Medicinal Plant Research 2024, Vol.14, No.2, 71-84
http://hortherbpublisher.com/index.php/mpr

Feature Review **Open Access**

Unveiling the Genome of *Chrysanthemum morifolium*: Adaptive Evolution and Medicinal Value

Lanjie Xu, Yongliang Yu, Zhengwei Tan, Chunming Li, Qing Yang, Hongqi Yang, Xiaoyu Su, Yao Sun, Huizhen Liang
Institute of Chinese Herbal Medicine, He'nan Academy of Agricultural Sciences, Zhengzhou, 450002, Henan, China
Corresponding author: lhzh66666@163.com

Medicinal Plant Research, 2024, Vol.14, No.2 doi: 10.5376/mpr.2024.14.0006
Received: 08 Feb., 2024
Accepted: 12 Mar., 2024
Published: 25 Mar., 2024

Preferred citation for this article:
Xu L.J., Yu Y.L., Tan Z.W., Li C.M., Yang Q., Yang H.Q., Su X.Y., Sun Y., and Liang H.Z., 2024, Unveiling the genome of *Chrysanthemum morifolium*: adaptive evolution and medicinal value, Medicinal Plant Research, 14(2): 71-84 (doi: 10.5376/mpr.2024.14.0006)

Abstract This study provides a comprehensive analysis of the genomics of *Chrysanthemum morifolium*, covering its genetic linkage map construction, whole-genome assembly, and transcriptomics research findings. It highlights key genes and regulatory networks involved in *Chrysanthemum morifolium* development and the accumulation of medicinal components. The study explores the application value of genomics research in improving *Chrysanthemum morifolium* quality and commercial value. High-throughput sequencing technology has identified key genes controlling the biosynthesis of compounds such as flavonoids, which are crucial for enhancing the plant's medicinal activity. Functional molecular markers accelerate the process of targeted breeding. Research in whole-genome and comparative genomics has elucidated the cultivation and evolutionary history of *Chrysanthemum morifolium*. Genetic linkage maps have identified QTLs for inflorescence and leaf traits, promoting marker-assisted selection in breeding programs. Polyploidy and DNA methylation contribute to its adaptability and resilience. The study analyzes the regulatory mechanisms of *Chrysanthemum morifolium*'s active medicinal components, such as flavonoids, phenolic acids, and terpenoids, and their roles in therapeutic effects. The study is expected to provide a road map for future research and applications in traditional medicine and modern healthcare, combining genomic data with traditional breeding techniques to accelerate the development of new varieties with strong disease resistance, broad adaptability, and high medicinal efficacy.

Keywords *Chrysanthemum morifolium*; Genomic research; Genetic map; Adaptive evolution; Medicinal value

1 Introduction

Chrysanthemum morifolium, a perennial herbaceous plant of *Chrysanthemum* genus in the family of Asteraceae, is not only a traditional famous flower in China but also one of the world's four major cut flowers. Native to China, *Chrysanthemum morifolium* has been cultivated for over 2,000 years, with more than 3,000 recorded varieties. There are 780 medicinal varieties across approximately 155 genera. The Asteraceae family is one of the largest plant families encompassing approximately 24,000~35,000 species (Song et al., 2018). Based on its applications, *Chrysanthemum morifolium* can be categorized into medicinal, ornamental, tea, and edible uses. It is rich in flavonoids, triterpenoids, and volatile oils, and possesses anti-inflammatory, anti-oxidative, and anti-bacterial properties (Pan et al., 2023). *Chrysanthemum morifolium* is an important economic crop with a wide cultivation range and high economic value due to its medicinal properties. The 2020 edition of the Chinese Pharmacopoeia includes “Boju”, “Gongju”, “Chuju”, “Huai Ju”, and “Hangju”. Although “Jiju”, “Qiju”, “Chuanju”, and “Fubaiju” are not listed in the Chinese Pharmacopoeia, they are still commonly found in the market. Among them, Hangbaiju (*Chrysanthemum morifolium* 'Hangbaiju') is one of the Source Plants of “Zhe Ba Wei (Eight Genuine Herbs of Zhejiang)” (Pan et al., 2023).

Chrysanthemum morifolium is a unique plant with medicinal properties, playing a crucial role in the development of human civilization and society, much like staple crops. With the advent of high-throughput sequencing technology and the development of genomics focused on medicinal plants, numerous genes involved in the synthesis and regulation of secondary metabolites have been identified. These genes provide genetic elements for the biosynthesis of compounds with various effects, enabling the biosynthesis of an increasing number of medicinal monomers. Sequencing and analysis of the complete chloroplast genomes of different *Chrysanthemum* *morifolium* varieties have revealed important phylogenetic relationships and evolutionary patterns of the plant (Tyagi et al., 2019; Xia et al., 2021a). Additionally, transcriptomic analyses have identified differentially expressed genes that play crucial roles in the development of *Chrysanthemum morifolium* and the biosynthesis of medicinal compounds (Ding et al., 2020; Liu et al., 2022). These superior genes can be used to enhance the ornamental value and medicinal quality of *Chrysanthemum morifolium*, thereby accelerating breeding efficiency.

This study comprehensively reviews the current state of *Chrysanthemum morifolium* genomics research, including the construction of genetic linkage maps, whole-genome assembly, and transcriptomics studies. It highlights key genes and regulatory networks involved in *Chrysanthemum morifolium* development and the accumulation of medicinal components, exploring the application value of genomics research in improving the quality and commercial value of *Chrysanthemum morifolium*. By integrating existing genomic research findings and synthesizing discoveries from multiple studies, the study elucidates the adaptability and evolutionary patterns of *Chrysanthemum morifolium*, enhancing its medicinal potential.

2 Botanical Characteristics of *Chrysanthemum morifolium*

2.1 Morphological description

Chrysanthemum morifoliumis is a perennial herbaceous plant of *Chrysanthemum* genus in the family of Asteraceae. As a highly heterozygous cultivated group, *Chrysanthemum morifoliumis* exhibits a complex genetic background and rich genetic diversity. Different varieties display a wide range of morphological traits, and even the same variety can show significant phenotypic differences under different cultivation conditions. The main classification criteria for *Chrysanthemum morifoliumis* varieties include inflorescence diameter, ray flower morphology, capitulum morphology, leaf morphology, flower color, and flowering period. For example, based on the flowering period, *Chrysanthemum morifoliumis* varieties can be classified into summer-flowering (June to September), autumn-flowering (October to November), winter-flowering (December to the following January), and year-round flowering. According to the diameter of the capitulum, they are divided into large-flowered types (greater than 6 cm) and small-flowered types (less than 6 cm), which are further classified into ray floret and disc floret types (Chen et al., 2009). The tubular petals in *Chrysanthemum morifoliumis* mainly arise from variations in disc florets and belong to the disc floret type. Compared to variations in the ray floret type, these are simpler and easier to distinguish. The leaves are shallowly serrated, and traits such as the number of leaf lobes, leaf width, leaf length, leaf area, and petiole length vary significantly among different varieties. *Chrysanthemum morifoliumis* exhibits a rich diversity of flower colors, including white, yellow, pink, red, and various intermediate shades. The capitulum is composed of numerous small florets, whose arrangement and size vary by variety (Shao et al., 2011). The plant's height and branching patterns also show considerable variability, enhancing its ornamental value (Sasaki et al., 2017).

2.2 Habitat and geographical distribution

Chrysanthemum morifoliumis is native to East Asia, particularly China, where it has been cultivated for over 2,000 years (Hao et al., 2022). *Chrysanthemum morifoliumis* is a short-day plant that thrives in warm climates and sunny environments, being highly sensitive to the length of daylight. It requires less than 10 hours of light per day to flower normally. *Chrysanthemum morifoliumis* prefers fertile soil rich in humus and well-drained sandy loam. It is relatively drought-tolerant, cold-resistant, but susceptible to waterlogging, and should not be continuously cultivated in the same soil. *Chrysanthemum morifoliumis* originated in China and belongs to the *Chrysanthemum* genus within the Anthemideae tribe of the Artemisiinae subtribe in the Asteraceae family. Globally, the Anthemideae tribe comprises approximately 111 genera and 1,800 species (Yang et al., 2022; Ye et al., 2022), with most species distributed in Central Asia, around the Mediterranean, and in southern Africa. While the genus *Chrysanthemum* is mainly distributed in East Asia, the closely related Ajania Poljak is mainly distributed in northwest China and other regions, the closely related genera such as *Brachanthemum* and *Kaschgaria* are mainly distributed in deserts, and the closely related monotypic genus *Stilpnolepis centiflora* is predominantly found in sand dunes. The geographical distribution of *Chrysanthemum morifolium* is closely linked to its cultivation for both ornamental and medicinal purposes. Different cultivars have been developed in various regions, leading to a rich diversity in morphological and chemical traits (Figure 1) (Feng et al., 2016b; Hao et al., 2022).

