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Chinese Medicine and Culture Listed in the World Journal Clout Index (WJCI) Report (2021 Edition)

Recently, the World Journal Clout Index (WJCI) 2021 report was published. It is a report jointly developed by the evaluation and research departments of six institutes, namely, the Institute of Scientific and Technical Information of China, *China Academic Journal* (CD version) Electronic Magazine Co., Ltd., Tsinghua University Library, Wanfang Data Co., Ltd., Society of China University Journals and China Editology Society of Science Periodicals. The *Chinese Medicine and Culture* has been successfully listed in the report.

Aimed at establishing a brand-new evaluating system, the WJCI report is a journal evaluation report reflecting the results of world wide's journals competing on the same platform. Journals listed in the report are considered exemplary and representative in their regions and disciplines. We are deeply indebted to the editorial board experts, reviewers, authors and colleagues from all walks of life for their support and assistance to this magazine! In the near future, the *Chinese Medicine and Culture* will continue to promote the interdisciplinary research of nature, humanities and history in traditional Chinese medicine (TCM), showcase the theoretical connotation of TCM and its profound cultural heritage in a multidimensional perspective, and build an influential international academic exchange platform in the field of TCM.

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Research Article

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OPEN

Discussion of Medicine and Religion: Study of Missionary Hospitals in Modern Shanghai, China

Lyu-Hua Chen, Li-Yun Chen✉

Abstract

In modern times, 15 missionary hospitals were established in Shanghai, including 6 Protestant hospitals and 9 Catholic hospitals. These hospitals were the products of Western missionaries in China. The establishment of missionary hospitals objectively introduced Western medicine into China and changed its original medical system. Based on documents and periodicals, Shanghai archives, Xujiahui library materials, hospital historical records, and domestic and foreign library historical materials, this paper systematically reviews the development of missionary hospitals in Shanghai, and discusses their balance between medicine and religion, to provide ideas and references for future research.

Keywords: Missionary hospital; Medical missionary; Modern Shanghai

1 Introduction

Since the beginning of the modern era, many Western missionaries have traveled to China with the purpose of preaching. However, at the beginning of this period, the Chinese people were relatively conservative and their understanding of medicine and health conditions were limited. The Chinese people were not generally inclined to listen to preaching. To convert the Chinese people to Christianity, Western missionaries found a shortcut: to "preach through medicine." They appointed medical missionaries to China who had the dual identity of doctors and missionaries. They established hospitals in an attempt to achieve the purpose of "healing the spirit" through "curing disease." Therefore, missionary hospitals and medical missionaries were the products of Western missionaries adapting to modern Chinese society. Western medicine was introduced to China by means of these medical missionaries. The introduction of Western medicine itself had a certain aggressiveness and ambition. At first, the Chinese attitude toward Western medicine was exclusion, suspicion, and resistance. By providing free medical services, missionary hospitals selected diseases for which immediate curative effects could be achieved, with a particular eye toward poor people. Therefore, Western medicine quickly became trusted and accepted by the Chinese people.

Medical missionaries are church members who preach while treating patients, and this treatment process is often free. However, over time, the medical treatment is gradually separated from missionary activity in medical missionary work. Throughout history, this special mode of "medical missionary" work made the missionary hospital more like a place for spreading modern culture. Shanghai, being the first batch of trading ports in the modern era, became one of the centers of domestic economy and culture. Western missionaries regarded this place as a key missionary area and successively set up many hospitals in Shanghai. The establishment of these hospitals has left a strong mark in the modern medical history of Shanghai. We sought to examine the existing research and historical literature to discuss the role of Shanghai missionary hospitals.

2 Origin of the missionary hospital

Since 1840, China has opened a number of trading ports. Western capitalist countries began to land in China, bringing with them an influx of Western missionaries (mainly divided into Protestantism and Catholicism). The purpose of these missionaries in China was to preach and spread the "Gospel of God." What they tried to salvage was the "soul" of the Chinese people. The missionaries used a variety of methods to achieve this goal, such as translating and publishing books, running schools, and conducting itinerant lectures. In practice, the Western missionaries found that the medical missionary approach, in which missionaries preach by providing medical services to Chinese people, was more in line with the pragmatic psychology of the Chinese people at that time. Therefore, a group of special medical missionaries appeared, who had the dual identity of doctor and missionary. Western medicine was introduced to China and completed the transformation of localization, secularization, commercialization, specialization, and cooperation.

The earliest missionary hospital in China was Boji Hospital, founded in Guangzhou in 1835. Its founder

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was Peter Parker (1804–1888), the first medical missionary to China. Western missionaries witnessed the infinite hope brought by the application of medicine to missionary activities. This is why the West gave Peter Parker great affirmation: "when the Western failed to open the horizontal bolt of China's door, he opened China's door with a scalpel." [1] Further missionaries followed suit. In just 31 years, there were 16 missionary hospitals and 24 missionary clinics in China, treating 41, 218 patients every year. [2] From 1860 to 1900, there were about 100 missionary hospitals in China. After 1900, this network had expanded all over the country, and the number increased by more than 400.[3] By the end of the Sino-Japanese War, the number of missionary hospitals among Chinese provinces and cities had become considerable, including 35 in Fujian, 28 in Guangdong and Jiangsu, 25 in Shandong, 22 in Hebei, 21 in Hubei and Sichuan, 16 in Hunan, 15 in Zhejiang, 12 in Liaoning, 10 in Anhui Province, six in Henan Province, four in Guangxi Province and Yunnan Province, three in Jilin Province, two in Guizhou Province and Heilongjiang Province, and one each in Gansu Province, Xinjiang Province, and Shanxi Province.[4]

In 1834, according to the provisions of the Nanjing Treaty, China opened five trading ports: Guangzhou, Xiamen, Fuzhou, Ningbo, and Shanghai. Following this Treaty, Shanghai gradually became the center of economy, trade, and culture. Western capitalist countries established docks, divided concessions, and opened shops and banks in Shanghai. The Western churches followed soon after and set up a sermon station to preach. William Lockhart (1811–1896), a medical missionary of the London Missionary Society, came to Shanghai for an investigation as soon as the port of Shanghai was opened, and there he established Renji Hospital, the first missionary hospital in Shanghai, in 1844. According to the existing historical data, there were 15 hospitals with a missionary background in Shanghai before the founding of the People's Republic of China, including 6 Protestant hospitals and 9 Catholic hospitals. (Table 1).

These modern missionary hospitals had several specific characteristics: they were missionary, medical, and charitable. First, in terms of their missionary nature, missionary hospitals usually have churches or rooms specially used for missionary work. Before 1860, William Lockhart rang the bell at 7:30 every morning to gather patients in Renji Hospital to listen to teaching and participate in prayer. Patients and accompanying family members also had to listen to the preacher while waiting for treatment. [5] There were churches and nunneries in Shanghai General Hospital; in 1904, after renovation, St. Luke's Hospital set up on the ground floor of the hospital a chapel that served patients during the day and was opened to surrounding residents at night. Founded in 1923, the Sacred Heart Hospital had six buildings, including an independent Sacred Heart Church. The missionary work in early missionary hospitals was undertaken by medical missionaries, who were professional doctors graduated from medical school. In addition to their religious beliefs, as doctors, benevolence and commitment to

Table 1 List of some missionary hospitals in modern Shanghai, China

Hospital Name	Missionary	Establishing time	Founder	Remarks
Shanghai Chinese Hospital	London Missionary Society	1844	William Lockhart	It is now Renji Hospital, affiliated with Shanghai Jiao Tong University School of Medicine.
Shanghai General Hospital	Archidioecesis Nanchinensis	1863	Diplomatic expatriate	It is now Shanghai General Hospital, affiliated with Shanghai Jiao Tong University School of Medicine.
St. Luke's Hospital	Episcopal Church in the United States of America	1866	Hony-Yu Wu	It is now Tong Ren Hospital, affiliated with Shanghai Jiao Tong University School of Medicine.
Hôpital St. Antoine	Catholic sisters of charity	1883	French sisters	It is especially for poor foreign teachers in China and was incorporated into Luwan District Central Hospital in the early 1980s.
Margaret Williamson Hospital	Woman's Union Missionary Society of America for Heathen Lands	1884	Margaret Williamson	It is also called Red House Hospital, now Obstetrics & Gynecology Hospital of Fudan University.
St. Elizabeth Hospital	Episcopal Church in the United States of America	1902	Steves	It was renamed Guangren Hospital in 1937.
Hôpital Sainte-Marie	Roman Catholic Metropolitan Archdiocese of Nanjing	1907	Monseigneur Prosper Paris	It is now Ruijin Hospital, affiliated with Shanghai Jiao Tong University School of Medicine.
Bethel Hospital	Bethel Mission	1920	Mary Stone	It is now Ninth People's Hospital, affiliated with Shanghai Jiao Tong University School of Medicine.
Shanghai Sanatorium Clinic	Seventh-day Adventist Church	1922	Miller	–
Sacred Heart Hospital	Ordine francescano	1923	Bo-Hong Lu	It is now Yangpu Hospital, affiliated with Tongji University.
St. Joseph's Hospital	Catholicism carries on the meeting	1926	Bo-Hong Lu	It was a clinic opened by Catholicism carries on the meeting in 1917.
Hôpital Coeur Immaculé De Marie	Catholicism carries on the meeting	1930	Bo-Hong Lu	It was destroyed by Japanese bombers in 1937.
Sino-Belgian Radium Institution	Roman Catholic Archdiocese of Cotabato	1931	H•vasslllsdis	It is now Fudan University Cancer Center.
Shanghai Mercy Hospital	Catholicism carries on the meeting	1935	Bo-Hong Lu	It specializes in mental health care.
Hôpital de la Saint Famille	Catholic sisters of charity	1948	French sisters	It was a clinic in Lujiazui, Pudong in the 14th year of Guangxu for missionary purposes.

saving the dying and healing the wounded were also part of their lifelong vows. Therefore, as missionary hospitals developed, more and more medical missionaries began to separate their identities of doctors and missionaries. They believed that "one person with two identities and work of missionary doctors and clergy will delay each other and fail at both ends. Missionary doctors should focus on medical treatment."[6] With the increasing number of patients in the hospital, the heavy hospital workload made these medical missionaries unable to accommodate the work of missionary activity and at the same time, medical treatment. Therefore, missionary work in the missionary hospital began to be handed over to missionaries who were specifically responsible for preaching, and missionary doctors no longer served as preachers concurrently. Medicine was thus separated from religion in the missionary hospital.

3 Protestant missionary hospitals

3.1 Shanghai Chinese Hospital (Renji Hospital)

The Shanghai Chinese Hospital, founded in 1844, was the first missionary hospital in Shanghai. It opened the way for Western medicine to establish its root in modern Shanghai.

The original site of the hospital was at the wharf outside the Dadongmen gate in Shanghai county. It was originally known as "Luo's clinic," run in a rented two-story house. The later name of the hospital, "Renji," means "benevolence and helping the world" in Chinese. In the long development history of Renji Hospital, it had many titles, including Luo's Clinic, China Hospital, Renji Medical Museum, Shandong Road Hospital, and Rexroth China Hospital.

Renji Hospital proved an exemplary model of hospital operation and management, clinical department setting, and medical education. In 1846, Renji Hospital moved to Maijiaquan and established its board of directors, laying the foundation for the standardized operation and management of the hospital. In 1854, Renji Hospital trained Huang Chunfu, the first doctor of Western medicine in China. In 1857, Benjamin Hobson became the second President of Renji Hospital. During this period, he compiled the earliest Western medical works in modern China, known as the "five kinds of Western medical books." They are the new editions of *Bowu Xinbian* (《博物新编》*Natural Philosophy*), *Quanti Xinlun* (《全体新论》*Treatise on Physiology*), *Xiyi Luelun* (《西医略论》*First Lines on the Practice of Surgery in the West*), *Fuyin Xinshuo* (《妇婴新说》*Treatise on Midwifery and Diseases of Children*), and *Neike Xinlun* (《内科新说》*Practice of Medicine and Materia Medica*). These works on Western medicine were given away free of charge in Renji Hospital, which greatly promoted the spread of Western medicine in China. In 1880, the British Government signed a contract to hand over the Renji Hospital to the Bureau of the Ministry of Work for a period of 25 years. In 1927, Lester, a famous British architect, real estate developer, and philanthropist in Shanghai, donated one million taels of silver and four lots of real estate to Renji Hospital to develop Shanghai's health care system. In 1945, Shanghai Municipal Health Bureau took over Renji Hospital and appointed Chen Bangdian, a specialist doctor of Renji Hospital, to preside over hospital affairs.

With a history of 177 years, Renji Hospital has become a level-A tertiary hospital today, integrating medical treatment, education, and scientific research in one place. It is affiliated with Shanghai Jiao Tong University School of Medicine.

3.2 St. Luke's Hospital (Tong Ren Hospital)

Founded in 1866, St. Luke's Hospital, was the third missionary hospital established in Shanghai. It was also the first missionary hospital founded by the Episcopal Church in the United States of America. The name of the hospital, Tongren, is taken from the meaning of "great harmony" and "benevolence" in the Bible.

Tong Ren Hospital was the first missionary hospital founded by Chinese people. In the autumn of 1866, the American Episcopal Church planned to establish a hospital in Shanghai. In the beginning, the Chinese priest Wu Hongyu rented a house and opened a clinic at the corner of Broadway Road and Wenjianshi Road, naming it Tong Ren Medical Bureau. Although Wu Hongyu was a Chinese American, he grew up in China, which gave him greater insight than Western missionaries into gaining acceptance among Chinese people. Wu Hongyu realized that "teaching through medicine" was the most practical psychology for Chinese people. Therefore, he asserted that "a good church doctor can create miracles."[7] In 1880, Henry William Boone came to China as the President of Tong Ren Hospital, and it was officially established under his auspices. The scale of the hospital continued to expand. In 1893, in addition to its inpatient department, the outpatient departments of Tong Ren Hospital included internal medicine, surgery, gynecology, dentistry, ophthalmology, pharmacy, and nursing, which was very rare in Western hospitals at that time.[8] In 1880, Henry William Boone opened a medical training course. Nine students were enrolled, seven of whom were recruited from St. John's College. This course serves as a precedent for the higher education of Western medicine in modern Shanghai, as well as a prototype for the medical school of St. John's University. In 1882, Boone also set up a nurse training school in Tong Ren Hospital to train local nurses. This is the earliest record of nurse training in China.

Today, Tong Ren Hospital is 155-year-old and has become a comprehensive tertiary hospital affiliated with the medical school of Shanghai Jiao Tong University.

3.3 Margaret Williamson Hospital (Red House Hospital)

Margaret Williamson Hospital, founded in 1884, was a missionary hospital of the Woman's Union Missionary Society of America for Heathen Lands.

The establishment of the hospital was closely related to the three women priests of the Woman's Union Missionary Society of America for Heathen Lands. They were Mrs. Margaret Williamson, the founding donor. Dr. Elizabeth Reifsnyder, the founder of the hospital, and Miss Elizabeth McKechnie, the nurse of the hospital.[9] In 1884, Williamson, who was in the United States, learned of the challenging health and medical conditions in Shanghai

and the difficulties of women and children in seeking medical treatment. In the act of Christian benevolence, she offered to donate $5,000 to build a hospital in Shanghai. This is also the origin of the English name of this hospital. Dr. Reifsnyder, the founder of the hospital, graduated from Women's Medical College of Pennsylvania in 1881 with a doctorate in medicine and became the first female medical missionary to come to China. In 1883, with the support of the Missionary Society, she opened a clinic in Shanghai to preach through medicine. The establishment of this clinic laid the foundation for the establishment of Margaret Williamson Hospital. Beginning in 1884, Dr. Reifsnyder began to serve as a medical missionary, which she did for the next 31 years until she returned to the United States in 1916. In 1884, Elizabeth McKechnie, who graduated from the nursing department, Women's Medical College of Pennsylvania, received an invitation from Dr. Reifsnyder to join the church and work at the hospital. McKechnie thus became the first female nurse to come to China. She made outstanding contributions to the development of nursing education in modern Shanghai.

At first, Margaret Williamson Hospital comprised only two private houses. It was not until 1885, after receiving donations, that a hospital of a larger scale was built. Therefore, the historical data also set 1885 as the founding year of Margaret Williamson Hospital. As the hospital was located outside the west gate of Shanghai at that time, it was called the "west gate." In addition, because its building roof was red, the hospital was also affectionately called the Red House Hospital. Margaret Williamson Hospital was the first hospital that dedicated to the care of women and children in Shanghai. It not only laid the foundation for the establishment of specialist hospitals in the history of modern medicine in Shanghai, but also contributed to the liberation of women in modern China.

3.4 St. Elizabeth Hospital (Guangren Hospital)

Guangren Hospital became independent from the Women's Department of Tong Ren Hospital in 1902.[10] The Clinic for Women and Children in Tong Ren Hospital was established in 1890. As a result of the large amount of money raised in 1902, it was able to construct a separate hospital, named Guangren Hospital, in its own building in Aiwenyi Road. Guangren Hospital was first presided over by Dr. Alex, and succeeded by Dr. Mei Yi. Beginning in 1907, Dr. Bolden oversaw hospital affairs for 33 years until his retirement. With his tireless efforts, Guangren Hospital became the largest hospital for women and children in China.[11]

3.5 Bethel Hospital

Bethel Hospital was founded in 1920 by sisters Shi Meiyu and Shi Feibi of the Bethel Mission in Shanghai. The hospital was located at 565 Chuangju Road, Nanshi. As Bethel means a temple or God's home in Hebrew, the name of the hospital means "God's home" or "Heaven's door." Today, Bethel hospital is known as the Ninth People's Hospital and is affiliated with Shanghai Jiao Tong University School of Medicine.

3.6 Shanghai Sanatorium Clinic

Shanghai Sanatorium Clinic, founded in 1929, was a missionary hospital founded by the Seventh-day Adventist Church. The hospital was located in Luobiegen Road (now known as Hami Road).

In 1927, H. W. Miller, a medical missionary of the Seventh-day Adventist Church, bought a piece of land on Luobiegen Road and built a 14-building hospital with a total of 60 beds. The hospital had an elegant environment and advanced equipment, including a spa, electrotherapy laboratory facilities, ice-making machine, as well as an X-ray department and a nutrition department.[12] The Seventh-day Adventist Church opened a number of missionary hospitals in China; in 1930, it opened a 150-bed branch hospital on Laobaizi Road (now Wujin Road) in Hongkou district, Shanghai.

4 Catholic missionary hospitals

4.1 Shanghai General Hospital (Gongji Hospital)

Shanghai General Hospital, founded in 1864, was the first missionary hospital run by the Roman Catholic Metropolitan Archdiocese of Nanjing, and the second missionary hospital in Shanghai. The original hospital was located near Rue Colbert (now 22 Shandong Second Road). At that time, the scale was very small, with only 17 wards and 35 beds. The difference between Shanghai General Hospital and other missionary hospitals was that before 1945, it was a convalescent hospital intended especially for overseas Chinese; after 1945, it became a hospital shared by foreigners and Chinese.

In addition to the Archdiocese of Nanjing, two important institutions were involved in the development of Shanghai General Hospital, The Conseil d'Administration Municipale de la Concession France, and the Bureau of Shanghai Ministry of Industry. The Shanghai General Hospital experienced two important transformations: one was that the hospital was moved in 1875 from the French concession to 190 North Suzhou Road, in the public concession; the other was that the hospital was taken over by the Shanghai Municipal Health Bureau of the national government in 1945. At that time, the sanatorium once dedicated to providing medical services for Westerners in Gongji Hospital became a sanatorium shared by Chinese and foreigners.

4.2 Hôpital St. Antoine (Andang Hospital)

Hôpital St. Antoine, founded in 1883, was a missionary hospital of the Catholic Church, first attached to the Gongji Hospital. This hospital offered free treatment, medication, and hospitalization for the poor and indigent. It was therefore originally known as Andang Poor Hospital and changed its name to Andang Hospital in 1951.[13] The hospital was located at 149 Luban Road (now Chongqing South Road).[14]

4.3 Hôpital Sainte-Marie (Guangci Hospital)

Hôpital Sainte-Marie, or St. Mary's Hospital, founded in 1907, was the second missionary hospital established by the Archdiocese of Nanjing (Fig. 1). The name of the

hospital, Guangci, means "wide charity" in Chinese. The hospital was located on Jinfu Road, the westernmost part of the French concession at that time (now Chongqing South Road). From its inception, Guangci Hospital was established to "spread the French medical concept through high-quality medical education, modern medical equipment, clinical service characteristics and relief for foreigners and poor patients in China."[15]

4.4 Sacred Heart Hospital

Sacred Heart Hospital, founded in 1923, was founded and supported by Lu Bohong, a famous industrialist, philanthropist, and Catholic in modern China.

Lu Bohong was a well-known philanthropist in modern China and a follower of Catholicism since childhood. Although he was not a clergyman, he enthusiastically participated in the church's charity work. The founding of the Sacred Heart Hospital was evidence of his kindness. In 1912, Lu Bohong saw sick workers in a factory in Yangshupu who did not seek medical treatment because they could not afford medical expenses. In response, he rented several houses near the factory and invited Catholic Franciscan nuns to assist doctors and administer medicine. From then on, as many as 500 or 600 people each day came for medical treatment. Every Sunday, the Catholic church sent members of the congregation and the priests of Hongkou Catholic Church to preach at the hospital. By 1923, rented housing was not enough for use. Lu Bohong called on enthusiastic philanthropists to raise funds to buy more than 4000 square metres of land on Ningguo Road, Yangshupu, and build new wards for men and women, with first-class, second-class and third-class wards. Each ward could accommodate 150 people of both men and women. One resident doctor and another specialist doctor from Britain, France, Germany, Austria, and Italy were included in each department of internal and external medicine.[16] In 1935, Sacred Heart nursing school was officially founded by the French Catholic Church and attached to Aurora University.

4.5 Hôpital Coeur Immaculé De Marie

Hôpital Coeur Immaculé De Marie was founded in 1930 by Lu Bohong on Beibaoxing Road. The name of the hospital means "the heart of a loving mother cures the disease of a red child." At that time, most residents in Zhabei District were poor. As one resident said, "I don't know how to pay attention to health at ordinary times, and I feel particularly poor in treatment in case of diseases."[17] Lu Bohong organized a fund donation event with the mission and raised more than 50,000 yuan, rented a house on North Baoxing Road, and established the hospital. The nursing work of the hospital was run by nuns. The hospital could accommodate a total of 200 patients, including 50 patients who would be granted free hospitalization.[18] Part of the operating capital came from an appropriation of the municipal government fund at that time. In addition to government funding, donations from businessmen living in Shanghai were also one of the principal funding sources for the hospital.

4.6 Sino-Belgian Radium Institution

The Sino-Belgian Radium Institution, formerly the Radium Department of Sacred Heart Hospital, was founded on

Figure 1 Sainte Mary's Hospital founded in 1904 (history exhibition hall of Ruijin Hospital now)

March 1, 1931 as a missionary hospital of the Archdiocese of Cotabato. The hospital was located within the Sacred Heart Hospital on Ningguo Road at that time; the president was Lu Bohong.

The establishment of this hospital was related to the Boxer Indemnity. In 1925, Belgium and the Republic of China government jointly established the Zhongbi Boxer Indemnity Committee to supervise the use of the Belgian "refunded" Boxer Indemnity. In 1931, the Sino-Belgian Charitable Institution, a subsidiary of the Sino-Belgian Boxer Rebellion Indemnity Committee, funded the purchase from France of the latest radium ingot therapeutic instrument, with a value of more than 200,000 yuan, and established a radium ingot department at the Sacred Heart Hospital. The Director of the radium ingot department was Ge Chengzhi. From 1931 to 1935, the Sino-Belgian Radium Institution was established in the Sacred Heart Hospital, and the hospital bed was also provided by Sacred Heart Hospital. During this period, patients were admitted to the hospital free of charge.[19] On January 1, 1936, the Sino-Belgian Radium Institution became independent from the Sacred Heart Hospital and was directly managed by the Boxer Indemnity Committee. In October 1937, it moved to 45 Qiqi Road (now Yueyang Road). By 1938, the treatment hospital was managed by the Catholic Franciscans and became a missionary hospital.

4.7 Shanghai Mercy Hospital

Shanghai Mercy Hospital was founded in 1935 in what was the southwest suburb of Shanghai at that time (now 3210 Humin Road, Zhuanqiao Town, Minhang District). There were 14 buildings in the hospital, including eight buildings for the sick and a construction area of about 30,000 square meters. Shanghai Mercy Hospital was one of the largest and most well-equipped psychiatric specialist hospitals in the Far East, with social service department and medical service department established within the hospital. It is now known as Shanghai Mental Health Center (Division).

5 Conclusions

Missionary hospitals in modern Shanghai have their own unique significance and have had an indelible influence on the formation of medical and healthcare systems in modern Shanghai.

The main purpose of a missionary hospital is to preach. In China, "more than half of the believers listen to the Bible for the first time in the missionary hospital."[20] In fact, medical missionary work was initially only one of the means to do missionary work; it was not a long-term plan. The missionary societies believed that medicine only played a role in the early stage of missionary work in order to eliminate prejudice, win trust, and establish churches. Once these objectives were achieved, the medical missionary approach could be abolished.[14,21] However, in practice, these missionary hospitals eventually took on more medical work than missionary work.

The emergence of missionary hospitals objectively changed the pattern of medical and healthcare services in modern China. At first, missionary hospitals had the dual attributes of missionary work and medical treatment, but these two attributes diverged and drifted apart in the process. Western missionaries found that the number of believers converted by medical missionaries via establishing of hospitals was less than expected, yet missionary hospitals still prospered in China. The main factors are as follows: First, given the dual identity of doctors and missionaries, medical missionaries prefer to perform the duties of doctors. They focus their work on operating hospitals and treating patients. Second, the missionary hospital has continuously cultivated Western medicine in China and fostered local medical and nursing talents, thus laying a foundation for the hospital to break away from the missionary medical support. Third, after the process of localization, specialization, and secularization of missionary medical undertakings in China, Western medicine is no longer the means of missionary work for Western churches but has evolved into a form of medicine that is accepted by Chinese society. Missionary hospitals have gradually shifted their religious purposes into the background and become pure medical institutions.

The introduction of Western medicine is not only a challenge to traditional Chinese medicine, but also a promotion. For a long time, traditional Chinese medicine and Western medicine were on opposing sides, and the farcical idea of "abolishing traditional Chinese medicine" even appeared. Facing the challenge from Western medicine, the traditional Chinese medicine practitioners accepted the fact that Western medicine will stay after its introduction and seek to develop a pathway integrating the advantages of both medicines. By learning from the model of Western medicine, they have built new traditional Chinese medicine hospitals and established traditional Chinese medicine colleges. These changes have made significant contributions to the revitalization and development of traditional Chinese medicine.

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Ethical approval

This article does not contain any studies with human or animal subjects performed by any of the authors.

Author contributions

Lyu-Hua Chen undertook the task of data collection, collation, writing and revision. Li-Yun Chen reviewed and revised the manuscript.

Conflicts of interest

The authors declare no financial or other conflicts of interest.

