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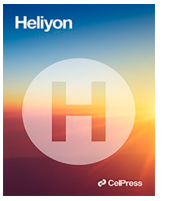

Review article

Research progress in the quality evaluation of Salvia miltiorrhiza based on the association of 'morphological features — functional substances — pharmacological action — clinical efficacy'

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ABSTRACT

Background: Salvia miltiorrhiza (Salvia miltiorrhiza Radix et Rhizoma) is the dried root and rhizome of *Salvia miltiorrhiza* Bge., a plant of the labiate family. It is a type of traditional Chinese medicine that can promote blood circulation for removing blood stasis. It is often used to treat cardiovascular and cerebrovascular diseases in a clinic.

Aim of the study: High-quality Chinese herbal medicines are the premise of the safe and effective use of Traditional Chinese Medicine (TCM) in clinics. We aim to prove the rationality of the traditional identification method, namely, 'the redder the root colour and the thicker the root, the better is the quality', to use the morphological features of Salvia miltiorrhiza as the main index to quickly and directly evaluate its quality.

Materials and methods: By referring to relevant ancient books, domestic and foreign literature, and academic papers, we summarised the research progress regarding the morphological features, functional substances, pharmacological action, and clinical efficacy of Salvia miltiorrhiza.

Results: The redder the colour, the thicker the root, and the denser the texture, the better is the quality of Salvia miltiorrhiza. In Salvia miltiorrhiza, tanshinone II_A and salvianolic acid B are the main functional substances that protect the cardiovascular and cerebrovascular functions. The higher the content of these two functional substances, the better is the clinical efficacy of Salvia miltiorrhiza.

Conclusion: The research idea of the correlation between the 'morphological features, functional substances, pharmacological action, and clinical efficacy' can be applied to evaluate the quality of Salvia miltiorrhiza. This research idea and method can also be applied to more Chinese herbal medicines.

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1. Introduction

The quality of Chinese herbal medicines will directly affect the clinical efficacy and medication safety. The identification methods of Traditional Chinese Medicine (TCM) include origin identification, character identification, microscopic identification, physical and chemical identification, and molecular identification. The purpose of identification is to effectively evaluate the quality of Chinese herbal medicines [1]. Character identification refers to identifying the quality of the medicinal materials in Chinese herbal medicines through the direct use of senses, such as visual observation, taste, touch, smell, etc. The character identification method is the traditional empirical identification method. Professor Xie Zongwan, a famous Chinese herbal medicine expert, called it 'quality evaluation through morphological identification' [2]. As one of the traditional identification methods of TCM, character identification has the advantages of simplicity, rapidity, and directness; however, its subjectivity is strong and no relevant research can satisfactorily explain the scientific principle of the traditional theory of 'quality evaluation through morphological identification'. The author believes that achieving a rapid and accurate evaluation of the quality of Chinese herbal medicines requires the use of modern scientific theories and methods to explain 'quality evaluation through morphological identification', to evaluate the quality of Chinese herbal medicines using their morphological features as the main index.

Salvia miltiorrhiza (Salvia miltiorrhiza Radix et Rhizoma) is the dried root and rhizome of *Salvia miltiorrhiza* Bge., a plant of the labiate family. The quality of Salvia miltiorrhiza with 'red colour and thick root' is known to be the best in past dynasties. This empirical identification method is still applicable in modern times. The efficacy of Salvia miltiorrhiza in promoting blood circulation for removing blood stasis, promoting menstruation, and relieving pain has been confirmed in long-term clinical application and has shown good efficacy in the treatment of cardiovascular and cerebrovascular system-related diseases [3]. In modern times, in-depth and comprehensive studies have been conducted on the morphological features, functional substances, pharmacological action, and clinical efficacy of Salvia miltiorrhiza, with a large amount of relevant literature, which is representative to a certain extent. Therefore, the author proposed the idea of quality evaluation of Salvia Miltiorrhiza that is related to its 'morphological features, functional substances, pharmacological action, and clinical efficacy' to provide new ideas and methods for the rapid and accurate quality evaluation of Salvia miltiorrhiza by considering its morphological features as the main index (Fig. 1).

2. Methods

2.1. Information retrieval from ancient books of the past dynasties

We consulted the relevant ancient books in the library of Gansu University of Traditional Chinese Medicine, sorted out and summarised the relevant records of morphological features and quality evaluation of Salvia miltiorrhiza.