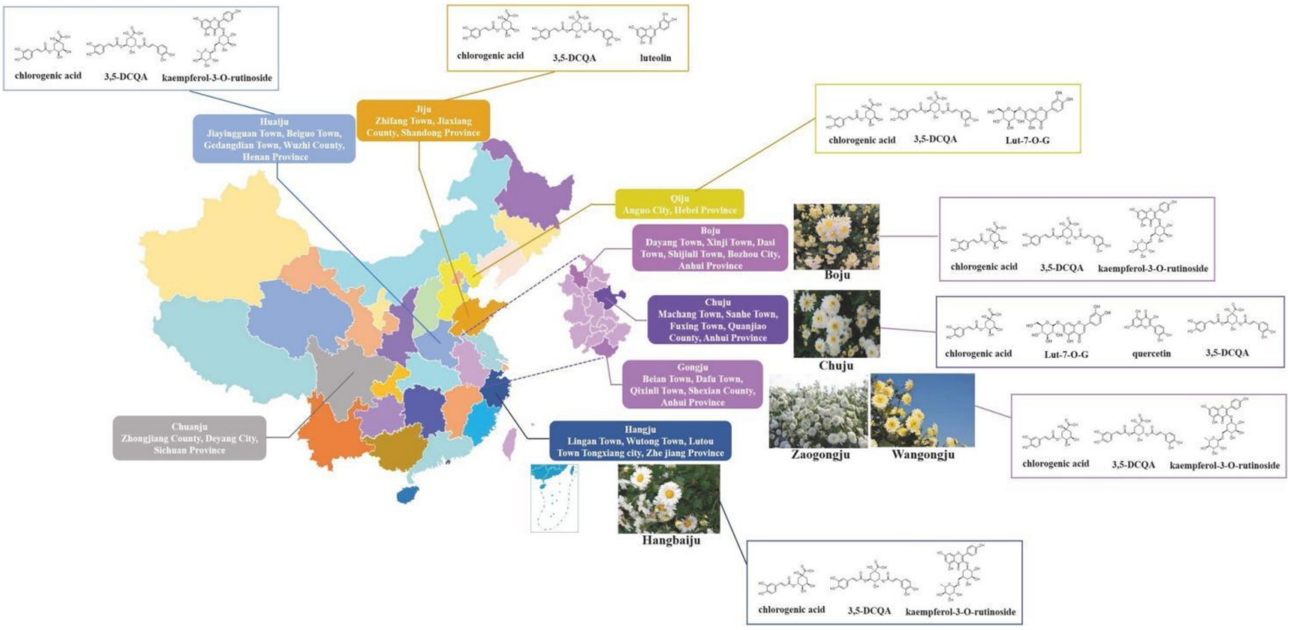


Figure 1 Geographical distribution, chemical and morphological characteristics of representative CM cultivars (Adopted from Hao et al., 2022)

Image caption: The medicinal quality (Q) markers of each cultivar are shown: Boju, Huaiju, Gongju and Hangju: chlorogenic acid, 3,5-DCQA, and kaempferol-3-O-rutinoside (Lu et al., 2022b); Chuju: chlorogenic acid, Lut-7-O-G, quercetin, 3,5-DCQA (Yang et al., 2018); Qiju: chlorogenic acid, 3,5-DCQA, and Lut-7-O-G (Peng et al., 2019); Jiju: chlorogenic acid, luteolin and 3,5-DCQA (Kang et al., 2022); The Q-marker of Chuanju of Zhongjiang, Sichuan Province is not reported (Adopted from Hao et al., 2022)

2.3 Application fields

Chrysanthemum morifolium has various uses and benefits, with widespread applications in the food, pharmaceutical, and beverage industries. Currently, products such as chrysanthemum tea, chrysanthemum wine, chrysanthemum pastries, and chrysanthemum cosmetics have been developed. Chrysanthemum tea refers to chrysanthemums used for brewing tea, known for their cooling properties that can relieve cold symptoms and improve vision (Zou et al., 2021; Hao et al., 2022). Edible chrysanthemums are those that can be consumed, containing high levels of proteins, fats, carbohydrates, vitamins, and minerals. They can be eaten fresh or dried, used in soups, stir-fries, fillings, or as food ingredients (Tang et al., 2024). Medicinal chrysanthemums contain many bioactive compounds, such as flavonoids, phenolic acids, and essential oils, which give them medicinal properties (Chen et al., 2020; Youssef et al., 2020). They are used to treat various ailments, including respiratory issues, hypertension, and inflammation (Hao et al., 2022; Ojha et al., 2023). Ornamental chrysanthemums come in numerous varieties with rich colors and beautiful flower shapes, displaying a wide range of forms. Depending on the cultivation method, they can be divided into four main categories: potted chrysanthemums, ground cover chrysanthemums, cut chrysanthemums, and styled chrysanthemums (art chrysanthemums). Due to their diverse colors and forms, and relatively easy cultivation and maintenance, they are popular in both professional and amateur horticulture (Sasaki et al., 2017).

3 Genomic Research in *Chrysanthemum morifolium*

3.1 History of genomic studies in chrysanthemums

In recent years, significant progress has been made in the genomics research of *Chrysanthemum morifolium*. DNA molecular markers have been widely used to construct genetic linkage maps of Chrysanthemum parents, but the average genetic distance between markers remains large, and the maps contain relatively few markers. Zhang et al. (2011) used RAPD markers to construct genetic maps for the varieties “Yuhualuoying” and “Aoyunhanxiao”, with 333 and 342 marker loci respectively, consisting of 57 and 55 linkage groups. The cumulative map lengths were 1,912.8 cM and 1,887.9 cM, with genome coverage rates of 65% and 66%, respectively. Peng et al. (2015) employed SSR and SRAP marker techniques to construct genetic maps for the cut flower Chrysanthemum variety

“QX-145” (mother) and “Nannong Yinshan” (father), containing 109 and 125 marker loci, respectively, and comprising 25 and 21 linkage groups. The cumulative map lengths were 1,465.6 cM and 1,972.7 cM. These early works laid a theoretical foundation for deciphering the genetic structure of *Chrysanthemum morifolium* and accelerated the development of marker-assisted breeding programs (Zhang et al., 2010). The advent of high-throughput sequencing technology has taken Chrysanthemum genomics research to a new level, providing crucial references for understanding the phenotypic characteristics and the mechanisms of medicinal compound synthesis in *Chrysanthemum morifolium* (Liu et al., 2015; Sasaki et al., 2017).

In 2017, the Chrysanthemum Whole Genome Project, jointly initiated by Institute of Chinese Materia Medica, China Academy of Chinese Medical Sciences and the Amway Plant Research and Development Center, made significant progress. The joint team utilized nanopore sequencing technology to overcome the challenges of sequencing complex higher plant genomes, completing the whole genome sequencing of the medicinal Chrysanthemum species for the first time. They also accomplished the full-length transcriptome genetic information extraction of Hangbaiju (*Chrysanthemum morifolium* 'Hangbaiju'). Subsequently, the genomes of *Chrysanthemum seticuspe* and *Chrysanthemum nankingense* were also assembled (Song et al., 2018; Hirakawa et al., 2019). In 2023, the team led by Chen Fadi from Nanjing Agricultural University decoded the genome of the hexaploid cultivated *Chrysanthemum morifolium*, reporting the world's first segmental allopolyploid genome. This research delved into the origin and breeding history of cultivated *Chrysanthemum morifolium*, laying a foundation for the next steps in deciphering the molecular mechanisms behind important horticultural traits (such as flower shape, flower color, plant form, and stress resistance) and targeted breeding.