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Research Article

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OPEN

Achievements of the Compendium *Bencao Tujing* (*Illustrated Classic of Materia Medica*): A Preliminary Study

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Abstract

Bencao Tujing (*Illustrated Classic of Materia Medica*) is a brilliant and monumental compendium of materia medica by Su Song, which was published in 1061 and gathered ancestral knowledge from the Song dynasty as a legacy for posterity. The compendium emphasized the clinical applications of medicinal materials collected nationwide, which used illustrated atlases as references. The descriptions for each medicinal material subsumed the prescriptions containing it and were supplemented with relevant medical cases. Medical prescriptions predating the Song dynasty were included, which enhanced the clinical usefulness of the pharmacopoeia. The ancestral knowledge of materia medica was extensively merged with natural history throughout the compendium, which also made extensive reference to more than 200 Chinese classics, local gazetteers, and published works from the social and natural sciences. The inclusion of natural history and literature works changed the convention used in earlier pharmacopoeias to present medicines based solely on pharmacological analyses. The compendium also pioneered the inclusion of natural history in pharmacopoeia. *Bencao Tujing* helped establish China's leading position in the field of materia medica. Su Song's meticulous nature, truth-seeking attitude, and adherence to scientific thinking are truly worthy of emulation and promotion.

Keywords: *Bencao Tujing* (*Illustrated Classic of Materia Medica*); Compendium; Chinese materia medica; Su Song

1 Introduction

Su Song (苏颂 1020 ACE–1101 ACE) (Fig. 1), a native of Quanzhou Tong'an (present day Tong'an district, Xiamen city, Fujian province) during the Song dynasty, was an outstanding scientist and naturalist. According to the chapter Su Song Zhuan (苏颂传 Su Song's Biography) of *Song Shi* (《宋史》*History of the Song Dynasty*), Su Song was well-versed in Confucian classics, natural history, divination, music, astrology, *Shan Hai Jing* (《山海经》*The Classic of Mountains and Seas*), and *Shen Nong Bencao Jing* (《神农本草经》*Shen Nong's Classic of the Materia Medica*). He was regarded as a great naturalist and consummate polymath. Su Song's greatest scientific achievements were in the fields of horology and mechanical engineering. He oversaw the construction of the Shuiyun Yixiang Tai (水运仪像台) (Fig. 2), that is, the "Water-Powered Armillary Sphere and Celestial Globe Tower," which was the world's first hydromechanical astronomical clock tower. In addition, he spearheaded the compilation of the *Bencao Tujing* (《本草图经》*Illustrated Classic of Materia Medica*), which is also known as *Tujing Bencao* and is a compendium in herbal pharmacology.[1] With its extensive collection of domestic herbal specimens and foreign medicinal materials, this pharmacopoeia succeeded *Xinxiu Bencao* (《新修本草》*Newly Revised Materia Medica*) from the Tang dynasty as the national pharmacopoeia. This brilliant and monumental compendium collated the texts about materia medica by herbal scholars from successive generations preceding the Northern Song dynasty and included a nationwide survey of medicinal materials in its showcase of the Song dynasty's ancestral knowledge of materia medica and scientific achievements.[2]

In the assessment of Su Song's book, Li Shizhen (李时珍) remarked that "Su Song's book made full and clear textual research, with further elaboration."[3] A British science historian, Joseph Needham, also observed, "In Europe, the expertise to have collected wild flora and fauna specimens intricately carved onto wood and printed was a monumental feat that was achieved only in the 15th century."[4] However, the pioneering work in this genre, the pharmacopoeia *Bencao Tujing*, had already been published in the 11th century.[5] The style used to compile this compendium was based on the illustrated atlas of medicinal herbs gathered from across China and extensive reference to more than 200 Chinese classics, local gazetteers, and published works from social and natural sciences. The physical descriptions,

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Figure 1 Portrait of Su Song (苏颂) from *Runzhou Xianxian Lu* (《润州先贤录》*The Records of Runzhou Sages*) (1933 edition, from Guo Xue Library)

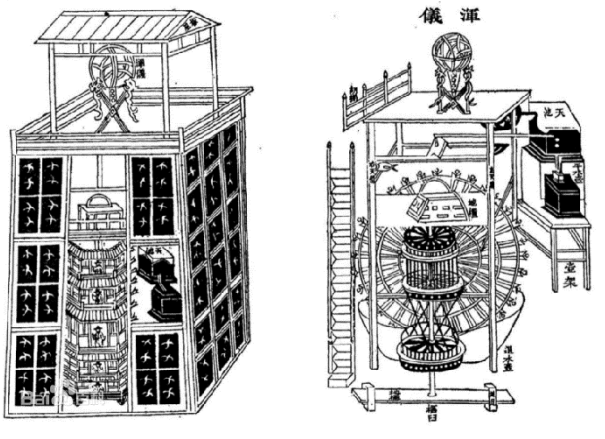

Figure 2 Shuiyun Yixiang Tai (水运仪象台) from *Siku Quanshu* (《四库全书》*Complete Library in the Four Branches of Literature*) (1937 edition, published by The Commercial Press)

geographical origins, pharmacological properties, harvest times, and indications for medicinal herbs also included references to various fields, from chemistry, zoology, botany in the natural sciences to military, economics, trade, religions, and cultural studies in the social sciences. This compendium marked a notable shift from the convention used by earlier pharmacopoeias to present medicines based on pharmacological analyses. This pharmacopoeia also pioneered the inclusion of natural history in the compendia of materia medica of succeeding generations. The publication of this book established China's leading position in the field of materia medica.[6]

Although the original version of *Bencao Tujing* was lost to history, its lost contents and illustrations had been recorded in *Jingshi Zhenglei Beiji Bencao* (《经史证类备急本草》*Classified Materia Medica from Historical Classics for Emergency*) by Tang Shenwei (唐慎微), abbreviated as *Zhenglei Bencao* (《证类本草》*Materia Medica Arranged According to Pattern*) during the Song dynasty.

When Zhang Cunhui (张存惠) inscribed *Zhenglei Bencao* in the Mongol Empire (1249), he amended his edition by inserting the contents of *Bencao Yanyi* (《本草衍义》*Elucidation of the Materia Medica*) into *Zhenglei Bencao*. He renamed the book as *Chongxiu Zhenghe Jingshi Zhenglei Beiyong Bencao* (《重修政和经史证类备急本草》*The Revised Zhenghe Classified Materia Medica from Historical Classics for Emergency*) (Fig. 3, Table 1).

2 Illustrated text focused on clinical use

Jiayou Bencao (《嘉祐本草》*Materia Medica of the Jiayou Era*) was published in the same period as *Bencao Tujing*. It leaned toward Chinese medical literature while *Bencao Tujing* used woodcut illustrations of herbal medicines and focused more on clinical applications.[7] Because of Su Song's skillful compilation, *Bencao Tujing* achieved structural unity with its clear taxonomic delineation. The compendium bridged the best of the ancestral knowledge of Chinese materia medica from the Song dynasty with innovations in medicines heralding China's future; thus, the pharmacopoeia epitomized the high standard of knowledge about medicinal materials in the Song dynasty. More than 640 medicines and 933 woodcut pictures of specimens from *Bencao Tujing* were recorded in *Zhenglei Bencao*, including more than 100 unclassified medicines that were not included in previous compendia of materia medica. The illustration of each medicine depicts its shape and colors while the accompanying text explicates the differences between medicines. Each medicine usually comes with one drawing, while some medicines have two or more drawings. For example, the description of Chai Hu (柴胡 *Radix Bupleuri*) included five drawings[8] (Fig. 4). More than 500 medicines were described accurately and realistically. Hence, *Bencao Tujing*'s achievements in medical botany and medical zoology were distinctive.

Su Song was a pioneer with his new style of compiling medicines, syndromes, prescriptions, and medical cases into a materia medica compendium. This resulted in the increased value and usefulness of *Bencao Tujing* in clinical applications. Before the publication of *Bencao Tujing*, the majority of materia medica compendia were focused on describing phytomorphology and pharmacological properties. *Bencao Tujing* included hundreds of prescriptions, such as 279 prescriptions of famous physicians before the Song dynasty, including Zhang Zhongjing (张仲景) and Sun Simiao (孙思邈). More than 130 prescriptions were widely circulated by the era's physicians in addition to folk remedies and efficacious prescriptions. More than 100 prescriptions were effective according to personal experience or had names, but lacked a description of their specific medicinal components.[9] The hallmark of these prescriptions was their use of common medicines. Some medicines were used in several prescriptions. For example, Zhi Zi (栀子 *Fructus Gardeniae*) is contained in innumerable prescriptions, and therefore cannot be fully explicated. Zhi Zi appears as a component in six prescriptions either empirically proven or traditionally used to treat diseases like jaundice, relapse

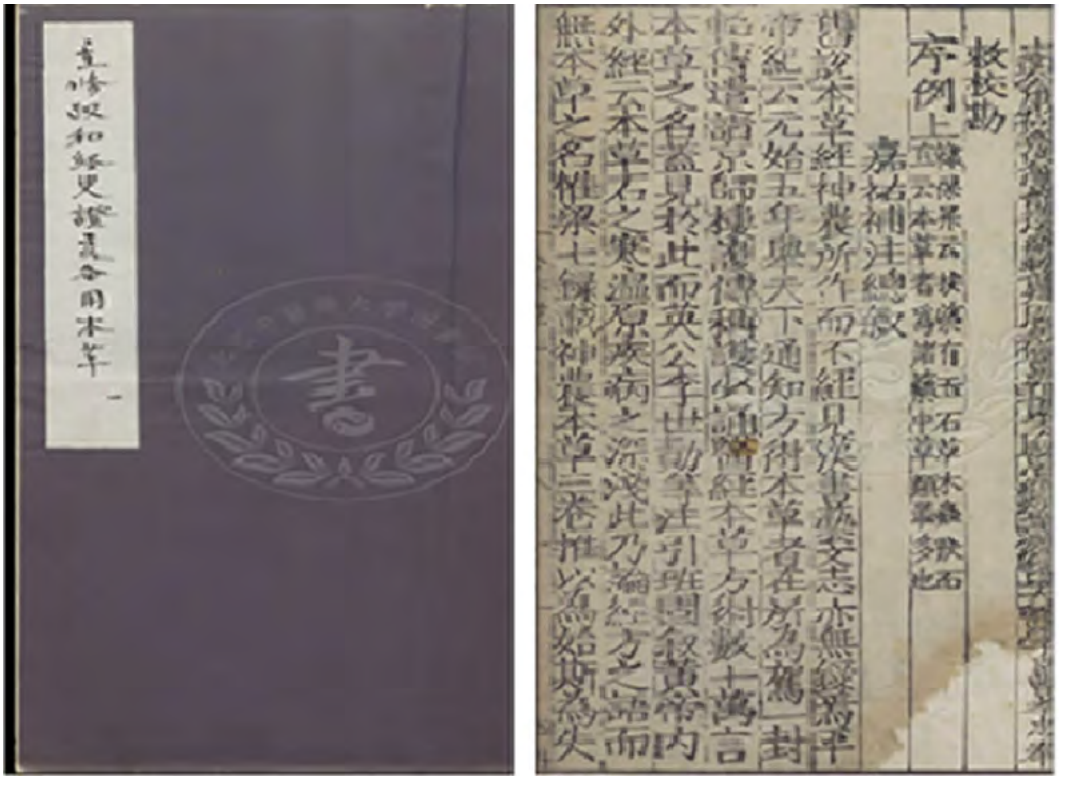

Figure 3 *Chongxiu Zhenghe Jingshi Zhenglei Beiyong Bencao* (《重修政和经史证类备急本草》*The Revised Zhenghe Classified Materia Medica from Historical Classics for Emergency*) (1523 eidition, from the Library of Beijing University of Chinese Medicine)

Table 1 Editions of ***Bencao Tujing*** (《本草图经》***Illustrated Classic of Materia Medica***) through the ages

Year	Author	Book	Description
Song dynasty 1061 ACE	Su Song	*Bencao Tujing*	Lost to history
Song dynasty 1097 ACE	Tang Shenwei	*Jingshi Zhenglei Beiji Bencao* (*Zhenglei Bencao*)	Some of *Bencao Tujing*'s lost contents and illustrations were included in this book
Mongol Empire 1249 ACE	Zhang Cunhui	*Chongxiu Zhenghe Jingshi Zhenglei Beiyong Bencao*	The contents of *Bencao Yanyi* were inserted into *Zhenglei Bencao* and *Zhenglei Becao* was renamed as *Chongxiu Zhenghe Jingshi Zhenglei Beiyong Bencao*

of serious illness or severe seasonal diseases caused by overexertion, toxic dysentery, and myospasm. Moreover, medical cases or contraindications were included. The integration of medicines with prescriptions markedly increased the clinical value of the materia medica compendium and was widely emulated by publications of materia medica in later generations. By the Ming dynasty, more than 10,000 prescriptions were included in *Bencao Gangmu* (《本草纲目》*The Grand Compendium of Materia Medica*) by Li Shizhen (李时珍).[10]

2.1 Integration of medicine with syndromes and prescriptions

The seamless integration of materia medica with prescriptions and natural history in this compendium pioneered the style of compiling medicines in pharmacopoeia. It allows emphasis to be placed equally on both the materia medica and relevant prescriptions. The entries of commonly used medicines would list prescriptions in which they function as the main medicine, including prescriptions for surgery, gynecology, internal medicine, cosmetology, dermatology, otorhinolaryngology, ophthalmology, and stomatology.[11] Thus, the contents of prescription books predating the Song dynasty were preserved, ensuring the dissemination of ancestral knowledge of treating the main diseases and syndromes of internal medicine, surgery, gynecology, and pediatric medicine (Table 2).

The entry of Fang Ji (防己 *Radix Stephaniae Tetrandrae*) in *Bencao Tujing* is an example. "In a treatment record, the patient feels shortness of breath with epigastric oppression; he has a sickly dark complexion and a tense pulse for dozens of days. Upon applying the Mu Fang Ji Decotion (木防己汤), the patient had vomiting and diarrhea, thereafter he recovered."[11] According to traditional Chinese medicine, emetic methods and purgative methods are used to expel pathogens out of the body and the application of Mu Fang Ji Decoction is a proven example of this treatment method.

The principles of choosing prescriptions are as follows: "Ancient compendia of prescription contain succinct records that have been clearly proven efficacious by people in the past and they are still frequently used today; medicines found to be efficacious based on experiences of medical practitioners are also recorded."[8] Whether the treatments described in compendium entries

Figure 4 Five drawings for Chai Hu (柴胡 *Radix Bupleuri*) in *Chongxiu Zhenghe Jingshi Zhenglei Beiyong Bencao* (1523 edition, from the Library of Beijing University of Chinese Medicine)

Table 2 **Main diseases and syndromes of internal medicine, surgery, gynecology, and pediatric medicine presented in *Bencao Tujing***

Medical Specialties	Diseases and Syndromes
Internal Medicine	angina pectoris, phlegm, febrile disease, amoebic dysentery, cholera, epigastric oppression, gastroparesis, abdominal bloating, flatulent dyspepsia, pharyngitis, chest discomfort, cough, degenerative lung disease, convulsion, vomiting, stroke, asthenic syndrome, insomnia, pulmonary abscess, jaundice, malaria, epilepsy and infectious diseases; common ailments and rare diseases, such as blurred vision, optic neuropathy, deafness, and oral diseases
Surgery	mastitis, goiter, bone injuries, carbuncles, boils, etc.
Gynecology	miscarriage, threatened abortion, and morbid leucorrhea
Pediatric medicine	malnutrition, ascariasis, infantile, and juvenile myoclonic epilepsy

are classic prescriptions, famous prescriptions, or folk prescriptions based on experience, all medicines were clinically tested, found to be efficacious, and carefully considered before they could be selected for compilation in the pharmacopoeia.

2.2 Enumeration of medical case studies with emphasis on clinical applications

Although *Bencao Tujing* combines materia medica with prescriptions, Su Song did not limit himself solely to the collation of medicines and treatments, but zealously examined the principles that underlie their medicinal use. In this regard, *Bencao Tujing* includes medical cases with prescriptions covering, for example, heart burn, gastritis, jaundice, and dysentery of internal medicine; wounds, sores, mange, favus, and hemorrhoids of surgery; orthopedic traumatic injuries, dysmenorrhea and infertility of gynecology; oral diseases, and toothache. Case studies of longevity are also included. By combining treatment records with materia medica, the contents of the pharmacopoeia are rich and engaging.[12]

For example, the entry of Da Huang (大黄 *Radix et Rhizoma Rhei*) records that "When Emperor Wu of the Liang dynasty wanted to take Da Huang as medicine for feverish sensations, the newly appointed physician Yao Sengyuan (姚僧垣) said, 'As Da Huang is a strong and fast-acting medicine, your majesty is now advanced in years and should use it with caution.' The emperor did not take the advice and he was consequently enervated after taking Da Huang. As the Emperor Yuan of the Liang dynasty often suffered from indigestion and constipation, all the physicians unanimously recommended the use of mild medicine to gradually induce bowel movements to unblock the intestine. However, physician Yao Sengyuan said: 'As the surging and replete pulse represented indigestion with constipation, to be adamant in using Da Huang renders the

disease treatable.' The emperor abided by this and gradually recovered."[11]

Da Huang has a purging effect; it also clears heat and promotes blood circulation. These two case studies on the use of Da Huang show that Chinese materia medica knowledge was applied according to individual's physical condition and diseases. Emperor Wu was old and frail, and therefore should not take Da Huang for the feverish sensation. However, Emperor Yuan was young and strong physically, and therefore could use Da Huang for constipation.

Su Song put equal emphasis on both prescriptions and medicines, and combined prescriptions and medical cases, which effectively ensured the preservation and dissemination of the prescriptions in the pre-Song dynasty. This format of pharmacopoeia improved its readability and enhanced its clinical utility as a materia medica textbook.

2.3 Pharmacological experimentation in the spirit of scientific inquiry

Records on the pharmacological effects of materia medica are the culmination of long-term clinical experience and the fruits of extensive experimental research. When "Shen Nong (神农) tasted a hundred herbs, and encountered seventy poisons in a day," he provided the prototype of human self-experimentation.[13] Subsequent generations of materia medica compendia recorded pharmacological experiments, which continuously enriched and refined our knowledge about the pharmacological effects and uses of Chinese medicinal herbs. In addition, *Bencao Tujing* included empirical records of pharmacological effects of medicines obtained by *in vivo* and *in vitro* experiments.

For example, the entry of Lan Shi (蓝实 *Polygonum tinctorium Ait.*) describes its ability to neutralize poisons and kill worms and insects. "After extracting 1 porcelain bowl of Lan Shi Decoction (蓝实汤), a spider was immersed into the decoction. After a good while, when the spider was removed from the decoction, it was severely paralyzed. In a separate Lan Shi Decoction, fine powder of She Xiang (麝香 *Moschus*) was added. When a spider was immersed in it, it died. Yet in another extracted Lan Shi Decoction with She Xiang, Xiong Huang (雄黄 *Realgar*) was additionally blended in; when another spider was immersed in it, it disintegrated into liquid."[8] (Table 3) The immersion of spider into Lan Shi Decoction and comparision of the reactions when She Xiang and Xiong Huang were separately added were pioneering *in vivo* experiment.

The genus and species of medicines could be differentiated by comparison and analogy. Through Su Song's vivid descriptions, the pharmacopoeia also provided methods to distinguish genuine medicines from counterfeit medicines, and superior specimens from inferior specimens for some medicines.

The entry of Ren Shen (人参 *Radix et Rhizoma Ginseng*) included this anecdote, "legend has it that Ren Shen can be tested by getting two people to walk together for three or five miles, with only one of them sucking it. The person who didn't suck the Ren Shen would surely be panting heavily; if the other one who sucked it is breathing smoothly, the Ren Shen is genuine."[14] By using this method, one could differentiate whether Ren Shen is genuine or not. In another example, the entry of Niu Huang (牛黄 *Calculus Bovis*) observes that "as counterfeits abound today, it can be tested by rubbing it on a nail as the genuine one would seep and stain the nail yellow."[14] The entry of Mu Xiang (木香 *Radix Aucklandiae*) suggests that "the one that is shaped like a shriveled bone, tastes bitter, and sticks to the teeth would be considered superior."[14] The authenticity of medicines can be distinguished based on these practical methods to ensure their clinical efficacy.

By today's scientific standards, these pharmacological research methods would be deemed simplistic because they lack scientific rigor in their experimental designs, use inaccurate observation indices, possess blind spots, and do not eliminate other confounding factors. However, to even possess a scientific spirit is praiseworthy when we consider the era and circumstances during which these experiments were conducted.

3 A wide variety of materia medica in natural history

Bencaojing Jizhu (《本草经集注》 *Collective Commentaries on the Classic of Materia Medica*) pioneered the trend of combining materia medica with natural history. *Bencao Tujing* made further progress by including natural history into works of materia medica. Its impressive contents are a kaleidoscope of multifarious references from more than 200 works that span the fields of zoology, botany, literature, history, philosophy, religion, politics, military studies, natural and social sciences, and natural history.[15] When *Bencao Gangmu* was published, this trend reached its peak. There are comments that "although named as a medical book, it's inherently physics" and "China's encyclopedia in the 16th century."[16] In the history of Chinese materia medica studies, *Bencao Gangmu* covers a wide range of subjects and truly pioneered the landmark integration of materia medica compendia with natural history. It was pivotal in bridging earlier materia medica development with innovations that heralded its future.

In terms of its conventions of naming medicinal herbs, *Bencao Tujing* relies on the herbs' biological characteristics, textual exegesis, and historical studies. Their names are informative and can be understood clearly, with verifiable references. For example, Xi Xin (细辛 *Radix et Rhizoma Asari*) is described as "thin (细) roots, yet extremely pungent (辛)."[15] (Fig. 5) The names of materia medica are logical and verifiable. In addition, they facilitate

Table 3 Experiments with Lan Shi Decoction (蓝实汤) from *Bencao Tujing*

Experiments	Results
1) A spider was immersed into the Lan Shi Decoction	The spider severely paralyzed
2) A spider was immersed into the Lan Shi Decoction with fine She Xiang (麝香 *Moschus*) Powder	The spider died
3) A spider was immersed into the Lan Shi Decoction with fine She Xiang Powder and Xiong Huang (雄黄 *Realgar*)	The spider disintegrated into liquid

Figure 5 The entry of Xi Xin (细辛 *Radix et Rhizoma Asari*) in *Chongxiu Zhenghe Jingshi Zhenglei Beiyong Bencao* (1523 edition, from the Library of Beijing University of Chinese Medicine)

understanding and help to recall the materia medica's characteristics.

3.1 Explanation with natural science

In *Bencao Tujing*, the textual explanation for each materia medica is comprehensive and accurate, describing its origins, production locations, alternative name(s), physical characteristics, other materia medica sharing its name, identification, processing methods, historical literature, main indications, included prescriptions, usage, preservation, cultivation, and domestication. [17] The biological traits of flora and fauna, such as the morphology of plants, structure of leaves, stem varieties, flowering and fruiting periods, as well as animal habits, such as the morphology of rhinoceros and the way of hunting, were described with vivid accuracy. The publication of *Bencao Tujing* had a significantly demonstrable effect on materia medica scholars of future generations when they differentiate between the different varieties of a particular species of medicinal herb.

For example, the entry of Di Huang (地黄 *Radix Rehmanniae*) states that its "leaves grow in February and it sprouts up from the ground everywhere; with wrinkled leaves that have no sheen, the taller ones are more than a feet, and the shorter ones are three or four inches; its flowers are purplish-red, but some are yellow followers; its ovary has extremely fine seeds that are sandy brown in color; its roots are like human fingers, entirely yellow, with uneven thickness and length."[8] The entry of Xu Duan (续断 *Radix Dipsaci*) observes that "germinating after March, it has a four-sided stem; the leaves grow in pairs and face each other; in April, it blossoms into red and white colors; its roots are yellow in color."[8] Therefore, outlining the general appearance of the plant is useful for the identification of plant morphology in research.

Some scholars classified the chemistry knowledge in *Bencao Tujing* into five categories: 1) explication and differentiation between various compounds; 2) illustrations of the preparation and manipulation of compounds, including drawings of the instruments; 3) newly added compounds; 4) inorganic minerals' geographic origins and characteristics; and 5) methods to differentiate elements and compounds. With its more than 20 detailed entries on chemistry, *Bencao Tujing* stimulated advancement in ancient chemistry and chemical engineering to a certain extent. [18] Therefore, this book occupies a relatively important place in the history of chemistry development.

3.2 Descriptions of materia medica from social perspectives

Through its descriptions of materia medica from various societal perspectives, *Bencao Tujing* reflected the reality of the social milieu of the Song dynasty by succinctly narrating the relevant content using skillful rhetoric. The scrolls present lifelike drawings of everyday life, which in turn serve as a valuable resource for sociological research. *Bencao Tujing* also included a fair amount of cultural knowledge drawn from historiography, such as the taboos in materia medica nomenclature, the historical names of geographical locations, and changes in geographical landscapes. Because *Bencao Tujing* is similar to natural history in its coverage, the book also provides an abundance of historical materials for research on the subdisciplines of historiography, including the history of technology, ethnohistory, folk history, and history of international relations.[4]

For example, the entry of Gou Gu Mu (枸骨木 *Cornus Wilsoniana Wanaer*) observes that, "when southerners obtain it, they twist it into an implement which is very useful."[6] Meanwhile, the entry for Suan Zao (酸枣 *Zizyphi Spinosae*) states, "extremely fine-grained, it is robust and heavy; townspeople use it as carriage axles and chopsticks."[6] The entry of Shan Cai (杉材 *Cunninghamia lanceolata*) notes that "made into pillars, it would not rot when buried. Additionally, people frequently use it to make rice buckets as it is water-resistant."[6] Finally, the entry of Qu Mai (瞿麦 *Herba Dianthi*) mentions that

it "has fine roots, so villagers get it to make brooms."[6] which describes how it was used in daily life. Accordingly, these descriptions cover the production equipment and tools used in everyday life, such as utensils, ropes, chests, wooden buckets, and brushes.

Another example of the utility of *Bencao Tujing* is a story about the use of Ji She Xiang (鸡舌香 *Syringa oblata*). "The Imperial Secretary sucks on Ji She Xiang to report to the Emperor and answer the Emperor's questions in the hope of making his breath fragrant."[6] The use of Ji She Xiang to treat bad breath stems from the attention paid to one's appearance and deportment, which reflects the society's emphasis on etiquette during the Song dynasty.

4 Conclusions

As a work of materia medica, *Bencao Tujing* synthesized the inherited ancestral knowledge during the Song dynasty and left a legacy for posterity. Su Song's compilation of materia medica by subsuming their related prescriptions and medical case studies enabled the transmission of the Song dynasty's medical prescriptions and their clinical applications to later generations. In addition, the use of experience-based folk prescriptions and empirically proven remedies was preserved. With its clinical usefulness enhanced by its organized contents, *Bencao Tujing* left a precious legacy for future generations. Furthermore, it merged the materia medica literature with the field of natural history. In doing so, Su Song pioneered a new style of materia medica compendia that introduced a brand-new thought process and method in the development of Chinese materia medica.[19] Thus, Su Song's meticulous nature, truth-seeking attitude, and adherence to scientific thinking are truly worthy of emulation and promotion.

