanese honeysuckle, is a perennial vine belonging to the Caprifoliaceae family. This plant is widely recognized for its ornamental value due to its dynamic flower coloration, which transitions from white to gold during development (Ge et al., 2018; Pu et al., 2020). Beyond its aesthetic appeal, *L. japonica* holds significant medicinal value. It has been extensively used in traditional Chinese medicine (TCM) for its anti-inflammatory, antibacterial, antiviral, and antioxidative properties (Shang et al., 2011). The plant's various parts, including leaves, flower buds, and stems, are utilized to treat a range of ailments, from febrile diseases to detoxifying poisons (Cai et al., 2020; Dai et al., 2023).

Historically, *Lonicera japonica* has been an integral part of traditional medicine practices, particularly in China. Known as Jin Yin Hua, it has been employed to treat exopathogenic wind-heat, epidemic febrile diseases, sores, and carbuncles (Shang et al., 2011; Yan et al., 2016). The plant's branches and unopened flower buds are specifically used to address external wind heat or febrile disease fever (Peng et al., 2010; Dai et al., 2023). Additionally, *L. japonica* has found applications in modern contexts, such as in the suppression of SARS-CoV-2 entry and the mitigation of COVID-19 related cytokine storms (Yeh et al., 2022; Gao et al., 2023). This rich history underscores the plant's enduring relevance and the potential for further medicinal applications.

Despite its established medicinal uses, there is a growing need to enhance the medicinal properties of *Lonicera japonica* through targeted breeding strategies. The identification of key phytochemical compounds and their differential expression in various plant parts can pave the way for optimizing the plant's therapeutic efficacy (Cai et al., 2020). Moreover, understanding the molecular mechanisms underlying its bioactive properties, such as the role of carotenoid metabolism in flower coloration, can inform breeding programs aimed at improving specific medicinal traits (Pu et al., 2020). Enhancing these properties not only holds promise for developing new drugs and therapeutics but also for ensuring the sustainable use of this valuable medicinal resource.



By integrating genomic, transcriptomic, and metabolomic data, this study identified key genetic and biochemical markers associated with the plant's therapeutic efficacy. The study will also investigate the potential for using different parts of the plant as alternative medicinal resources, thereby promoting comprehensive exploitation and utilization of *L. japonica*. This study hopes to contribute to the development of improved medicinal varieties of *Lonicera japonica*, ensuring its continued relevance and efficacy in traditional and modern medicine. By focusing on these aspects, the study provides a robust framework for enhancing the medicinal properties of *Lonicera japonica*, thereby supporting its continued use and development in both traditional and contemporary medical practices.

2 Genetic Basis of Medicinal Properties

2.1 Identification of key medicinal compounds in Lonicera japonica

Flavonoids are one of the primary active components in *Lonicera japonica*, contributing significantly to its medicinal properties. The R2R3-MYB transcription factor gene *LjaMYB12* has been identified as a key regulator in the biosynthesis of flavonoids. Ectopic expression of *LjaMYB12* in *Arabidopsis thaliana* has been shown to increase flavonoid accumulation, suggesting that this gene plays a crucial role in enhancing the therapeutic effects of flavonoids in *L. japonica* (Qi et al., 2019). Additionally, tetraploid *L. japonica* plants have been found to contain higher levels of flavonoids compared to their diploid counterparts, indicating that polyploidy may also influence flavonoid biosynthesis (Wang et al., 2020).

Phenolic acids, such as chlorogenic acid, are another important group of bioactive compounds in *Lonicera japonica*. These compounds are known for their antioxidant properties, which contribute to the plant's medicinal efficacy. Comparative transcriptomic analyses have revealed that tetraploid *L. japonica* plants exhibit higher levels of phenolic acids than diploid plants, suggesting that genetic factors play a significant role in the biosynthesis of these compounds (Wang et al., 2020). Furthermore, phenolic acids have been shown to reduce oxidative damage by enhancing antioxidant enzyme activity, particularly under stress conditions such as salt stress (Cai et al., 2021).

2.2 Genetic diversity and its role in enhancing medicinal properties

Genetic variation within wild populations of *Lonicera japonica* is crucial for the plant's adaptability and the diversity of its medicinal compounds. Transcriptomic analyses have identified significant differences in gene expression profiles between different varieties of *L. japonica*, which may explain the variability in medicinal efficacy (Yuan et al., 2012). This genetic diversity is crucial for the development of breeding strategies to enhance the medicinal properties of plants.

The production of bioactive compounds in *Lonicera japonica* is closely linked to its genetic diversity. Studies have shown that tetraploid plants, which possess greater genetic variation, produce higher levels of key medicinal compounds such as flavonoids and phenolic acids compared to diploid plants (Wang et al., 2020). This suggests that increasing genetic diversity through breeding or polyploidy can enhance the production of bioactive compounds, thereby improving the medicinal quality of *L. japonica*.