The release of the Chrysanthemum genome facilitates the in-depth study of high-density genetic map construction and advances the research in the biology and molecular breeding of flowering plants (Hirakawa et al., 2019).

3.2 Methods and technologies used in genome sequencing

The methodologies employed in the genomic studies of *Chrysanthemum morifolium* have evolved with technological advancements. Early studies utilized molecular markers such as RAPD, ISSR, and AFLP to construct genetic linkage maps (Zhang et al., 2010), but these maps had relatively large average genetic distances between markers and contained fewer markers. The rapid development of high-throughput sequencing technologies, including whole genome sequencing, reduced representation genome sequencing, and RNA-Seq, has provided more cost-effective and efficient means for molecular marker development.

First-generation sequencing technologies primarily included the Sanger method of chain-termination sequencing and the chemical degradation method (Sanger et al., 1977). The main advantages of first-generation sequencing were long read lengths and high base reading accuracy, but these methods also had significant drawbacks of low throughput and high cost.

Second-generation sequencing technologies, also known as next-generation sequencing (NGS) or deep sequencing (Sultan et al., 2008), include four main sequencing technologies developed over time: pyrosequencing by Roche 454, Solexa sequencing by Illumina, Supported Oligo Ligation Detection (SOLiD) sequencing by ABI, and DNBSEQ sequencing by BGI. Among these, Roche 454's pyrosequencing and ABI's SOLiD have been phased out. Second-generation sequencing technologies have facilitated the acquisition of large-scale transcriptome data and EST markers, promoting the identification of genes related to various traits (Sasaki et al., 2017; Yue et al., 2018).

Unlike the SMRT sequencing technology by PacBio, which converts biochemical signals into fluorescence signals for sequencing, Oxford Nanopore Technology's nanopore sequencing technology uses electrical signals for sequencing. Some classify this new nanopore sequencing technology as fourth-generation sequencing (Feng et al., 2015), but due to its long read length characteristic, it is considered third-generation sequencing in this context. Compared to second-generation sequencing, third-generation single-molecule sequencing technology offers significant advantages such as long read lengths, fast sequencing speed, and the ability to sequence complex genomic regions. This makes it indispensable for assembling complex genomes, detecting large structural variations, analyzing different types of base modifications, and direct RNA sequencing (Ardui et al., 2018). It plays a crucial role in assembling complex genomes and identifying structural variations (Song et al., 2018).

The combined use of bioinformatics tools and comparative genomics tools is employed to analyze gene expression patterns, identify differentially expressed genes, and elucidate the evolutionary mechanisms of traits and quality indicators (Zhang et al., 2010; Shulga et al., 2017; Won et al., 2017).

3.3 Key findings from genomic studies

Genomic studies on *Chrysanthemum morifolium* have achieved significant breakthroughs, advancing our understanding of its economic and medicinal value. The construction of genetic linkage maps has obtained numerous quantitative trait loci (QTLs) associated with important traits such as flower diameter, ray floret layer number, and ray floret length, which are crucial for breeding programs (Zhang et al., 2011). Transcriptome analyses have revealed the gene regulatory networks involved in flavonoid biosynthesis and flower development, thereby comprehensively revealing the current life activity status of various cells or tissues (Liu et al., 2015; Yue et al., 2018). The whole genome sequencing of related species has provided in-depth insights into the origin and breeding history of cultivated *Chrysanthemum morifolium*. The research has also laid the foundation for future studies to decipher the molecular mechanisms underlying important horticultural traits (such as flower shape, flower color, plant form, and stress resistance) and for targeted breeding efforts (Won et al., 2017; Song et al., 2018; Hirakawa et al., 2019). Additionally, studies on the biosynthesis of bioactive components, such as flavonoids and caffeoylquinic acids, provides technical support for enhancing the economic and medicinal value of *Chrysanthemum morifolium* (Chen et al., 2020).

By integrating these findings, researchers have been able to develop a comprehensive understanding of the current state of the genomic landscape of *Chrysanthemum morifolium*, paving the way for future studies aimed at improving its ornamental and medicinal properties.

4 Adaptive Evolution of *Chrysanthemum morifolium*

4.1 Genetic diversity and phylogenetic relationships

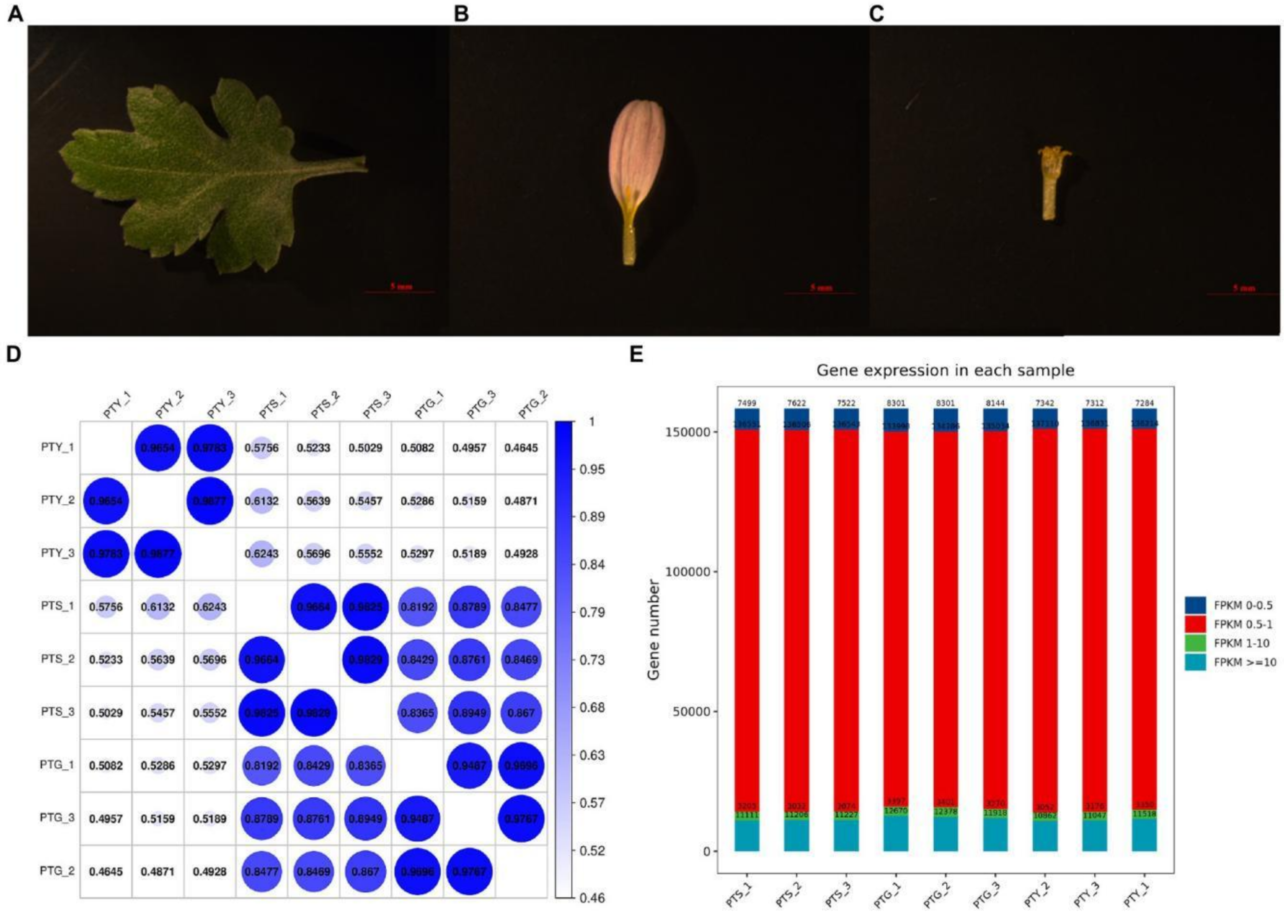
Genetic diversity is an important genetic foundation for a species, playing a crucial role in its survival and reproduction. The higher the genetic diversity within a species population, the stronger its adaptability to harsh environments, making it easier for the species to reproduce and evolve. DNA molecular marker technologies, such as RFLP, RAPD, ISSR, and SCoT, are widely used methods for analyzing the genetic diversity of *Chrysanthemum morifolium*, offering advantages such as speed, efficiency, and accuracy.