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Ethical approval

This study does not contain any studies with human or animal subjects performed by any of the authors.

Author contributions

Lin-Lin Xiu and Gan-Sheng Zhong contributed to the design; Shao-Hong Chen and Hai-Yan Liu performed the literature search; Lin-Lin Xiu and Qi-Xuan Wang contributed to manuscript preparation and manuscript editing; Shi-Chun Xu and Qi-Xuan Wang revised the manuscripts.

Conflicts of interest

The authors declare no financial or other conflicts of interest.

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Research Article

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OPEN

Art of Nourishing Life According to the Kidney Meridian in *Zhenjiu Dacheng* (*The Great Compendium of Acupuncture and Moxibustion*)

Anita Bui[1,2,✉]

Abstract

"Daoyin Benjing" (Art of Nourishing Life) discusses the kidney meridian in depth. It is a dense and heterogeneous text that is heavily influenced by Daoism. The text proposes rules for the maintenance of life using language that is often cryptic and understandable only to the initiated. This language is closely interwoven with the classical terms of traditional Chinese medicine. The kidney is the home of vital energy, which is a type of sexual energy and the root of life. Engagement in moderate sexual activity nourishes life and leads to a long life. This is the goal of every Daoist follower and the goal of every doctor.

Keywords: Daoyin; Kidney; Art of nourishing life; Yang Jizhou; *The Great Compendium of Acupuncture and Moxibustion*

1 Introduction

"Daoyin Benjing" (导引本经 Art of Nourishing Life) has been translated into Vietnamese from *Zhenjiu Dacheng* (《针灸大成》*The Great Compendium of Acupuncture and Moxibustion*), a famous text written by Yang Jizhou (杨继洲) in 1601[1].

Daoyin Benjing focuses on discussions of the protection of life, and supplements the descriptions of the five yin meridians of the system: the foot shaoyin meridian of the kidney (Fig. 1), the foot jueyin meridian of the liver, the foot taiyin meridian of the spleen, the hand shaoyin meridian of the heart, and the hand taiyin meridian of the lung. It takes into account the five zang organs: kidney, liver, spleen, heart, and lung.

The originality of this text lies in its language, which is almost mystical but is closely interwoven with the classical terms of traditional Chinese medicine. This prompted H. Maspero to comment that "One of the most curious features of the Taoist religion is the constant and intimate mixture of practices of a very absorbing public and private cult, of mystical practices going as far as concentration and ecstasy, and of practices of moral life, with practices that have only a purely physiological value and interest, diets of food, diets of sexual union, gymnastics of breathing, etc."[2]

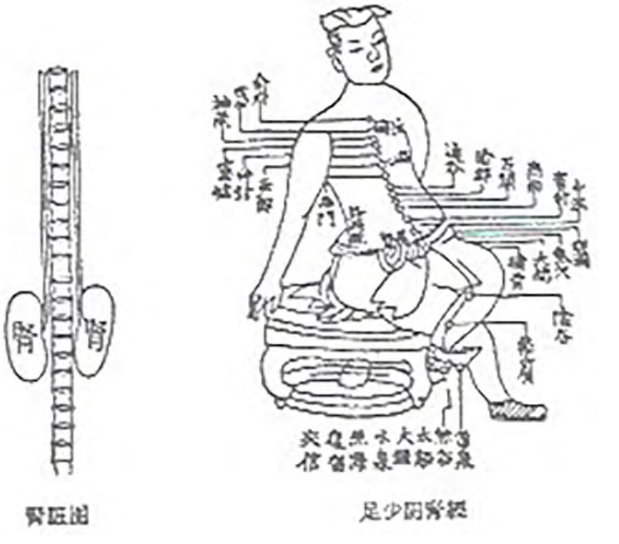

Figure 1 Foot shaoyin meridian of the kidney in *Zhenjiu Dacheng* (《针灸大成》*The Great Compendium of Acupuncture and Moxibustion*)

Some of the original texts are written in verse. This gives a poetic quality and provides a different and more original perspective on the text.

2 Comments on the original texts

Physiologically, the kidney is part of a group of five zang organs. According to the correspondences of the five-element system, the kidney is linked to the cosmos (i.e., to the seasons, planets, space, and time). From a Daoist perspective, the kidney is the precosmic yang in the Kan trigram (Fig. 2). It contains the seminal quintessence *jing* (精), and thus comes directly from the energy of heaven and earth, which is why human longevity depends upon it.

Anatomically, the existence of two kidneys is associated with mingmen (命门) or the gate of life. This has

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Figure 2 Kan trigram

produced much discussion over the long history of Chinese medicine, which indicates the importance of the role of kidneys in medicine and in the art of nourishing life. A documented review of the theory of mingmen (命门学说) was published in French by Dr. Jean-Claude Dubois in the journal *Knowledge of Acupuncture* (*Connaissance de l'Acupuncture*) in 2010. In his foreword, the author points out that "Mingmen is not a univocal expression. It is of interest to medicine, traditional philosophy, Taoism and the highest metaphysics."[3] In this fascinating debate, Dubois quotes a study by Song Zhixing published in the journal *Xin Zhongyi* (《新中医》*Journal of New Chinese Medicine*) in 1980, "Mingmen's Theories: History and Clinical Applications," which returns to the enigmatic description of this concept in chapter 52 of the *Su Wen* (《素问》*Basic Questions*) in relation to the "small heart" and the 7th vertebra. Furthermore, he returns to the case of the *Yixue Rumen* (《医学入门》*Introduction to Medicine*) and the transmission of the mingmen theory in France in the 1950s by George Soulié de Morant, whose work influenced all French acupuncture practices.

The influence of this philosophy on traditional Chinese medicine therefore remains, and is particularly strong in this text and other texts on daoyin. We can see that it is sometimes difficult to separate this philosophy from purely medical conceptions.

2.1 Paragraph 1

Man is born and lives by the energy of heaven and earth. Within man remains the Original Breath, an ancestral treasure rooted in the center, radiating life and abundance.

This inner breath that dwells in every person is the original breath, yuan qi (元气). It is one of the primordial breaths formed at the creation of heaven and earth. "Man on being born receives the original breath of heaven and earth, which becomes his spirits (神) and his body (形), he receives the breath of the original one qi (元一之气) which becomes his saliva and essence."[2] Similarly, "The original breath of heaven and earth begins at the north place, belongs to Water, has the Kan trigram, and presides over the northern region and the Heng Peak, the region of ji. The original breath of man is the same as that of heaven and earth; in man it is born in the kidneys."[2] The original breath is the vital principle; it occupies and fills the lower cinnabar field.

The kidney is the home of this original breath; it is the seat of an "ancestral treasure radiating life and abundance." To nourish life is to preserve this breath. All methods of prolonging life consist of internalizing this treasure, as explained by Zhuang Zi (庄子). "Man's life is due to the accumulation of breath; if the breath accumulates there is life, if it scatters, there is death."[4]

The end of this paragraph is illustrated by a metaphor warning against the dispersion of the heavenly breath. This breath is compared to the master of the house; if the master leaves the house, a hundred thieves will break in and seize the estate, and there will be ruin. If emptied of its energy, the kidney, the receptacle of the root of life, weakens the whole body and causes its ruin. In this respect, we read that "If the root is cut, the viscera, the nerves, the veins are like branches and leaves; when the root is destroyed, the branches wither."[2]

2.2 Paragraph 2

The reference to the sages discovering the secrets of longevity immerses us into the mysteries of Daoism. After denouncing the agitation that troubles and disperses the celestial spirit, the sages propose techniques of breathing to remedy this, "the breathing technique for breathing out and breathing in (expiration and inspiration) in the supine and prone position." [Note 1] The text gives no indications other than these two positions and the importance of this technique, because this technique alone can restore health. Here, we attempt a deeper understanding of this technique drawing on the writings of the daozang. The procedures for "nourishing the vital principle," particularly the techniques of the breath, are abundantly developed there. Among these techniques, embryonic breathing is the most important. "Those who practice the Dao, if they want to obtain embryonic breathing taixi, must first know the source of embryonic breathing and then practice it, which is like the fetus in the womb. By going back to the base, by going back to the origin, one drives out old age, and one returns to the state of the fetus. Really this exercise has a reason to be."[2] The practice of this method is extremely complex; it has been modified over time according to the inspiration of the spiritual Masters and is only for the initiated. It consists of making the internal breath circulate. "This internal breath ... is naturally in the body, it is not a breath that one goes to seek outside."[2] The two internal and external breaths move in perfect correspondence. This is the mechanism that governs the circulation of the original breath, which is achieved in two steps: swallowing the primary qi and circulating it.

However, this circulation of the breath is not easy; there are many obstacles to overcome so the breath must be helped to circulate. Master Ning [Note 2] used to say, "The control of the breath regulates the interior, and the gymnastics regulates the exterior." Therefore, there is a close relationship between these two techniques. Thus, in the text, the term "breathing" is immediately followed by "position." It is therefore essential to associate these two techniques, the breathing technique and the gymnastic technique, because together they can restore health to the body.

The prone position or lying on the back is undoubtedly the first of the *daoyin* movements. There are many

daoyin methods, and it is not clear whether the text refers to the *Pengzu daoyin fa,* which is first practiced in the prone position, or the *Chisongzi daoyin fa,* which also includes this position. However, it does not matter which text discusses the prone position first, for all methods transmitted by spiritual Masters must be adapted and dosed like remedies to obtain beneficial results and thus live harmoniously and achieve longevity.

2.3 Paragraph 3

Prophylaxis is of paramount importance in traditional Chinese medicine. Without minimizing the importance of therapeutics, the emphasis here is on preventive medicine. "Prevent disease before it happens," says Lao Zi[5]. Chapter 2 of the *Su Wen* contains the same idea:

"The Sages cure themselves before the disease arises and ensure peace before the trouble arises. Thus, waiting for illness to apply remedies or waiting for disturbance to impose peace is like waiting for thirst to dig a well or waiting for war to forge weapons."[6]

This concept in *Huangdi Neijing* (《黄帝内经》*The Yellow Emperor's Inner Classic*) reveals a profound influence of *Yi Jing* (《易经》*The Book of Changes*). *Yi Jing* uses broken and solid lines (yin and yang) to describe the movement of life in its process of continuous transformation. All things evolve and transform according to certain laws. The orientation of the lines in *Yi Jing* represents auspicious or harmful influences. This is why it is good to be able to prevent harm and to observe the predictive nature of small details. "The noble man in time of peace does not forget the danger; while living does not forget the death; when the country is well governed does not forget the disorder, thus the bodies are in peace and the country is well protected."[7]

This concept of preventive awareness that characterizes *Yi Jing* is apparent in *Huangdi Neijing*, where it underlies the theory of the art of nourishing life, i. e., "treating illness before being sick." The commentaries on chapter two of the *Su Wen* give an example of the practice of this art by the famous physician of the Later Han dyansty, Zhang Zhongjing (张仲景). To the question, "What do you mean by 'Good doctors treat before the disease occurs?" Master Zhang answered, "Let us take for example a disease of the liver. This disease will spread to the spleen (liver-wood destroys spleen-earth). The spleen must be tonified so that it has enough strength to resist the destruction caused by the liver. Thus, the energy of the liver is obliged to follow its normal evolution towards the heart-fire (Fig. 3). To act in this way is to try to make normal what is abnormal, and to subdue rebellion to ensure peace. If we wait until the five organs are disturbed, how can we heal them?"[6]

Carelessness in one season harms health in the following season; knowledge of pathological processes allows one to take necessary measures from one season to the next season. Thus, to maintain the body in vigor and health, it is necessary to treat diseases before they appear, to nourish life before becoming old, and not to let diseases set in. This enables one to prolong life and slow down old age.

The use of the body's natural resources is advocated. The notion of "stone metal," which is abundantly present

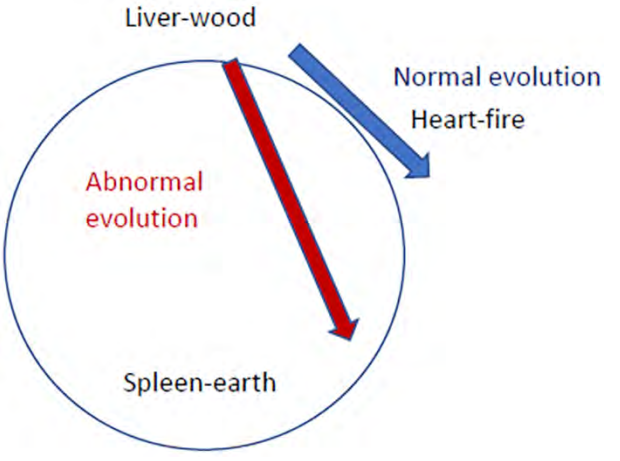

Figure 3 Normal and abnormal evolution of the liver-wood

in the body may mean the natural exploitation of one's body to practice a method of internal alchemy to prolong life. Indeed, the great Daoist Masters realized very quickly that alchemical remedies had beneficial effects on health, although their effects on "immortality" were limited. The Masters thus turned to other practices. Drawing on external (operative) alchemy as a basis, they developed the practice of internal alchemy (内丹) using their own bodies as laboratories. The alchemical tools of the athanor, alembic, vessel, and the products of mercury, lead, and cinnabar were conceptualized as being within the body. On this subject, Ge Hong exclaimed, "When I study the books of yangsheng (养生), I collect the recipes of longevity, there is not one that does not end with alchemy!"[8]

Finally, the paragraph concludes with a dialogue between Qi Bo and Huang Di. "One must maintain the mind in serenity to keep the vital energy" provides more details of this dialogue. "The ancient sages advise to avoid perverse energy and wind, to have the heart always in a state of 'serenity and emptiness,' so that the ancestral energy remains harmonious, the *jing* and the *shen* remain solid inside. Thus, how could illness arise?"[6]

2.4 Paragraph 4

Wang Ziqiao asked Peng Zu [Note 3], "What is the essence of human energy?" Peng Zu replied, "No human energy is more essential than sexual energy."[9] In humans, vital energy is the most precious resource and its integrity must be absolutely preserved. Nothing is more dangerous than wasting this energy through uncontrolled and dissolute sexuality. Reckless sexual union compromises the prolongation of life. This does not mean abstinence from all sexual acts; sexual union is useful to those who know how to engage in it properly. A Daoist author has the Daoist goddess say rather naively: "One does not fight against the natural inclination of man, and one can increase longevity, is this not also a pleasure?" However, it is advisable to be a master of oneself to avoid falling into debauchery. Specific principles and rules must be followed so that one does not destroy this essential energy capital; it must be cultivated to achieve harmony between body and mind.

The famous manuscripts of Mawangdui reveal an abundant literature on techniques for ensuring a healthy sex life. The rules are clear: "Sexual energy has eight pluses and seven minuses. If you cannot make use of the eight pluses and seven minuses, your physical energy will decrease by half when you are forty; when you are fifty, your activities will decline; when you are sixty, your hearing and sight will lose their acuity; and when you are seventy, you will be atrophied in the lower part and debilitated in the upper part; your sexual energy will no longer function, tears and mucus will flow. The eight pluses are as follows: the first is the mastery of energy, the second is the production of salivary secretion, the third is the knowledge of the right moment, the fourth is the accumulation of energy, the fifth is the continuous production of seminal fluid, the sixth is the aspiration of heaven's energy, the seventh is the maintenance of fullness, and the eighth is the stabilization of the erection. The seven minuses are as follows: The first is closure, the second is flight, the third is exhaustion, the fourth is impotence, the fifth is emotional disturbance, the sixth is alienation, the seventh is waste ... so if you skillfully put the eight pluses to good use and eliminate the seven minuses, your eyes and ears will be bright and clear, your body will be light and alert, your sexual energy will be stronger and stronger, you will have a happy and long life."[9]

Finally, treatments are recommended to cure the abuse of the seven minuses; it is advised to "take herbs, do moxibustion to induce energy, take food supplements to increase physical strength."[10]

Following this advice, sex can provide good health, increase the power of concentration, reduce stress, and develop physical and mental serenity.

2.5 Paragraph 5

The sages say that, "When the oil runs out, the lamp goes out; when the marrow runs out, the man dies." However, if we fill the oil, the lamp lights up again; when we strengthen the marrow, the man becomes strong again.

The marrow is compared here to the oil of a lamp, and is the energy that ensures the vitality of the body. First, one should not waste this energy, but seek to conserve it by practicing different methods to obtain "regeneration" of the marrow. These methods are the application of measures such as tonic medicines, acupuncture, moxibustion, dietetics, living in accordance with nature, massages, and gymnastic techniques. The use of acupuncture and moxibustion can maintain health and combat aging. Bian Que (扁鹊) [Note 4] says, "When the man is not sick, frequent moxibustion on Guanyuan (关元 CV 4), Qihai (气海 CV 6), Mingmen (命门 GV 4), Zhongwan (中脘 CV 12) can also maintain longevity of more than one hundred years."

A clinical case observed in the Pain Treatment and Evaluation Center of the Cochin-Tarnier Hospital in Paris illustrates well the importance of the moxibustion method.

Mr. S, 84 years old, former engineer, referred on January 28, 2005, to the Center for chronic daily disabling headaches lasting more than two years. The patient had a left temporal hemicrania, also called chronic paroxysmal hemicranias, and this affection is frequent in older adults. The patient had sought multiple consultations and treatments for the pain, with no satisfactory results.

In the history, nothing particular was noted except for headaches that occurred in youth, the characteristics of which strongly suggested migraines without aura.

On examination, Mr. S was well groomed, alert, and very intelligent. The visual analog scale (VAS) of the pain was between four and five.

The face was pale, but turned pink during the painful attacks; the tongue was pinkish, without coating; the pulse was quite wide and superficial at the first consultation.

Mr. S complained particularly of reduced concentration, memory, and intellectual activity, which was an important aspect of his life.

The neurological examination data were completely normal. Two magnetic resonance imaging brain scans indicated no obvious pathological changes.

His current treatment was low-dose Elavil® and Dolipprane® as needed. Attempts at drug withdrawal for chronic daily headache were unsuccessful; Mr. S. did not tolerate other allopathic treatments.

First acupuncture session: I treated the temporal headache by puncturing the gallbladder meridian points Fengchi (风池 GB 20), Shuaigu (率谷 GB 8), Yanglingquan (阳陵泉 GB 34), then Yintang (印堂 EX-HN3), Taiyang (太阳 EX-HN5), Hegu (合谷 LI 4), and Baihui (百会 GV 20).

After the session, the patient experienced relief. A second session was planned for the following week. The same points were used for a few sessions; the results were positive but lasted only a few hours. During a session in May 2005, after having removed the needles, I decided to tonify the kidneys by moxibustion on Shenfeng (神封 KI 23) and Mingmen. The following week, the patient reported remarkable results: Mr. S. had experienced no more pain (even from the bunion on his foot, which had been hurting him). He was radiant and had recovered most of his intellectual faculties. Since then, I have seen him occasionally to maintain this state, which he describes as "miraculous!" Moxibustion is a method of choice for elderly subjects. Bian Que's words are still relevant today [Note 5].

2.6 Paragraph 6

This paragraph focuses on rules for the maintenance of life in winter. It is a transcription of *Su Wen* chapter 2, entitled "Laws of Harmonization of the Mental Mind by the Four Energies." I translate here the text of the 1953 Hoang De Noi Kinh edition (reprinted 2001 VHTT Hanoi), starting at the beginning of the text to facilitate the understanding of Dr. Nguyen Tu Sieu's annotations.

The explanation of "paralysis of all four limbs" (*wei jue* 痿厥) is an illustration of Chinese preventive medicine. Indeed, according to the law of the five elements, kidney-water precedes liver-wood. A deficiency of kidney energy in winter necessarily leads to a deficiency of liver-wood energy in spring, thus causing specific pathologies of liver energy insufficiency.[3]

The decrease in the energy of kidney-water leads to a deficiency of liver-wood energy; the nutritive function of the muscles becomes deficient, resulting in paralysis of the four limbs with a feeling of cold (Fig. 4).

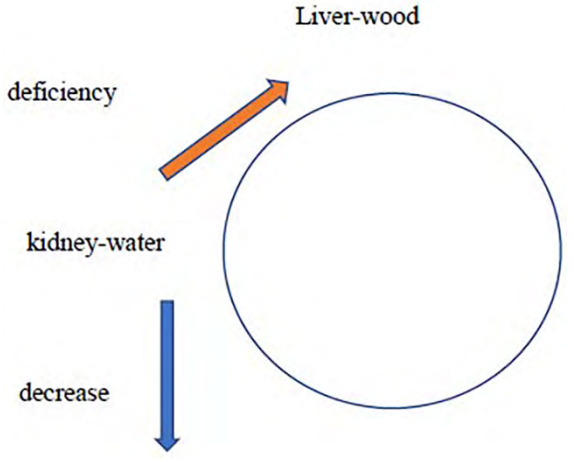

Figure 4 Relationship between kidney-water and liver-wood

In this commentary, importance is placed on the imitation of nature, an essential aspect of yangsheng (养生). To conform to the natural order is to nourish life, to slow down aging, and to prolong vigor. The person who conforms to the natural order of heaven and earth will have a happy and long life. This idea is based on conforming to the variations of the four seasons and the yin and yang; we must use these factors to our advantage to neutralize and avoid the unfavorable aspects of these natural variations. In short, to ensure vigor and longevity, we must conform to the times and preserve ourselves from perverse energies.

This includes circadian and seasonal conformity. Thus, at dawn, the energy of the human body increases, so it is advisable to get up early and do exercises. At dusk, the yang energy collects, so it is advisable to withdraw and to gather, as this time is conducive to meditation. The climate of the four seasons is divided into the warmth of spring, the heat of summer, the coolness of autumn, and the cold of winter. The process of growth and development of living beings is growth in spring, development in summer, recollection in autumn, and conservation in winter. Humans must follow these seasonal variations and order their activities and rest according to the season: in spring and summer, one should get up early and go to bed late; in autumn and winter, one should go to bed early and wake up late.

Humans are affected by environmental factors such as wind, rain, fog, frost, and other complex variations in weather. Traditional Chinese medicine groups these into six energies: wind, cold, heat, dampness, dryness, and fire. When these energies are in excess or deficiency, they are unfavorable to the human body and are called the six perverse energies. A powerful way to nourish life is therefore to conform to the normal conditions of the six qi and to preserve oneself from the abnormal situations generated by the six energies.

2.7 Paragraph 7

A small poem of four stanzas and a commentary ends this text. The rhythm of the verses is broken into seven syllables, and its meaning is difficult to grasp, "Naturally man must keep his Pure Spirit intact. To have the form is like not having it, that is to follow the Way. In the dark door of the woman is life."

The key is undoubtedly in the third stanza, which refers to *Dao De Jing* (《道德经》*Tao Te Ching*) chapter 6 "In the dark female door, resides the root of heaven and earth." In the context of sexual energy and sexual hygiene, we can interpret these verses as describing the creative act of life. Keeping the spirit intact can be translated as keeping the seminal essence intact. One way to achieve immortality through the sexual act is to avoid ejaculation, which saves sexual energy.

This is why the commentaries emphasize the expression *jiao gan jing* (Tinh Giao Cam), which can be interpreted as "the essence of compenetration" or as "sexual energy," or simply as indicating semen. The maintenance of life through sexual techniques consists of keeping the seminal essence intact. This strengthens the original essence and thus prolongs life.

3 Conclusions

The kidney, an organ that comes directly from the energy of heaven and earth, contains the seminal essence that is the origin of human life. The essence is the "precious good" sought by the sages of antiquity. All the rules of protection of life can be summed up in one rule: keep the seminal essence intact. The apostrophe, which ends this text "To speak like this is to say everything!" is well significant. The author incites us to act, to react in order to obtain long life and happiness.

Notes

Note 1. The Baihui (百会 DU 20) and Huiyin (会阴 RN 1) points are also considered as zi and wu according to Van Nghi. Zi refers to mid-day and wu refers to mid-night. Anterior zi may be the meeting of yin (hui yin), and posterior wu may be the point of Baihui. It may be the zi, wu, mao and you: four times and four regions of the body. To make the breath circulate in the governor vessel and the conception vessel, Daoists meditated according to the rule of the 12 periods of 2 hours each of the day; these are represented by twelve hexagrams symbolizing the modulation of the breath and the circulation in these two vessels.
Note 2. To my knowledge, this notion has not been mentioned in other translations.
Note 3. Master Ning was a contemporary of the Yellow Emperor and was Director of the Taozheng Potters. He was able to gather fire and not burn himself. He could place himself in the center of a fire and move up and down with the smoke; his clothes never got burned (*Zeng Zao, Daoshu*).
Note 4. Peng Zu, a great officer of the Shang dynasty, lived successively under the Xia and Shang dynasties and reached, the age of 700 years. He obtained the Dao by constantly eating cinnamon.
Note 5. Bian Que's real name was Qin Yueren (秦越人). Ancient records suggest that he was the first famous physician in history whose biography was published by Sima Qian (司马迁) in the *Shi Ji* (《史记》*Historical Annals*) "Biographies of Bian Que." In addition to the *Historical Annals*, there are later fragmentary notes on Bian Que in *Zhanguo Ce* (《战国策》*Stratagems of the Warring*

States), *Hanfei Zi* (《韩非子》*Han Fei Zi*), *Lie Zi* (《列子》*Lie Zi*), and other ancient books.

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Ethical approval

This study does not contain any studies with human or animal subjects performed by the author.

Author contributions

Anita Bui wrote and revised the manuscript.

Conflicts of interest

The author declares no financial or other conflicts of interest.

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Review

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Efficacy of Shugan Hewei Therapy for Chronic Atrophic Gastritis: A Systematic Review and Meta-Analysis

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Abstract

Objective: Shugan Hewei therapy (SHT) acts to soothe the liver and harmonize the stomach. It is a classical traditional Chinese medicine method widely used in China to treat chronic atrophic gastritis (CAG) due to liver qi invading the stomach. However, the clinical effects of SHT remain unclear. We aimed to evaluate the overall clinical effective rate and safety of SHT in treating CAG.

Methods: We used the Jadad scale and Cochrane Collaboration risk of bias tool to evaluate the methodological quality of studies investigating SHT. Eight medical databases were searched to identify relevant studies. After data extraction and quality evaluation, 27 randomized controlled trials, including 2,441 patients, were considered eligible for analysis. No serious heterogeneity or publication bias was observed across the included studies. We used Revman 5.3 statistical software to evaluate the general clinical effective rate and safety of SHT.

Results: The results showed that SHT was more effective (RR=1.25; 95% CI [1.20, 1.29]; $P<0.01$) and safer (MD=0.24, 95% CI [0.08, 0.75]; $P<0.01$) than control interventions comprising western medicine, Chinese patent medicine, and/or western medicine + Chinese patent medicine. Compared with the control interventions, SHT resulted in greater improvements in the symptom scores for stomach distension and stomachache, serum gastrin level, histopathologic changes, *Helicobacter pylori* (HP) inhibition rate, and gastric mucosal inflammation.

Conclusion: SHT was more effective and safer than control interventions for CAG.