2.3 Molecular markers associated with medicinal traits

The identification and development of molecular markers associated with the biosynthesis of key medicinal compounds are essential for marker-assisted selection (MAS) in breeding programs. Transcriptomic studies have provided valuable insights into the genes and metabolic pathways involved in the production of flavonoids and phenolic acids in *Lonicera japonica* (Yuan et al., 2012; Wang et al., 2020). These findings can be used to develop molecular markers that can facilitate the selection of plants with enhanced medicinal properties.

Marker-assisted selection (MAS) is a powerful tool for improving the medicinal properties of *Lonicera japonica*. By using molecular markers linked to the biosynthesis of key compounds, breeders can efficiently select plants with desirable traits. The application of MAS can accelerate the development of new varieties with higher levels of bioactive compounds, thereby enhancing the overall medicinal value of *L. japonica* (Yuan et al., 2012; Wang et al., 2020).



3 Traditional Breeding Methods

3.1 Selection of superior genotypes

The selection of superior genotypes in *Lonicera japonica* involves identifying varieties that exhibit high yield and enhanced medicinal properties. Key criteria include the concentration of bioactive compounds, resistance to environmental stressors, and overall plant vigor. For instance, research has shown that certain varieties of *Lonicera japonica*, such as 'Yujin2', have been bred for their strong aroma and high content of bioactive compounds like terpenoids and phenolic acids, which are crucial for their medicinal efficacy (Li et al., 2022). Additionally, the ability to withstand salt stress while maintaining high levels of bioactive constituents is another important criterion, as demonstrated by studies on the impact of salt stress on the quality of *Lonicera japonica* (Cai et al., 2021).

Once superior genotypes are identified, effective propagation techniques are essential to maintain and multiply these desirable traits. Traditional methods such as cuttings and layering are commonly used. For example, propagation through cuttings ensures that the genetic makeup of high-yielding varieties is preserved, allowing for consistent medicinal quality across generations. Advanced techniques like tissue culture can also be employed to propagate selected genotypes rapidly and in large quantities, ensuring a steady supply of high-quality medicinal plants.

3.2 Crossbreeding strategies

Crossbreeding strategies aim to combine desirable traits from different parent plants to produce hybrids with superior medicinal properties. Hybridization efforts focus on enhancing the content of bioactive compounds such as terpenoids, phenolic acids, and flavonoids. For instance, integrating volatile metabolomic and transcriptomic analyses has identified key biosynthetic pathways and genes involved in the production of these compounds, which can be targeted in hybridization programs to develop varieties with enhanced medicinal properties (Li et al., 2022).

Evaluating hybrid vigor, or heterosis, is crucial in determining the success of crossbreeding efforts. This involves assessing the growth, yield, and medicinal quality of hybrid plants compared to their parent varieties. Studies have shown that hybrids can exhibit improved resistance to environmental stressors and higher concentrations of bioactive compounds, making them more effective for medicinal use. For example, hybrids developed through polyploidy breeding have shown significant improvements in both yield and quality of *Lonicera japonica*.

3.3 Field trials and performance evaluation

Field trials are essential for evaluating the performance of selected and hybrid genotypes under real-world conditions. Experimental plots should be established in diverse environments to assess the adaptability and stability of the plants. Proper plot design, including randomized block designs, ensures that the data collected is statistically valid and reliable. These trials help in understanding how different genotypes perform in terms of growth, yield, and medicinal quality under various environmental conditions (Li et al., 2023).

The analysis of growth and medicinal quality in field trials involves measuring various parameters such as plant height, biomass, and the concentration of bioactive compounds. Advanced analytical techniques like UFLC-QTRAP-MS/MS can be used to quantify the levels of multiple bioactive constituents, providing a comprehensive assessment of the medicinal quality of the plants. Additionally, statistical analyses such as partial least squares discrimination analysis and gray relational analysis can be employed to systematically evaluate and distinguish the performance of different genotypes, ensuring that the best-performing varieties are selected for further development (Cai et al., 2021).

4 Advanced Breeding Techniques

4.1 Genomic selection and its application

Genomic selection (GS) represents a significant advancement in plant breeding, leveraging the power of high-density DNA markers to predict the performance of breeding lines. Unlike traditional marker-assisted selection, which focuses on identifying individual loci associated with traits, GS uses all available marker data to



predict the genetic value of an individual. This approach allows for more accurate and comprehensive selection, particularly for complex traits controlled by multiple genes with small effects (Jannink et al., 2010; Merrick et al., 2022). The integration of GS into breeding programs has shown promise in accelerating genetic gains and reducing the breeding cycle time, making it a valuable tool for modern plant breeding (Heslot et al., 2015; Crossa et al., 2017).