Chrysanthemum morifolium exhibits rich genetic diversity, which is crucial for maintaining its adaptability and evolution. The use of various molecular markers such as SCoT, ISSR, and SSR, plays an important role in evaluating this diversity. Tang et al. (2018) used eight ISSR primers to analyze the genetic diversity and relationships of 40 medicinal plant samples from 40 genera of the Asteraceae family. Feng et al. (2016a) screened 32 SCoT primers and used them to analyze the genetic diversity of 32 individual plants from the “Xiaoyangju” population of Hangbaiju in Tongxiang, Zhejiang. This method can be effectively applied to the genetic diversity analysis and phylogenetic analysis of *Chrysanthemum morifolium* germplasm. Genetic diversity provides essential information for the rational use and conservation of *Chrysanthemum morifolium*. The extent of genetic diversity in *Chrysanthemum morifolium* germplasm is a product of long-term evolution and is a prerequisite for its survival, adaptation, and development. Higher genetic diversity or richer genetic variation implies a stronger ability of the organism to adapt to environmental changes.

Molecular phylogenetic analysis is a fundamental method in bioinformatics, primarily used to study the evolutionary patterns, directions, rates, and the impacts of various molecular mechanisms on the structure and function of genes and genomes at the molecular level. Phylogenetic analysis can elucidate the evolutionary relationships between *Chrysanthemum morifolium* and its closely related species. Liu et al. (2012) used the chloroplast genome to construct a phylogenetic tree, clarifying its unique evolutionary history and speciation events. These studies indicate that *Chrysanthemum morifolium* has a close evolutionary relationship with related species. Wild chrysanthemums, due to their unique genetic makeup and superior traits, are often used as genetic resources for introducing new traits. Understanding the evolutionary history and genetic relationships of *Chrysanthemum morifolium*, as well as the genetic characteristics of specific traits, provides a theoretical basis for breeding strategies aimed at improving the ornamental and medicinal properties of *Chrysanthemum morifolium*.

4.2 Adaptation to environmental stresses

In recent years, due to global climate change, excessive use of water resources, and intensified human activities, *Chrysanthemum morifolium* has significantly declined or degraded. Maintaining a certain level of genetic diversity is crucial for the adaptation and evolution of organisms and is of great importance for the management and conservation of species. Li et al. (2023) studied the phenotypic and genetic changes in *Chrysanthemum morifolium* to analyze its environmental adaptation mechanisms. Heterosis, or hybrid vigor, is a common genetic phenomenon in the biological world. *Chrysanthemum morifolium* is a predominantly outcrossing plant, and hybridization can produce a wide range of variation types and gene combinations. DNA methylation is a highly conserved epigenetic modification that primarily regulates gene transcription and expression, playing a crucial role in maintaining genome stability and responding to abiotic stresses (Xin et al., 2015). DNA methylation is closely related to heterosis; hybridization results in significant changes in DNA methylation levels as well as the loss and gain of genetic fragments, which can produce genotypes adapted to new environmental conditions (Wang et al., 2014). The expression levels of genes, such as CmTM6-mu, can regulate flowering time in plants and their stress responses to external environmental factors affecting growth and development. Liu et al. (2022) identified key regulatory genes controlling flower development and flowering time (Figure 2).



	PTY_1	PTY_2	PTY_3	PTS_1	PTS_2	PTS_3	PTG_1	PTG_3	PTG_2
PTY_1		0.9654	0.9783	0.5756	0.5233	0.5029	0.5082	0.4957	0.4645
PTY_2	0.9654		0.9877	0.6132	0.5639	0.5457	0.5286	0.5159	0.4871
PTY_3	0.9783	0.9877		0.6243	0.5696	0.5552	0.5297	0.5189	0.4928
PTS_1	0.5756	0.6132	0.6243		0.9664	0.9825	0.8192	0.8789	0.8477
PTS_2	0.5233	0.5639	0.5696	0.9664		0.9829	0.8429	0.8761	0.8469
PTS_3	0.5029	0.5457	0.5552	0.9825	0.9829		0.8365	0.8949	0.867
PTG_1	0.5082	0.5286	0.5297	0.8192	0.8429	0.8365		0.9487	0.9696
PTG_3	0.4957	0.5159	0.5189	0.8789	0.8761	0.8949	0.9487		0.9767
PTG_2	0.4645	0.4871	0.4928	0.8477	0.8469	0.867	0.9696	0.9767	

Figure 2 Chrysanthemum samples used for transcriptome sequencing and gene expression levels and correlation analysis results (Adopted from Liu et al., 2022)

Image caption: (A–C) Leaf, ray floret, and disc floret, respectively, of *Chrysanthemum morifolium* Ramat “Pink Carpet”; (D) Gene expression levels in each sample; (E) Gene expression level statistics of each sample (Adopted from Liu et al., 2022)

4.3 Evolutionary significance of polyploidy in *Chrysanthemum morifolium*

Chrysanthemum morifolium is an allohexaploid that has undergone whole-genome duplication (WGD) events. Comparative transcriptome analysis of *Chrysanthemum morifolium* and its wild relative, *Chrysanthemum boreale*, indicates that both species have experienced polyploidization events, which have enhanced their genetic complexity and adaptability (Won et al., 2017). Transcriptome analysis shows that the genetic pattern of *Chrysanthemum morifolium* is primarily hexaploid, with polyploidy acting as a driving force in its evolutionary history (Fan et al., 2021). *Chrysanthemum lavandulifolium* has undergone two WGD events, the most recent one being shared by all Asteraceae plants, and an earlier one being the γ event common to core eudicots. *Chrysanthemum lavandulifolium* itself has not experienced additional WGD events, with its genomic evolution mainly driven by tandem duplication events. This ongoing genomic change contributes to the diversity and adaptability of the genus (Wen et al., 2022).

5 Medicinal Value of *Chrysanthemum morifolium*

5.1 Bioactive compounds and their therapeutic properties

Chrysanthemum morifoliumis renowned not only for its ornamental value but also for its significant medicinal properties. The plant contains a variety of bioactive compounds, including flavonoids, phenolic acids, and essential oils, which contribute to its therapeutic effects (Yue et al., 2018).

Flavonoids: The flowers of *Chrysanthemum morifolium* are rich in flavonoids such as luteolin, apigenin, and quercetin. These compounds exhibit potent antioxidant properties, neutralizing free radicals and protecting cells from oxidative damage. They also have anti-inflammatory and anti-carcinogenic effects, making them valuable in the prevention and treatment of various diseases.

Phenolic Acids: Compounds like chlorogenic acid and caffeic acid are abundant in *Chrysanthemum morifolium*. These phenolic acids possess strong antioxidant activities and contribute to the plant's anti-inflammatory, antimicrobial, and antiviral properties. They also play a role in modulating immune responses and protecting against cardiovascular diseases (Dong et al., 2023).

Terpenoids: *Chrysanthemum morifolium* contains several terpenoids, including sesquiterpene lactones, which have demonstrated anti-inflammatory, anti-tumor, and hepatoprotective effects. These compounds are also known for their ability to inhibit the growth of various pathogens, including bacteria and fungi.

Essential Oils: The essential oils extracted from *Chrysanthemum morifolium* flowers contain a mix of volatile compounds that exhibit antimicrobial, antifungal, and anti-inflammatory properties. These oils are commonly used in aromatherapy and traditional medicine for their soothing and healing effects.

5.2 Pharmacological activities and clinical applications

The pharmacological activities of *Chrysanthemum morifolium* are diverse, reflecting its extensive use in traditional and modern medicine. Key clinical applications include:

Anti-inflammatory and Antioxidant Effects: The antioxidant and anti-inflammatory properties of *Chrysanthemum morifolium* are well-documented. These effects help in managing oxidative stress and inflammation-related conditions, such as arthritis, cardiovascular diseases, and neurodegenerative disorders (Yue et al., 2018; Wang et al., 2022).

Antimicrobial Activity: The plant's bioactive compounds exhibit significant antimicrobial properties, making it effective against a range of bacterial, viral, and fungal infections (Figure 3) (Youssef et al., 2020). This antimicrobial activity supports its traditional use in treating respiratory infections, skin conditions, and gastrointestinal disorders (Yuan et al., 2020).