Keywords: Chinese herbal medicine; Chronic atrophic gastritis; Efficacy; Meta-analysis; Shugan Hewei therapy

1 Introduction

Chronic atrophic gastritis (CAG) is characterized by reduced gastric acid secretion, atrophic gastric mucosa (GM), and metaplasia of the intestinal epithelium.[1] This condition is an important pre-cancerous lesion of gastric cancer, which is the fifth most frequent cancer and the third leading cause of cancer death. [2] CAG has a global incidence of 0% to 10.9%.[3] However, the prevalence of CAG is higher in China. In a population of Chinese patients, the prevalence of atrophic gastritis was 17.7% on endoscopy and 25.8% on pathologic examination.[4–5]

CAG is associated with *Helicobacter pylori* (HP) infection, and HP eradication is recommended in most cases.[6] Although CAG resulting from HP infection is commonly treated with antibiotics, antibiotic administration may give rise to long-term antibiotic resistance.[7] Another treatment for HP is chemotherapy; however, some patients cannot tolerate chemotherapy because of its adverse effects and drug interactions.[8] Furthermore, the incidence and detection rate of CAG are positively correlated with age, and older adults have many concomitant diseases and lower immunity, which is conducive to the deterioration and development of some primary diseases.[9]

The efficacy of some traditional Chinese medicine (TCM) therapies has been confirmed in recent years.[10] TCM may reduce the symptoms of CAG and improve patient's quality of life. In TCM theory, CAG is commonly caused by liver qi invading the stomach.[11] One TCM method widely used to treat CAG patients with liver qi invading the stomach is Shugan Hewei (疏肝和胃) therapy (SHT), which soothes the liver and harmonizes the stomach.[12] However, the overall clinical effective rate and safety of SHT remain unclear. This systematic

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review and meta-analysis were conducted to evaluate the efficacy and safety of SHT for CAG.

2 Methods

2.1 Search strategy

We searched for articles published from inception until December 1, 2020, in English databases (PubMed, Embase, SpringerLink, SciVerse, Science Direct) and Chinese databases [Chinese Scientific Journals Database (VIP), China National Knowledge Infrastructure (CNKI), Wanfang Database (Wan-fang), and SinoMed]. The following search terms were used alone or in combination: "chronic atrophic gastritis," "atrophic gastritis," "precancerous disease of gastric cancer," "shugan hewei therapy," "soothingliver (Shu Gan)," "regulating qi to harmonize stomach (Liqi Hewei)," "syndrome of liver qi invading the stomach," "Chaihu Shugan Powder," and "randomized controlled trial."

2.2 Selection criteria

Retrieved articles underwent initial screening of the title and abstract. Studies were excluded if they were animal studies, case reports, reviews, experience introductions, non-randomized controlled trials, or if the intervention measures were combined with other therapies.

Two researchers independently read the full text of retrieved studies that were not excluded in the initial screening. The studies were strictly screened in accordance with the eligibility criteria. Disagreements were resolved via discussion with a third researcher. In accordance with a previous systematic review and meta-analysis of Ban Xia Xie Xin Decoction (半夏泻心汤) for CAG,[13] the inclusion criteria were: 1) patients diagnosed with CAG via endoscopy and pathology; 2) randomized controlled trials (RCTs); 3) all participants were older than 18 years; 4) comparison of an experimental group treated with SHT versus a control group treated with conventional western medicine (WM), Chinese patent medicine (CPM), or WM+CPM; 5) with treatment course ≥1 month; and 6) Jadad score ≥2.

2.3 Outcomes

2.3.1 Main outcome

The overall clinical effective rate.

The evaluation criteria were based on the *Zhongyao Xinyao Linchuang Yanjiu Zhidao Yuanze* (《中药新药临床研究指导原则》*Guiding Principles for Clinical Research of New Chinese Medicines*).[14] Cure: the disappearance or basic disappearance of clinical signs and symptoms; significantly effective: obvious improvement in main clinical symptoms and signs; effective: clinical symptoms and signs improved or significantly reduced; invalid: either no obvious improvement or aggravation of clinical symptoms and signs.

2.3.2 Additional outcomes

1. Improvement in GM inflammation;
2. Improvement in histopathologic changes;
3. HP inhibition rate;
4. Serum gastrin level;
5. Improvements in symptom scores;
6. Stomachache symptom score;
7. Gastric acid reflux symptom score;
8. Belching symptom score;
9. Poor appetite symptom score;
10. Safety evaluation.

2.4 Data extraction and quality assessment

Two researchers independently extracted the data, including the first author, publication year, sample size, sex, age, course of disease, intervention, duration, outcome measures, follow-up, adverse effects, and Jadad score. The Jadad scale and Cochrane Collaboration risk of bias tool were used to evaluate the methodological quality. Disagreements were resolved via discussion with a third researcher. The modified Jadad score ranges from 0 to 7, and includes the following domains: randomization, concealment of allocation, blinding, and patient dropouts. The Cochrane Collaboration risk of bias tool addresses the sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias.

2.5 Data synthesis and analysis

Statistical analysis was performed using Review Manager 5.3 software. The pooled risk ratio (RR) was calculated to assess dichotomous data, while the weighted mean difference (MD) was used for continuous variables, with both adopting 95% confidence intervals (CI). Heterogeneity was assessed using the χ^2 test and inconsistency index statistic (I^2). A random-effect model was used if substantial heterogeneity existed (I^2>50% or P<0.05); otherwise, a fixed-effect model or subgroup analysis was used. The Z-test was used to assess the overall effect. Pooled results were considered statistically significant at P<0.05. The potential publication bias was analyzed using funnel plots.

3 Results

3.1 Characteristics of included studies

The database search retrieved a total of 617 studies, including 155 from CNKI, 424 from Wan-fang database, 31 from VIP, and none from SinoMed, PubMed, Ebscore Medline, Cochrane Library, and Embase. Twenty-seven clinical RCTs including a total of 2,441 patients (1,248 in the experimental group and 1,193 in the control group) satisfied our selection criteria and were included in this meta-analysis.[15–41] The flowchart of the literature search is shown in Figure 1. The sample size of the included studies was 58 to 200 participants, the participant age ranged from 18 to 81 years, and the treatment course ranged from 4 to 48 weeks. The characteristics of the included studies are described in Table S1. The constituents of the herbal formulas are listed in Table S2. The frequencies of the usage and distribution of TCM are listed in Table S3, and the classification of Chinese

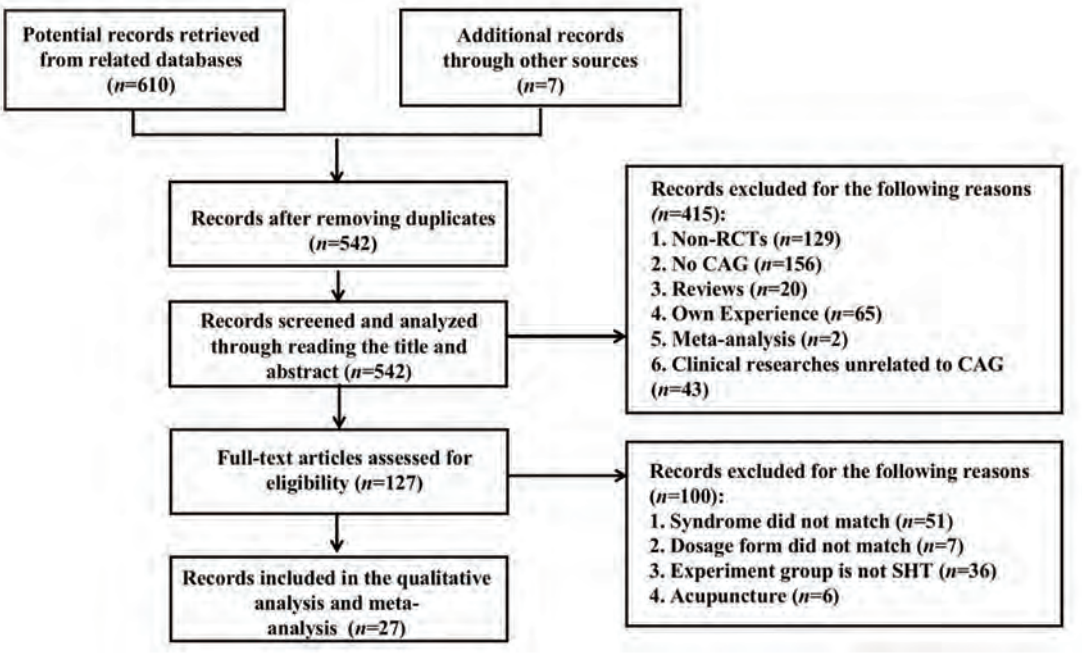

Figure 1 PRISMA flowchart depicting the study selection process

herbs are listed in Table S4. The proportions of patients treated with Liqi Hewei (理气和胃 regulates qi to harmonize the stomach) therapy and Shu Gan (疏肝 soothes the liver) therapy were 27.6% and 25.4%, respectively; these were the most commonly administered herbs in the included studies (Fig. 2).

3.2 Risk of bias assessment

The details of the evaluation of the methodological quality of the included studies are shown in Table S5. Randomization was achieved with random number tables in three studies [26, 28, 33] and patients in three studies were randomly divided into groups,[17, 21, 22] while 13 studies used the word "randomization" without any explanation of the randomization process. The blinding method was only reported in one study, [35] while 18 studies did not mention blinding. None of the included studies reported the allocation concealment method. Two studies provided the number of dropouts[18, 25] but did not conduct an intention-to-treat analysis to deal with the missing data. Because of the relative lack of specific information, it was not possible to determine whether the processes of random sequence generation, blinding, and allocation concealment were conducted adequately, leading to a high risk of bias in the present review (Fig. 3). The patients' age, sex, and other characteristics were comparable in all studies.[15–41]

All 27 included studies reported the overall clinical effective rate. Heterogeneity analysis indicated homogeneity among the 27 studies (P=0.13, I^2=24%), so the fixed-effect model was used. The experimental group had a significantly different overall clinical effective rate compared with the control group (RR=1.25; 95% CI [1.20, 1.29]; P<0.01). The overall effect was significant (Z=11.60) (Fig. 4). The results demonstrated that the overall clinical

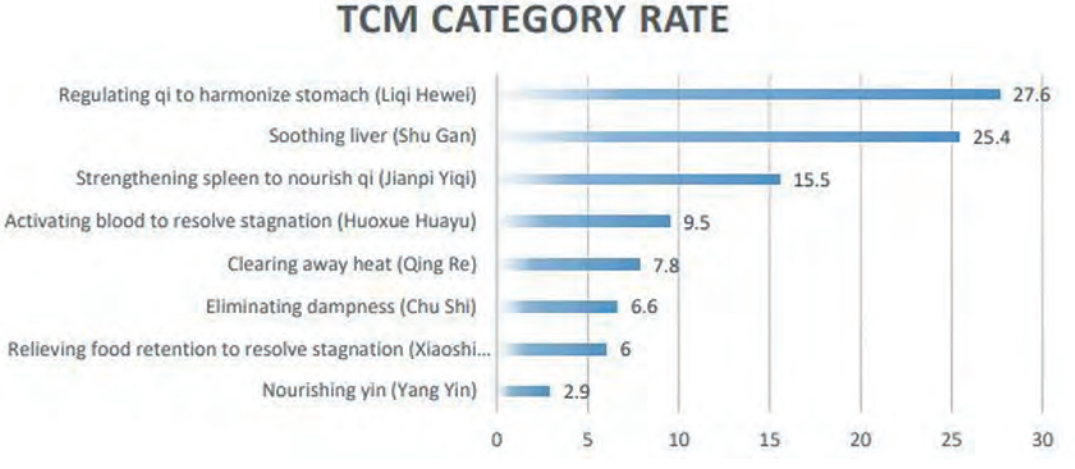

Figure 2 TCM category rate

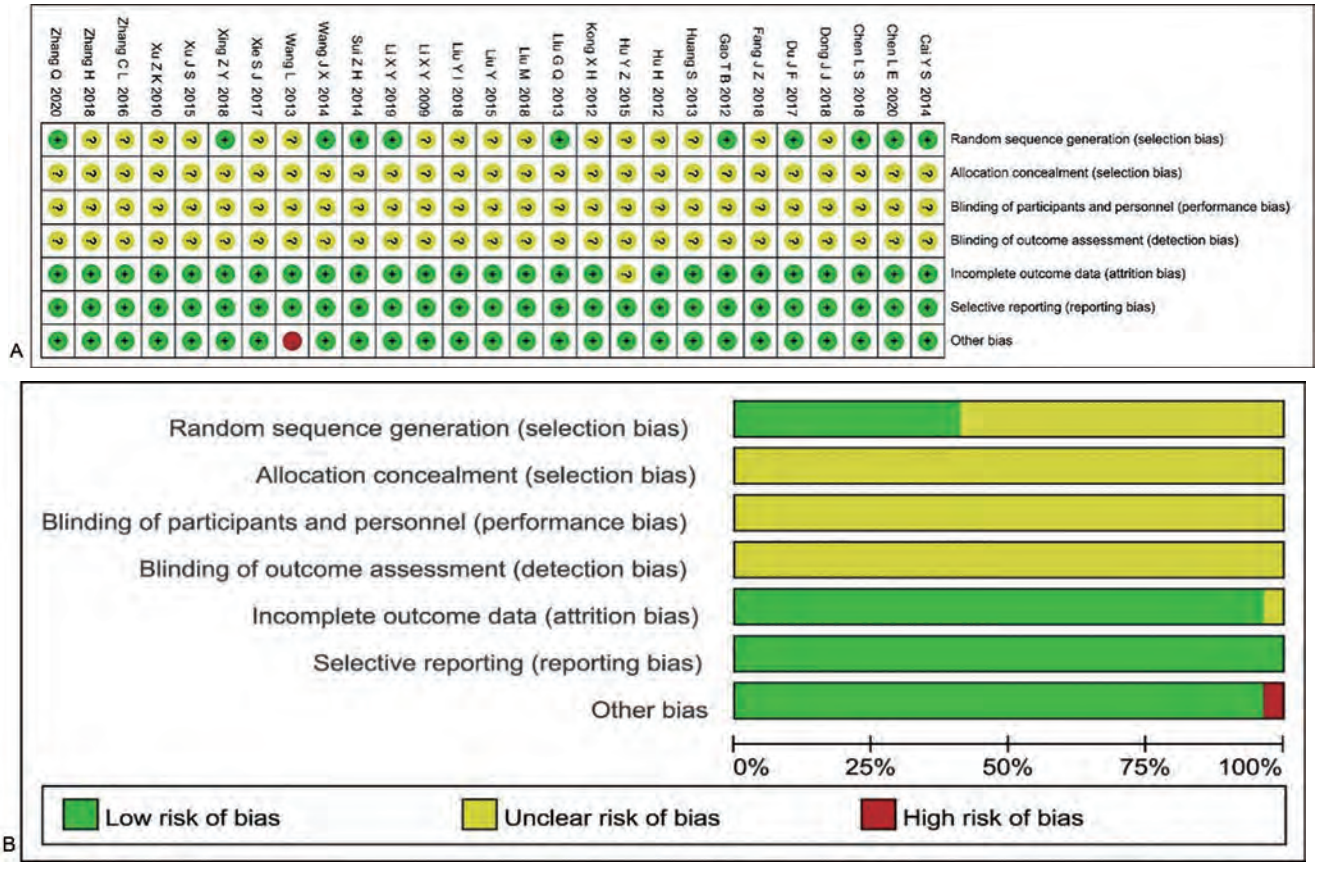

Figure 3 (A) Risk of bias graph (B) Risk of bias summary

effective rate of SHT was better than that of the control intervention.

3.3 Publication bias

The potential publication bias of the 27 studies[15–41] was identified by an asymmetrical funnel plot (Fig. 5).

3.4 Improvement in GM inflammation

Improvement in GM inflammation after SHT was reported in eight studies.[18, 24, 25, 31, 32, 34, 35, 39] The studies were homogeneous (P=0.48, I^2=0%), so the fixed-effect model was adopted for analysis.

The improvement in GM inflammation was significantly different in the experimental group compared with the control group (RR=1.23; 95% CI [1.14, 1.33]; P<0.01), with a significant overall effect (Z=5.22). The results demonstrated that SHT achieved a greater improvement in GM inflammation than the control intervention (Fig. 6).

3.5 Improvement in histopathologic changes

Improvement in histopathologic changes after treatment was reported in four studies.[22, 32, 35, 39] The studies were homogeneous (P=0.45, I^2=0%), so the fixed-effect model was adopted for analysis. The improvement in histopathologic changes was significantly different in the experimental group compared with the control group (RR=1.31; 95% CI [1.13, 1.50]; P<0.01), with a significant overall effect (Z=3.72). The results demonstrated that SHT achieved a greater improvement in histopathologic changes than the control intervention (Fig. 7).

3.6 HP inhibition rate

Improvement in the HP inhibition rate after treatment was reported in four studies.[18, 22, 25, 34] The studies were homogeneous (P=0.62, I^2=0%), so the fixed-effect model was adopted for analysis. Meta-analysis results showed a significant difference in the HP inhibition rate between the experimental and control groups (RR=1.28; 95% CI [1.05, 1.56]; P=0.01), with a significant overall effect (Z=2.47). The results demonstrated that SHT achieved a greater HP inhibition rate than the control intervention (Fig. 8).

3.7 Serum gastrin level

Improvement in the serum gastrin level after treatment was reported in three studies.[18, 30, 34] The studies were homogeneous (P=0.86, I^2=0%), so the fixed-effect model was adopted for analysis. The serum gastrin level was significantly different in the experimental group compared with the control group (MD=3.56; 95% CI [2.86, 4.26]; P<0.01), with a significant overall effect (Z=9.99). The results demonstrated that SHT achieved a greater improvement in the serum gastrin level than the control intervention (Fig. 9).

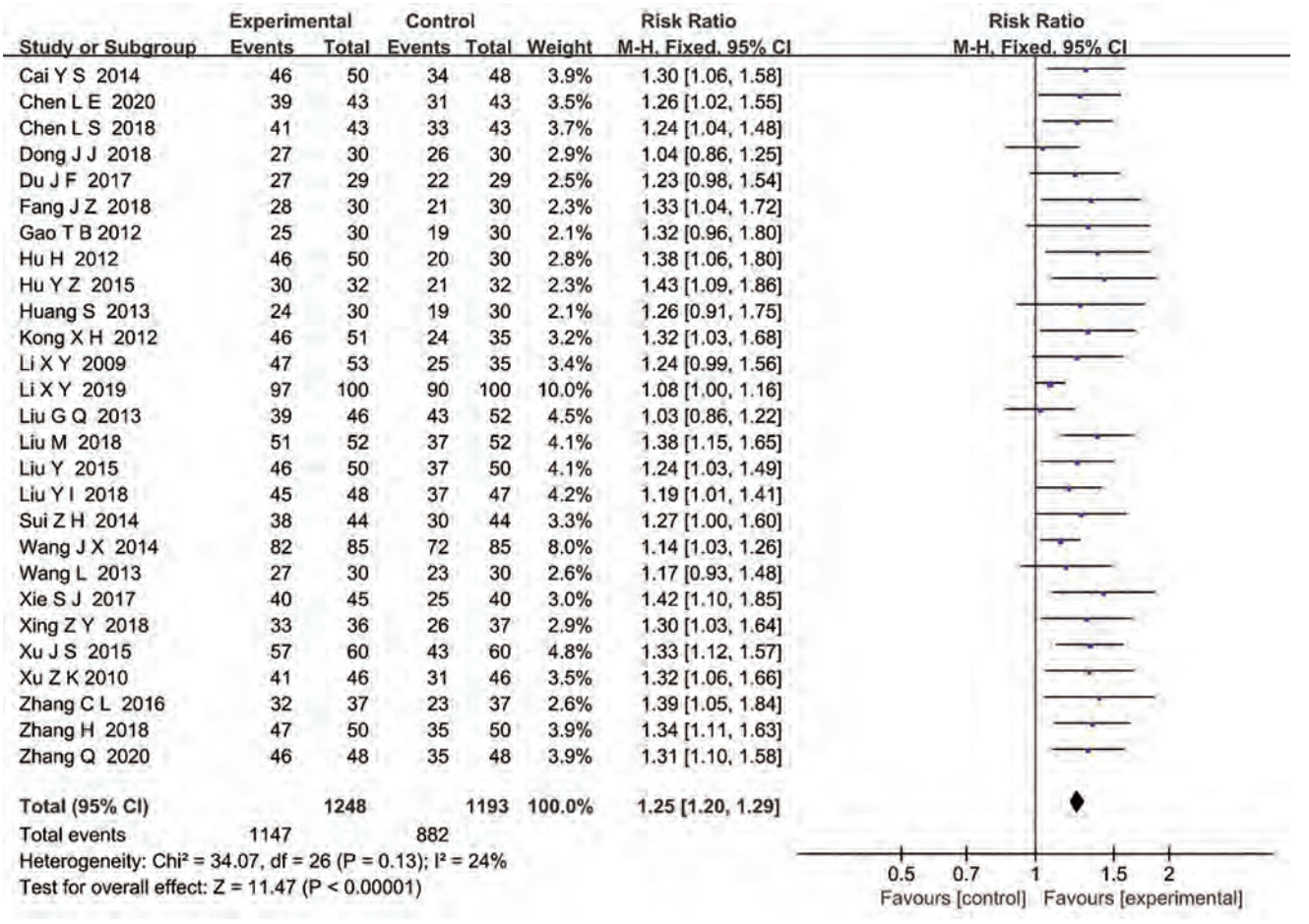

Figure 4 Forest plot of the overall clinical effective rate (fixed-effect model)

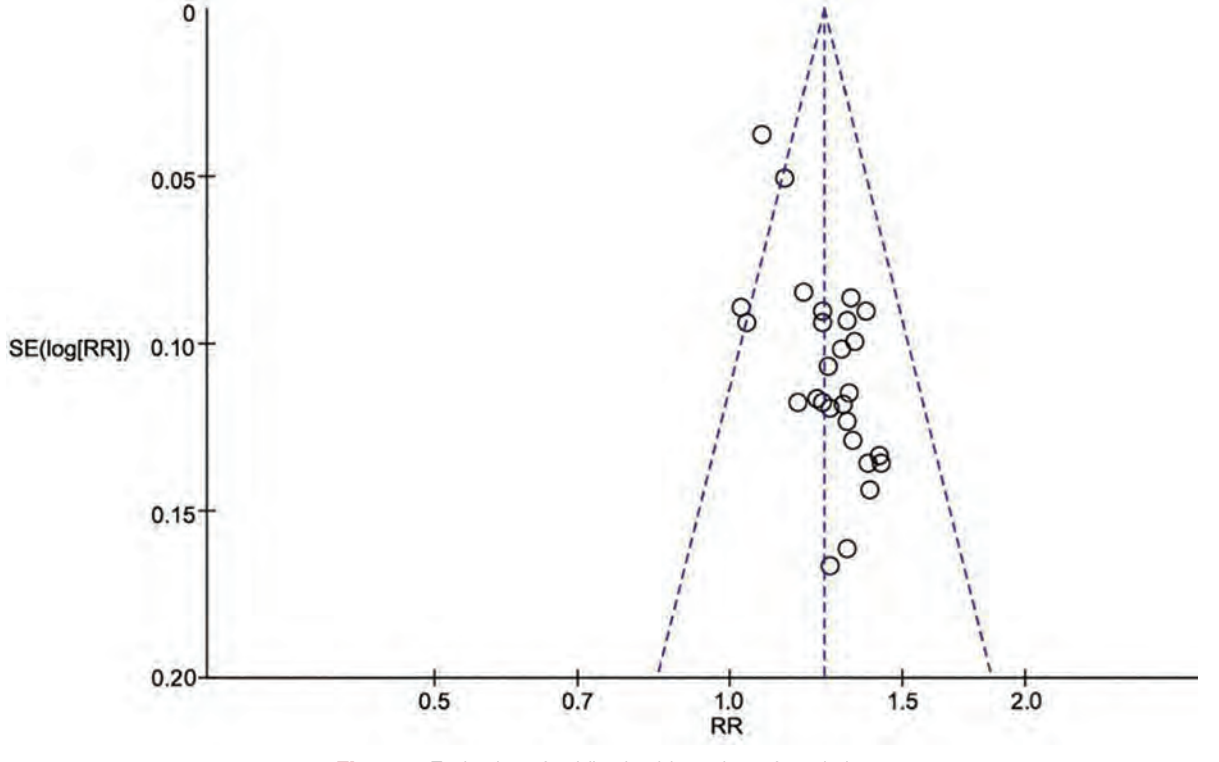

Figure 5 Evaluation of publication bias using a funnel plot

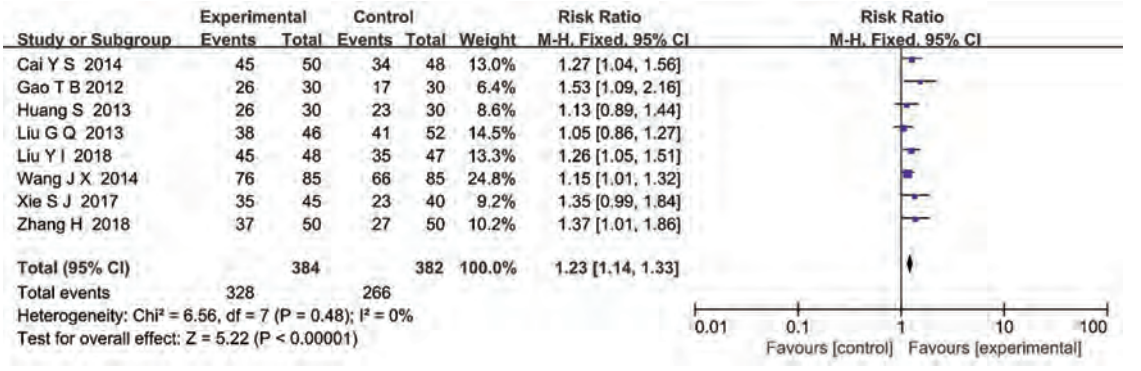

Figure 6 Forest plot of improvement of GM inflammation (fixed-effect model)

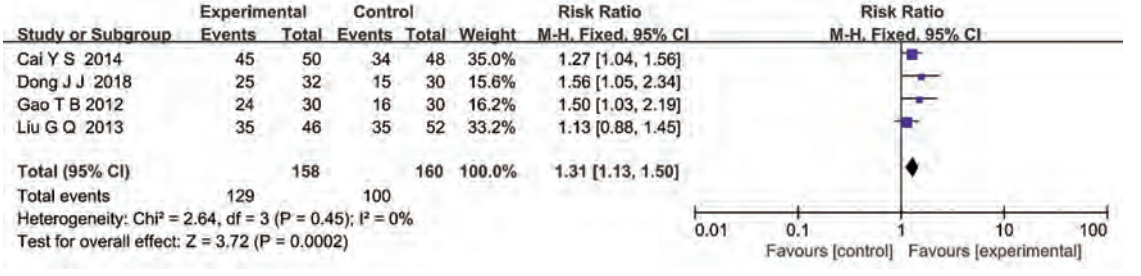

Figure 7 Forest plot of improvement in histopathological changes (fixed-effect model)

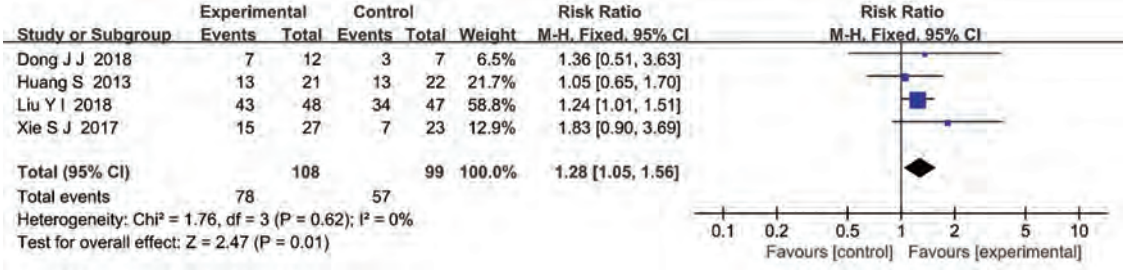

Figure 8 Forest plot of the HP inhibition rate (fixed-effect model)

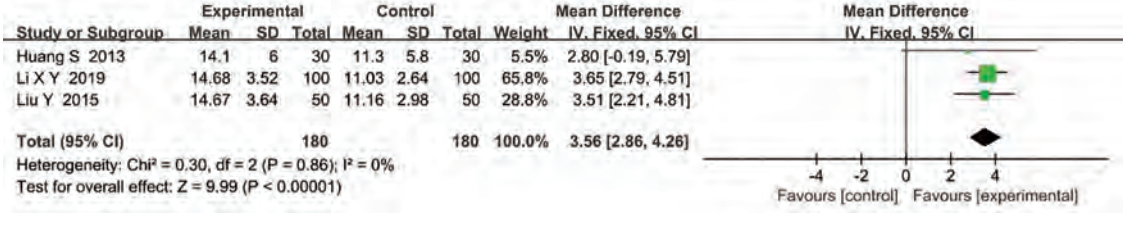

Figure 9 Forest plot of improvement in serum gastrin (fixed-effect model)

3.8 Improvement in symptom scores

3.8.1 Stomach distension symptom score

Improvement in the stomach distension symptom score was reported in five studies.[18, 19, 21, 22, 39] The studies were heterogeneous (P<0.01, I^2=90%), so the random-effect model was adopted for analysis. Improvement in the stomach distension symptom score was significantly different in the experimental group compared with the control group (MD=–1.17; 95% CI [–1.52, –0.82]; P<0.01), with a significant overall effect (Z=6.61). The results demonstrated that SHT achieved a greater improvement in the stomach distension of patients with CAG than the control intervention (Fig. 10).