The application of GS in enhancing medicinal traits of *Lonicera japonica* involves the identification and selection of genotypes with superior bioactive compound profiles. By analyzing phenotypic data and high-density marker scores, GS can predict the breeding values of lines, facilitating the selection of individuals with desirable medicinal properties. This method has been shown to improve the accuracy of selection and increase genetic gains per unit time, making it an effective strategy for breeding *Lonicera japonica* with enhanced medicinal traits (Heslot et al., 2012; Xu et al., 2019). Additionally, the use of GS can help in managing genotype-by-environment interactions, further optimizing the breeding process for specific medicinal traits (Wang et al., 2018; Jeon et al., 2023).

4.2 Genetic modification and CRISPR/Cas9 technology

Genetic modification, particularly through CRISPR/Cas9 technology, offers precise and efficient tools for editing genes associated with the production of bioactive compounds in *Lonicera japonica*. This technology allows for the targeted modification of specific genes, enabling the enhancement of desirable traits such as increased concentration of medicinal compounds. By knocking out or modifying genes involved in metabolic pathways, researchers can directly influence the biosynthesis of key bioactive compounds, leading to improved medicinal properties (Jannink et al., 2010; Heslot et al., 2015; Crossa et al., 2017).

The use of genetic modification and CRISPR/Cas9 technology in plant breeding raises several ethical and regulatory challenges. Concerns about the safety and environmental impact of genetically modified organisms (GMOs) necessitate stringent regulatory frameworks to ensure responsible use. Additionally, ethical considerations regarding the manipulation of genetic material must be addressed, including issues related to biodiversity, ecological balance, and potential long-term effects. Navigating these challenges requires a balanced approach that considers both the potential benefits and risks associated with genetic modification technologies (Heslot et al., 2012; Merrick et al., 2022).

4.3 Biotechnology in *Lonicera japonica* breeding

In vitro culture techniques are essential biotechnological tools in the breeding of *Lonicera japonica*. These techniques involve the cultivation of plant cells, tissues, or organs under controlled conditions, allowing for the rapid propagation of plants with desirable traits. In vitro culture can be used for clonal propagation, somatic embryogenesis, and the production of genetically uniform plants. This method is particularly useful for preserving and multiplying elite genotypes with enhanced medicinal properties, ensuring a consistent supply of high-quality plant material for further breeding and research (Jannink et al., 2010; Crossa et al., 2017; Jeon et al., 2023).

Transgenic approaches involve the introduction of foreign genes into the *Lonicera japonica* genome to confer new traits or enhance existing ones. This method can be used to improve various traits, including resistance to pests and diseases, tolerance to abiotic stresses, and the production of specific bioactive compounds. By incorporating genes from other species or synthetic constructs, researchers can create transgenic lines with superior medicinal properties. These approaches, combined with traditional breeding methods, can significantly accelerate the development of *Lonicera japonica* varieties with enhanced medicinal traits (Xu et al., 2019; Merrick et al., 2022).

5 Role of Environmental Factors

5.1 Influence of climate on medicinal properties

Climate plays a significant role in determining the medicinal properties of *Lonicera japonica*. Various environmental stresses, such as salt stress, can influence the plant's morphology, physiology, and the accumulation of bioactive constituents. For instance, under salt stress, *Lonicera japonica* exhibited changes in growth, photosynthetic pigments, osmolytes, lipid peroxidation, and antioxidant enzyme activities. These changes were



correlated with the accumulation of phenolic acids, which are known to reduce oxidative damage, thereby enhancing the medicinal quality of the plant (Cai et al., 2021). Additionally, the electric field has been shown to enhance cadmium accumulation and photosynthesis in *Lonicera japonica*, suggesting that controlled environmental conditions can optimize the plant's growth and medicinal properties (Liu et al., 2022).

5.2 Soil health and nutrient management

Soil health and nutrient management are critical for the optimal growth and medicinal quality of *Lonicera japonica*. Planting *Lonicera japonica* in gravel-mulched land significantly improved soil properties, including increased concentrations of soil organic carbon, available nitrogen, phosphorus, and potassium. Enzyme activities such as urease, phosphatase, and catalase were also enhanced, leading to improved soil bacterial community diversity. These improvements in soil health directly contribute to the better growth and medicinal quality of *Lonicera japonica* (Wang et al., 2023). Furthermore, the presence of arbuscular mycorrhizal fungi, such as *Glomus versiforme* and *Rhizophagus intraradices*, can enhance nutrient uptake, reduce cadmium toxicity, and improve antioxidant activities, thereby promoting healthier plant growth and higher medicinal value (Jiang et al., 2016).