2.2. Chinese literature data retrieval

We used Chinese databases, such as CNKI (中国知网), WanFang (万方), and VIP (维普), as the data sources. The literature types

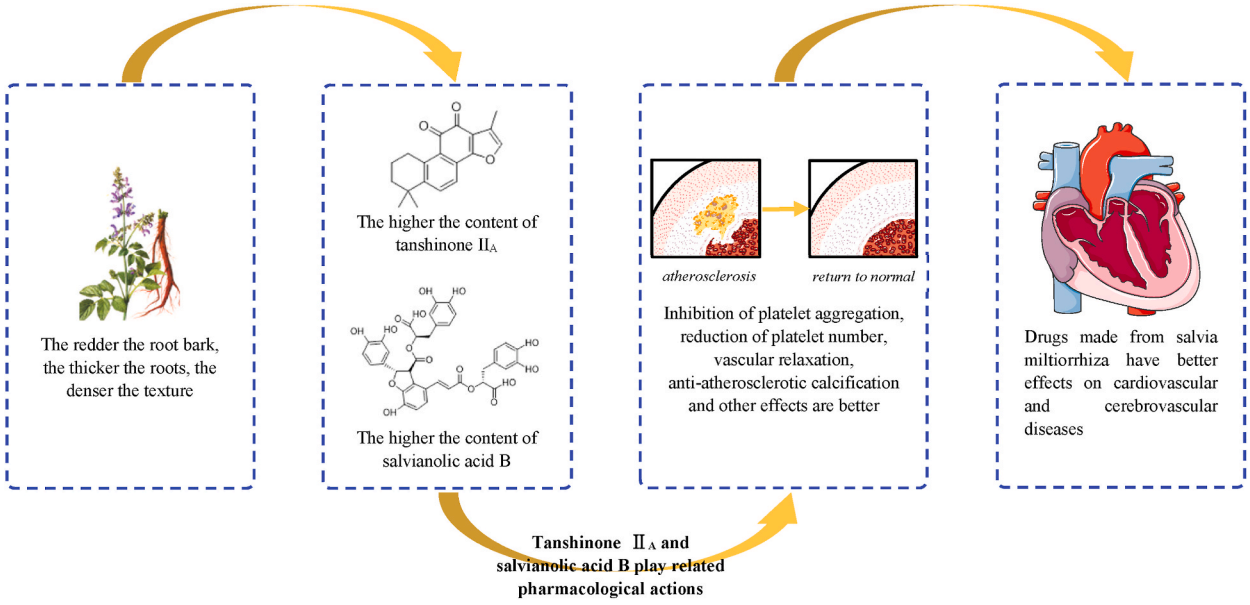

Fig. 1. Quality evaluation of Salvia miltiorrhiza associated with its 'morphological features, functional substances, pharmacological action, and clinical efficacy'.

were selected as '期刊' (journal) and '学位论文' (dissertation). The search terms were set as '丹参' (Salvia miltiorrhiza), '外观性状' (morphological features), '功效物质' (functional substances), '药理作用' (pharmacological action), and '临床疗效' (clinical efficacy), and the language was selected as 'Chinese'; the time span was not limited.

2.3. English literature data retrieval

We used international databases, such as PubMed and Web of Science (WOS), as the data sources. The literature types were selected as 'Article or Review'. The search terms were set as 'Salvia miltiorrhiza', 'danshen', '*Salvia miltiorrhiza* Bge.', 'Salvia miltiorrhiza Radix et Rhizoma', 'morphological features', 'functional substances', 'pharmacological action', and 'clinical efficacy'; the time span was not limited.

We read and summarised all kinds of literature specified above, and the specific analysis results are as follows.

3. Research progress on morphological features, functional substances, pharmacological action, and clinical efficacy of Salvia miltiorrhiza