3.8.2 Stomachache symptom score

Improvement in the stomach distension symptom score was reported in four studies.[18, 19, 21, 22] The studies were heterogeneous (P<0.01, I^2=93%), so the random-effect model was adopted for analysis. Improvement in the stomach distension symptom score after treatment was significantly different in the experimental group compared with the control group (MD=–0.79; 95% CI

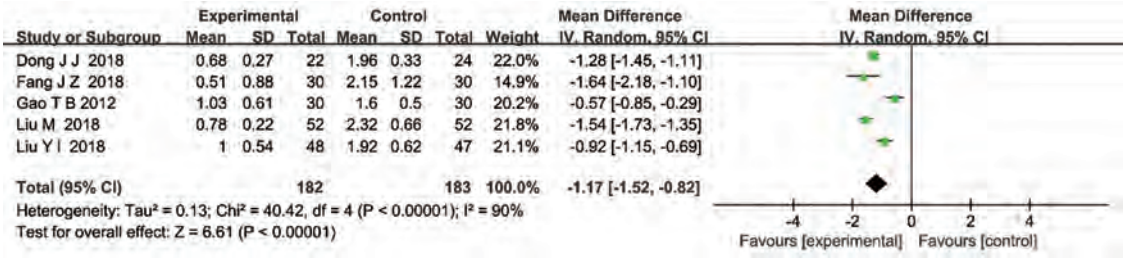

Figure 10 Forest plot of improvement in the stomach distension symptom score (random-effect model)

[–1.17, –0.41]; P<0.01), with a significant overall effect (Z=4.08). The results demonstrated that SHT achieved a greater improvement in the stomachache symptom score of patients with CAG than the control intervention (Fig. 11).

3.8.3 Gastric acid reflux symptom score

Improvement in the gastric acid reflux symptom score was reported in four studies. [19, 21, 39] The studies were homogeneous (P=0.27, I^2=23%), so the fixed-effect model was adopted for analysis. Improvement in the gastric acid reflux symptom score was significantly different in the experimental group compared with the control group (MD=–0.74; 95% CI [–0.87, –0.61]; P<0.01), with a significant overall effect (Z=11.44). The results demonstrated that SHT achieved a greater improvement in the gastric acid reflux symptom score of patients with CAG than the control intervention (Fig. 12).

3.8.4 Belching symptom score

Improvement in the belching symptom score was reported in four studies. [19, 21, 22] The studies were heterogeneous (P<0.01, I^2=86%), so the random-effect model was adopted for analysis. Improvement in the belching symptom score was significantly different in the experimental group compared with the control group (MD=–0.56; 95% CI [–0.87, –0.25]; P<0.01), with a significant overall effect (Z=3.51). The results demonstrated that SHT achieved a greater improvement in the belching symptom score of patients with CAG than the control intervention (Fig. 13).

3.8.5 Poor appetite symptom score

Improvement in the poor appetite symptom score was reported in two studies. [18, 39] The studies were homogeneous (P=0.36, I^2=0%), so the random-effect model was adopted for analysis. Improvement in the poor appetite symptom

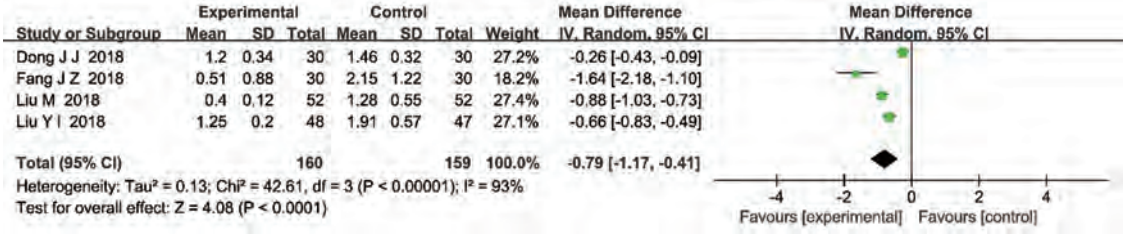

Figure 11 Forest plot of improvement in the stomachache symptom score (random-effect model)

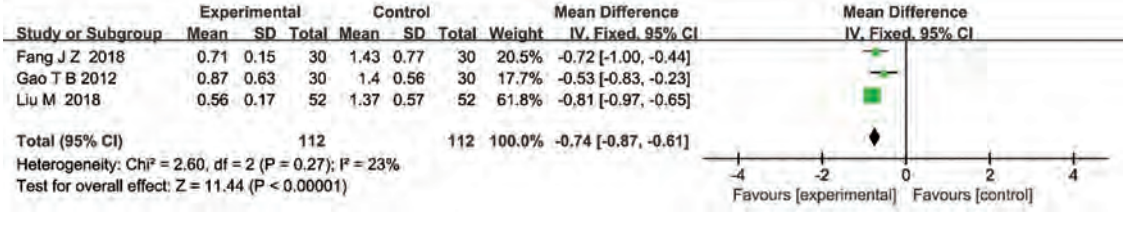

Figure 12 Forest plot of improvement in the gastric acid reflux symptom score (fixed-effect model)

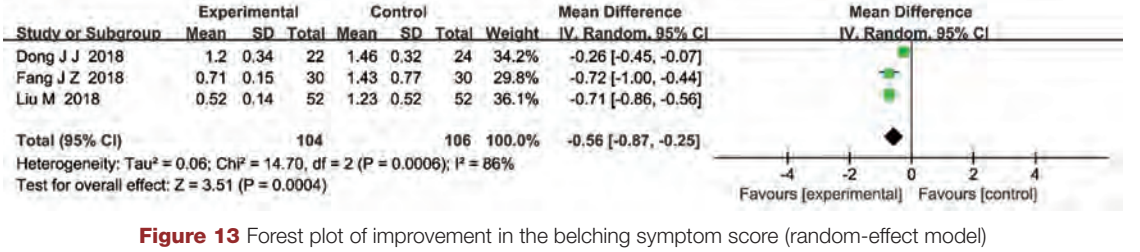

Figure 13 Forest plot of improvement in the belching symptom score (random-effect model)

score was significantly different in the experimental group compared with the control group (MD=–0.19; 95% CI [–0.32, –0.06]; P<0.01), with a significant overall effect (Z=2.89). The results demonstrated that SHT achieved a greater improvement in the poor appetite symptom score of patients with CAG than the control intervention (Fig. 14).

3.8.6 Safety evaluation

All 27 studies were included in the safety evaluation. Six studies mentioned whether adverse reactions were observed in the treatment course.[15, 16, 25, 28, 33, 39] Three of these six studies stated that no adverse reactions were observed in the treatment course,[25, 33, 39] while the other three studies mentioned a specific number of patients with adverse reactions observed in the treatment course. [15, 17, 28] One study reported that no adverse reactions occurred in the experimental group;[28] the other two studies reported the occurrence of allergic dermatitis, nausea, vomiting, arthralgia, and myasthenia.[15, 17] Twenty-two studies did not mention whether adverse reactions were observed. The studies were homogeneous (P=0.80, I^2=0%), so the fixed-effect model was adopted for analysis. Meta-analysis showed a significant overall effect (P<0.01, Z=2.46); the incidence of adverse reactions was significantly greater in the control group than in the experimental group (MD=0.24; 95% CI [0.08, 0.75]; P<0.01). Therefore, SHT was safer and had fewer associated adverse events than the control intervention (Fig. 15).

3.9 Subgroup analyses

3.9.1 SHT versus WM

Fourteen studies[15, 17, 18, 19, 21, 24, 26, 28, 31, 34, 35, 37, 40, 41] compared SHT and WM in a total of 1,257 patients (643 cases in the experimental group and 614 in the control group). The studies were homogeneous (P=0.50, I^2=0%), so the fixed-effect model was adopted for analysis. The general clinical effective rate was significantly different in the experimental group compared with the control group (RR 1.25; 95% CI [1.19, 1.32]; P<0.01), with a significant overall effect (Z=8.41). The results demonstrated that SHT achieved a higher overall clinical effective rate than WM (Fig. 16 A).

3.9.2 SHT versus CPM

Nine studies[20, 22, 25, 27, 29, 32, 36, 38, 39] compared SHT and CPM in a total of 710 patients (368 in the experimental group and 342 in the control group). The studies were homogeneous (P=0.50, I^2=0%), so the fixed-effect model was adopted for analysis. The general clinical effective rate was significantly different in the experimental group compared with the control group (RR 1.30; 95% CI [1.20, 1.40]; P<0.01), with a significant overall effect (Z=6.57). The results demonstrated that SHT achieved a higher overall clinical effective rate than CPM (Fig. 16 A).

3.9.3 SHT versus WM+CPM

Four studies[15, 17, 30, 33] compared SHT and WM+CPM in a total of 474 patients (237 in the experimental group and 237 in the control group). The studies were homogenous. (P=0.11, I^2=0%), so the fixed-effect model was adopted for analysis. The general clinical effective rate was significantly different in the experimental group compared with the control group (RR=1.17; 95% CI [1.09, 1.26]; P<0.01), with a significant overall effect (Z=4.22). The results demonstrated that SHT achieved a higher overall clinical effective rate than WM+CPM (Fig. 16 A).

Excluding each of the four studies in a one-by-one manner and then performing a sensitivity analysis revealed that the heterogeneity was largely caused by one study.[17] The study had no substantial heterogeneity between

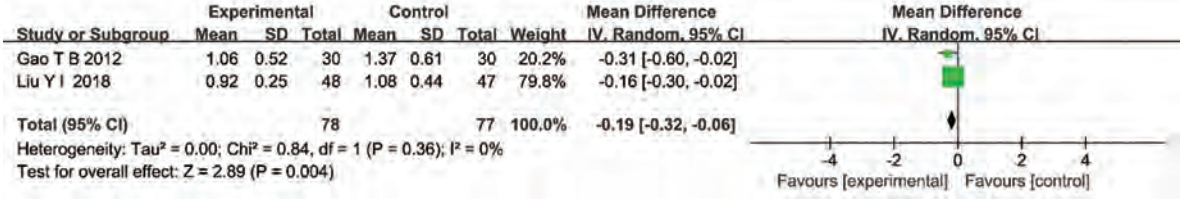

Figure 14 Forest plot of improvement in the poor appetite symptom score (random-effect model)

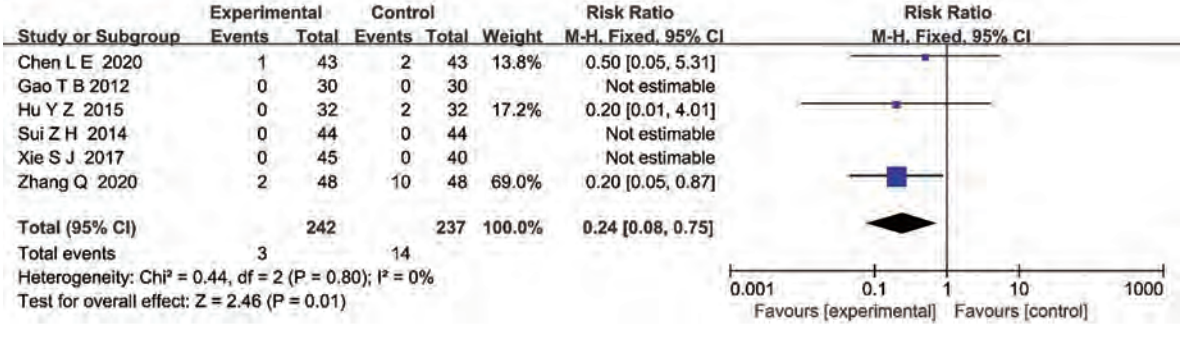

Figure 15 Forest plot of the safety evaluation (fixed-effect model)

groups (P=0.99, I^2=0%) (RR=1.26; 95% CI [1.11, 1.41]; P<0.01). The subgroup analysis revealed that the heterogeneity was not significantly related to the sample size (Fig. 16 B). The possible reason for the heterogeneity is that the study[17] did not clearly describe the diagnostic criteria of CAG and the TCM syndrome types. In terms of the general clinical effective rate, SHT was superior to WM, WM+CPM, and CPM.

3.10 Sensitivity analysis

Eliminating individual studies in a one-by-one manner revealed that most of the combined effect sizes were relatively minor, which indicated that the results of the meta-analysis were relatively stable.

3.11 Dropouts and follow-up

Only two of the 27 included studies mentioned the number of patients who were withdrawn or dropped out during the treatment course.[22,34] Dong[22] reported the withdrawal of one patient in the experimental group and one in the control group due to drug withdrawal, while Huang[34] reported that no patients were withdrawn or dropped out during the treatment course.

Three studies mentioned follow-up. One study[39] reported a follow-up period of 6 months, during which recurrence developed in seven patients (14.89%) in the experimental group and 12 (48%) in the control group. One study[15] reported a follow-up period of 3 months, during which no recurrence developed in the experimental

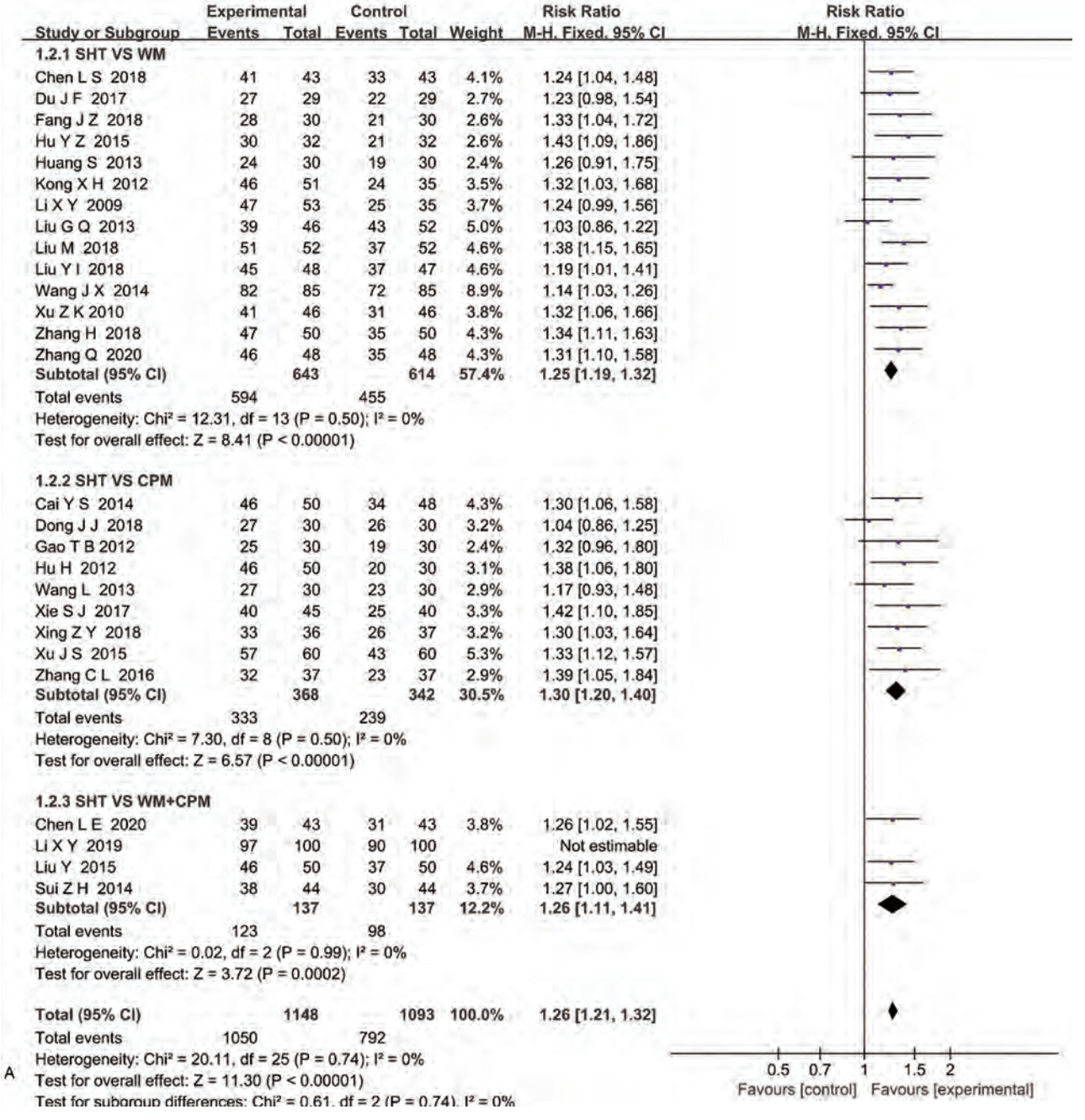

Figure 16 (A) Forest plot of the subgroup analyses (fixed-effect model)

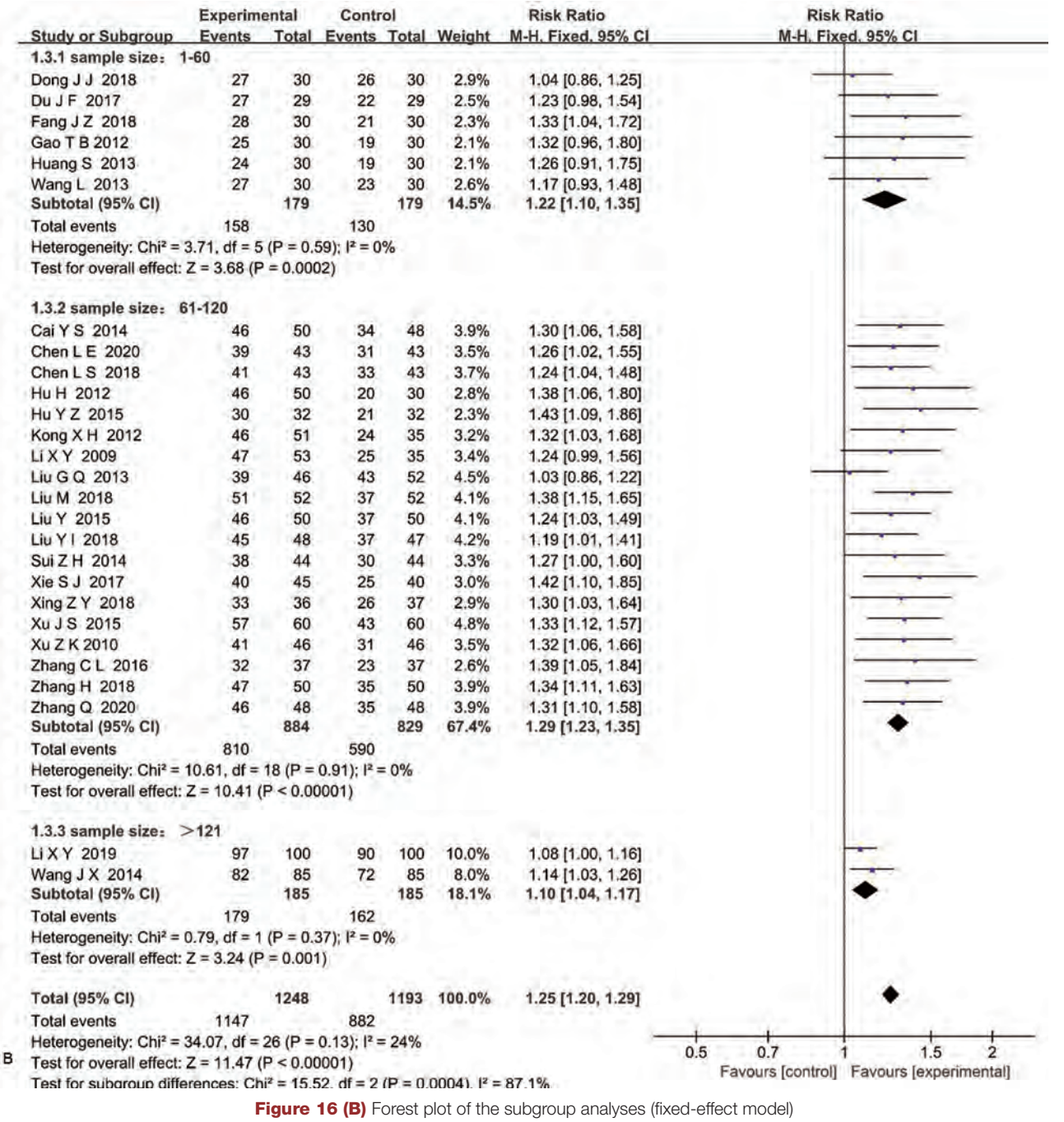

Figure 16 (B) Forest plot of the subgroup analyses (fixed-effect model)

group or the control group. One study[25] reported a follow-up period of 6 months but did not report whether there were any recurrences.

4 Discussion

Studies have showed that 54.5% of patients with CAG not only experience symptoms of physical discomfort such as stomachache, stomach distension, and poor appetite, but also experience symptoms of emotional instability such as anxiety, depression, and irritability.[42–43] In TCM, patients with CAG with stomach symptoms and emotional instability are diagnosed with liver qi invading the stomach, which is one of the most common patterns of CAG. Negative emotions can affect gastrointestinal motility and sensitivity, and eventually affect the brain-gut signaling pathway, leading to the mutual reinforcement of gastrointestinal and affective symptoms.[44–46] In clinical practice, SHT is the preferred treatment for patients with CAG with both stomach discomfort and emotional instability. Many studies have reported the unique advantages of SHT.[47–50]

Our study revealed the following five main findings: 1) The overall clinical effective rate of SHT was superior to that of WM, WM+CPM, and CPM; 2) SHT achieved better improvements in the serum gastrin level, histopathologic changes, HP inhibition rate, and inflammation of GM than the control interventions; 3) SHT

achieved better improvements in the symptoms of stomach distension, stomachache, and emotional instability than the control interventions; 4) The long-term efficacy of SHT was better than that of the control interventions; 5) SHT was safer and had fewer adverse events than the control interventions.

Chai Hu (柴胡 *Radix Bupleuri*), Bai Shao (白芍 *Radix Paeoniae Alba*), Gan Cao (甘草 *Radix et Rhizoma Glycyrrhizae*), Zhi Qiao (枳壳 *Fructus Aurantii*), Xiang Fu (香附 *Rhizoma Cyperi*), and Chen Pi (陈皮 *Pericarpium Citri Reticulatae*) are commonly used for SHT. Most of these herbs are the components of Chaihu Shugan Powder (柴胡疏肝散 CSP). The formula of CSP is recorded in the book of *Jingyue Quanshu*(《景岳全书》*The Complete Works of Zhang Jing-yue*), which was written by Zhang Jiebin (张介宾) during the Ming dynasty. This formula acts by soothing the liver qi to resolve qi stagnation, and moving qi to relieve pain, thus regulating the liver and stomach simultaneously.[51]

CSP protects the GM and exerts antidepressant effects.[52] Many clinical trials and pharmacological studies have indicated that CSP promotes gastric acid secretion and strengthens gastric motility, [53] which is consistent with our results. Our study demonstrated that the serum gastrin secretion was increased after treatment with SHT compared with the control intervention. Serum gastrin promotes gastric acid secretion, thereby promoting gastric emptying. [54] Furthermore, ferulic acid and meranzin hydrate, the components of Chai Hu and Zhi Qiao, significantly strengthen gastrointestinal motility, [55–56] thus improving the symptoms of stomach distension and belching. Among the herbs contained in CSP, Chai Hu, Bai Shao, Zhi Qiao, and Gan Cao all have anti-inflammatory, anti-ulcer, and gastrointestinal tract protective effects.[50, 57, 58] Therefore, CSP is effective in improving the stomach symptoms. CSP exerts anti-depressant effects by affecting the hippocampus and hypothalamus and inhibiting hypothalamic-pituitary-adrenal hyperactivity. [52] Studies have showed that Chai Hu, Xiang Fu, Gan Cao, Bai Shao, and Zhi Qiao all have antidepressant effects.[59–66]

By strictly following the TCM theory of pattern identification, the dosage and/or formula of a certain decoction can be modified in accordance with the individual symptoms of patients with CAG.[67] Hence, SHT has the advantage of flexibility in treating CAG, especially in the treatment of patients with stomach symptoms and emotional instability.

Several limitations of this meta-analysis must be acknowledged. First, the methodological quality of the included studies was not ideal, and caution is required when interpreting the results. Secondly, the courses of disease and treatments were not consistent across the included studies. This might compromise the validity of some results and lead to overestimations of the effects of treatment. Thirdly, all included studies were conducted in China, where SHT is well known, widely researched, and commonly administered. Therefore, the results might be affected by language and reporting biases. Fourthly, only three of the 27 included studies mentioned the follow-up period. As atrophic gastritis is a chronic recurrent disease, more follow-up data are needed to better assess the long-term efficacy of SHT.

