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Research Progress on Chemical Components and Pharmacological Activities of Hylotelephium Erythrostictum

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Fund Project: Transfer and Transformation of Scientific and Technological Achievements of Henan Academy of Sciences (241614035); Henan Academy of Sciences Talent Team Building Special Project (241814076); Henan Province Zhongke Science and Technology Achievement Transfer and Transformation Project (2025102).

Abstract: Hylotelephium erythrostictum, a perennial herb of the genus Sedum in the Crassulaceae family, possesses documented ethnopharmacological properties including dispelling wind and dampness, promoting blood circulation and removing blood stasis, and clearing heat and detoxifying. Contemporary phytochemical analyses demonstrate Sedum spectabile is rich in various active components such as flavonoids, phenolic acids, steroids, and terpenoids, and has significant pharmacological activities such as antioxidant, hypoglycemic, antibacterial, and anti-inflammatory effects. This article systematically reviews the research progress in recent years on the separation and identification of chemical components, optimization of extraction processes, and pharmacological mechanisms of Sedum spectabile, and discusses its development and utilization prospects, aiming to provide a scientific basis for the subsequent in-depth research and rational development of this medicinal plant.

Keywords: Hylotelephium erythrostictum; Chemical components; Extraction process; Pharmacological activities; Mechanism of action

1. Introduction

Hylotelephium erythrostictum (Miq.) H. Ohba, also known as Scorpion Grass, Hylotelephium spectabile, magnificent Sedum, Eight Treasures, Blood-Activating Sanqi, double-leaf Sedum, White Flower Scorpion Grass, etc [1,2], It is an herbaceous plant belonging to the genus Echeveria of the Crassulaceae family. The leaves are thick or opposite, with thick roots and stems. The whole plant is slightly covered with white powder and appears grayish green. Hylotelephium erythrostictum is mainly distributed in the northeastern, southwestern and central regions of China. The whole plant of the Eight Treasures Rhodiola can be used as medicine and has a long history of folk medicinal use. The “Compendium of Materia Medica” records that it has the functions of “promoting blood circulation and stopping bleeding, clearing heat and detoxifying, dispelling wind and promoting diuresis”, and is often used to treat pharyngitis, mastitis, urticaria and other diseases.

In recent years, with the in-depth research on traditional medicinal plants, the medicinal value of Hylotelephium erythrostictum has attracted increasing attention. Studies have shown that Hylotelephium erythrostictum is abundant in bioactive secondary metabolites, including various active components such as flavonoids, phenolic acids, and steroids, which endow the plant with extensive pharmacological activities. However, at present, most of the research on Hylotelephium erythrostictum focuses on horticultural cultivation and ecological adaptability, while there are relatively few systematic studies on its medicinal value and mechanism of action. Therefore, this paper conducts a comprehensive review of the research progress in aspects such as the chemical composition, extraction process and pharmacological activity of Hylotelephium erythrostictum, with the aim of providing a reference for the in-depth research and development application of this medicinal plant.

Table 1 lists the common hylotelephium plant species and their distribution in China. As can be seen from the table, hylotelephium plants are widely distributed in China, with a rich variety of species and great potential for development and utilization.

Table 1: Common Types of Hylotelephium and Their Distribution.

Latin Name	Distribution
Hylotelephium ewersii	Xinjiang, China; Pakistan; Mongolia and the Soviet Union
Hylotelephium tatarinowii	Shanxi, Hebei and Inner Mongolia in China
Hylotelephium spectabile	Heilongjiang, Jilin, Liaoning, Hebei, Shandong, Henan, Shaanxi, Anhui
Hylotelephium mingjinianum	Anhui, Zhejiang, Hubei, Hunan, Guangxi
Hylotelephium angustum	Hubei, Sichuan, Qinghai, Yunnan, Shaanxi, Shanxi, Gansu
Hylotelephium verticillatum	Jilin, Liaoning, Hebei, Shanxi, Shaanxi, Gansu, Shandong, Jiangsu, Anhui, Zhejiang
Hylotelephium pallescens	Jilin, Inner Mongolia, Shanxi, Hebei, Heilongjiang, Liaoning
Hylotelephium sieboldii	Lichuan, Hubei Province, China
Hylotelephium purpureum	Heilongjiang, Jilin, Liaoning, Xinjiang and other places.
Hylotelephium maximum	Eurasia and North America, Yunnan, Guizhou, Sichuan, Hubei

2. Chemical Composition

Hylotelephium erythrostictum is rich in secondary metabolites, mainly including flavonoids, phenolic acids, sterols and terpenoids, etc. These components have diverse structures and significant biological activities, serving as an important material basis for the plant to exert its pharmacological effects.