3.1. Research progress on the relationship between morphological features and quality of Salvia miltiorrhiza

3.1.1. Records of the morphological features and quality evaluation of Salvia miltiorrhiza in past dynasties

Salvia miltiorrhiza was first recorded in Shennong Bencao Jing. The description of Salvia miltiorrhiza in *Bencao Tujing* is as follows: 'the root is red, as big as a finger, more than a foot long, and several roots per seedling'. The description of the quality evaluation of Salvia miltiorrhiza in *Bencao Pinhui Jingyao* is as follows: 'it is better to use with thick roots'. In *Bencao Gangmu* written by Li Shizhen of the Ming Dynasty, Salvia miltiorrhiza was believed to have a red root bark and purple interior. In *Bencao Chengya Banji*, its description is as follows: 'the root is as big as a finger, more than a foot long, and it is good to pick in winter'. The morphological features of Salvia miltiorrhiza were recorded in *Zengding Weiyao Tiaobian* of the Republic of China as follows: 'red root bark, purple, and streaked interior. A dry and loose body, large above ground parts and without a root head has the best quality'. In *Zhongyaocai Chuantong Jianbie Jingyan*, Jin Shiyuan recorded that Salvia miltiorrhiza with 'a dry body, thick root, red root bark, lack of a root head, fibrous roots, and impurity is of good quality'. Consequently, 'red colour' and 'thick root' are important identification indicators of the morphological features of Salvia miltiorrhiza. In summary, the quality evaluation of Salvia miltiorrhiza in the past dynasties mostly emphasised the characteristics, colour of roots, and other features, and most of specimens were those with thick roots, red root bark, purple interior, no root head, fibrous root, and impurity, as presented in Table 1.

3.2. Research progress on the relationship between the morphological features and functional substances of Salvia miltiorrhiza in modern times

Shi et al. [4] observed the characteristics of wild Salvia miltiorrhiza from 14 places of origin in Anhui Province by field investigation and sample collection and determined the content of fat-soluble components of wild Salvia miltiorrhiza by high-performance liquid chromatography (HPLC). The results indicated significant differences in the colour of the corolla, compound leaf, and root bark of Salvia miltiorrhiza from different places of origin in Anhui Province, among which the contents of fat-soluble components of Salvia miltiorrhiza with deep purple flowers, deep green leaves, and red root bark were high, and those of Salvia miltiorrhiza with light purple flowers, yellow-green leaves, and brown root bark were low. Li et al. [5] determined the correlation between the morphological features (texture, diameter, and colour) and salvianolic acid B content of Salvia miltiorrhiza pieces. Through visual observation, they found that the colour of Salvia miltiorrhiza pieces from the same place of origin was not significantly different. The higher the density and texture of Salvia miltiorrhiza pieces, the higher was the content of salvianolic acid B; the larger the diameter of Salvia miltiorrhiza pieces, the higher was the content of salvianolic acid B. Therefore, they speculate that the thicker and denser the root of Salvia miltiorrhiza, the higher was the content of salvianolic acid B. Wang et al. [6] used phenotypic group technology to systematically

Table 1
Records of morphological features of Salvia miltiorrhiza in ancient literature.

Dynasty	Origin	Original record (in Chinese)	Morphological features
Song	*Bencao Tujing*（本草图经）	'根赤，大如指，长亦尺余，一苗数根'	The root is red, as big as a finger, and more than a foot long.
Ming	*Bencao Pinhui Jingyao*（本草品汇精要）	'用：根粗壮者佳'	Thick roots.
	Compendium of Materia Medica（本草纲目）	'根皮丹而肉紫'	Red root bark, purple interior.
	Bencao Chengya Banji（本草乘雅半偈）	'根大如指，长尺余，冬采者良'	The root is as big as a finger, and more than a foot long.
Republic of China	*Zengding Weiyao Tiaobian*（增订伪药条辨）	'皮色红，肉紫有纹。质燥体松，头大无芦为最佳。丹参芦细质松，多细枝次。头小枝粗，肉糯有白心，亦次'	Red root bark, purple and streaked interior, large, and without root head above ground.
Modern	*Zhongyaocai Chuantong Jianbie Jingyan*（中药材传统鉴别经验）	'以身干、条粗壮、色红、无芦头、须根杂质者为佳'	Dry body, thick root, red root bark, without root head, fibrous root, and contains impurity.