5 Conclusions

SHT is one of the effective treatments for CAG. Our results suggest that the overall clinical effective rate of SHT was superior to that of WM+CPM, WM, and CPM. However, due to the limitations of poor methodological quality and the small sample size of the included studies, the overall clinical effective rate and safety of SHT require confirmation in large-scale, multicenter, well-designed RCTs.

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Ethical approval

This study does not contain any studies with human or animal subjects performed by any of the authors.

Author contributions

Guo-Ping Liu and Hai-Xia Yan were responsible for the conception and design of the study. Hua-Ling Song provided methodological advice for the study. Jing-Bin Niu and Xiao Gai were responsible for literature searching, data acquisition, and first draft of the manuscript. De-Cai Yang and Chun-Mei Zhu assisted in research preparation and were involved in data analysis acquisition. Yi-Xin Zheng and Yang Cao assessed the quality of the included studies. Peng Qian analyzed and interpreted the data. All authors read and approved the final manuscript.

Conflicts of interest

The authors declare no financial or other conflicts of interest.

Supplementary Information

Supplementary data to this article can be found online at: http://links.lww.com/CMC/A1.

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Review

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Systematic Review and Meta-Analysis on the Effect of Transdermal Preparations of *Sinomenium Acutum* on Rheumatoid Arthritis

Si-Si Du[1], Qin-Hui Fu[1]✉, Jian Pei[1], Hua Zhou[2]

Abstract

Objective: We evaluated the efficacy and safety of transdermal preparations of *Sinomenium acutum* (SA) for rheumatoid arthritis (RA).

Methods: Randomized controlled trials (RCTs) of SA transdermal preparations for RA were extracted from relevant databases and screened in accordance with the inclusion criteria. The Cochrane System Evaluation Manual (version 5.1.0) was used to assess the quality of the included trials. We used the Cochrane Review Manager (version 5.4) to conduct the meta-analysis.

Results: Six trials comprising 436 patients (220 patients in the treatment group and 216 patients in the control group) were analyzed. The meta-analysis indicated that SA transdermal preparations in combination with disease-modifying antirheumatic drugs (DMARDs) enhanced the overall effect (odds ratio [OR] 3.97, 95% confidence interval [CI] [2.25, 7.00], $P<0.00001$), decreased visual analogue scale (VAS) results (mean difference [MD] −0.64, 95% CI [−1.20, −0.09], $P=0.02$), decreased laboratory indexes including the erythrocyte sedimentation rate (ESR) (MD −4.36, 95% CI [−5.63, −3.08], $P<0.00001$) and C-reactive protein (CRP) (MD −3.6, 95% CI [−3.99, −3.21, $P<0.00001$]), and decreased the Disease Activity Score-28 (DAS28) (MD −0.41, 95% CI [−0.78, −0.03], $P=0.03$). The results suggest that combination therapy did not shorten the duration of morning stiffness (DMS; standardized MD [SMD] −6.13, 95% CI [−17.33, 5.06], $P=0.28$) or reduce rheumatoid factor (RF) laboratory indexes (SMD −0.85; 95% CI [−2.19, 0.49], $P=0.21$). Only one study reported adverse reactions, and thus, it was difficult to determine whether adverse drug reactions in the combination therapy group were significantly different from those in the control group.

Conclusion: We found that SA transdermal preparations combined with DMARDs may have greater clinical efficacy than DMARDs for RA. More well-designed and high-quality RCTs are required to verify the findings and determine whether transdermal preparations cause fewer adverse events.

Keywords: *Sinomenium acutum*; Sinomenine; Transdermal drug delivery system (TDDS); Rheumatoid arthritis; Systematic review

1 Introduction

Rheumatoid arthritis (RA) is an autoimmune disease that usually presents in clinical settings as symmetrical polyarthritis. It is characterized by chronic inflammatory synovitis resulting in progressive joint destruction. Currently, RA affects approximately 1.0% of the population worldwide, with a prevalence rate of 0.32%–0.34% in China. Within China, RA is a main cause of disability and labor force loss.[1] Although RA may develop at any age, women aged between 45 and 55 are most commonly affected, and the prevalence increases with age. RA affects more women than men by a ratio of approximately 3:1.[2]

Current RA treatments aim to reduce the severity of symptoms including joint pain, swelling, and stiffness; prevent or slow joint damage; reduce disability; and improve patients' ability for self-care.[3] Clinically, RA treatment drugs are divided into the following four categories: disease-modifying anti-rheumatic drugs (DMARDs), nonsteroidal anti-inflammatory drugs (NSAIDs), biologics, and corticosteroids. Although these drugs have strong anti-inflammatory and immunosuppressive effects, their drawbacks include considerable side effects, high cost, and a limited ability to reverse bone destruction.[4]

The stem of *Sinomenium acutum* (SA) is known as Qing Feng Teng (青风藤 *Caulis Sinomenii*) (Fig. 1). It enters the liver and spleen meridians and acts to dispel wind, unblock vessels, warm meridians and thus relieve

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Figure 1 Qing Feng Teng (青风藤 *Caulis Sinomenii*). (A) *Sinomenium acutum* (Thunb.) Rehd. et Wils. var. *cinereum* Rehd. et Wils; (B) *Sinomenium acutum* (Thunb.) Rehd. et Wils; (C) *Caulis Sinomenii*; (D) *Caulis Sinomenii*.

pain. A published study[5] indicated that SA was mainly used to alleviate pain, swelling, stiffness, and joint deformity. The use of SA was first recorded in *Bencao Tujing* (《本草图经》*Illustrated Classic of Materia Medica*) (Fig. 2). According to *Bencao Gangmu* (《本草纲目》*The Grand Compendium of Materia Medica*), SA acts to remove wind and alleviate Bi-impediment caused by wind and dampness, joint swelling, knee joint pain, numbness, and itching. It is often soaked in medicinal wine prior to treatment.[6]

Sinomenine (SIN) is an alkaloid isolated from SA. It has significant pharmacological effects and possesses analgesic, anti-inflammatory, immunosuppressant, antihypertensive, and anti-arrhythmic activity. It can also shorten the course of disease and improve the prognosis of RA.[7]

SA is receiving more attention from researchers within China and abroad. In China, SIN preparations such as Zhengqing Fengtongning (ZQFTN) tablets and injection, hydrochloride tablets and injection, total alkaloid tablets, and sustained-release agents have been widely used in clinical settings. A meta-analysis[8] of 16 clinical trials involving 1,500 RA patients showed that SIN demonstrated better performance and fewer side effects in treating RA compared with methotrexate (MTX), especially when used in combination with MTX. Another meta-analysis[9] of 956 RA patients across 11 clinical studies also indicated that ZQFTN combined with MTX demonstrated greater efficacy in treating RA than MTX alone and that it might have an advantage over MTX in terms of adverse drug reactions.

SIN has low oral bioavailability and a short half-life, and thus it generally requires long-term and frequent clinical treatment at high doses.[10] *In vivo*, SIN can promote histamine release and cause skin rashes, gastrointestinal issues, and other adverse clinical reactions. SIN can be unstable, and it decomposes at a faster rate when exposed to light and heat.[11] There has recently been an increasing interest in developing a transdermal system involving SIN that can overcome these disadvantages. SIN can bypass the liver's first-pass effect, avoid destruction by the gastrointestinal tract, and maintain a stable and lasting blood concentration.[12] This study investigated clinical randomized controlled trials (RCTs) involving SA transdermal preparations combined with disease-modifying antirheumatic drugs (DMARDs) to treat RA and provided an evidence-based foundation for future use.

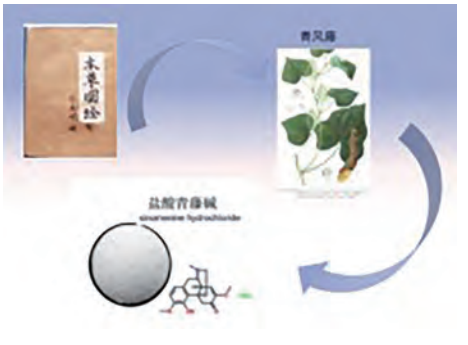

Figure 2 Discovery of sinomenine hydrochloride and its historical records

2 Methods

We conducted the meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA)[13] guidelines. The protocol was registered with INPLASY (No. INPLASY202160085).

2.1 Search strategy

The databases searched within this study were China National Knowledge Infrastructure (CNKI), Web of Science, Wanfang Data, SinoMed, VIP, Embase, EBSCO CINAHL, PubMed, and the Cochrane Library. We searched the databases from the date of inception to December 2020 without language restrictions. Search terms such as "Qingfengteng" or "ZhengqingFengtongning" or "Sinomenine" or "Sinomenine acutum" and "Rheumatoid arthritis" or "RA" were used.

2.2 Inclusion criteria

The inclusion criteria were as follows: (1) the included participants met the diagnostic criteria for RA;[14-15] (2) the participants received transdermal SIN or an external SA preparation combined with DMARDs versus DMARDs only; (3) outcome indicators included the total efficacy rate, visual analogue scale (VAS), duration of morning stiffness (DMS), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), Disease Activity Score-28 (DAS28), and safety evaluation; and (4) a randomized controlled trial (RCT) design was used.

2.3 Exclusion criteria

The exclusion criteria were as follows: (1) duplicate studies; (2) unrelated outcome indicators; and (3) conference materials.

2.4 Data extraction

Two reviewers independently screened the articles and extracted the data. Differences of opinions were discussed and resolved. If necessary, a third reviewer resolved differences of the two opinions. During screening, duplicate studies were excluded first, and then the titles and abstracts were read for preliminary screening to exclude irrelevant articles. The remaining articles were read and screened again to determine studies to be included. The following data were extracted: (1) basic information from the included studies, including author and publication date; (2) basic features of the included studies, including the sample size in each group; (3) intervention measures; (4) outcome indicators; and (5) adverse reactions.

2.5 Quality assessment

Quality assessment of the included trials was conducted using the Cochrane Handbook for Systematic Reviews of Interventions (version 5.1.0).[15] Attention was paid to the following details: (1) random allocation method; (2) allocation concealment; (3) method of blinding; (4) data integrity; (5) selective presentation of research outcomes; and (6) bias from other sources. Each item was evaluated as "low" (low risk of bias), "high" (high risk of bias), or "unclear" (moderate or unknown risk of bias).[16]

2.6 Statistical analysis

We used Review Manager (RevMan) software, version 5.4.1 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2020) to perform data analysis.

Binary variables are expressed as odds ratio (OR) and 95% confidence interval (CI). A value <0.05 was considered to suggest statistical heterogeneity. We selected the mean difference (MD) or standardized mean difference (SMD) as the combined statistic when encountering continuous variables, and each effect quantity is expressed with 95% CI. A fixed or random-effects model was applied depending on the heterogeneity, which was determined using the I^2 statistic. I^2>50% was considered to indicate significant heterogeneity.

3 Results

3.1 Literature search

The preliminary database search identified 750 related articles that were screened. Among them, 493 duplicate articles were excluded, 209 articles were excluded after reading the title and abstract, and six RCTs[17-22] were included after reading the whole article. The specific screening details are presented in figure 3. The characteristics of the included RCTs are summarized in Table 1. Among the included articles, there were 436 participants (220 in the treatment group and 216 in the control group). Four experimental groups were administered ZQFTN transdermally, and two experimental groups were administered SA *via* an external preparation. Two control groups received diclofenac sodium (DS) + MTX + Paeoniae Radix Alba (TGP), one control group received loxoprofen sodium (LOX) + leflunomide (LEF) + MTX, one control group received DS + MTX + sulfasalazine (SSZ), one control group received MTX + tripterygium glycoside tablets (TGT), and one control group received MTX + meloxicam (MLX).

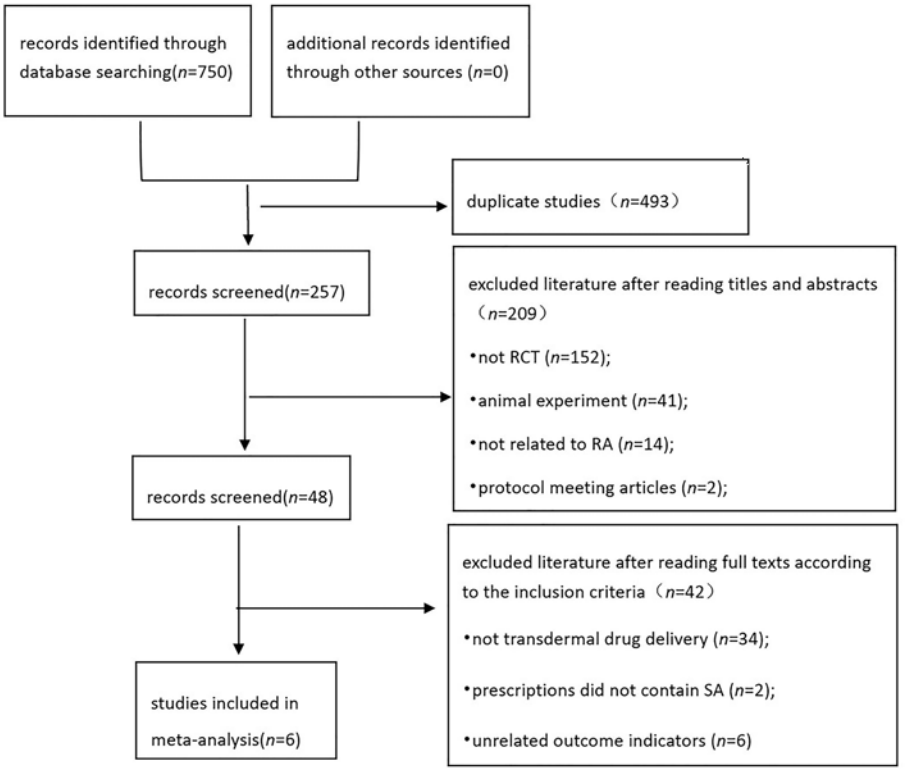

Figure 3 Flowchart of the literature search

Table 1 Randomized controlled trial characteristics

Study	Sample size		Intervention treatment		Total effective rate		Course	Outcome
	TG	CG	TG	CG	TG	CG		
Zhong 2010[17]	36	36	ZQFTN+LOX+LEF+MTX	LOX+LEF+ MTX	94%	72%	10 days	TE,VAS
Zhang 2012[18]	39	39	ZQFTN+DS+MTX+TGP	DS+MTX+TGP	94.9%	79.5%	30 days	DMS,ESR,CRP,RF, DAS28
Huang 2014[19]	40	39	ZQFTN+DS+MTX+SSZ	DS+MTX+SSZ	45%	17.9%	10 days	TE,VAS, DMS,AE
Zhu 2015[20]	44	44	ZQFTN+DS+MTX+TGP	DS+MTX+TGP	90.9%	81.8%	2 months	TE,VAS, DMS, RF ESR
Huang 2018[21]	31	30	Zhongyao Laliao Fang TDD+ MTX+ TGT	MTX+ TGT	90.32%	76.67%	3 months	TE,VAS, DMS,CRP,ESR,DAS28
Shu 2019[22]	30	28	Zhongyao Waifu Fang TDD+ MTX+ MLX	MTX+ MLX	96.7%	75%	4 weeks	TE,VAS, DMS,CRP,ESR,RF, DAS28

The treatment course varied, ranging from 10 days to 3 months.

3.2 Quality assessment

Two studies[20,22] used the random number table method for randomization, resulting in a low risk of bias. One study[17] randomized its order of admission, resulting in a high risk of bias. The remaining three studies mentioned "randomization," but no specific randomization method was introduced within the studies. Two studies[19,22] mentioned that patients were lost to follow-up or dropped out, and incomplete data resulted in a high risk of bias. One study[22] selectively reported its outcome, resulting in a high risk of bias. None of the articles stated whether there were other biases. The quality evaluation showed that the included trials were of relatively low quality (Figs. 4 and 5).

3.3 Total efficacy of the SA transdermal drug delivery system

Six studies[17-22] compared the effects of SA transdermal preparations combined with DMARDs to those of DMARDs only. There was little significant heterogeneity in the studies (P=0.84; I^2=0%). The fixed-effects model was used for our analysis. The overall effect test results

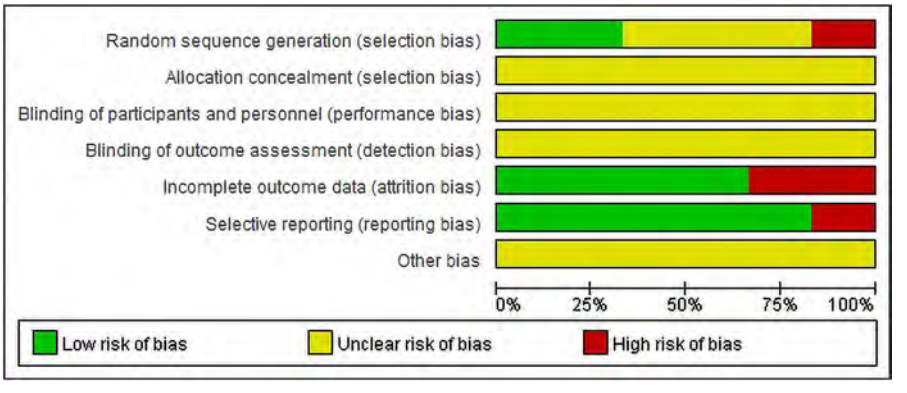

Figure 4 Risk-of-bias graph

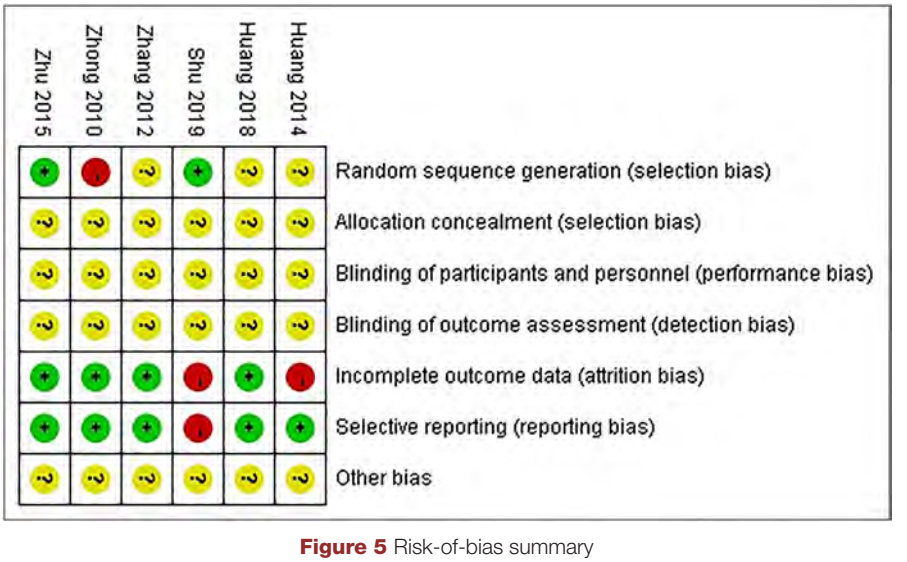

Figure 5 Risk-of-bias summary

suggested that combination SA transdermal drug delivery (TDD) showed a more significant effective rate in treating RA than that of the DMARDs group (OR 3.97, 95% CI [2.25, 7.00]; P<0.00001) (Fig. 6).

3.4 Visual analogue scale

Two studies[17-21] provided VAS data. Heterogeneity tests indicated a small degree of heterogeneity between the included studies (P=0.32, I^2=0%); therefore, data analysis was conducted using the fixed-effects model.

The overall effect test (MD – 0.64, 95% CI [– 1.20, – 0.09], P=0.02) indicated that the experimental group that received the combination SA TDD had a lower VAS score than that of the DMARDs alone group (Fig. 7).

3.5 Duration of morning stiffness

Two studies[18,21] used DMS as an outcome measure. The random effects model was selected for the combined analysis on the basis of the heterogeneity test results (P<0.00001; I^2=99%). There was no statistical significance between SA TDD in combination with DMARDs and DMARDs alone in reducing DMS (SMD= – 6.13; 95% CI [–17.33, 5.06], P=0.28) (Fig. 8).

3.6 Rheumatoid factor

Three studies[18,20,22] provided the serum RF concentration. Because there was high heterogeneity (P<0.00001; I^2=95%), the random-effects model was used to analyze the studies. There was no difference in RF between the SA TDD in combination with DMARDs group and the DMARDs alone group (SMD – 0.85, 95% CI [– 2.19, 0.49], P=0.21) (Fig. 9).

3.7 Erythrocyte sedimentation rate

Four studies[18,20-22] investigated approaches for decreasing the ESR. Due to the presence of heterogeneity (P=0.07;

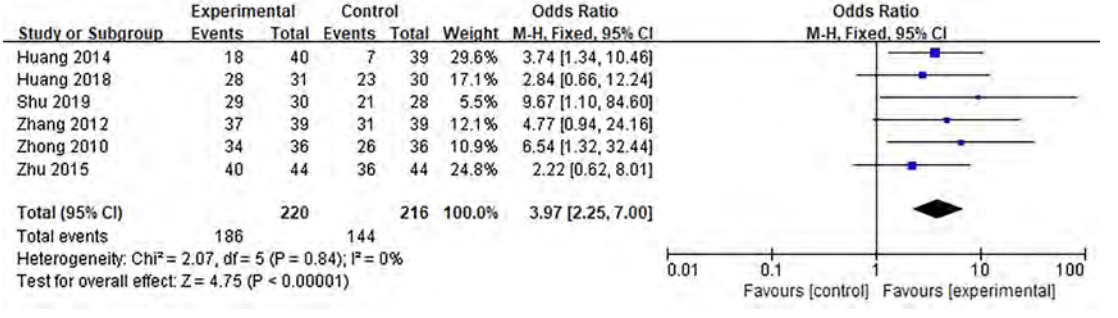

Figure 6 Analysis of the total effect of SA TDD combined with DMARDs group vs. DMARDs group

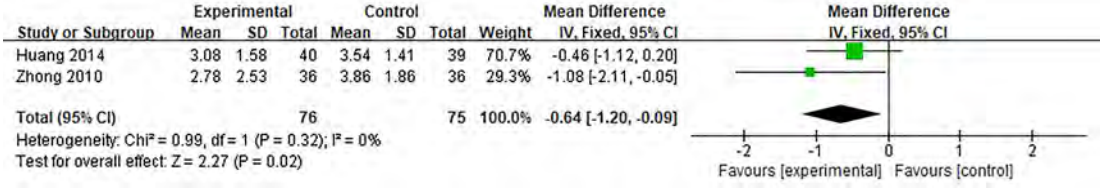

Figure 7 Analysis of VAS results in SA TDD combined with DMARDs group vs. DMARDs group

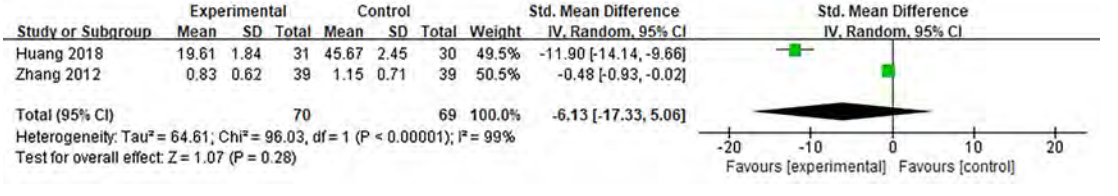

Figure 8 Analysis of the DMS results in SA TDD combined with DMARDs group vs. DMARDs group

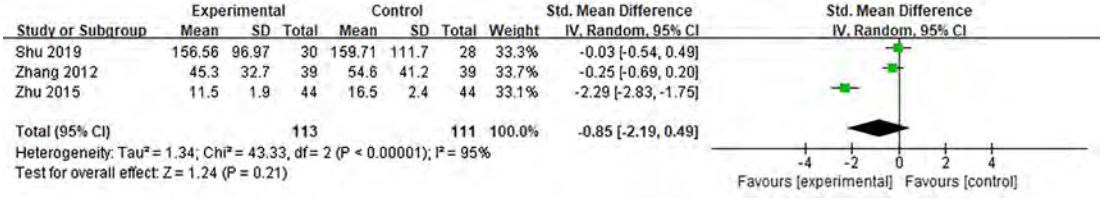

Figure 9 Analysis of RF results in SA TDD combined with DMARDs group vs. DMARDs group

I^2=57%), we chose the random-effects model for data analysis. SA TDD combined with DMARDs group showed greater treatment efficacy in decreasing ESR (MD −4.36, 95% CI [−5.63, −3.08], P<0.00001) compared with that of the DMARDs alone group (Fig. 10).

3.8 C-reactive protein

Three studies[18,21-22] reported an amelioration of CRP levels. Owing to a lack of heterogeneity (P=0.71; I^2= 0%), we performed the analysis using the fixed-effects model. SA TDD in combination with DMARDs demonstrated greater efficacy in improving the CRP concentration (MD, 3.6, 95% CI [–3.99, –3.21], P<0.00001) (Fig. 11).

3.9 Disease activity score-28

Two studies[18,22] included the DAS28. Because these studies showed little heterogeneity based on the heterogeneity test results (P=0.24; I^2=26%), the fixed-effects model was used. SA TDD in combination with DMARDs had lower scores compared with the DMARDs alone group. The results showed clear differences between the two treatments in decreasing the DAS28 scores (MD −0.41, 95% CI [–0.78, –0.03], P=0.03) (Fig. 12).

3.10 Adverse effects

Among the six included studies, one reported adverse reactions.[19] In the treatment group, there was one case of local skin itching and rash, which resolved after stopping the external treatment. Sixteen people (seven from the treatment group and nine from the control group) withdrew from the study during the treatment due to aggravated and intolerable joint pain.

3.11 Publication bias

Publication bias in the six included articles was assessed using a funnel plot. Because the plot was symmetrical, we concluded that there was no publication bias in these studies (Fig. 13).

4 Discussion

RA is a chronic autoimmune condition that can cause inflammation in multiple areas of the body. If not treated in a timely and effective manner, it causes joint deformity and ankylosis. In severe cases, RA results in the loss of joint function and varying degrees of disability, which is detrimental and painful to patients.[23] The World Health Organization has designated RA as a refractory disease.[24] Traditional Chinese medicine (TCM) has a long history of treating RA, including the use of SA.