5.3 Biotic factors influencing Lonicera japonica

Biotic factors, including microbial interactions and plant-microbe symbiosis, significantly influence the growth and medicinal properties of *Lonicera japonica*. The symbiotic relationship with arbuscular mycorrhizal fungi has been shown to alleviate cadmium toxicity and improve nutrient uptake, which in turn enhances the plant's growth and medicinal properties (Jiang et al., 2016). Additionally, the diversity of soil bacterial communities, influenced by the cultivation of *Lonicera japonica*, plays a crucial role in maintaining soil health and promoting plant growth. The presence of beneficial bacteria such as *Firmicutes*, *Proteobacteria*, and *Bacteroidetes* can enhance soil nutrient availability and enzyme activities, further supporting the medicinal quality of the plant (Wang et al., 2023).

In summary, environmental factors such as climate, soil health, and biotic interactions play a pivotal role in determining the medicinal properties of *Lonicera japonica*. Understanding and managing these factors can lead to improved cultivation practices and enhanced medicinal quality of this valuable plant.

6 Case Study

6.1 Successful breeding programs in enhancing *Lonicera japonica*

Several breeding programs have successfully enhanced the medicinal properties of *Lonicera japonica*. One notable example is the breeding of the elite variety 'Yujin2', which has a strong aroma and is used in functional drinks and cosmetics. This variety was developed through selective breeding and has been shown to have a significantly higher concentration of terpenoids, tryptophan derivatives, and fatty acid derivatives compared to other varieties like 'Fengjin1' (Figure 1) (Li et al., 2022). The integrated volatile metabolomic and transcriptomic analysis revealed that the biosynthetic pathways of these compounds were major contributors to the stronger aroma of 'Yujin2', providing insights into the metabolic mechanisms and molecular basis of floral scents in *Lonicera japonica* (Figure 2) (Li et al., 2022).

6.2 Field applications of high-medicinal-value cultivars

High-medicinal-value cultivars of *Lonicera japonica* have been applied in various fields, including medicine, cosmetics, and environmental remediation. For instance, the polysaccharides extracted from *Lonicera japonica* have been used to develop functional products such as lozenges, soy sauce, and toothpaste, highlighting their broad-spectrum antibacterial activity and therapeutic effects on various infectious diseases (Yang et al., 2023). Additionally, the leaves and stems of *Lonicera japonica*, which have similar chemical components and anti-inflammatory properties as the flower buds, have been proposed as alternative or supplementary sources for medicinal use (Li et al., 2020). Furthermore, the application of electric fields has been shown to enhance cadmium accumulation and photosynthesis in *Lonicera japonica*, making it a promising candidate for environmental remediation (Liu et al., 2022).



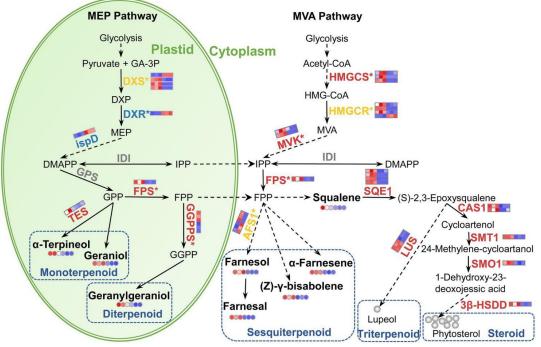


Figure 1 Schematic presentation of terpenoid biosynthetic pathway in LJFs of 'Yujin2' compared to 'Fengjin1' (Adopted from Li et al., 2022)

Image caption: the upregulated, downregulated, mix-regulated, and unchanged genes (bold fonts) and metabolites (small circles) in 'Yujin2' are represented in red, blue, yellow, and gray, respectively. The first three and the latter three squares of a bar represent the normalized abundance values of DEGs or DAVs from 'Yujin2' and 'Fengjin1', respectively. Red and blue colors reflect high and low expression levels, respectively. The asterisk followed by the gene name indicate that the gene expression was validated by qRT-PCR. The solid line, dashed line, and dotted line indicate a single-step reaction, a multi-step reaction, and the movement of substances, respectively (Adopted from Li et al., 2022)

6.3 Lessons learned from case studies and future prospects

The case studies on breeding and field applications of *Lonicera japonica* provide several valuable lessons and future prospects. Firstly, the success of breeding programs like 'Yujin2' underscores the importance of integrating metabolomic and transcriptomic analyses to understand the regulatory mechanisms of key medicinal compounds (Li et al., 2022). Secondly, the utilization of all aerial parts of *Lonicera japonica*, including leaves and stems, can maximize the medicinal value of the plant and provide alternative sources for traditional medicine (Cai et al., 2020; Li et al., 2020). Thirdly, the application of electric fields to enhance the growth and hyperaccumulation abilities of *Lonicera japonica* demonstrates the potential for innovative approaches in environmental remediation (Liu et al., 2022).