2.1 Flavonoids

Flavonoids are the main active components of Hylotelephium erythrostictum (Table 2). So far, more than 30 kinds of flavonoids have been isolated and identified from this plant. These compounds are mainly kaempferol, quercetin and its glycoside derivatives (Figure 1). Among them, kaempferol -3-O-α -L-rhamnoside (compound 6) and quercetin -3-O glucoside (compound 7), etc. Structural analysis indicates that the flavonoids in Hylotelephium erythrostictum mostly feature undergo glycosylation modification predominantly at the C-3 and C-7 positions, and this structural feature is closely related to its biological activity.

Table 2: Flavonoids in Plants of the Hylotelephium.

Compound Number	Compound Name	Origin of Species	Part	References
1	Apigenin	Hylotelephium erythrostictum	Flowers, The whole plant	[2, 3]
2	Diosmetin	Hylotelephium erythrostictum	Flowers, The whole plant	[2, 3]
3	Kaempferol	Hylotelephium erythrostictum, Hylotelephium ewersii	Flowers, The whole plant	[2-5]
4	Artemisinin	Hylotelephium erythrostictum	The whole plant	[3]
5	Rhamnetin	Hylotelephium erythrostictum	The whole plant	[3]
6	Kaenophen-3-o-α-L-pyran rhamnose -(1→6)-β-D-pyran glucoside	Hylotelephium erythrostictum	Leaf	[4]
7	Quercetin-3-O-8-D-pyranoside	Hylotelephium erythrostictum	Leaf	[4]
8	Rutin	Hylotelephium ewersii	The whole plant	[5, 41]
9	Kaempferol -7-O-α-L-rhamnoside	Hylotelephium ewersii, Hylotelephium pallescens	The whole plant	[5, 6]
10	Quercetin	Hylotelephium ewersii, Hylotelephium erythrostictum	The whole plant	[3, 5]
11	Arbutin	Hylotelephium ewersii	The whole plant	[5]
12	Kaempferol 4 '-O-β-D-glucoside	Hylotelephium ewersii	The whole plant	[5]
13	3,7-bis-O-α-L-rhamnoside	Hylotelephium pallescens	The whole plant	[6]
14	Acanthin-7-o-β-D-glucoside	Hylotelephium erythrostictum	The whole plant	[7]
15	Kaempferol 3,7-di-O-rhamnoside	Hylotelephium sieboldii var. sieboldii and var. ettyuense	Leaf, stems	[8]
16	Kaempferol 3-O-neohesperidoside-7-O-rhamnoside			[8]
17	Kaempferol 3-O-glucosyl-(1 →2)-rhamnoside-7-O-rhamnoside			[8]

18	Kaempferol 3-O-sambubioside-7-O-rhamnoside	[8]
19	Kaempferol 3-O-glucoside-7-O-rhamnoside	[8]
20	Kaempferol 3-O-xylorhamnorhamnoside-7-O-rhamnoside	[8]
21	Quercetin 3-O-neohesperidoside-7-O-rhamnoside	[8]
22	Quercetin 3,7-O-glycoside which attached each 1 mol of glucose and rhamnose	[8]
23	Quercetin 3-O-glucoside-7-O-rhamnoside	[8]
24	kaempferol 3-O-sophoroside-7-O-rhamnoside	[8]
25	Kaempferol 3-O-diglucoside-7-O-rhamnoside	[8]
26	Quercetin 3,7-O-glycoside which attached each 1 mol of xylose and glucuronic acid	[8]
27	Kaempferol 3-O-sophoroside	[8]
28	Kaempferol 3-O-neohesperidoside	[8]
29	Quercetin 3-O-xylorhamnoside	[8]
30	Quercetin 3-O-neohesperidoside	[8]
31	Quercetin 3-O-sophoroside	[8]
32	Kaempferol 3-O-glucoside	[8]
33	Kaempferol 3-O-rhamnoside	[8]
34	Quercetin 3-O-glucoside	[8]
35	Quercetin 3-O-rhamnoside	[8]