SIN is a main active component of *Sinomenium acutum*. It exerts powerful anti-inflammatory and analgesic effects through different mechanisms of action. SIN has a moderate analgesic effect due to its structural similarity to morphine,[25] but it does not lead to addiction. A study using a model of chronic sciatic nerve compression in rats showed that SIN could relieve neuropathic pain by regulating glutamate transporter-1 (GLT-1) and glutamate-aspartate transporter (GLAST) mRNA levels.[26] SIN was also found to alleviate formaldehyde-induced

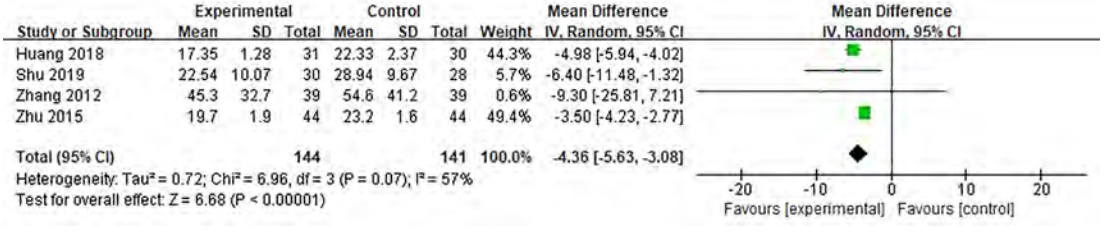

Figure 10 Analysis of ESR in SA TDD combined with DMARDs group vs. DMARDs group

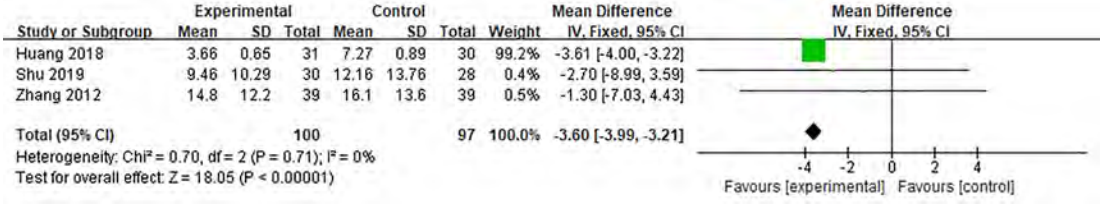

Figure 11 Analysis of CRP in SA TDD combined with DMARDs group vs. DMARDs group

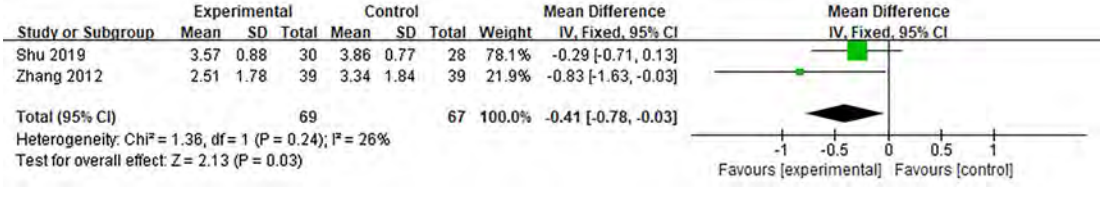

Figure 12 Analysis of DAS28 in SA TDD combined with DMARDs group vs. DMARDs group

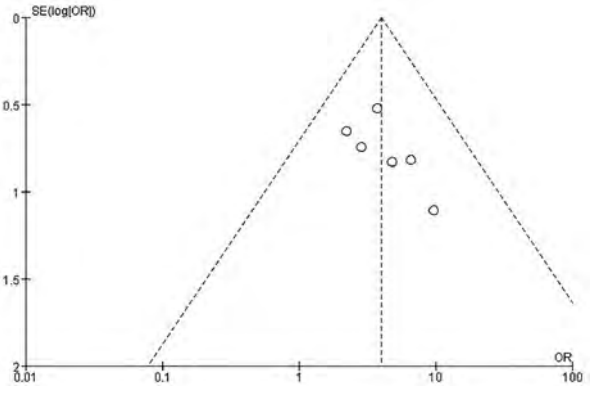

Figure 13 Funnel plot of the overall clinical effect

inflammatory pain in mice and exerted peripheral analgesic effects by reducing neuron excitability.[27]

SIN exerts a powerful anti-inflammatory effect through several mechanisms. SIN selectively inhibits the binding activity of the furthest downstream nuclear factor kappa-B (NF-κB) and DNA to reduce the mRNA expression of inflammatory factors, including tumor necrosis factor-α, interleukin (IL)-1β, and IL-6.[28] SIN also inhibits the production of serum IL-1 and IL-6 by inhibiting metalloproteinase activity. [29] Additionally, SIN is involved in various signaling pathways. For example, SIN plays a role in the Toll-like receptor(TLR) signal transduction pathway, exerting anti-inflammatory effects by inhibiting the core protein MyD88 in this pathway. [30] SIN acts on the CD14/toll-like receptor 4 pathway, the Janus kinase 2 (JAK2)/ signal transducer and activator of transcription 3 (STAT3) pathway, and calcium signaling by inhibiting the key receptor alpha-7 nicotinic acetylcholine receptor (α7nAChR) within the cholinergic anti-inflammatory pathway, thereby inhibiting the inflammatory response of macrophages. [31] SIN affects the extracellular signal-regulated kinases (ERK)/early growth response gene-1(Egr-1) signaling pathway by inhibiting α 7nAChR, thereby inhibiting fibroblast-like synovial cell proliferation.[32-33]

Prostaglandin E2 (PGE2) is a vital inflammatory mediator;, and cyclooxygenase (COX) is considered to be a significant rate-limiting enzyme in PGE2 synthesis. The irritation caused by non-steroidal anti-inflammatory drugs (NSAIDs) is related to COX-2 inhibition, but these medications also inhibit the normal physiological support functions of enzymes. Although gastrointestinal side effects of COX-1 inhibition could be relieved using selective COX-2 inhibitors, research is beginning to focus more on their adverse cardiovascular effects. [34] SIN is a specific microsomal prostaglandin E synthase (mPGES)-1 inhibitor, and it directly targets mPGES-1 without interfering with the balance between prostacyclin and thromboxane, thereby avoiding the cardiovascular side effects induced by COX-2 inhibitors.[35-36]

The advantages of transdermal administration include its ability to bypass the liver, reduced histamine response, and maintenance of a steady-state concentration, which reduces the inter- and intra-patient variability. Topical SA preparations provide potential value for clinical applications.

Application of the TDD system is limited because some hydrophilic macromolecular drugs have a low skin barrier penetration rate, especially the stratum corneum, which leads to a low blood concentration for these drugs. This demonstrates the importance of studying enhancement methods for drug percutaneous absorption. SIN is an ideal drug because the hydrophobic lipid structure between the stratum corneum is the rate-limiting barrier for its penetration. Common methods to promote SIN transdermal absorption mainly include adding transdermal absorption enhancers (such as azone, propylene glycol, menthol, borneol, and oleic acid), improving the SIN intermediate carrier (using carriers such as liposomes, alcohols, liquid crystals, and nanoparticles), and using related physical methods (such as electroporation, microneedles, and ultrasound). Among the penetration enhancers, azone is the most widely used because of its high efficiency, lack of toxicity, and non-irritating properties. [37] Clinically, electroporation is the most common method of promoting permeation. The instant high-voltage pulsed electric field is used to form temporary and reversible hydrophilic pores in the lipid bilayers to increase the permeability of both cell and tissue membranes. [38] Clinical studies have found that electroporation transdermal administration of ZQFTN combined with conventional Western medical treatment significantly reduces joint pain and swelling, improves mobility in RA, and shows significant efficacy in treating knee osteoarthritis, gouty arthritis, and vertebral artery-type cervical spondylosis.[38-41]

Chinese medicine has two distinctive features: a holistic view and treatment based on pattern identification. One of the essential principles is to address the symptoms first in acute conditions and to focus on the root cause in remissive stages. As for the treatment of RA, the following three kinds of sequential administration (or triple-sequential therapy) are suggested: transdermal intra-articular administration, oral administration, and intra-muscular injection. For example, during the active stage, intra-articular administration combined with intramuscular injection or oral administration is a useful treatment. During the remissive stage, oral administration alone or combined with transdermal intra-articular administration is beneficial. Using different administration methods in different RA stages can maximize the treatment efficacy. If taken for an extended period of time, almost all herbs and DMARDs can easily damage e stomach qi and compromise the further treatment. External treatment can reduce the required dose of internal medicine and protect stomach qi.[42] In Chinese medicine, there is an old saying goes that, "If you stomach qi is good, then almost always you have a good chance of recovering from any illness."

5 Conclusions

Previous meta-analyses have indicated that SA preparations, such as ZQFTN, combined with synthetic DMARDs may have a greater benefit and fewer side effects than the synthetic DMARDs alone. However, in almost all of the included studies, ZQFTN was only administered orally. Through this meta-analysis, we can

conclude that SIN transdermal preparations combined with DMARDs demonstrated greater clinical efficacy than DMARDs alone, and they showed similar effects as oral SA preparations. We suggest that SA transdermal preparations do not have a greater efficacy than oral administration to help ameliorate major RA symptoms, which was supported by the laboratory marker results. Side effects were not mentioned in most of the included studies, so it was difficult to determine whether TDD systems reduced SA side effects. Because the included RCTs showed low methodological quality, further RCTs are required to determine whether SA transdermal preparations could replace or be combined with synthetic DMARDs to reduce the DMARDs dose.

Notes

Note 1: Zhong Yao La Liao Formula (中药蜡疗方): Lei Gong Teng (雷公藤 *Radix Tripterygii Wilfordii*), Hong Hua (红花 *Flos Carthami*), Ru Xiang (乳香 *Olibanum*), Mo Yao (没药 *Myrrha*), Chuang Xiong (川芎 *Rhizoma Chuanxiong*), San Leng (三棱 *Rhizoma Sparganii*), E Zhu (莪术 *Rhizoma Curcumae*), Gui Jian Yu (鬼箭羽 *Ramulus Euonymi*), Qing Feng Teng (青风藤 *Caulis Sinomenii*), Chuan Wu (制川乌 *Radix Aconiti Praeparata*), and Tian Nan Xing (天南星 *Rhizoma Arisaematis*). Note 2: Zhong Yao Wai Fu Formula (中药外敷方): Ku Shen (苦参 *Radix Sophorae Flavescentis*), Huang Bai (黄柏 *Cortex Phellodendri Chinensis*), Qing Feng Teng (青风藤 *Caulis Sinomenii*), Bi Xie (萆薢 *Rhizoma Dioscoreae Spongiosae*), Dang Gui (当归 *Radix Angelicae Sinensis*), Chuang Xiong (川芎 *Rhizoma Chuanxiong*), Quan Xie (全蝎 *Scorpio*), Da Xue Teng (大血藤 *Caulis Sargentodoxae*), and Ji Xue Teng (鸡血藤 *Caulis Spatholobi*).

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Ethical approval

This study does not contain any studies with human or animal subjects performed by any of the authors.

Author contributions

Si-Si Du performed the literature search and drafted the manuscript. Hua Zhou conducted the statistical analysis. Jian Pei contributed to article screening and data extraction. Qin-Hui Fu designed the study and revised the manuscript.

Conflicts of interest

The authors declare no financial or other conflicts of interest.

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Review

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OPEN

Progress of Research on *Aṣṭāṅgahṛdaya Saṃhitā*

Li-Ying Zhang[1], Xing-Yi Wang[2,✉]

Abstract

Aṣṭāṅgahṛdaya Saṃhitā (*Compendium of the Essence of the Eight Branches*) is one of the most important works on Ayurvedic medicine from ancient India. It provides a comprehensive overview and synthesis of Ayurvedic theories from different schools of thought. With concise and clear contents, it was an essential textbook for Ayurvedic medicine in India and many other regions at the time it was written. This article summarizes the main contents of the book, reviews the current status of research, and finds that the modern research on *Aṣṭāṅgahṛdaya Saṃhitā* focuses on religious philosophy, the theory of bodily humors, discussion of drug use, and its relationship with Chinese medicine. The book was widely disseminated in the areas surrounding India and influenced Tibetan and Arabic medicine, as well as multiethnic medicine along the Silk Road.

Keywords: *Aṣṭāṅgahṛdaya Saṃhitā* (*Compendium of the Essence of the Eight Branches*); Ayurveda; Tibetan medicine; Silk Road

1 Introduction

Aṣṭāṅgahṛdaya Saṃhitā (*Compendium of the Essence of the Eight Branches*) is one of the most important works of Ayurvedic medicine from ancient India. It is known as one of the *bṛhattrayī* (great trilogy) of Ayurveda, along with *Caraka Saṃhitā* (*Charaka's Compendium*) and *Suśruta Saṃhitā* (*Suśruta's Compendium*). *Caraka Saṃhitā* represents knowledge from the school of *Ātrēya*, the god of internal medicine (*Kāyacikitsā*),[1] while the contents of *Suśruta Saṃhitā* originate from the school of *Dhañvañtari*, the god of surgery (*Śalya*),[2] so the medical understanding of the two is quite different. *Aṣṭāṅgahṛdaya Saṃhitā*, however, integrates the theories of these different schools of medicine and draws on the essence of *Caraka Saṃhitā*, *Suśruta Saṃhitā*, and *Bhela Saṃhitā* (*Bhela's Compendium*).[3] The full text, which has a total of 7,120[4] verses, is cohesively written and organized in a systematic and easy-to-remember manner that served the learning needs of Ayurvedic researchers and physicians very well. After the book was published, it became particularly popular in southern India, where its readership surpassed even that of the *Caraka Saṃhitā* and *Suśruta Saṃhitā*.[5] The southern Dravidians subsequently wrote several medicinal books based on the contents of *Aṣṭāṅgahṛdaya Saṃhitā*.[6] People in the southern state of Kerala, which, with its rich medicinal resources and long-established medicinal culture, was an important place for Ayurveda, also adopted *Aṣṭāṅgahṛdaya Saṃhitā* as their guide to practice.[7] As a work from the mature period of Ayurvedic medicine in ancient India,[8] *Aṣṭāṅgahṛdaya Saṃhitā* is of great significance to the subsequent development and dissemination of Ayurveda.

2 Authorship and date of *Aṣṭāṅgahṛdaya Saṃhitā*

In recent years, many Indian and European scholars have attempted to identify the author of this book, but so far, there have been no conclusive findings.[4] Some scholars believed that Vāgbhaṭa was the author of both *Aṣṭāṅgahṛdaya Saṃhitā* and *Aṣṭāṅgasaṃgraha* (*Compendium of the Eight Branches*). One piece of evidence that best supports this point of view is that a large number of texts in *Aṣṭāṅgasaṃgraha* are quoted without modification in *Aṣṭāṅgahṛdaya Saṃhitā*, and the two works have many similarities in terms of chapter arrangement, medical thoughts, and practical points of view.[4] However, the vast majority of scholars argued that the two works were not written by the same author, despite the authors of both books are called Vāgbhaṭa. Because of the citation relationship mentioned above, *Aṣṭāṅgasaṃgraha* may have preceded *Aṣṭāṅgahṛdaya Saṃhitā*, so their respective authors are referred to as "Vāgbhaṭa I" and "Vāgbhaṭa II"[9] or "Vṛddha-Vāgbhaṭa" and "Vāgbhaṭa"[10] to indicate their differences. However, the popularity of *Aṣṭāṅgahṛdaya Saṃhitā* in the areas surrounding India was much higher than that of *Aṣṭāṅgasaṃgraha*,[4] so some scholars have proposed that *Aṣṭāṅgahṛdaya Saṃhitā* may have appeared first.[11] In 1941, Hilgenberg and Kirfel translated the full text of *Aṣṭāṅgahṛdaya Saṃhitā* into German. In their preface, they argued that *Aṣṭāṅgahṛdaya Saṃhitā*

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must have predated *Aṣṭāṅgasaṃgraha* and suggested that the transformation from the former to the latter was a relatively slow process.[12] Drawing on some newly discovered manuscripts, Dominik Wujastyk created a family tree for Vāgbhaṭa and concluded that he was a descendant of Ravigupta, the author of *Siddhasāra* (*Essence of the medical theories*).[13]

The religious beliefs of Vāgbhaṭa are also a topic of considerable academic controversy. There is still no clear conclusion as to whether he was a Brahmanist, a Buddhist, or a combination of both.[14] There are also different opinions about the specific time for the writing of *Aṣṭāṅgahṛdaya Saṃhitā*, ranging from the 2nd century BC to the 13th century AD. Meulenbeld[14] argued that a more reliable timeframe would be after Dṛḍhabala's revision of *Caraka Saṃhitā*, i.e., the 4th century,[15] and before the publication of *Mādhavanidāna* (*Mādhava*'s *Pathology*) in the 7th or 8th century.[11] The reason for this judgment is that much of the content of *Aṣṭāṅgahṛdaya Saṃhitā* is quoted from Dṛḍhabala's revision of *Caraka Saṃhitā*, and much of the content of *Mādhavanidāna* is quoted from *Aṣṭāṅgahṛdaya Saṃhitā*. Although the issues of the authorship and date of the book are still unresolved, this does not affect its important position in the history of Ayurvedic medicine in India.

3 Main contents of *Aṣṭāṅgahṛdaya Saṃhitā*

Aṣṭāṅgahṛdaya Saṃhitā is divided into six sections: the introduction (*sūtra sthāna*), body (*śārīra sthāna*), pathology (*nidāna sthāna*), treatment (*cikitsita sthāna*), medicinal and purification therapy (*kalpasiddhi sthāna*), and the supplement (*uttara sthāna*). The first five sections of the book are concerned with internal medicine, which is one of the eight branches of Ayurveda, while the last section deals with the remaining seven branches, namely pediatrics, demonology, head and neck diseases (including diseases of the ears, throat, nose, and eyes), surgery, toxicology and detoxification, rejuvenation, and virility.

The introductory section is considered to be the most comprehensive exposition of medical theory in any ancient Ayurvedic medical text, surpassing even the relevant parts of *Caraka Saṃhitā* and *Suśruta Saṃhitā*.[16] It has 30 chapters, with a highly systematic organization. It emphasizes the concepts of disease prevention and health maintenance, the basic theories of Ayurveda, the classification of the bodily humors and the treatment of their corresponding diseases, various methods of drug delivery, such as purification therapy, the use of surgical and medical devices, etc.[17] The first chapter "*Āyuṣkāmīya* (Desire for Long Life)" is considered to be the essence of the introductory section.[18-19] This chapter deals in turn with the eight branches of Ayurveda, the theory of humors, food digestion, bodily constitution, bodily tissues, excreta, diagnostics, etiology, disease precursors, symptomatology, climatic and geographical types, treatment methods, and treatment of mental illnesses. At the end of this chapter, the author lists the titles of all 120 chapters of the book.

The "body" section contains 6 chapters on embryology, the process of pregnancy and childbirth, bodily structure and vital areas, signs of poor prognosis, and signs of death. Among the "great trilogy of Ayurveda," only *Aṣṭāṅgahṛdaya Saṃhitā* places the "body" section before "pathology." This arrangement is considered an improvement[14] in that general knowledge is covered before the description of specific diseases, which makes the sections more coherent. The third section of "pathology" contains 16 chapters describing the classification, causes, and clinical manifestations of twenty-four types of diseases, including fever, cough, respiratory distress, and tuberculosis. A striking feature of the arrangement of this section of *Aṣṭāṅgahṛdaya Saṃhitā* is the more detailed classification of internal diseases, many of which are not mentioned in the "pathology" section of *Caraka Saṃhitā* and *Suśruta Saṃhitā*. The section on "treatment" contains 22 chapters on the treatment of the diseases mentioned in the previous section, including prescriptions, theories on the use of medicines, methods of administration, and daily diet. The "medicinal and purification therapy" section, which has 6 chapters, covers purification therapies (including emetics, purgation, and enemas) and the preparation of remedies, principles of pharmacology, etc. The final section, "the supplement," contains 40 chapters, including 2 on the treatment of pediatric diseases, 5 on the treatment of evil spirits and psychological diseases, 17 on the treatment of head and neck diseases (including 9 on eye diseases, 2 on ear diseases, 2 on nose diseases, 2 on mouth, teeth, and throat diseases, and 2 on head diseases), 10 on surgery-related diseases, 4 on detoxification methods, and 1 on methods for rejuvenation and virility, respectively.

Although *Aṣṭāṅgahṛdaya Saṃhitā* is a synthesis of *Caraka Saṃhitā* and *Suśruta Saṃhitā*, the book is not entirely organized in accordance with either of them. Its orderly arrangement of topics and clear descriptions of medical ideas and clinical practice greatly condenses the contents of previously written medical books. However, the clarity of the text is not without flaws. Dominic Wujastyk noted that although the book is well written, it lacks the plurality and complexity of previous medical texts and he surmized that the reader might miss out on a sense of what had been involved historically in identifying and summarizing the core theories from these complex treatises.[20]

4 Dissemination of *Aṣṭāṅgahṛdaya Saṃhitā*

Vāgbhaṭa and his *Aṣṭāṅgahṛdaya Saṃhitā* were known far and wide at the time of the book's writing. The well-known Chinese pilgrim I-Tsing, who spent 671 A.D. to 695 A.D.[21] in India, wrote *Nanhai Jigui Neifa Zhuan* (《南海寄归内法传》*A Record of Buddhist Practices Sent Home From the Southern Sea*), based on his experiences in India and Southeast Asia. In Volume 3 of this book, I-Tsing introduced the eight branches of ancient Indian medicine and noted that "These eight arts formerly existed in eight books, but lately a man epitomized them and made them into one bundle. All physicians in the five parts of India practice according to this book, and any physician who is well versed in it never fail to live by the official pay."[22] The name of the author was not mentioned here, but many scholars believed that the person to whom I-Tsing was referring was Vāgbhaṭa.[10] To a certain extent, I-Tsing's record reflected the influence of both Vāgbhaṭa and *Aṣṭāṅgahṛdaya Saṃhitā*. In fact, *Aṣṭāṅgahṛdaya*

Saṃhitā did spread to many regions outside India.

More importantly, *Aṣṭāṅgahṛdaya Saṃhitā* had an influence on Tibetan medicine. Indian medicine's period of the greatest influence on Tibetan medicine began around 600 AD when Imperial Tibet invited many famous Indian doctors to Tibet for exchanges and sent many scholars to India to study.[23] This continuous exchange not only led to the incorporation of Indian medical ideas into Imperial Tibet but also led to the creation of a group of Tibetan translators who were well versed in Indian medical culture and translated many Indian medical texts into Tibetan, including *Aṣṭāṅgahṛdaya Saṃhitā*. Some scholars believe that abridged translations of *Aṣṭāṅgahṛdaya Saṃhitā* were circulating in Tibet before the 10th century or during the reign of Imperial Tibet.[24] Around the first half of the 11th century,[25] the famous Tibetan translator Rin-chen-bzan-po and the Indian pundit Jārandhara jointly translated the full text of *Aṣṭāṅgahṛdaya Saṃhitā* into Tibetan.[10] This Tibetan version of *Aṣṭāṅgahṛdaya Saṃhitā* continued to exert great influence until the 13th century, when *rGyud-bZhi* (*Four Tantras of Tibetan Medicine*) gained a central position in Tibetan medicine.[26] Some scholars compared the Tibetan version of *Aṣṭāṅgahṛdaya Saṃhitā* with *rGyud-bZhi* and found that many of the verses in the two works were identical. And in some cases, there were only slight differences in the number of syllables.[27] Other scholars pointed out that in terms of both content and organization, *Aṣṭāṅgahṛdaya Saṃhitā* was the closest among the "great trilogy of Ayurveda" to *rGyud-bZhi*.[28] These findings undoubtedly indicate that *Aṣṭāṅgahṛdaya Saṃhitā* is one of the most important sources for the enrichment of Tibetan medicine. Around the same time that the entire text of *Aṣṭāṅgahṛdaya Saṃhitā* was translated into Tibetan, Rin-chen-bzan-po also translated the Kashmiri scholar Candranandana's commentary on the book, *Padārthacandrikā* (*Word Meaning and Elucidation*), into Tibetan.[14] *Aṣṭāṅgahṛdaya Saṃhitā* was later included in the Tanjur Division of the *Great Chinese Tripitaka*. After the 13th century, the Tibetan text of *Aṣṭāṅgahṛdaya Saṃhitā* was translated into Mongolian, and during the period of the Phagmodrupa dynasty (1354–1617), the Tibetan version was transmitted to China.[26]

Aṣṭāṅgahṛdaya Saṃhitā was also translated into Arabic. The family of Barmakid, who came from Bactria and had a long Buddhist tradition, ran a hospital in Baghdad. During the reign of Harun Rashid of the Abbasid dynasty (786–809), Yaḥyā al-Barmakī, a descendant of the Barmakid family and an important official of the dynasty, became particularly interested in Indian medicine, so he hired two Indian doctors to work in his hospital in Baghdad and invited them to translate three medical works from Sanskrit.[29] One of them, an Indian physician named Ibn Dahn, translated *Aṣṭāṅgahṛdaya Saṃhitā* into Arabic around 800 AD.[30] Later, around 850 AD, *Aṣṭāṅgahṛdaya Saṃhitā* was quoted in the medical work *Firdaws al-Ḥikma* (*Paradise of Wisdom*) by the court physician Alī ibn Rabban al-Ṭabarī.[31] Around the 10th century, the famous "Arabian Galen" Al-Razi also quoted eight passages from the Arabic version of *Aṣṭāṅgahṛdaya Saṃhitā* in his classic work *al- Ḥāwī* (*Comprehensive Book on Medicine*).[30]

The medical documents unearthed in the Turfan region are an important embodiment of the exchange between Chinese and foreign medicine, and to some extent reflect the spread of Indian medicine along the Silk Road. A number of manuscripts of *Aṣṭāṅgahṛdaya Saṃhitā* were unearthed in the Turfan region. Twelve of these, written in Uyghur alone, were found in Sängim [U 6871 b, U 6871 c, U 6871 a, Mainz 209, U 6866 (Fig. 1), Mainz 187, U 6883, U 6851, U 6905 d, U 6821(Fig. 2), U 6879, U 6834], three of which (Mainz 187, U 6883 and U 6851) were joined together into a large and more complete fragment. Maue traced back the original Sanskrit correspondences of these manuscripts.[32] He also completed the transcriptions and translations of the manuscripts and explained some of the differences between the Uyghur editions and their Sanskrit originals.[33] Another two monolingual manuscripts in Sogdian [So 15900 (Fig.3) and So 10789(3)] that originated from *Aṣṭāṅgahṛdaya Saṃhitā* were found: one of which, excavated in Qočo, described the treatment of epilepsy and eye diseases; the other mentioned laxatives, exercise, and fitness.[34] There is also a piece of a bilingual Uyghur – Sanskrit manuscript of *Aṣṭāṅgahṛdaya Saṃhitā* (U 6817) (Fig. 4) with six lines of text written on both sides. Maue transcribed and translated this manuscript and provided annotations on some of the phrases. This manuscript originated from the 29th chapter of the "introduction" part of the book.[32] In addition, three late Indian Sanskrit medical manuscripts were collected by the Japanese Ōtani expedition team, one of which, *Aṣṭāṅgahṛdaya Saṃhitā*, was found in Nepal in the 18th century.[35] It was evident that *Aṣṭāṅgahṛdaya Saṃhitā* had a certain influence on medicine in the multiethnic and multilingual regions along the Silk Road and played an important role in the exchange of medical cultures.