evaluate the parameters of root morphological characteristics of Salvia miltiorrhiza through high-throughput digital collection and modeling of root morphological characteristics, and determine the correlation between key morphological characteristics and active components. They found that tanshinone compounds were mostly orange and accumulated in a large amount in the periderm structure, making the root appear red; thus, 'the redder the colour' indicates a higher content of tanshinones in Salvia miltiorrhiza. Ran et al. [7] used HPLC to compare the content of tanshinone II_A in Salvia miltiorrhiza from different provenances, places of origin, and harvest periods, and found that when the surface of Salvia miltiorrhiza was brownish red or reddish brown, the content of tanshinone II_A was higher; when the surface of Salvia miltiorrhiza was grayish brown, the content of tanshinone II_A was lower. Additionally, many experiments have been conducted to study the correlation between 'morphological features and functional substances' of Salvia miltiorrhiza through more accurate, objective, and transmissible bionic technology. Diao [8] found that the redder the root bark, the higher was the content of tanshinones; the denser the texture, the higher was the content of salvianolic acid B. Wei et al. [9] studied the correlation between the root colour of Salvia miltiorrhiza and the content of its active components using colorimeter and HPLC. Their experimental results showed that the redder the colour, the higher were the contents of fat-soluble and water-soluble components of Salvia miltiorrhiza. The change in colour has a greater impact on the content of tanshinone II_A and salvianolic acid B, and has a greater impact on the content of fat-soluble components than the water-soluble components. Liu et al. [10] used a colorimeter and HPLC to study the correlation between the colour of Salvia miltiorrhiza powder and content of functional substances. The results showed that the colour index Δa^* has a significant positive correlation with the content of functional substances. Shen [11] quantitatively analysed the redness of Salvia miltiorrhiza using a colorimeter and visible spectrophotometry, and analysed the correlation between the morphological characteristics of Salvia miltiorrhiza and its active components. They found that the redness of Salvia miltiorrhiza was positively correlated with its fat-soluble active components. Shi et al. [12] used HPLC to determine the content of tanshinones and salvianolic acid B in Salvia miltiorrhiza. The chroma value of the methanol solution of Salvia miltiorrhiza powder was determined by a colorimeter. The results showed that the larger the value of a*, the higher were the contents of tanshinones and salvianolic acid B. Wang et al. [13] conducted experiments with a colorimeter and HPLC, and found that the chromaticity value a* of the surface colour of Salvia miltiorrhiza was positively correlated with the content of tanshinones.

In summary, the redder the root colour and the larger the diameter, the higher was the content of related functional substances, which is consistent with the 'thick root, red root bark, and purple interior' features recorded in ancient literature of all dynasties. Table 2 presents the specific results of the correlation studies.

3.3. Research progress on the functional substances of Salvia miltiorrhiza and their pharmacological action

The effective components of Salvia miltiorrhiza refer to the chemical substances contained in Salvia miltiorrhiza that can reflect its pharmacological action and express its clinical efficacy [14]. Relevant research has shown that the main functional substances in Salvia miltiorrhiza are water-soluble phenolic acids (salvianolic acid A, salvianolic acid B, salvianolic acid, etc.) and fat-soluble tanshinones (tanshinone I, tanshinone II_A, cryptotanshinone, etc.) [15]. The quality evaluation standard of Salvia miltiorrhiza stipulated by *The Chinese Pharmacopoeia (2020)* states that the total content of tanshinone II_A, cryptotanshinone, and tanshinone I must not be less than 0.25%, and the content of salvianolic acid B must not be less than 3.0%, indicating that the contents of tanshinone II_A and salvianolic acid B represent the quality of Salvia miltiorrhiza to a certain extent.

The pharmacological action of TCM is the summary of the research on the therapeutic effect of Chinese herbal medicines using modern pharmacology, which is most closely related to the traditional efficacy of Chinese herbal medicines. Therefore, studying the relationship between the 'traditional efficacy and pharmacological action' of Chinese herbal medicines is one important method to clarify the modern biological basis of the efficacy of TCM [16]. The traditional effects of Salvia miltiorrhiza include the promotion of blood circulation for removing blood stasis, promoting menstruation and relieving pain, clearing the heart and preventing uneasiness, cooling blood, and eliminating carbuncle. Salvia miltiorrhiza is a representative Chinese herbal medicine for promoting blood circulation and removing blood stasis. At present, relevant studies have found that the syndrome of blood stasis in TCM has the following pathophysiological changes: high blood viscosity, blood circulation and microcirculation disorders, platelet activation and adhesion, blood coagulation, fibrinolysis system changes, and thrombosis, among others. Cardiovascular and cerebrovascular diseases are general terms for heart and brain diseases. Western medicine generally refers to diseases in the heart, brain, and whole body tissues caused by blood viscosity, hyperlipidemia, and atherosclerosis as ischemic or hemorrhagic diseases [17]. TCM believes that the fundamental pathogenesis of cardio-cerebrovascular diseases is 'blood stasis', and the method of promoting blood circulation to alleviate blood stasis is the main method used to treat the syndrome of blood stasis in TCM [18]. Therefore, Salvia miltiorrhiza can effectively treat cardiovascular and cerebrovascular diseases to a certain extent.