Future research should focus on further optimizing breeding strategies to enhance specific medicinal properties, exploring the full potential of different plant parts, and developing new applications for high-medicinal-value cultivars. Additionally, the integration of advanced genomic and metabolomic techniques will be crucial in identifying and manipulating key genes and pathways involved in the biosynthesis of medicinal compounds (Ran et al., 2023; Yin et al., 2023). By building on these lessons and prospects, the medicinal value of *Lonicera japonica* can be further enhanced and diversified for various applications.

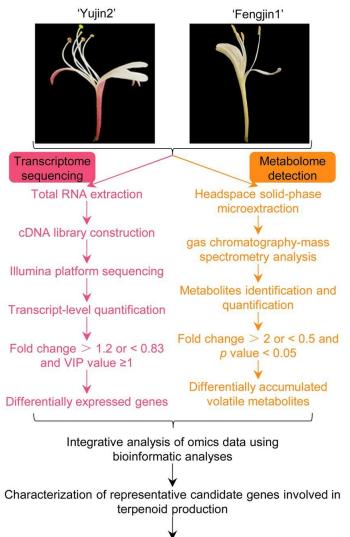
7 Challenges and Future Directions

7.1 Current limitations in Lonicera japonica breeding

Breeding *Lonicera japonica*, a plant with significant medicinal and economic value, faces several challenges. One major limitation is the incomplete understanding of the regulatory mechanisms underlying its desirable traits, such as floral scent and bioactive compound production. For instance, while studies have identified key metabolites and genes involved in the biosynthesis of floral scents, the precise regulatory networks remain largely unknown (Li et



al., 2022). Additionally, the quality and yield of *L. japonica* are significantly affected by environmental stressors, such as salt stress, which complicates breeding efforts aimed at enhancing these traits (Cai et al., 2021). Another challenge is the limited genetic diversity available for breeding programs, which restricts the potential for developing new varieties with improved characteristics.



The mechanisms of floral scent regulation in Lonicera japonica

Figure 2 Overview of the metabolomics and transcriptomics workflow (Adopted from Li et al., 2022)

Image caption: *Lonicera japonica* flowers (LJFs) at the silver flowering stage of two contrasting varieties of *L. japonica*, 'Yujin2' and 'Fengjin1' were collected. Headspace solid-phase microextraction (HS-SPME) coupled with gas chromatography-mass spectrometry (GC-MS) and transcriptomics analysis were performed for volatile organic compound (VOC) profiling and global gene expression patterns, respectively. Integrated metabolomics and transcriptomics analysis serves to elucidate the regulatory mechanism of floral scents of LJFs by bioinformatic analyses (Adopted from Li et al., 2022)

7.2 Potential breakthroughs in breeding strategies

Recent advancements in omics technologies, such as metabolomics and transcriptomics, offer promising avenues for overcoming some of the current limitations in *L. japonica* breeding. Integrated analyses of volatile metabolites and gene expression have provided insights into the metabolic pathways and regulatory genes responsible for floral scent production, which could be targeted in future breeding programs to develop more fragrant varieties (Li et al., 2022). Polyploid breeding is another promising strategy that has been explored to enhance the yield and quality of *L. japonica*. This approach involves inducing polyploidy to create plants with multiple sets of chromosomes, which can result in increased biomass and improved stress tolerance. Additionally, the application of advanced statistical methods, such as partial least squares discriminant analysis (PLS-DA), can help identify



key chemical markers and differentiate between various plant parts, aiding in the selection of superior varieties (Cai et al., 2020).

7.3 Future directions for research and application

Future research should focus on elucidating the complex regulatory networks governing the biosynthesis of bioactive compounds and floral scents in *L. japonica*. This could involve the use of advanced genomic and transcriptomic techniques to identify key regulatory genes and pathways (Li et al., 2022). Another important direction is the development of stress-tolerant varieties through genetic and biotechnological approaches, such as CRISPR/Cas9-mediated gene editing, to enhance the plant's resilience to environmental stressors like salt stress (Cai et al., 2021). Additionally, expanding the genetic diversity available for breeding programs through the collection and characterization of wild *L. japonica* populations could provide new genetic resources for developing improved varieties.