Cardiovascular Health: *Chrysanthemum morifolium* has been shown to improve cardiovascular health by reducing blood pressure, lowering cholesterol levels, and enhancing blood circulation. These effects are largely attributed to its flavonoids and phenolic acids, which help in preventing atherosclerosis and other heart-related issues (Feng et al., 2016b).

Eye Health: In traditional Chinese medicine, *Chrysanthemum morifolium* is widely used to treat eye conditions such as conjunctivitis and dry eyes. The plant's anti-inflammatory and antioxidant properties help alleviate eye strain and improve vision (Yuan et al., 2020).

Cancer Prevention and Treatment: Some studies suggest that the bioactive compounds in *Chrysanthemum morifolium*, particularly flavonoids and terpenoids, possess anti-carcinogenic properties. They inhibit the growth and proliferation of cancer cells, induce apoptosis, and enhance the efficacy of conventional cancer treatments (Yue et al., 2018).

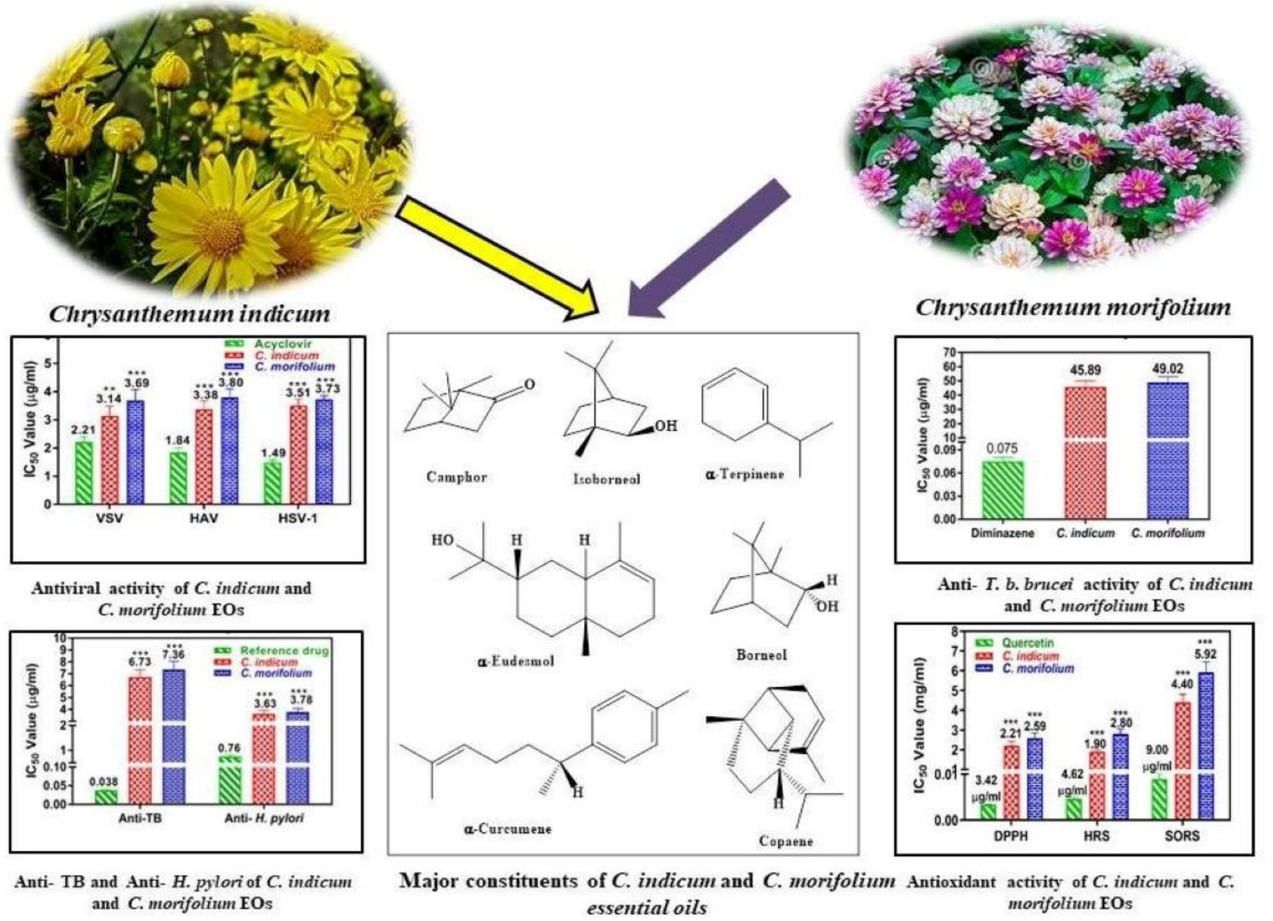


Figure 3 Major constituents, antiviral activity, anti-mycobacterial activity, anti-Helicobacter pylori activity, anti-trypanosomal activity and antioxidant activities of *Chrysanthemum indicum* and *Chrysanthemum morifolium* essential oils (Adopted from Youssef et al., 2020)

5.3 Comparison with other medicinal plants

When compared to other medicinal plants, *Chrysanthemum morifolium* stands out due to its unique combination of bioactive compounds and wide range of pharmacological activities. For instance, while many medicinal plants are known for their antioxidant properties, *Chrysanthemum morifolium*'s high flavonoid content provides a particularly potent antioxidant effect (Yue et al., 2018). Moreover, its anti-inflammatory and antimicrobial properties are comparable to those found in well-known medicinal herbs such as turmeric and garlic. However, the specific combination of compounds in *Chrysanthemum morifolium* offers a distinct therapeutic profile that is particularly effective in treating cardiovascular and respiratory conditions (Feng et al., 2016b; Yue et al., 2018). This makes it a valuable addition to the repertoire of medicinal plants used in traditional and modern medicine.

6 Integrative Analysis of Genome and Medicinal Value

6.1 Correlation between genetic traits and medicinal properties

The genetic traits of *Chrysanthemum morifolium* have been extensively studied. Previous researchers have used DNA molecular markers such as RAPD, ISSR, and AFLP to construct genetic linkage maps for *Chrysanthemum morifolium*, obtaining molecular markers closely linked to specific traits, thereby providing technical support for marker-assisted breeding (Zhang et al., 2011). Genetic maps constructed using EST-SSR markers have identified QTL loci associated with traits such as inflorescence and leaf characteristics, which are important for the medicinal quality of chrysanthemum (Fan et al., 2020). The genetic diversity among different cultivars, assessed using SSR markers, has also provided insights into the phylogenetic relationships and the potential medicinal value of various cultivars (Feng et al., 2016b).

6.2 Genomic basis for the production of bioactive compounds

The production of bioactive compounds in *Chrysanthemum morifolium* is closely linked to its genomic makeup. Transcriptome analysis has revealed numerous genes involved in the biosynthesis of flavonoids, which are key bioactive compounds with medicinal properties (Yue et al., 2018). The identification of structural and regulatory genes in the flavonoid biosynthetic pathway has elucidated the genomic basis for the production of these compounds. Techniques like ultrasonic-assisted extraction have optimized the methods for extracting bioactive compounds, accelerating the process of rapid and comprehensive analysis of these compounds (Yuan et al., 2015). Modern biotechnologies have identified flavonoids and caffeoylquinic acids in chrysanthemum flowers, further elucidating the genomic basis for the production of these compounds (Chen et al., 2020).

6.3 Potential for genetic improvement and biotechnological applications

The genetic information obtained from *Chrysanthemum morifolium* genome research provides extensive data for genetic improvement and the breeding of new varieties. The whole-genome assembly of *Chrysanthemum seticuspe* has identified numerous candidate genes controlling Chrysanthemum traits, which can be applied to cultivated chrysanthemums (Hirakawa et al., 2019). Candidate genes controlling flower characteristics have been cloned, and a series of functional molecular markers have been developed, providing technical support for targeted breeding (Sasaki et al., 2017). Comparative transcriptome analysis between wild and cultivated species has revealed patterns of genome duplication and gene selection, elucidating the evolutionary patterns of Chrysanthemum, which can guide future breeding efforts (Won et al., 2017). The integration of these genomic resources and biotechnological approaches holds promise for breeding Chrysanthemum varieties with superior phenotypic and medicinal properties.