Modern pharmacological research shows that tanshinone II_A and salvianolic acid B can significantly alleviate the syndrome of blood stasis and play a role in protecting cardio-cerebral blood vessels by dilating blood vessels, reducing arterial pressure, inhibiting platelet aggregation, anticoagulation, and other mechanisms. The specific pharmacological functions are presented in Table 3. This

Table 2
Correlation study on 'morphological features and functional substances' of Salvia miltiorrhiza.

Morphological features	Effective components
The flowers are deep purple, leaves are dark green, and root bark is red.	The higher is the content of fat-soluble components.
The redder the root bark.	The higher is the content of tanshinone II_A.
The larger the diameter and the denser the texture of the pieces.	The higher is the content of salvianolic acid B.

Table 3
Pharmacological functions of tanshinone II_A and salvianolic acid B on cardio-cerebrovascular protection.

Functional substances	Pharmacological action	References
Tanshinone II_A	Reduce the number of platelets, inhibit platelet aggregation, and has a certain anticoagulation effect	[19–22]
	Diastolic blood vessel	[23–25]
	Anti-atherosclerotic calcification	[26–30]
	Significant cardiac protective effect	[31,32]
Salvianolic acid B	Inhibit platelet activation and aggregation	[33–37]
	Anti-atherosclerosis	[38,39]
	Alleviate acute myocardial ischemia injury in rats	[40]
	Reduce lipid deposition in the thoracic aorta, aortic arch, and intimal thickness of the thoracic aorta	[41]

proves that tanshinone II_A and salvianolic acid B could represent the quality of Salvia miltiorrhiza to some extent.

3.4. Research progress on the correlation between dosing concentration and efficacy of functional substances of Salvia miltiorrhiza

Hou et al. [42] selected 24-month-old aging guinea pigs as animal experimental models and fed them diets containing 75, 100, and 150 mg/kg of water-soluble extract of Salvia miltiorrhiza every day for 28 days to evaluate its effect on abnormal hemorheological parameters of aging guinea pigs. The results showed that when the dosage of a water-soluble extract of Salvia miltiorrhiza in guinea pigs' diet was 150 mg/kg, the blood viscosity of aging guinea pigs significantly decreased. Tang et al. [28] found that tanshinone II_A can reduce the atherosclerotic plaque of the aortic arch by 23, 34, and 47% at doses of 10, 30, and 90 mg/kg, respectively, through in-vivo experiments, indicating that when the content of tanshinone II_A was high in the dose range of 10–90 mg/kg, the improvement of atherosclerosis was better. Maione et al. [20] found that tanshinone II_A can inhibit platelet aggregation in rats in a concentration-dependent manner. Tang et al. [27] found that tanshinone II_A could reduce the pathological changes of atherosclerosis calcification in a dose-dependent manner through experiments. Fang et al. [29] established a rabbit model with a high-fat diet and administered 6.25, 15, and 37.5 mg/kg of tanshinone II_A. They found that 37.5 mg/kg of tanshinone II_A could effectively improve atherosclerosis. Chen et al. [43] found that tanshinone II_A at an oral dose of 3–30 mg/kg could inhibit the formation of atherosclerosis in rabbits, and the inhibitory effect was the strongest when the oral dose was 30 mg/kg. Zhong et al. [44] used reverse transcriptase-polymerase chain reaction (RT-PCR) to study the effect of tanshinone II_A at different mass concentrations (0, 3.13, 6.25, 12.5, 25, 50 ng/ml) on the expression of thrombomodulin in vascular endothelial cells of rats. The results showed that the expression of thrombomodulin decreased significantly with the increase in the mass concentration of tanshinone II_A. Hu et al. [40] established a rat myocardial ischemia model and treated rats with salvianolic acid B at doses of 5, 10, and 15 mg/kg, respectively. They found that salvianolic acid B could not improve myocardial ischemia in rats at doses of 5 mg/kg but could improve myocardial ischemia in rats at doses of 10 and 15 mg/kg; they also found that salvianolic acid B had better effects at doses of 15 mg/kg. Lin et al. [45] found that salvianolic acid B can reduce myocardial ischemia-reperfusion injury in rats in a dose-dependent manner when the dose is in the range of 4–64 mg/kg.

In summary, both tanshinone II_A and salvianolic acid B play a protective role on cardio-cerebral vessels in a dose-dependent manner; namely, within a certain dose range, the higher the contents of tanshinone II_A and salvianolic acid B, the better is the efficacy of Salvia miltiorrhiza. However, the specific dose range requires further study.