In terms of application, there is significant potential for the use of *L. japonica* in various industries, including medicine, cosmetics, and food. For instance, the bioactive polysaccharides isolated from *L. japonica* have shown a wide range of health benefits, such as anti-inflammatory and antioxidant properties, which could be harnessed in the development of new therapeutic products (Yang et al., 2023). Moreover, the plant's ability to improve soil properties and microbial diversity suggests its potential use in ecological restoration projects, particularly in degraded environments like gravel-mulched lands (Wang et al., 2023). Overall, a multidisciplinary approach combining advanced breeding techniques, genetic research, and practical applications will be essential for fully realizing the potential of *L. japonica*.

8 Concluding Remarks

The research on *Lonicera japonica* has revealed significant insights into its medicinal properties and the potential for breeding strategies to enhance these properties. Studies have identified numerous metabolites and genes involved in the biosynthesis of terpenoids, tryptophan derivatives, and fatty acid derivatives, which contribute to the floral scent of *Lonicera japonica*. This knowledge is crucial for breeding more fragrant varieties for ornamental and functional uses. Different parts of *Lonicera japonica*, including flower buds, leaves, and stems, have been shown to contain similar chemical components with significant anti-inflammatory properties. This suggests that leaves and stems could serve as alternative medicinal resources. Polysaccharides extracted from *Lonicera japonica* exhibit a wide range of health benefits, including anti-diabetic, anti-inflammatory, and immunoregulatory effects. These findings highlight the potential for developing functional products from these polysaccharides. The stage at which *Lonicera japonica* is harvested significantly affects the accumulation of phenylpropanoid metabolites, which are important for its medicinal properties. This information can guide optimal harvesting practices to maximize medicinal value.

The findings from these studies have several implications for future breeding efforts aimed at enhancing the medicinal properties of *Lonicera japonica*. By understanding the metabolic pathways and genes involved in floral scent production, breeders can develop varieties with enhanced aromatic properties, which are desirable for both ornamental and functional uses. The discovery that leaves and stems have similar bioactive compounds as flower buds opens up new avenues for utilizing these parts, which are often considered less valuable. This can lead to more sustainable and cost-effective use of the plant. Knowledge about the optimal harvesting stages for maximum phenylpropanoid accumulation can be used to improve the quality and efficacy of *Lonicera japonica* as a medicinal plant. The diverse health benefits of *Lonicera japonica* polysaccharides suggest that future breeding efforts could focus on enhancing the yield and quality of these compounds, leading to the development of new functional foods and medicinal products.

Lonicera japonica holds immense potential as a medicinal plant, with a wide range of bioactive compounds that offer various health benefits. The integration of metabolomic, transcriptomic, and genomic analyses has provided a deeper understanding of the plant's chemical composition and the underlying mechanisms that contribute to its medicinal properties. Future breeding efforts, guided by these insights, can lead to the development of superior



varieties with enhanced medicinal qualities, thereby expanding the applications of *Lonicera japonica* in traditional medicine, functional foods, and other industries. Continued research and innovation in this field will ensure that the full potential of this valuable plant is realized.

♦------

Acknowledgments

We are grateful to Julie Luo for critically reading the manuscript and providing valuable feedback that improved the clarity of the text. We also appreciate two anonymous peer reviewers who contributed to the evaluation 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.

References

- Cai Z., Liao H., Wang C., Chen J., Tan M., Mei Y., Wei L., Chen H., Yang R., and Liu X., 2020, A comprehensive study of the aerial parts of *Lonicera japonica* Thunb. based on metabolite profiling coupled with PLS-DA, Phytochemical Analysis, 31(6): 786-800. https://doi.org/10.1002/pca.2943
- Cai Z., Liu X., Chen H., Yang R., Chen J., Zou L., Wang C., Chen J., Tan M., Mei Y., and Wei L., 2021, Variations in morphology, physiology, and multiple bioactive constituents of *Lonicerae Japonicae* Flos under salt stress, Scientific Reports, 11: 3939. <u>https://doi.org/10.1038/s41598-021-83566-6</u>
- Crossa J., Pérez-Rodríguez P., Cuevas J., Montesinos-López O., Jarquín D., Campos G., Burgueño J., González-Camacho J., Pérez-Elizalde S., Beyene Y., Dreisigacker S., Singh R., Zhang X., Gowda M., Roorkiwal M., Rutkoski J., and Varshney R., 2017, Genomic selection in plant breeding: methods, models, and perspectives, Trends in Plant Science, 22(11): 961-975. <u>https://doi.org/10.1016/j.tplants.2017.08.011</u>
- Dai X., Li X., Yang B., Guo C., Jiang C., and Niu D., 2023, First report of leaf rot on *Lonicera japonica* caused by *Rhizopus arrhizus* in China, Plant Disease, 107(9): 2873.