7 Future Directions in *Chrysanthemum morifolium* Research

7.1 Emerging trends in genomic research

The field of genomic research is rapidly evolving, and the future prospects for *Chrysanthemum morifolium* are promising. Integrating genomics with transcriptomics, proteomics, and metabolomics will enable a deeper understanding of the complex biological networks and interactions that control plant development, stress responses, and medicinal properties (Won et al., 2017).

Combining single-cell transcriptome sequencing technology allows for the acquisition of gene expression information from individual cells within *Chrysanthemum morifolium* tissues. This approach can be used to distinguish the transcriptomic characteristics of different cell types and identify specific cell types involved in the biosynthesis of bioactive compounds and their regulation (Liu et al., 2015).

Further utilizing artificial intelligence (AI) and machine learning to analyze complex genomic data can enhance the understanding of *Chrysanthemum morifolium*. AI-driven predictive models can identify key genetic markers and pathways associated with desirable traits, facilitating more efficient breeding and genetic engineering efforts (Hirakawa et al., 2019).

7.2 Prospects for developing new medicinal varieties

The results obtained from genomics research can accelerate the breeding of new *Chrysanthemum morifolium* varieties. Marker-assisted selection (MAS) can be used to expedite targeted breeding. By identifying functional molecular markers associated with high concentrations of bioactive compounds, breeders can develop new varieties with enhanced medicinal efficacy (Fan et al., 2020).

CRISPR/Cas9 and other gene engineering technologies provide another avenue for creating novel varieties. These tools enable precise modifications of the plant genome through transgenic techniques, thereby enhancing the content or expression of specific traits. For example, by editing genes involved in the flavonoid biosynthesis pathway, researchers can develop varieties with enhanced medicinal efficacy (Kishi-Kaboshi et al., 2017). Furthermore, metabolic engineering can be employed to optimize the production of specific bioactive compounds. By manipulating the plant's metabolic pathways, it is possible to increase the yield of desired therapeutic agents, making *Chrysanthemum morifolium* an even more potent medicinal resource (Zou et al., 2021).

7.3 Challenges and opportunities in translating genomic research into practical applications

While significant progress has been made in the genomic research of *Chrysanthemum morifolium*, it has not yet been applied to production. As a hexaploid plant with a complex genetic background, genetic improvement of *Chrysanthemum morifolium* is challenging (Fan et al., 2020). The construction of genetic maps has developed QTLs for key traits such as inflorescence and leaf characteristics, providing promising opportunities for breeding programs (Fan et al., 2020). Chloroplast whole-genome analysis offers valuable resources for studying the phylogeny and evolutionary patterns of *Chrysanthemum morifolium* (Xia et al., 2021a; Xia et al., 2021b). Specific genes, such as *CmTCP20*, can regulate flowering time, thereby enhancing the ornamental value and economic benefits of *Chrysanthemum morifolium*. By comprehensively utilizing genomic research findings and through the collaborative efforts of researchers, the rapid application of genomic research results to practical production can be achieved (Wang et al., 2019).

8 Concluding Remarks

The genome of *Chrysanthemum morifolium* has been extensively studied, leading to significant breakthroughs in understanding its genetic makeup, adaptive evolution, and medicinal value. High-throughput sequencing technologies have identified key genes involved in flavonoid biosynthesis, which are crucial for enhancing the plant's medicinal activity. The generation of expressed sequence tags (ESTs) has provided potential targets for genetic manipulation to enhance medicinal properties. The de novo whole-genome assembly of *Chrysanthemum seticuspe*, a model species, has further expanded our knowledge of the genetic and gene discovery processes in cultivated chrysanthemums. Functional molecular markers accelerate the process of targeted breeding. Whole-genome and comparative genomic studies have elucidated the cultivation and evolutionary history of *Chrysanthemum morifolium*. Genetic linkage maps have identified QTL loci for inflorescence and leaf traits, promoting marker-assisted selection in breeding programs.

The genomic data obtained from various studies provide a solid foundation for future research aimed at improving the ornamental and medicinal qualities of *Chrysanthemum morifolium*. Future research should focus on leveraging the genetic resources and molecular insights gained from these studies to develop new chrysanthemum cultivars with improved nutritional and medicinal qualities. The integration of genomic data with traditional breeding techniques can accelerate the development of varieties with strong disease resistance, broad adaptability, and high medicinal efficacy, thereby increasing their commercial and medicinal value. The continued exploration of the genetic and molecular bases of *Chrysanthemum morifolium* will not only contribute to the plant's ornamental and medicinal applications but also provide valuable insights into the evolutionary processes that shape plant diversity.

◆

Acknowledgments

The HortHerb Publisher appreciate the two anonymous peer reviewers for their critical assessment and constructive suggestions on our manuscript.

Funding

This work was supported by China Agriculture Research System of MOF and MARA (CARS-21); Key Research and Development Program of Henan (241111310200, 231111110800); Key project at central government level: The ability establishment of sustainable use for valuable Chinese medicine resources (2060302); Major Science and Technology Projects in Henan Province (221100310400); Henan Academy of Agricultural Sciences Emerging Discipline Development Project (2024XK01); Henan Academy of Agricultural Sciences Independent Innovation Special Fund (2024ZC040); Henan Academy of Agricultural Sciences Outstanding Youth Science and Technology Fund (2024YQ15、2024YQ16); Henan Province Science and Technology Research Projects (232102110198, 232102110243, 232102110262, 242102110248, 242102110260); (Provincial Key Laboratory of Conservation and Utilization of Traditional Chinese Medicine Resources, Institute of Chinese Herbel Medicines, Henan Academy of Agricultural Sciences, Zhengzhou, Henan, China).

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

Chen F.D., Li F.T., Chen S.M., Guan Z.Y., and Fang W.M., 2009, Meiosis and pollen germinability in small-flowered anemone type chrysanthemum cultivars, Plant Systematics and Evolution, 280: 143-151.
https://doi.org/10.1007/s00606-009-0173-9

Chen S., Liu J., Dong G., Zhang X., Liu Y., Sun W., and Liu A., 2021, Flavonoids and caffeoylquinic acids in *Chrysanthemum morifolium* Ramat flowers: A potentially rich source of bioactive compounds, Food Chemistry, 344: 128733.
https://doi.org/10.1016/j.foodchem.2020.128733
PMid:33280963

Ding L., Song A., Zhang X., Li S., Su J., Xia W., Zhao K., Zhao W., Guan Y., Fang W., Chen S., Jiang J., and Chen F., 2020, The core regulatory networks and hub genes regulating flower development in *Chrysanthemum morifolium*, Plant Molecular Biology, 103: 669-688.
https://doi.org/10.1007/s11103-020-01017-8
PMid:32472481

Dong X., Huang H., Wang R., Luo S., Mi Y., Pan Y., Shen W., Cui J., Hu X., Cheng X., Shi X., and Wang H., 2023, High-speed counter-current chromatography assisted preparative isolation of phenolic compounds from the flowers of *Chrysanthemum morifolium* cv. *Fubaiju*, Journal of Separation Science, 46(19): 2300172.
https://doi.org/10.1002/jssc.202300172
PMid:37528737

Fan M., Gao Y., Wu Z., and Zhang Q., 2020, Linkage map development by EST-SSR markers and QTL analysis for inflorescence and leaf traits in Chrysanthemum (*Chrysanthemum morifolium* Ramat.), Plants, 9(10): 1342.
https://doi.org/10.3390/plants9101342
PMid:33050665 PMCid:PMC7600071

Fan M., Gao Y., Wu Z., Haider S., and Zhang Q., 2022, Evidence for hexasomic inheritance in *Chrysanthemum morifolium* Ramat. based on analysis of EST-SSR markers, Genome, 65(2): 75-81.
https://doi.org/10.1139/gen-2020-0155
PMid:34756106

Feng S.G., He R.F., Jiang M.Y., Lu J.J., Shen X.X., Liu J.J., Wang Z.A., and Wang H.Z., 2016a, Genetic diversity and relationships of medicinal *Chrysanthemum morifolium* revealed by start codon targeted (SCoT) markers, Scientia Horticulturae, 201: 118-123.
https://doi.org/10.1016/j.scienta.2016.01.042