3.5. Research progress on the clinical efficacy of Salvia miltiorrhiza

In modern clinical practice, Salvia miltiorrhiza has mainly been used for the prevention and treatment of cardio-cerebrovascular diseases, such as angina pectoris, coronary heart disease, hypertension, and stroke [46]. It has a good auxiliary treatment effect, can improve the cure rate of patients, and can significantly improve the clinical symptoms of patients, all of which help realise the clinical application value of Salvia miltiorrhiza [47]. The China Food and Drug Administration (CFDA) has approved the use of more than 300 preparations related to Salvia miltiorrhiza. The clinical effect of compound danshen (Salvia miltiorrhiza) dripping pills on cerebral infarction is significant [48], and when these are combined with rosuvastatin calcium tablets in the treatment of unstable angina pectoris, the results are effective and safe [49]. Compound danshen injection combined with astragalus injection can effectively improve the cardiac function and serum indices of patients, and has a better effect on the treatment of elderly patients with chronic congestive heart failure during acute attacks [50]. Sodium tanshinone II_A sulfonate injection can effectively improve hemorheology, reduce blood viscosity, reduce pulmonary hypertension, and improve cardiac function, which is worthy of clinical application [51]. It can also effectively treat coronary heart disease, improve related indices of coronary heart disease, optimise hemorheology indexes, and has good safety [52]. The use of compound danshen capsules can reduce the systolic blood pressure and pulse rate of hypertensive patients, and it is well tolerated by the body [53].

Relevant literature has shown that the promotion and application of blood circulation-promoting and blood stasis-removing drugs for the prevention and treatment of cardiovascular diseases are the original contributions of Chinese medical experts [18]. All these findings further prove that the traditional effect of Salvia miltiorrhiza on promoting blood circulation for removing blood stasis has a certain correlation with protecting cardio-cerebrovascular diseases in modern pharmacology. Thus, Salvia miltiorrhiza can be used to effectively prevent cardio-cerebrovascular diseases.

4. Correlation analysis of 'morphological features — functional substances — pharmacological action — clinical efficacy'

Based on the above series of summaries and research progress on Salvia miltiorrhiza, we produced the quality evaluation model pattern of Salvia miltiorrhiza, as shown in Fig. 2. In addition to Salvia miltiorrhiza, the correlation analysis between 'morphological features, functional substances, pharmacological action, and clinical efficacy' can also be conducted for many Chinese herbal medicines.

The author believes that if this correlation analysis is to be applied to more Chinese herbal medicines, a series of experimental studies, as shown in Fig. 3, can be conducted to establish the research model for the quality evaluation of Chinese herbal medicines. In particular, determining the correlation between the 'morphological features, functional substances, pharmacological action, and clinical efficacy' of Chinese herbal medicines can help realise their rapid and accurate quality evaluation.

5. Summary and outlook

The above summary of relevant studies satisfactorily explains the scientific nature of the traditional quality evaluation method that is as follows: 'the redder the colour and stronger the root, the better is the quality of Salvia miltiorrhiza'; our summary proves the rationality and reliability of the correlation analysis between the 'morphological features, functional substances, pharmacological action, and clinical efficacy' of Salvia miltiorrhiza. Simultaneously, this correlation analysis also conforms to the holistic concept and systematic thinking of TCM theory. However, the following problems still exist: ① in addition to tanshinone II_A and salvianolic acid B, tanshinone I and cryptotanshinone are also used as quality evaluation criteria of Salvia mltiorrhiza in the 2020 edition of Chinese Pharmacopoeia. Moreover, many other components are also present in Salvia miltiorrhiza, such as Danshensu, salvianolic acid A, protocatechualdehyde, and rosmarinic acid, which also have different pharmacological functions [54]; however, only few reports exist regarding the correlation between the morphological features of Salvia miltiorrhiza and these functional substances. ② In this study, the correlation analysis between 'morphological features, functional substances, pharmacological action, and clinical efficacy' was only conducted to elucidate the traditional efficacy of Salvia miltiorrhiza in promoting blood circulation for removing blood stasis. However, modern pharmacological studies have shown that Salvia miltiorrhiza has other pharmacological effects, such as anti-tumor, anti-liver damage, nervous system protection effects [54], but the main functional substances responsible for these pharmacological functions are still unclear. Only few studies have been conducted on these clinical effects; thus, these pharmacological functions are not described here. ③ Only few clinical studies have been conducted on the dose-effect relationship of Salvia miltiorrhiza. ④ At present, most studies on the clinical efficacy of Salvia miltiorrhiza have mainly focused on the efficacy and mechanism of the related preparations of Salvia miltiorrhiza and the combination of these preparations with western medicines or Chinese herbal medicines for the prevention and treatment of related diseases. However, most reports on the clinical efficacy of a single medicine of Salvia miltiorrhiza comprised pharmacological experiments using animal models, which could not completely represent the clinical efficacy of Chinese