https://doi.org/10.1094/PDIS-05-23-0964-PDN

- Gao B., Zhu L., Liu Z., Li Y., He X., Wu X., Pehrsson P., Sun J., Xie Z., Slavin M., and Yu L., 2023, Chemical composition of honeysuckle (*Lonicerae japonicae*) extracts and their potential in inhibiting the SARS-CoV-2 spike protein and ACE2 binding, suppressing ACE2, and scavenging radicals, Journal of Agricultural and Food Chemistry, 71(15): 6133-6143. https://doi.org/10.1021/acs.jafc.3c00584
- Ge L., Li J., Wan H., Zhang K., Wu W., Zou X., Wu S., Zhou B., Tian J., and Zeng X., 2018, Novel flavonoids from *Lonicera japonica* flower buds and validation of their anti-hepatoma and hepatoprotective activity *in vitro* studies, Industrial Crops and Products, 125: 114-122. https://doi.org/10.1016/J.INDCROP.2018.08.073
- Heslot N., Jannink J., and Sorrells M., 2015, Perspectives for genomic selection applications and research in plants, Crop Science, 55(1): 1-12. https://doi.org/10.2135/CROPSCI2014.03.0249
- Heslot N., Yang H., Sorrells M., and Jannink J., 2012, Genomic selection in plant breeding: a comparison of models, Crop Science, 52(1): 146-160. https://doi.org/10.2135/CROPSCI2011.06.0297
- Jannink J., Lorenz A., and Iwata H., 2010, Genomic selection in plant breeding: from theory to practice, Briefings in Functional Genomics, 9(2): 166-177. https://doi.org/10.1093/bfgp/elq001
- Jeon D., Kang Y., Lee S., Choi S., Sung Y., Lee T., and Kim C., 2023, Digitalizing breeding in plants: a new trend of next-generation breeding based on genomic prediction, Frontiers in Plant Science, 14: 1092584. <u>https://doi.org/10.3389/fpls.2023.1092584</u>
- Jiang Q., Zhuo F., Long S., Zhao H., Yang D., Ye Z., Li S., and Jing Y., 2016, Can arbuscular mycorrhizal fungi reduce Cd uptake and alleviate Cd toxicity of Lonicera japonica grown in Cd-added soils? Scientific Reports, 6: 21805. https://doi.org/10.1038/srep21805
- Li J., Chang X., Huang Q., Liu P., Zhao X., Li F., Wang Y., and Chang C., 2023, Construction of SNP fingerprint and population genetic analysis of honeysuckle germplasm resources in China, Frontiers in Plant Science, 14: 1080691. <u>https://doi.org/10.3389/fpls.2023.1080691</u>
- Li J., Yu X., Shan Q., Shi Z., Li J., Zhao X., Chang C., and Yu J., 2022, Integrated volatile metabolomic and transcriptomic analysis provides insights into the regulation of floral scents between two contrasting varieties of *Lonicera japonica*, Frontiers in Plant Science, 13: 989036. <u>https://doi.org/10.3389/fpls.2022.989036</u>
- Li R., Kuang X., Wang W., Wan C., and Li W., 2020, Comparison of the chemical constitution and bioactivity among different parts of *Lonicera japonica* Thunb., Journal of the Science of Food and Agriculture, 100(2): 614-622. https://doi.org/10.1002/jsfa.10056