Feng S., He R., Lu J., Jiang M., Shen X., Jiang Y., Wang Z., and Wang H., 2016b, Development of SSR markers and assessment of genetic diversity in medicinal *Chrysanthemum morifolium* cultivars, Frontiers in Genetics, 7: 113.
https://doi.org/10.3389/fgene.2016.00113
PMid:27379163 PMCid:PMC4908101

Feng Y., Zhang Y., Ying C., Wang D., and Du C., 2015, Nanopore-based fourth-generation DNA sequencing technology, Genomics, Proteomics and Bioinformatics, 13(1): 4-16.
https://doi.org/10.1016/j.gpb.2015.01.009
PMid:25743089 PMCid:PMC4411503

Hao D.C., Song Y., Xiao P., Zhong Y., Wu P., and Xu L., 2022, The genus *Chrysanthemum*: Phylogeny, biodiversity, phytometabolites, and chemodiversity, Frontiers in Plant Science, 13: 973197.
https://doi.org/10.3389/fpls.2022.973197
PMid:36035721 PMCid:PMC9403765

Hirakawa H., Sumitomo K., Hisamatsu T., Nagano S., Shirasawa K., Higuchi Y., Kusaba M., Koshioka M., Nakano Y., Yagi M., Yamaguchi H., Taniguchi K., Nakano M., and Isobe S., 2019, De novo whole-genome assembly in *Chrysanthemum seticuspe*, a model species of Chrysanthemums, and its application to genetic and gene discovery analysis, DNA Research, 26(3): 195-203.
https://doi.org/10.1093/dnares/dsy048
PMid:30689773 PMCid:PMC6589549

Kang S.H., Nie J., Chen K.L., and Deng H.Y., 2022, Comparison of morphological characteristics and quality evaluation of *Chrysanthemum morifolium*, Journal of Chinese Medicinal Materials, 2022: 49-57.

Kishi-Kaboshi M., Aida R., and Sasaki K., 2017, Generation of gene-edited *Chrysanthemum morifolium* using multicopy transgenes as targets and markers, Plant and Cell Physiology, 58(2): 216-226.
https://doi.org/10.1093/pcp/pcw222
PMid:28049122

Li Z., Mao C., Wu X., Zhou H., Zhao K., Jiang J., Chen S., Fang W., Guan Z., Zhang J., Liao Y., Wang Z., Chen F., and Wang H., 2023, Hybrid weakness and continuous flowering caused by compound expression of FTLs in *Chrysanthemum morifolium* × *Leucanthemum paludosum* intergeneric hybridization, Frontiers in Plant Science, 14: 1120820.
https://doi.org/10.3389/fpls.2023.1120820
PMid:36778705 PMCid:PMC9911212

Liu H., Jia Y., Chai Y., Wang S., Chen H., Zhou X., Huang C., Guo S., and Chen D., 2022, Whole-transcriptome analysis of differentially expressed genes between ray and disc florets and identification of flowering regulatory genes in *Chrysanthemum morifolium*, Frontiers in Plant Science, 13: 947331.
https://doi.org/10.3389/fpls.2022.947331
PMid:35991433 PMCid:PMC9388166

Liu H., Sun M., Du D., Pan H., Cheng T., Wang J., and Zhang Q., 2015, Whole-transcriptome analysis of differentially expressed genes in the vegetative buds, floral buds and buds of *Chrysanthemum morifolium*, PLoS One, 10(5): e0128009.
https://doi.org/10.1371/journal.pone.0128009
PMid:26009891 PMCid:PMC4444331

Liu P.L., Wan Q., Guo Y.P., Yang J., and Rao G.Y., 2012, Phylogeny of the genus *Chrysanthemum* L.: evidence from single-copy nuclear gene and chloroplast DNA sequences, PLoS One, 7(11): e48970.
https://doi.org/10.1371/journal.pone.0048970
PMid:23133665 PMCid:PMC3486802

Lu Y.F., Li D.X., Zhang R., Zhao L.L., Qiu Z., Du Y., et al., 2022, Chemical antioxidant quality markers of *Chrysanthemum morifolium* using a spectrum-effect approach, Frontiers in Pharmacology, 13: 809482.
https://doi.org/10.3389/fphar.2022.809482
PMid:35197853 PMCid:PMC8859431

Ojha S., Vishwakarma P.K., Tripathi S.M., and Mishra S., 2024, Exploring the therapeutic potential of *Chrysanthemum morifolium*: An ethnopharmacological perspective, Current Nutrition & Food Science, 20(5): 646-657.
https://doi.org/10.2174/1573401319666230803092050

Pan C., He X., Song S., Zou L., Wang M., and Han B., 2023, Identification and analysis of phosphatidylethanolamine-binding protein family genes in the Hangzhou white chrysanthemum (*Chrysanthemum morifolium* Ramat.), Agriculture, 13(2): 374.
https://doi.org/10.3390/agriculture13020374

Peng H., Chen F.D., Fang W.M., Jiang J.F., Chen S.M., Guan Z.Y., and Liao Y., 2013, Heterosis and mixed genetic analysis of branch traits of cut chrysanthemum, Acta Horticulturae Sinica, 40(7): 1327-1336.

Peng H., Zhang F., Jiang J., Chen S., Fang W., Guan Z., and Chen F., 2015, Identification of quantitative trait loci for branching traits of spray cut chrysanthemum, Euphytica, 202: 385-392.
https://doi.org/10.1007/s10681-014-1259-1

Peng A., Lin L., Zhao M., and Sun B., 2019, Classification of edible chrysanthemums based on phenolic profiles and mechanisms underlying the protective effects of characteristic phenolics on oxidatively damaged erythrocytes, Food Research International, 123: 64-74.
https://doi.org/10.1016/j.foodres.2019.04.046
PMid:31285013

Sanger F., Nicklen S., and Coulson A.R., 1977, DNA sequencing with chain-terminating inhibitors, Proceedings of the National Academy of Sciences, 74(12): 5463-5467.
https://doi.org/10.1073/pnas.74.12.5463
PMid:271968 PMCid:PMC431765

Sasaki K., Mitsuda N., Nashima K., Kishimoto K., Katayose Y., Kanamori H., and Ohmiya A., 2017, Generation of expressed sequence tags for discovery of genes responsible for floral traits of *Chrysanthemum morifolium* by next-generation sequencing technology, BMC Genomics, 18: 1-14.
https://doi.org/10.1186/s12864-017-4061-3
PMid:28870156 PMCid:PMC5584320

Shao Q., Guo Q., Li Y., and Mao P., 2011, Numerical analysis of morphological variation of germplasm resources of *Chrysanthemum morifolium* for medicine, Zhongguo Zhong Yao Za Zhi= Zhongguo Zhongyao Zazhi= China Journal of Chinese Materia Medica, 36(10): 1261-1265.

Shulga O., Nedoluzhko A., Shchennikova A., Gruzdeva N., Shelenkov A., Sharko F., Sokolov A., Pantiukh E., Rastorguev S., Prokhortchouk E., Skryabin K., 2017, Profiling of microRNAs in wild type and early flowering transgenic *Chrysanthemum morifolium* by deep sequencing, Plant Cell, Tissue and Organ Culture (PCTOC), 128: 283-301.
https://doi.org/10.1007/s11240-016-1109-z

Song C., Liu Y., Song A., Dong G., Zhao H., Sun W., Ramakrishnan S., Wang Y., Wang S., Li T., Niu Y., Jiang J., Dong B., Xia Y., Chen S., Hu Z., Chen F., and Chen S., 2018, The *Chrysanthemum nankingense* genome provides insights into the evolution and diversification of chrysanthemum flowers and medicinal traits, Molecular Plant, 11(12): 1482-1491.
https://doi.org/10.1016/j.molp.2018.10.003
PMid:30342096

Sultan M., Schulz M.H., Richard H., Magen A., Klingenhoff A., Scherf M., Borodina T., Soldatov A., Parkhomchuk D., Schmidt D., O'Keeffe S., Haas S., Vingron M., Lehrach H., and Yaspo M.L., 2008, A global view of gene activity and alternative splicing by deep sequencing of the human transcriptome, Science, 321(5891): 956-960.
https://doi.org/10.1126/science.1160342
PMid:18599741

Tang G.M., Li W.D., Huang G.L., Zhang L., Fu H.Y., Xiao X.L., and Yang J.L., 2024, Research on resource classification and product development of functional *Chrysanthemum morifolium*, China Fruit & Vegetable, 2024, 44(4): 54-57.