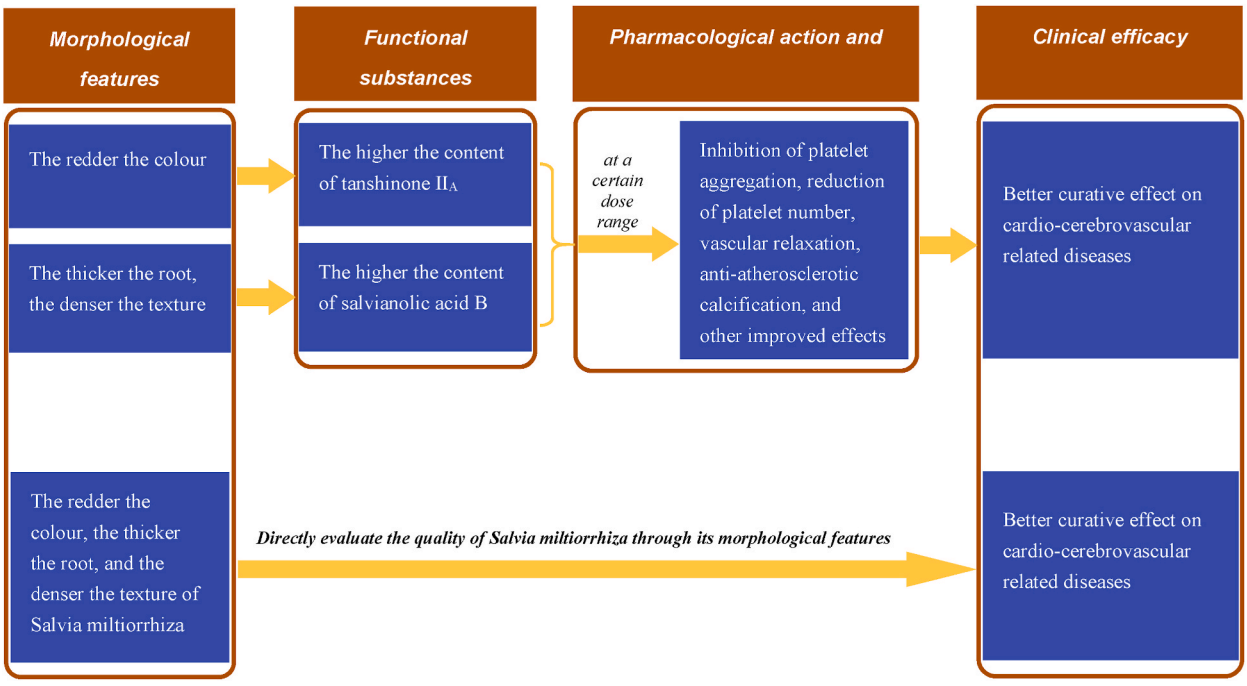

Fig. 2. Quality evaluation model pattern of Salvia miltiorrhiza based on the association between 'morphological features, functional substances, pharmacological action, and clinical efficacy'.