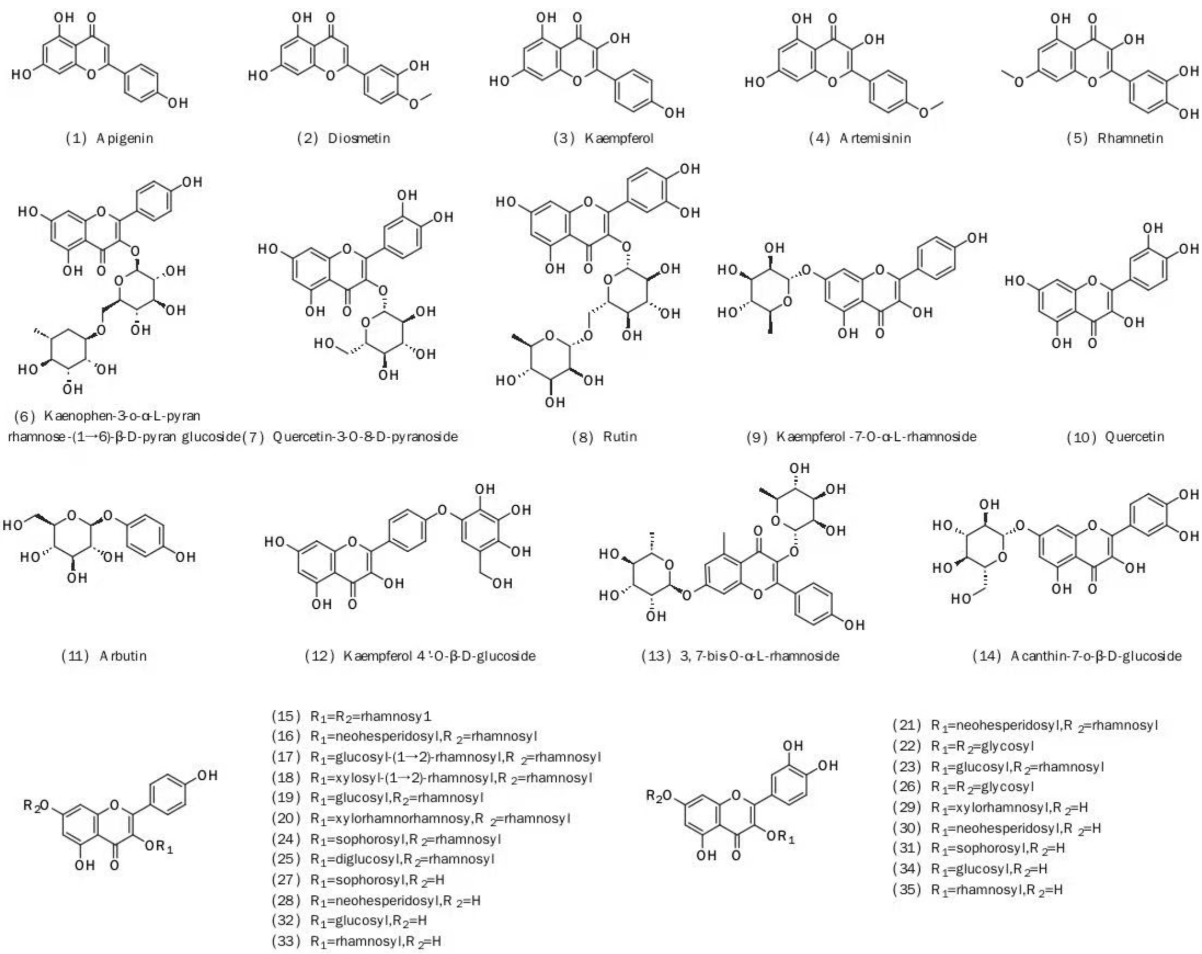

Figure 1: Shows the Structure of Flavonoids in the Hylotelephium.

The structural characteristics of flavonoids are closely related to their biological activities. Studies have shown that the phenolic hydroxyl groups in the aglycone structures of kaolin and quercetin are the key groups for their antioxidant activity, while the introduction of sugar groups can improve their solubility and bioavailability. It is particularly worth noting that kasanferol -3-O-α -L-rhamnoside and quercetin -3-O glucoside demonstrated significant activity in antioxidant and anti-inflammatory experiments, which provides important clues for the development of related drug lead compounds.