Tang X.H., Hu J., Ren C.X., Song J., Pei J., Wu Q.H., and Chen J., 2018, Analysis of genetic diversity and relationship in medicinal plants of Compositae by ISSR, Tianran Chanwu Yanjiu yu Kaifa (Natural Product Research and Development), 30(10): 1764-1768.

Tyagi S., Jung J.A., Kim J.S., Kwon S.J., and Won S.Y., 2019, The complete chloroplast genome of an economic plant, *Chrysanthemum morifolium* 'Baekma', Mitochondrial DNA Part B, 4(2): 3133-3134.
https://doi.org/10.1080/23802359.2019.1666682
PMid:33365886 PMCid:PMC7706905

Wang H., Jiang J., Chen S., Qi X., Fang W., Guan Z., Teng N., Liao Y., and Chen F., 2014, Rapid genetic and epigenetic alterations under intergeneric genomic shock in newly synthesized *Chrysanthemum morifolium* × *Leucanthemum paludosum* hybrids (Asteraceae), Genome Biology and Evolution, 6(1): 247-259.
https://doi.org/10.1093/gbe/evu008
PMid:24407856 PMCid:PMC3914698

Wang J., Guan Y., Ding L., Li P., Zhao W., Jiang J., Chen S., and Chen F., 2019, The *CmTCP20* gene regulates petal elongation growth in *Chrysanthemum morifolium*, Plant Science, 280: 248-257.
https://doi.org/10.1016/j.plantsci.2018.12.008
PMid:30824003

Wang S.Q., Liu D., Ye X.C., Zhu Q.Q., Zhang D.D., Wang B., and Nie J., 2022, Pharmacodynamic material basis and anti-inflammatory mechanism of *Chrysanthemum morifolium* cv. *Fubaiju* based on UPLC-Q-TOF-MS/MS combined with network pharmacology, Zhongguo Zhong Yao Za Zhi= Zhongguo Zhongyao Zazhi= China Journal of Chinese Materia Medica, 47(15): 4190-4201.

Wen X., Li J., Wang L., Lu C., Gao Q., Xu P., Pu Y., Zhang Q., Hong Y., Hong L., Huang H., Xin H., Wu X., Kang D., Gao K., Li Y., Ma C., Li X., Zheng H., Wang Z., Jiao Y., Zhang L., and Dai S., 2022, The *Chrysanthemum lavandulifolium* genome and the molecular mechanism underlying diverse capitulum types, Horticulture Research, 9: uhab022.
https://doi.org/10.1093/hr/uhab022
PMid:35039834 PMCid:PMC8771455

Won S.Y., Kwon S.J., Lee T.H., Jung J.A., Kim J.S., Kang S.H., and Sohn S.H., 2017, Comparative transcriptome analysis reveals whole-genome duplications and gene selection patterns in cultivated and wild Chrysanthemum species, Plant Molecular Biology, 95: 451-461.
https://doi.org/10.1007/s11103-017-0663-z
PMid:29052098 PMCid:PMC5727146

Xia H., Xu Y., Liao B., Huang Z., and Wang F., 2021a, Complete chloroplast genome sequence of a Chinese traditional cultivar in Chrysanthemum, *Chrysanthemum morifolium* 'Anhuishiliuye', Mitochondrial DNA Part B, 6(4): 1281-1282.
https://doi.org/10.1080/23802359.2020.1866451
PMid:33855177 PMCid:PMC8018469

Xia H., Xu Y., Zhang J., Huang Z., Luo H., Ye Z., and Zhou H., 2021b, Complete chloroplast genome sequence of a Dutch cultivar of Chrysanthemum, *Chrysanthemum morifolium* 'Orizaba'(Asteraceae), Mitochondrial DNA Part B, 6(7): 1937-1938.
https://doi.org/10.1080/23802359.2021.1936672
PMid:34179473 PMCid:PMC8205100

Xin C.H., Hou R.K., Wu F., Zhao Y.B., Xiao H.H., Si W.T., Ali M.E., Cai L., and Guo J., 2015, Analysis of cytosine methylation status in potato by methylation-sensitive amplified polymorphisms under low-temperature stress, Journal of Plant Biology, 58: 383-390.
https://doi.org/10.1007/s12374-015-0316-1

Yang Q., Li Z.D., Che K.M., Wang H.F., Li D.B., Zhi Z., Liu X., Liao W.C., and Sun S.J., 2022, Herbal textual research on the origin, habitat and efficacy of Chrysanthemum, Shizhen Guoyi Guoyao, 33(11): 2675-2678.

Yang Y.J., Jiang Z.F., Guo J.N., Yang X.L., Xu N., Chen Z.H., Hao J., Li J.X., Pang J.L., Shen C.J., and Xu M.J., 2018, Transcriptomic analyses of *Chrysanthemum morifolium* Ramat under UV-B radiation treatment reveal variations in the metabolisms associated with bioactive components, Industrial Crops and Products, 124: 475-486.
https://doi.org/10.1016/j.indcrop.2018.08.011

Ye M.Q., Deng J., Peng J., Zhang R.R., Wu M.H., Ma Z.G., and Cao H., 2022, Herbalogical study, Chinese Traditional Patent Medicine, 44(06): 1912-1917.

Youssef F.S., Eid S.Y., Alshammari E., Ashour M.L., Wink M., and El-Readi M.Z., 2020, Chrysanthemum indicum and *Chrysanthemum morifolium*: Chemical composition of their essential oils and their potential use as natural preservatives with antimicrobial and antioxidant activities, Foods, 9(10): 1460.
https://doi.org/10.3390/foods9101460
PMid:33066507 PMCid:PMC7602131

Yuan H., Jiang S., Liu Y., Daniyal M., Jian Y., Peng C., Shen J., Liu S., and Wang W., 2020, The flower head of *Chrysanthemum morifolium* Ramat.(Juhua): A paradigm of flowers serving as Chinese dietary herbal medicine, Journal of Ethnopharmacology, 261: 113043.
https://doi.org/10.1016/j.jep.2020.113043
PMid:32593689

Yuan J., Huang J., Wu G., Tong J., Xie G., Duan J.A., and Qin M., 2015, Multiple responses optimization of ultrasonic-assisted extraction by response surface methodology (RSM) for rapid analysis of bioactive compounds in the flower head of *Chrysanthemum morifolium* Ramat, Industrial Crops and Products, 74: 192-199.
https://doi.org/10.1016/j.indcrop.2015.04.057

Yue J., Zhu C., Zhou Y., Niu X., Miao M., Tang X., Chen F., Zhao W., and Liu Y., 2018, Transcriptome analysis of differentially expressed unigenes involved in flavonoid biosynthesis during flower development of *Chrysanthemum morifolium* 'Chuju', Scientific Reports, 8(1): 13414.
https://doi.org/10.1038/s41598-018-31831-6
PMid:30194355 PMCid:PMC6128863

Zhang F., Chen F.D., Fang W.M., Chen S.M., Liu P.S., and Yin D.M., 2011, Heterosis and mixed genetic analysis of inflorescence traits of Chrysanthemum, Nanjing Nongye Daxue Xuebao (Journal of Nanjing Agricultural University), 34(4): 31-36.

Zhang F., Chen S., Chen F., Fang W., and Li F., 2010, A preliminary genetic linkage map of chrysanthemum (*Chrysanthemum morifolium*) cultivars using RAPD, ISSR and AFLP markers, Scientia Horticulturae, 125(3): 422-428.
https://doi.org/10.1016/j.scienta.2010.03.028

Zou Q., Wang T., Guo Q., Yang F., Chen J., and Zhang W., 2021, Combined metabolomic and transcriptomic analysis reveals redirection of the phenylpropanoid metabolic flux in different colored medicinal *Chrysanthemum morifolium*, Industrial Crops and Products, 164: 113343.
https://doi.org/10.1016/j.indcrop.2021.113343