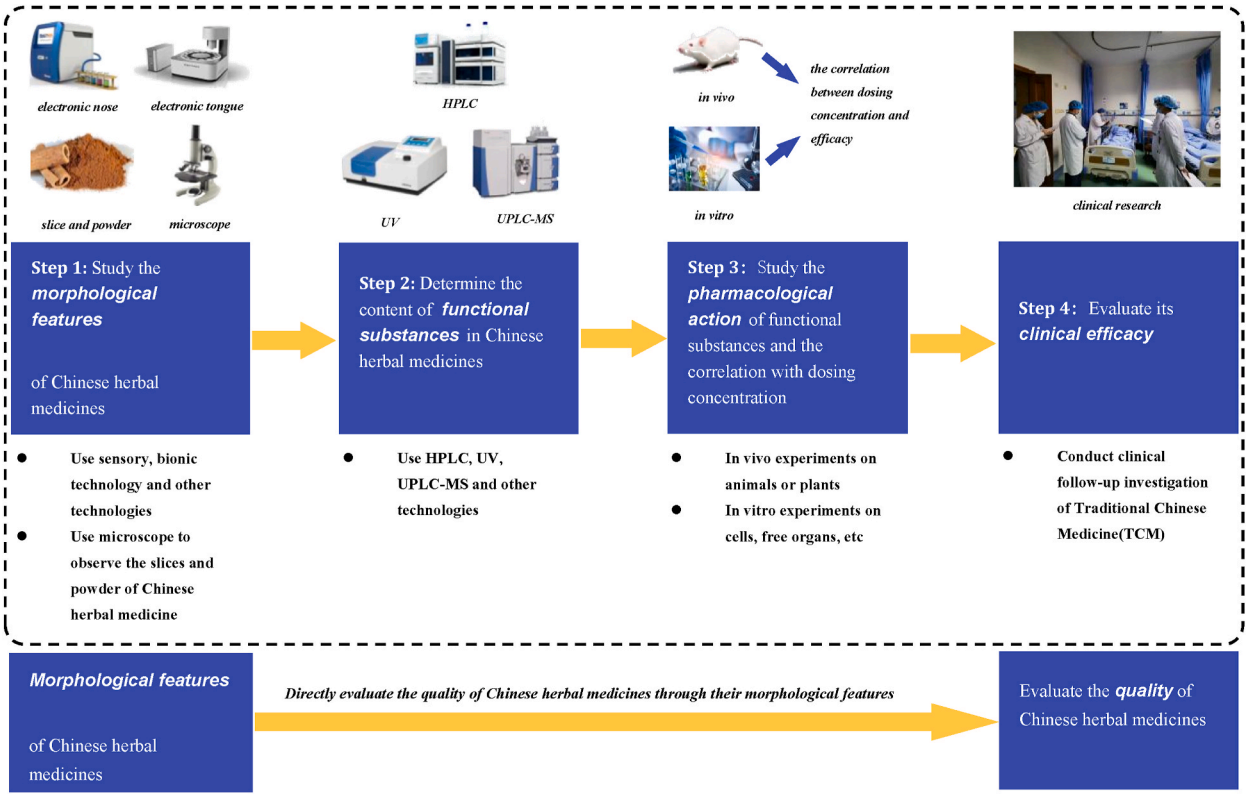

Fig. 3. Quality evaluation of the modern pattern of Chinese herbal medicines based on the association between 'morphological features, functional substances, pharmacological action, and clinical efficacy'.

herbal medicines.

With the modernisation of TCM in recent years, a modern TCM quality evaluation and control system centred on index components has been established. However, the existence of index components is not closely related to the clinical efficacy and safety, thereby hindering the evaluation and control of the quality of TCM [55]. Based on this correlation analysis, the author proposes the following suggestions for the future development of the quality evaluation of Chinese herbal medicines: ① with the development of science and technology, a series of bionic technologies can be used to digitally evaluate the range of morphological features, such as the colour, smell, and taste of high-quality Chinese herbal medicines in the future. ② For one or several key substances whose clinical efficacy has been determined, the clear chemical structure, efficacy, and easy detection of these substances must be realised. ③ The clinical-oriented safety and efficacy of evaluation studies must be strengthened. ④ The research and application of biological assays for Chinese herbal medicines must be increased with 'clinical effect' as the guideline, 'active organism' as the technical means, and 'quality of Chinese herbal medicines' as the objective of evaluation [56]. ⑤ Clinical research on Chinese herbal medicines must be conducted, such as the collection of pieces of Chinese herbal medicines with different morphological features from large TCM hospitals. First, a correlation study between their 'morphological features and functional substances' must be conducted. Subsequently, in-vivo or in-vitro experiments must be conducted to compare their pharmacological actions. Finally, a clinical follow-up investigation must be conducted to investigate the efficacy of pieces of Chinese herbal medicines with different morphological features in patients. The quality of Chinese herbal medicines was evaluated based on their morphological features. This study was conducted with the following objectives: to establish the guiding significance and reference value to improve the quality standard of Chinese herbal medicines based on their clinical efficacy for safe and rational clinical drug use; and to provide a strong theoretical basis for ensuring the clinical safety and effectiveness of Chinese herbal medicines, realising the high quality of Chinese herbal medicine products, and promoting the high-quality development of the TCM industry.

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Data availability statement

No data was used for the research described in the article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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