2.2 Phenolic Acid Compounds

Phenolic acid compounds are potential highly efficient and pure natural antioxidants and an important source of medical and health products for human disease prevention. The phenolic acid compounds isolated from the hylotelephium are shown in Table 3. At present, various phenolic acids such as rogogallic acid (compound 6), protocatechuic acid (compound 1), and p-hydroxycinnamic acid have been isolated and identified. These compounds exhibit low molecular mass characteristics and good bioavailability, making them potential natural antioxidants and anti-inflammatory agents. Studies have shown that gallic acid can exert antioxidant effects by activating the Nrf2/ARE pathway [9], while trans-hydroxycinnamic acid (compound 3) can inhibit the activation of the NF-κB signaling pathway and reduce the release of inflammatory factors [10]. These findings provide a scientific basis for explaining the traditional medicinal effects of the eight-treasure Sedum.

Table 3: Phenolic Acid Compounds in Plants of the Hylotelephium.

Compound Number	Compound Name	Origin of Species	Part	References
1	Protocatechuic acid	Hylotelephium erythrostictum	Flowers	[2]
2	p-Hydroxybenzoic acid	Hylotelephium erythrostictum	Flowers	[2]
3	p-Coumaric acid	Hylotelephium spectabile	Rhizome	[11]
4	Cis-p-hydroxycinnamic acid	Hylotelephium spectabile	Rhizome	[11]
5	3-Hydroxy-4-methoxybenzoic acid	Hylotelephium spectabile	Rhizome	[11]
6	Gallic acid	Hylotelephium erythrostictum , Hylotelephium spectabile	The whole plant, Rhizome	[3,11]

3. Research on Extraction Process

The extraction process of the active ingredients of Hylotelephium erythrostictum directly affects its yield and biological activity. The commonly used extraction methods at present include ultrasonic extraction, enzymatic hydrolysis and solvent extraction, etc. Each method has its own characteristics and should be selected and optimized according to the properties of the target components.

3.1 Ultrasonic Extraction Method

Ultrasonic extraction technology can induce ultrastructural disruption of plant cell walls via cavitation effects by taking advantage of the cavitation effect, thermal effect and mechanical effect of ultrasonic waves, promoting the release of active components [18,19]. This method has the advantages of high extraction efficiency, simple operation and low solvent consumption, and is particularly suitable for the extraction of thermally unstable components [20,21]. In the extraction of total flavonoids from Hylotelephium erythrostictum, the ultrasonic method demonstrates superior extraction efficiency. Feng G L [22] extracted total flavonoids from Hylotelephium erythrostictum by ultrasonic technology. Orthogonal experiments were conducted. When the extraction temperature was 60℃ and the extraction was carried out five times, the yield of total flavonoids was significantly increased under these conditions. Wu X F [23] established optimal parameters through response surface methodology by using the response surface method and found that the ultrasonic extraction temperature was 64 ℃, the ultrasonic time was 48 minutes, and the ultrasonic extraction was carried out three times. The extraction rate of total flavonoids was 3.116%. Tang Z S [16] is research on the ultrasonic extraction of Hylotelephium erythrostictum shows that the best extraction effect is achieved when the methanol concentration is 70%, the ratio of material to liquid is 1:30 (W/V), the temperature is 45℃, and the extraction time is 30 minutes.

3.2 Enzymatic Hydrolysis Method

Enzymatic hydrolysis is a method that utilizes specific enzymes (such as cellulase, pectase, etc.) to degrade the components of plant cell walls, destroy cell structures, and thereby increase the dissolution rate of active ingredients [24,25]. It features high efficiency, mildness, safety, and strong specificity [26,27], and is particularly suitable for plant materials with dense cell wall structures. Fu D D [28] optimized the enzymatic extraction process of total polyphenols from Hylotelephium erythrostictum by the response surface method. The optimal conditions were as follows: extraction time 1 hour, cellulase content 15.8 mg, enzymatic hydrolysis temperature 50℃, and enzymatic hydrolysis time 30 min. Under these conditions, the average yield of polyphenols was 24.22 mg/g. Zhang L H [29] studied the process of extracting salidroside from Rhodiola rosea by cellulase hydrolysis and found that when the hydrolysis temperature was 45℃, the dosage of cellulase was 0.36%, and the pH was 5.5, the extraction rate of salidroside could reach 1.39%.Yue X W [30] demonstrated through orthogonal experiments that the efficiency of extracting salidroside by enzymatic hydrolysis (65℃, enzyme dosage of 1.75%, time of 60 minutes) was 74.16% higher than that of the traditional water extraction method. The order of influence of each factor was enzyme dosage > enzymatic hydrolysis temperature > enzymatic hydrolysis time.