- Liu Z., Chen Q., Lin M., Chen M., Zhao C., Lu Q., and Meng X., 2022, Electric field-enhanced cadmium accumulation and photosynthesis in a woody ornamental hyperaccumulator- *Lonicera japonica* Thunb., Plants, 11(8): 1040. <u>https://doi.org/10.3390/plants11081040</u>
- Merrick L., Herr A., Sandhu K., Lozada D., and Carter A., 2022, Optimizing plant breeding programs for genomic selection, Agronomy, 12: 714. https://doi.org/10.20944/preprints202202.0048.v1
- Peng X., Li W., Wang W., and Bai G., 2010, Identification of *Lonicera japonica* by PCR-RFLP and allele-specific diagnostic PCR based on sequences of internal transcribed spacer regions, Planta Medica, 76(5): 497-499. <u>https://doi.org/10.1055/s-0029-1186235</u>
- Pu X., Li Z., Tian Y., Gao R., Hao L., Hu Y., He C., Sun W., Xu M., Peters R., Peer Y., Xu Z., and Song J., 2020, The honeysuckle genome provides insight into the molecular mechanism of carotenoid metabolism underlying dynamic flower coloration, The New Phytologist, 227(3): 930-943. https://doi.org/10.1111/nph.16552
- Qi X., Fang H., Chen Z., Liu Z., Yu X., and Liang C., 2019, Ectopic expression of a R2R3-MYB transcription factor gene LjaMYB12 from Lonicera japonica increases flavonoid accumulation in Arabidopsis thaliana, International Journal of Molecular Sciences, 20(18): 4494. <u>https://doi.org/10.3390/ijms20184494</u>
- Ran Z., Ding W., Yu H., Zhang L., Fang L., Guo L., and Zhou J., 2023, Combinatorial transcriptomics and metabolomics analysis reveals the effects of the harvesting stages on the accumulation of phenylpropanoid metabolites in *Lonicera japonica*, Functional Plant Biology, 50(10): 808-820. <u>https://doi.org/10.1071/FP23033</u>
- Shang X., Pan H., Li M., Miao X., and Ding H., 2011, Lonicera japonica Thunb.: ethnopharmacology, phytochemistry and pharmacology of an important traditional Chinese medicine, Journal of Ethnopharmacology, 138(1): 1-21. <u>https://doi.org/10.1016/j.jep.2011.08.016</u>
- Wang H., Li Y., Wang S., Kong D., Sahu S., Bai M., Li H., Li L., Xu Y., Liang H., Liu H., and Wu H., 2020, Comparative transcriptomic analyses of chlorogenic acid and luteolosides biosynthesis pathways at different flowering stages of diploid and tetraploid *Lonicera japonica*, PeerJ, 8: e8690. <u>https://doi.org/10.7717/peerj.8690</u>
- Wang X., Ma B., Liu H., Bao Y., Li M., McLaughlin N., and Guo L., 2023, Improvement in gravel-mulched land soil nutrient and bacterial community diversity with *Lonicera japonica*, Frontiers in Microbiology, 14: 1225503. https://doi.org/10.3389/fmicb.2023.1225503
- Wang X., Wang X., Xu Y., Hu Z., and Xu C., 2018, Genomic selection methods for crop improvement: current status and prospects, The Crop Journal, 6(4): 330-340.

https://doi.org/10.1016/J.CJ.2018.03.001

- Xu Y., Liu X., Fu J., Wang H., Wang J., Huang C., Prasanna B., Olsen M., Wang G., and Zhang A., 2019, Enhancing genetic gain through genomic selection: from livestock to plants, Plant Communications, 1(1): 100005. <u>https://doi.org/10.1016/j.xplc.2019.100005</u>
- Yan K., Cui M., Zhao S., Chen X., and Tang X., 2016, Salinity stress is beneficial to the accumulation of chlorogenic acids in honeysuckle (*Lonicera japonica* Thunb.), Frontiers in Plant Science, 7: 1563. <u>https://doi.org/10.3389/fpls.2016.01563</u>
- Yang X., Yu A., Hu W., Zhang Z., Ruan Y., Kuang H., and Wang M., 2023, Extraction, purification, structural characteristics, health benefits, and application of the polysaccharides from *Lonicera japonica* Thunb.: a review, Molecules, 28(12): 4828. <u>https://doi.org/10.3390/molecules28124828</u>
- Yeh Y., Doan L., Huang Z., Chu L., Shi T., Lee Y., Wu C., Lin C., Chiang S., Liu H., Chuang T., Ping Y., Liu H., and Huang C., 2022, Honeysuckle (Lonicera japonica) and Huangqi (Astragalus membranaceus) suppress SARS-CoV-2 entry and COVID-19 related cytokine storm in vitro, Frontiers in Pharmacology, 12: 765553.

https://doi.org/10.3389/fphar.2021.765553

- Yin X., Xiang Y., Huang F., Chen Y., Ding H., Du J., Chen X., Wang X., Wei X., Cai Y., Gao W., Guo D., Alolga R., Kan X., Zhang B., Alejo-Jacuinde G., Li P., Tran L., Herrera-Estrella L., Lu X., and Qi L., 2023, Comparative genomics of the medicinal plants *Lonicera macranthoides* and *L. japonica* provides insight into genus genome evolution and hederagenin-based saponin biosynthesis, Plant Biotechnology Journal, 21(11): 2209-2223. https://doi.org/10.1111/pbi.14123
- Yuan Y., Song L., Li M., Liu G., Chu Y., Ma L., Zhou Y., Wang X., Gao W., Qin S., Yu J., Wang X., and Huang L., 2012, Genetic variation and metabolic pathway intricacy govern the active compound content and quality of the Chinese medicinal plant *Lonicera japonica* Thunb., BMC Genomics, 13: 195. <u>https://doi.org/10.1186/1471-2164-13-195</u>



Disclaimer/Publisher's Note

The statements, opinions, and data contained in all publications are solely those of the individual authors and contributors and do not represent the views of the publishing house and/or its editors. The publisher and/or its editors disclaim all responsibility for any harm or damage to persons or property that may result from the application of ideas, methods, instructions, or products discussed in the content. Publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.