3.3 Solvent Extraction Method

Solvent extraction is the most traditional method for extracting active components from plants. Its principle is to utilize the principle of like dissolves like and select solvents of appropriate polarity to dissolve the target components from plant tissues. It has the characteristics of operational simplicity, cost-effectiveness and wide application range [31-33].

Sun T L[34] compared the extraction effects of total flavonoids from Hylotelephium erythrostictum by water extraction and alcohol extraction, and found that the total flavonoid content (5.62%) obtained by 70% ethanol reflux extraction (material-to-liquid ratio 1:15, 3 times, 2 hours each time) was significantly higher than that obtained by water extraction (2.80%).Hao Y J[35] studied the extraction effects of different solvents on the antioxidant components of the wound tissue in Rhodiola rosea. The results showed that the total flavonoid content in the four extracts was ethanol > methanol > water > n-butanol in sequence. The total flavonoid content in the ethanol extract was the highest at 80.50mg/g, and the DPPH free radical scavenging rate reached 87.60%.

4.Pharmacological Activity

4.1 Antioxidant Activity

The extract of Sedum officinale exhibits potent free radical scavenging capacity against DPPH/ABTS radicals, effectively eliminating various free radicals such as DPPH and ABTS, and reducing oxidative stress damage. Studies have shown that its antioxidant activity is mainly attributed to the synergistic effect of flavonoids and phenolic acids. The extract of Hylotelephium erythrostictum exhibits remarkable antioxidant capacity, effectively eliminating various free radicals such as DPPH and ABTS, and alleviating oxidative stress damage. Studies have shown that its antioxidant activity is mainly attributed to the synergistic effect of flavonoids and phenolic acids. Liu X Y [36] compared the antioxidant activities of Hylotelephium erythrostictum extracts obtained by different extraction methods. The results showed that the antioxidant activity of the reflux extract was superior to that of the soaking extract. Further component analysis revealed that the different extracts obtained from petroleum ether, ethyl acetate, chloroform, n-butanol, water, etc., with the ethyl acetate extraction site at a concentration of 0.1mg/mL, achieved a DPPH free radical scavenging efficiency of 96%, which was comparable to the antioxidant activity of the positive control VC. The study by Wu X F [4] also confirmed that when the concentration of ethyl acetate in the leaves of Hylotelephium erythrostictum was 0.9mg/mL, the clearance rate of DPPH free radicals was 95.18%, demonstrating extremely strong antioxidant capacity. Suk et al [37] found through multiple antioxidant evaluation systems that the above-ground part extract of Hylotelephium erythrostictum had the highest antioxidant activity, which was positively correlated with its high phenolic content (230mg/g gallic acid equivalent).

4.2 Hypoglycemic Effect

Hylotelephium erythrostictum exhibits multi-target and multi-pathway action characteristics in hypoglycemic effects. Studies have shown that its hypoglycemic mechanism involves multiple links such as inhibiting the digestion and absorption of carbohydrates, protecting the function of pancreatic beta cells, and improving insulin resistance. Sun T L [34] studied that the inhibitory activity of total flavonoids from Hylotelephium erythrostictum on α -glucosidase was displays inhibitory potency comparable to the clinical drug acarbose in clinical practice. 2-α -glucosidase is a key enzyme responsible for oligosaccharide decomposition on the brush border of the small intestine. Inhibiting its activity can delay the hydrolysis of carbohydrates, delay the entry of glucose into the blood, and prevent the postprandial blood glucose increase in diabetic patients. Zhao D H [38] confirmed through the alloxan-induced diabetic rat model that total flavonoids of Hylotelephium erythrostictum can significantly increase the levels of serum insulin and C-peptide and reduce the content of glycated hemoglobin, indicating that it has the effect of protecting pancreatic β cells and improving long-term blood glucose control. The mechanism might be to repair pancreatic β cells while regulating disorders of glucose metabolism and enhancing antioxidant effects. Quan [3] isolated a special benzofuranone compound from Hylotelephium erythrostictum. The half-maximal inhibitory concentration (IC50) of this compound against α -glucosidase was only 1.8μM, with IC50=1.8μM and an inhibitory constant (Ki) of 709 nM. It is a potent natural alpha-glucosidase inhibitor.

4.3 Antibacterial

Yin X M [2] systematically evaluated the antibacterial activities of different solvent extracts of Hylotelephium erythrostictum. The experimental results showed that the ethyl acetate layer had inhibitory effects on all 20 tested strains, and the minimum inhibitory concentration range was 16-256 μg/mL.Zhao C A [39] studied the inhibitory effect of ethanol extract of Hylotelephium erythrostictum on plant pathogenic fungi. The results showed that at a mass concentration of 200g/L, the inhibition rates of 9 plant pathogenic fungi were all above 75%. It also has inhibitory effects on the mycelial growth of Campylobacter maize and the spore germination of Campylobacter maize, and the antibacterial activity increases with the increase of the extract concentration. Zhao CA, Yu M Y [40], et al., studied the anti-feeding and contact killing effects of ethanol extract of Hylotelephium erythrostictum on the third-stage larvae of cabbage worms. The results showed that the lethal median concentrations of Hylotelephium erythrostictum ethanol extract for the 3rd instar larvae of cabbage worm at 48h and 72h were 7.768 g/L and 0.183g/L, respectively. The absenteeism rates at 24 and 48 hours were 99.15% and 91.94% respectively, and the concentrations during absenteeism were 4.819 and 15.442g/L respectively. This indicates that the ethanol extract of Hylotelephium erythrostictum has a high absenteeism and contact killing activity against the third-stage larvae of cabbage worm.

4.4 Anti-inflammatory Effect

Hylotelephium erythrostictum has demonstrated excellent anti-inflammatory effects in various inflammatory models, and its action involves multiple links of the inflammatory signaling pathway. Phenolic acid components enhance the antioxidant capacity of cells by regulating the Nrf2/ARE pathway, while inhibiting the expression of pro-inflammatory factors (such as TNF-α and IL-6), thereby reducing inflammatory responses [41].

Zang M Q [42] investigated the inhibitory effect of the aqueous extract of Hylotelephium erythrostictum on the excessive proliferation and differentiation of drosophila intestinal stem cells caused by the inflammatory factor sodium dodecyl sulfate (SDS). The results showed that the extract of Hylotelephium erythrostictum can significantly increase the survival rate of fruit flies with inflammatory injury (from 11.11% to 100%), reduce the level of reactive oxygen species in the intestine, maintain intestinal morphology, protect intestinal epithelial cells from induced damage, and maintain intestinal homeostasis. Suk [37] found that the ethanol extract of Hylotelephium erythrostictum could concentration-dependently suppressed pro-inflammatory cytokine production of pro-inflammatory factors such as TNF-α, IL-1β and IL-6 in LPS-induced RAW264.7 macrophages. Therefore, Hylotelephium erythrostictum extract is a natural anti-inflammatory drug material. The hylotelephium telephium gel developed by Wang X F [43] has shown significant anti-inflammatory effects in various animal inflammation models (ear swelling, increased peritoneal permeability, paw edema), and can increase serum SOD and GPx activities and reduce MDA content.

5.Research Prospects

At present, there are relatively few studies on the chemical composition, medicinal value and other aspects of Hylotelephium erythrostictum. Therefore, this article reviews the research on the chemical composition, extraction process, pharmacological activity and other aspects of Hylotelephium erythrostictum. The chemical composition of Hylotelephium erythrostictum has pharmacological effects such as antioxidation, hypoglycemic, anti-inflammatory and antibacterial, and has high medicinal value. In the future, metabolomics can be used to analyze the dynamic changes of active ingredients in vivo, network pharmacology methods can be adopted to explain the compatibility mechanism of compound prescriptions, and preclinical research can be combined to promote the development of new natural product drugs, thereby fully releasing their application potential in the fields of biomedicine, natural antioxidants, etc.

Acknowledgements

We gratefully acknowledge the financial support from the Project for the Transfer and Transformation of Scientific and Technological Achievements of Henan Academy of Sciences (241614035), Henan Academy of Sciences Talent Team Building Special Project (241814076), Henan Province Zhongke Science and Technology Achievement Transfer and Transformation Project (2025102). Thank you to Henan Academy of Sciences, Henan High-tech Industrial Co., Ltd. and Zhongyuan Meigu (Luoyang) Technology Industry Co., Ltd. for their scientific collaboration and instrumental support.

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