The wide range of influence of *Aṣṭāṅgahṛdaya Saṃhitā* can also be seen in the number of copies of commentaries about it. *Aṣṭāṅgahṛdaya Saṃhitā* has the signal honor of having been the subject of the highest number of commentaries of all the Ayurvedic treatises,[4] of which a total of 33 editions are known (although most have been lost) in Sanskrit, Hindi, Telugu, Malayalam, and Tibetan.[36]

5 Status of the study of *Aṣṭāṅgahṛdaya Saṃhitā*

5.1 Religious and philosophical background of *Aṣṭāṅgahṛdaya Saṃhitā*

Vogel identified a number of Buddhist elements in *Aṣṭāṅgahṛdaya Saṃhitā*.[10] For example, the opening section of the first chapter "*Āyuṣkāmīya*" reads: "Obeisance be, to that *Apūrva Vaidya* (unique/unparalleled/rare physician) who has destroyed, without any residue (all) the diseases, such as *rāga* (passion/desire), etc., which are constantly associated (innate/inherent) with and spread all over the body, giving rise to *outṣukya* (anxiety), *moha* (delusion), and *arati* (restlessness)." The *Vaidya* here was believed to be the Buddha. Chapter two included this passage: "All (human) activities are meant for the happiness of all the living beings; such happiness is based on *dharma* (righteousness, right moral conduct); therefore every person should adopt (follow) righteousness always;" "…ten sins pertaining to the body, speech, and

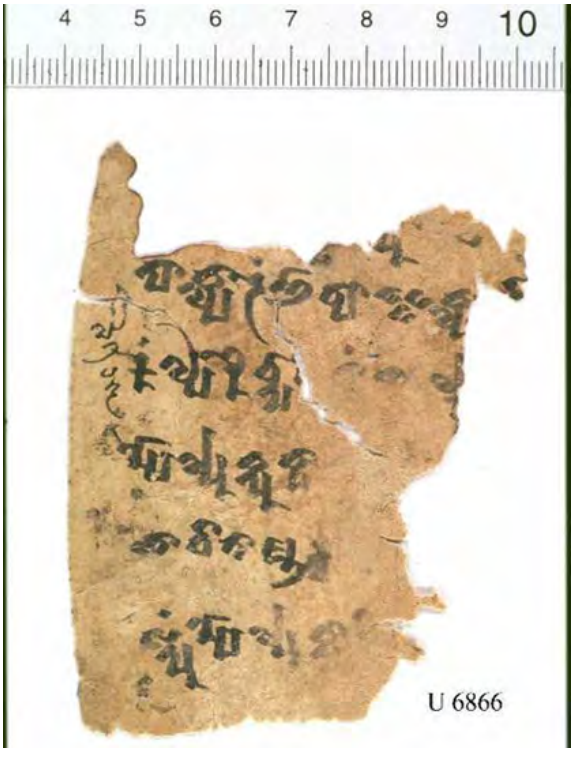

Figure 1 U 6866, recto (from Deposit of the BERLIN-BRANDENBURG ACADEMY OF SCIENCES AND HUMANITIES in the STATE LIBRARY OF BERLIN - Prussian Cultural Heritage Orient Department)

Figure 2 U 6821, recto (from Deposit of the BERLIN-BRANDENBURG ACADEMY OF SCIENCES AND HUMANITIES in the STATE LIBRARY OF BERLIN - Prussian Cultural Heritage Orient Department)

Figure 3 So 15900, recto (from Deposit of the BERLIN-BRANDENBURG ACADEMY OF SCIENCES AND HUMANITIES in the STATE LIBRARY OF BERLIN - Prussian Cultural Heritage Orient Department)

Figure 4 U 6817, recto (from Deposit of the BERLIN-BRANDENBURG ACADEMY OF SCIENCES AND HUMANITIES in the STATE LIBRARY OF BERLIN - Prussian Cultural Heritage Orient Department)

mind should be avoided." He suggested that the Buddhist elements in the book were in part responsible for its high degree of acceptance in Tibet. In addition, Vogel noted that the book also contained elements of Brahminism, such as the "three pursuits of life (justice, wealth, and pleasure)" and "good daily behavior, including avoidance of Buddhist shrines" that appeared in chapter 2.[10] Meulenbeld summarized a number of Buddhist figures who appeared in *Aṣṭāṅgahṛdaya Saṃhitā*.[14] Zysk examined the transformation of ancient Indian medicine from the unorthodox medical approach of the Vedic mantra chanting to an orthodox view of medicine based on etiology and treatment around the three *doṣas* (humors) system and found that this transformation relied on the intervention of Hindu mythology, Brahminical ideology, and corresponding practices in medical works, which gradually made Ayurveda an orthodox sci-

ence.[8] Of the "great trilogy of Ayurveda," *Caraka Saṃhitā* and *Suśruta Saṃhitā* reflected both Vedic concepts and Brahmanical influences, whereas *Aṣṭāṅgahṛdaya Saṃhitā* entered a new phase when the momentum of the Brahminization of Ayurveda no longer existed, so the book, while retaining a Brahminical orthodoxy, also incorporated more boldly and freely the unorthodox elements of Buddhism.[8] Conceicao's research found that *Aṣṭāṅgahṛdaya Saṃhitā* more or less embodied the six philosophical systems of ancient India, i.e., Samkhya, Yoga, Vaisheshika, Nyaya, Mimansa and Vedanta. Therefore, the Ayurvedic knowledge contained in this book is highly comprehensive and systematic.[16]

5.2 Doctrine of the three humors in *Aṣṭāṅgahṛdaya Saṃhitā*

The doctrine of the three humors or *tridoṣa-vidyā* is an important element of Ayurvedic medical theory. It refers to the idea that there are three humors circulating in the human body, which are wind (*vāta*), bile (*pitta*), and phlegm (*kapha* or *śleṣman*). In a healthy state, the three humors are in equilibrium; if one of them is out of balance, the body becomes ill.[19,37-38] *Aṣṭāṅgahṛdaya Saṃhitā* expanded and refined the theory of humors on the basis of its predecessors. Each humor has general characteristics, and *Aṣṭāṅgahṛdaya Saṃhitā*, for the first time, divided each of the humors into five subtypes. These five subtypes depicted a more detailed picture of the characteristics of the body's humors.[39] Scharfe found that the understanding of the doctrine of the three humors in *Aṣṭāṅgahṛdaya Saṃhitā* was more influenced by *Suśruta Saṃhitā*, and the theory of humors was further refined and gradually fixed in *Aṣṭāṅgahṛdaya Saṃhitā*. The first chapter of the introductory section of the book stated that "plasma, blood, muscles, fat, bone, bone marrow, and semen are the seven body tissues (*dhātu*s) and are also known as *dusya*s after they get vitiated by the humors" (Sū. 1.13). The author explicitly identified the concepts of *dhātu*s and *dusya*s, which first appeard in *Aṣṭāṅgahṛdaya Saṃhitā* and *Aṣṭāṅgasaṃgraha*.[40] Other scholars carried out research on the body's constitution based on the doctrine of humors. After comparing the chapter *Vimānasthāna* (the Science of Right Measure or Proportion, 8.95–100) of *Caraka Saṃhitā* and *Aṣṭāṅgahṛdaya Saṃhitā*, Maas[41] found that the ranks of their humoral constitutions were slightly different. The former considered a constitution composed of three humors to be superior to two-humor and single-humor constitutions. A phlegmatic constitution was the best of the single-humor constitutions, a bilious constitution was intermediate, and a windy constitution was of a lower quality. However, the quality of the constitutions resulting from a mixture of two humors was not specified. The latter clearly classified three levels of humoral constitutions: the most desirable was a suitable amount of all three humors, while the worst originated from two humors. Dagmar Wujastyk[42] found that the theory of humors was originally described only in the branch of "internal medicine" in Ayurveda but in *Aṣṭāṅgahṛdaya Saṃhitā*, the author incorporated the theory of humors into the branch of "rejuvenation." By treating imbalances of humors, the aim of maintaining health and prolonging life can be achieved. Although short in length, this incorporation was more evident in subsequent medical books. In comparing the "bodily winds" described in *Caraka Saṃhitā*, *Suśruta Saṃhitā*, *Aṣṭāṅgahṛdaya Saṃhitā*, and *Aṣṭāṅgasaṃgraha*, Zysk[43] suggested that *Aṣṭāṅgahṛdaya Saṃhitā* and *Aṣṭāṅgasaṃgraha* were the most well-developed Ayurvedic treatises on the theory of the five bodily winds (*Prāṇa, Udāna, Vyāna, Samāna, Apāna*). *Aṣṭāṅgahṛdaya Saṃhitā* and *Aṣṭāṅgasaṃgraha* provided more details in describing the causes of the intensification of the five bodily winds and the resulting diseases. At the same time, the two medical texts also concisely related the specific wind to its corresponding mental and sensory activities, which points to certain Yoga–ascetic influences in the formulation of the doctrine of the bodily winds in the late classical period.

5.3 Use of drugs in *Aṣṭāṅgahṛdaya Saṃhitā*

In 1966, Godbole and others sorted out the medicinal plants in *Aṣṭāṅgahṛdaya Saṃhitā* and constructed a list of equivalents in Sanskrit, Bengali, Hindi, Marathi, Tamil, and English.[44] Singh examined the plant alias "*Kumbhika*" in *Aṣṭāṅgahṛdaya Saṃhitā* and found that this represented the first instance of a Sanskrit word being used to refer to the fruit of the water lily, which was not found in other texts.[45] Dominik Wujastyk argued that references to items that intensify the delivery of a drug were relatively rare in early Ayurvedic texts but greatly increased in *Aṣṭāṅgahṛdaya Saṃhitā*.[46] Dighe analyzed the eight types of metal and exotic mineral remedies mentioned in *Aṣṭāṅgahṛdaya Saṃhitā* in terms of treatment, diagnosis, efficacy, the five purification therapies, surgical applications, and medicinal dosage forms.[47]

5.4 *Aṣṭāṅgahṛdaya Saṃhitā* in relation to Chinese medicine

Emmerick compared the chapter on epilepsy in *rGyud-bZhi* with the Tibetan version of *Aṣṭāṅgahṛdaya Saṃhitā*. He found that with respect to epilepsy, *rGyud-bZhi* did not rely much on *Aṣṭāṅgahṛdaya Saṃhitā* and that there were some significant differences. For example, *rGyud-bZhi* grouped the causes of epilepsy into five categories, whereas *Aṣṭāṅgahṛdaya Saṃhitā* divided them into four.[48] Li Qinpu (李勤璞) found that the doctrine of pregnancy based on the lunar cycle in *Aṣṭāṅgahṛdaya Saṃhitā* was one of the sources of the Tibetan medical doctrine of pregnancy that could be traced to rGyud-*bZhi*.[49] In addition, he thought that *Jiva's Idea on Viscera* might have stemmed from *Aṣṭāṅgahṛdaya Saṃhitā* or its mother edition and that the doctrine of pregnancy in *Jiva's Idea on Viscera* might be a citation of *Aṣṭāṅgahṛdaya Saṃhitā* or its mother edition in a Chinese version.[50] By comparing the earliest written record of harelip repair, the Dunhuang Tibetan manuscript S.t.756, with *Aṣṭāṅgahṛdaya Saṃhitā* and *Aṣṭāṅgasaṃgraha* which were the earliest medical books discussing this technique, Liu Yinghua (刘英华) found that the materials and formulas used in Tibetan lip restoration surgery differed significantly from those discussed in Ayurveda, indicating that Tibetan plastic surgery had its own characteristics.[51] In a comparative study of two ancient Tibetan medical texts newly discov-

ered in the last two years, Gongbao Dongzhu (公保东主) found that both *Sgrongsalgdamspa sum cu pa* (*Thirty Teachings of the Medical Beacon*) and *Dri med gzibrjid* (*Immaculate Majesty*), written in the early twelfth century, summarized the essence of Tibetan medicine and incorporated the contents of *Aṣṭāṅgahṛdaya Saṃhitā*, reflecting the fusion of Tibetan and Indian medicine.[52] Deshpande found similarities in some respects between *Bodhisattva Nāgārjuna's Work on Ophthalmology* (the original book was lost but part of the lost text can be found in *Collections of Medical Recipes*) and *Aṣṭāṅgahṛdaya Saṃhitā*, especially in their understanding of cataract surgery, suggesting that the former made a reference to the latter.[53] In the book *Ayurveda: India's Traditional Medicine*, Liao Yuqun (廖育群) suggested that *Aṣṭāṅgahṛdaya Saṃhitā* began to use mercury and other medicinal minerals as orally given medicines, which may have been influenced by traditional Chinese medicine.[54]

6 Conclusions

Aṣṭāṅgahṛdaya Saṃhitā integrates the contents of *Caraka Saṃhitā* and *Suśruta Saṃhitā* in beautiful and concise language, making it a classic work in the history of Ayurveda. This book is an important repository for understanding the essence of Ayurvedic theory. *Aṣṭāṅgahṛdaya Saṃhitā* has been widely disseminated outside India. It has connections with both Tibetan and Arabic medicine. The Uyghur and Sogdian manuscripts of *Aṣṭāṅgahṛdaya Saṃhitā* unearthed in Turfan also serve as proof of the enormous impact of the book and the significant impact of Ayurvedic medicine on multiethnic medicine along the Silk Road. A systematic study of Ayurvedic medical diagnosis and the treatment ideas behind *Aṣṭāṅgahṛdaya Saṃhitā* would help to summarize the characteristics of traditional Indian medicine and the medical characteristics of ethnic groups along the Silk Road and would contribute to the current medical exchanges and coordinated development under the Belt and Road Initiative.

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Ethical approval

This study does not contain any studies with human or animal subjects performed by the authors.

Author contributions

Xing-Yi Wang contributed to the conception of the study; Li-Ying Zhang contributed to the manuscript preparation.

Conflicts of interest

The authors declare no financial or other conflicts of interest.

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Voyage of Ben Cao, Part II: Development of Chinese Medicinal Specimens in the British Museum

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1 Introduction

In 2015, an on-site field investigation was conducted by the authors' research group to authenticate a batch of ancient Chinese medicinal decoction pieces that have been preserved in a rare collection at the Natural History Museum in London.

These treasured artifacts comprise a portion of the Sloane Collection, and the nearly 100 Chinese medicinal specimens examined within provide an objective record of the real situation regarding Chinese medicinal materials in commercial circulation 300 years ago. The precious data from this collection provide an extremely valuable reference for research into the history of medicinal exchange between China and the West during the Age of Exploration, shedding light on the evolution and historical changes in the species used in Chinese medicine as well as the history of medicinal processing and decoction pieces.

2 The Sloane Collection and the British Museum

The British Museum (Fig. 1) was established in 1753. Its collections originate from all of the major continents and range from antiquity to the present; the museum is in a leading international position in terms of the number of its artifacts. The story of the origin of the British Museum begins with Sir Hans Sloane. Sir Hans Sloane (1660–1753) was born in Ireland; he became an outstanding British doctor and served as the physician to the governor of Jamaica. Sir Hans's life was dedicated to scientific research, and he had a deep love for collecting objects, with a particular enthusiasm for plant and animal materials. His botanical specimens represent an embryonic form of the style used for voucher specimens in the modern day. His specimens formed the basis for many descriptions of new species and names adopted by the Swedish botanist Linnaeus, who laid the foundation for the modern system of binomial nomenclature. Sir Hans is credited with patenting the combination of chocolate and milk, which brought him a considerable income. This economic abundance supported his collections and his generous philanthropy.

Figure 1 The British Museum

When Sir Hans Sloane passed away in 1753, his collection contained over 70,000 objects; amazingly, this substantial number does not even include his vast collections of botanical specimens, books, and manuscripts. At the time of his death, he bequeathed his vast collection to the nation. The British government honored his dying wish and built a museum to preserve this precious collection; thus, Sir Hans's collection became the foundation of the British Museum. Today, Sir Hans's contributions are memorialized through the dedication of place names such as "Sloane's Square" in central London. As the collections of the British Museum increased over time, the objects were divided to form the British Library, the Natural History Museum (Figs.2 and 3), and the British Museum.

The Natural History Museum is situated in the South Kensington district of London. The building itself is an architectural masterpiece designed by Alfred Waterhouse, and it was established and opened to the public in 1881. The Natural History Museum stores over seventy million objects, encompassing animals, plants, fossils, and minerals. Upon entry, visitors are greeted by a colos-

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Figure 2 The Natural History Museum

Figure 3 Entrance hall of the Natural History Museum

sal dinosaur skeleton (Fig.4), and on the wall is a display of extinct ancient creatures and fossils. On the hall of the second floor, to the left is a white marble statue of Darwin, while to the right lies the cut surface of a North American redwood tree over 3 m wide; looking at its annual rings reminds us that time brings great changes. From the thousands of years in the history of man to the billions of years in the history of the Earth, visitors are inspired by the evolution of our world. Featuring permanent and temporary exhibits for the popularization of science, it can be visited continuously.

According to the introduction by our guide, the exhibits on display account for only one-tenth of the collection. If the entire collection were to be put on display, one would need to walk for 27 km to see all the exhibits.

At the Darwin Research Center, the color of the plants against a snow-white background radiates the vitality of life. Upon entering the collection room, the temperature, humidity, and security are closely controlled. Many specimens from Sir Hans Sloane and Charles Darwin are stored within. An oil portrait of Sir Hans sits on the wall, with bright eyes and an aura of peace, calmly watching over and accompanying his collection of treasured artifacts (Fig. 5). In the absence of special permission, ordinary visitors are not allowed to see this sacred scientific space. Because many of the specimens in the storehouse have not yet been authenticated, it is not possible to look up the items online; it is even hard to find all the information within the collection itself. Fortunately, the authors had been invited to examine the collection: a historic moment and a special opportunity (Fig. 6).

Figure 4 Dinosaur skeleton hanging from the ceiling

Figure 5 Prof. Zhao with the portrait of Sir Hans Sloane

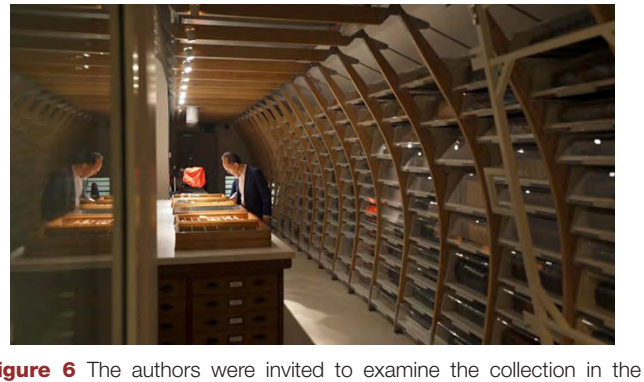

Figure 6 The authors were invited to examine the collection in the closed area

Prior to our visit, the staff at the Natural History Museum had already prepared a number of specimens (Fig. 7). A broad table with four cabinets of specimens was laid out, and within the cabinets, many boxes were stored. Each box featured transparent glass, and the size of each box varied depending on the specimens stored within (Fig. 8). The specimen boxes were identified by four-digit codes, and each box was wrapped in a plastic cover with a bar code. Additional records of the collection were written in eighteenth-century English and occasionally French. The medicinal names featured an archaic style of Pinyin that is no longer in use; for example, Wu Yao (乌药 *Radix Linderae*) was labeled "u jo," Zhi Shi (枳实 *Fructus Aurantii Immaturus*) was labeled "cj xe," and Huo Xiang (藿香 *Herba Agastachis*) was labeled "ho hian." A number of specimens featured labels with English or Latin names, and a number of people had evidently attempted to authenticate the materials in the past. Although some items were identified inaccurately, such as a Ju Hua (菊花 *Flos Chrysanthemi*) specimen that was labeled "camomilla," it is clear that these specimens have consistently attracted the attention of experts in botany and pharmacy.

Figure 7 Sir Hans Sloane's plant collections

Figure 8 Cabinets of specimen boxes

Most of the specimens observed were decoction pieces. The collection contained commonly used Chinese medicines as well as herbs that are locally used in southern regions and a number of foreign medicinals. Based on the varieties observed, it appears likely that many specimens came from a pharmacy in southern China; thus, the collection likely reflects the real clinical situation in a particular region and time. According to the introduction from the caretakers responsible for the collection, these specimens were obtained for Sir Hans Sloane by the East India Company, and the current set represents only a portion of the original collection.

These specimens offer evidence of historical changes in the species used in Chinese medicine. For example, in the case of the herb Mu Tong (木通 *Caulis Akebiae*) (Fig.9), the Chinese *Ben Cao* literature indicates that the species originally used was *Akebia quinata* (Thunb.) Decne. In the 1990s, renal failure was reported in Europe owing to the mistaken use of *Aristolochia manshuriensis* Kom as Mu Tong, and the topic of "Chinese herb nephrotoxicity" continues to arise in discussions of Chinese herbal toxicity.[1] Based on this identification, it is clear that the Mu Tong medicinal material sent to Europe from China during Sloane's era was derived from *Akebia quinata* (Thunb.) Decne. Confusion with *Aristolochia manshuriensis*, known as Guan Mu Tong (关木通 *Caulis Aristolochiae Manshuriensis*), may thus have occurred during the Qing dynasty owing to influence from the northern regions.[2]

Figure 9 Mu Tong (木通 *Caulis Akebiae*)

Opium poppy is very effective for relieving cough and stopping diarrhea. It was clearly recorded as early as the Song dynasty, and the Ming dynasty *Bencao Gangmu* (《本草纲目》*The Grand Compendium of Materia Medica*) notes that it cannot be taken for a prolonged period of time.[3] The extraction of morphine or opium from the poppy did not arise until later, in the period surrounding the Opium Wars. Currently, the poppy capsules on the market all show evidence of cutting by knife, and these cuts have become regarded as a special identifying characteristic in Chinese medicinal authentication textbooks. However, the outer capsule is intact in the specimens observed here, suggesting that the opium capsules of the time were not previously cut to extract opium for use as a drug.

Customary differences between the northern and southern regions of China are reflected in the parts used for medicinal purposes of some plants in the observed specimens.[4] Within this collection, the Chinese names are not standardized, meaning that a number of folk

medicines used in southern regions can also be seen, such as Mu Bie Zi (木鳖子 *Semen Momordicae*), Zi Cao Rong (紫草茸 *Lacciferi Secretio*), and Chu Shi Zi (楮实子 *Fructus Broussonetiae*). Many characters are written in shorthand to save strokes, such as Lai Fu Zi (莱菔子 *Semen Raphani*) and Zhu Ling (猪苓 *Polyporus*) (Fig. 10). Chinese herbal medicines are commercial materials, so the level of cultural sophistication varies among traders.

Figure 10 Zhu Ling (猪苓 *Polyporus*)

Foreign medicines are present in the collection, including Mo Shi Zi (没食子 *Galla Halepensis*), Ru Xiang (乳香 *Olibanum*) (Fig. 11), Ding Xiang (丁香 *Flos Caryophylli*), Ying Su Qiao (罂粟壳 *Pericarpium Papaveris*) (Fig. 12), Bing Lang (槟榔 *Semen Arecae*), and Sha Ren (砂仁 *Fructus Amomi*). This demonstrates that foreign medicines have long entered China and have long become assimilated for use in Chinese medicine.[5] Animal products such as Wu Ling Zhi (五灵脂 *Faeces Trogopterori*) and Lu Bian (鹿鞭 *Cervi Testis et Penis*) can be seen in the collection. One approximately 2.5 cm-sized piece of Lu Bian was surrounded by unidentifiable plant material that had broken down into powder. This suggests that some plant material was originally used to facilitate the storage of animal products, presumably by preventing insect damage.

In the context of minerals, one oval-shaped specimen of Yang Qi Shi (阳起石 *Actinolitum*) was striking. Its texture was smooth and moist, with fiberglass shards that sparkle.

Figure 11 Ru Xiang (乳香 *Olibanum*)

Figure 12 Ying Su Qiao (罂粟壳 *Pericarpium Papaveris*)

Dried nuts such as chestnuts, hazelnuts, walnuts, and pine nuts are often sold through the same commercial channels as Chinese herbal medicines. One walnut specimen had been sliced horizontally with its shell intact, as though it had been made into a specially prepared specimen; this was unique within the collection. A number of items featured marks that were indicative of medicinal processing, such as the smoke-processed Wu Mei (乌梅 *Fructus Mume*) and stir-fried Bi Ma Zi (蓖麻子 *Semen Ricini*). Additional preparation techniques can be observed by the cutting methods used to produce thin slices or strips for the herbs Zhi Shi, Hou Po (厚朴 *Cortex Magnoliae Officinalis*), Gan Cao (甘草 *Radix* et *Rhizoma Glycyrrhizae*), Chen Pi (陈皮 *Pericarpium Citri Reticulatae*), and Bing Lang.

The color of many specimens has changed owing to prolonged storage over the past 300 years. Insect damage and oxidation have caused many specimens to become dark brown. The latex threads seen in Du Zhong (杜仲 *Cortex Eucommiae*) are no longer present. Most specimens no longer had an aroma, with the exception of one specimen of chili pepper that was still spicy and irritating to the nose. The shape of the chili pepper differed from the long, thin chili that is common in China today, but its characteristic seeds could still be clearly seen. Chili entered China during the Ming dynasty, but the precise shape of these early chilies remains unknown. Owing to limitations of time and equipment, a number of species could not be identified at that time. For example, one box labeled Dang Gui (当归 *Radix Angelicae Sinensis*) did not contain any medicinal material. In other cases, the external features of the material were not adequately intact for clear identification, as in the case of Ying Shi (营实 *Fructus Rosae Rugosae*), Qing Guo (青果 *Fructus Canarii*), He Shi (鹤虱 *Fructus Carpesii*), Rou Gui (肉桂 *Cortex Cinnamomi*), Xuan Shen (玄参 *Radix Scrophulariae*), Mao Dong Qing (毛冬青 *Radix Ilex Pubescens*), and Ji Dan Guo (鸡蛋果 *Passiflora edulis* Sims). Additionally, some specimens such as camphor wood from Japan and hemp cloth-like material from Thailand require further verification before they can be identified.

Voucher specimens are the cornerstone of modern scientific research in the discipline of authentication, and they also provide strong evidence helpful in researching the medicinal materials used in ancient times. At present, known collections of Chinese medicinal specimens include

nine medicinal spices that were unearthed at the Mawangdui tombs in Changsha, as well as sixty varieties of Chinese medicines that have been stored in Japan since the Tang dynasty in the Shosoin storehouse. Additional collections include aromatic woods recovered from a Song-dynasty shipwreck site in Quanzhou, Chinese medicinal specimens with a history of more than one thousand years at the Liao Shangjing Museum at Balin Left Banner in Inner Mongolia, and a number of Qing-dynasty medicinal materials that were preserved in the Forbidden City in Beijing. These treasured specimens offer firsthand evidence that cannot be replaced by references in the literature alone.

The specimens in the British Natural History Museum have survived the waves of the sea and the fires of dry land, making them all the more precious for discovery and identification. Upon investigation, it is apparent that the British Museum and the National Library are valuable resources for early botanical illustrations, as well as medical classics from both the East and the West. This area is worthy of deep investigation, discussion, research, and development, and represents a rich resource for the history of natural sciences that must be approached via a multinational, multidisciplinary effort. Our research is just beginning, and we will continue in this direction.

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Ethical approval

This study does not contain any studies with human or animal subjects performed by any of the authors.

Author contributions

Zhong-Zhen Zhao wrote and reviewed the article. Eric Brand translated and revised the article.

Conflicts of interest

The authors declare no financial or other conflicts of interest. Zhong-Zhen Zhao is an editorial board member of Chinese Medicine and Culture. The article was subject to the journal's standard procedures, with peer review handled independently of this editorial board member and his research group.

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News and Views

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"Eastern" Xi Yang Qian (*Rubia tirctorum* L.) and "Western" Zhong Guo Qian (*Rubia cordifolia* L.): Across the Regions

Min Shao✉

Abstract

Qian Cao (*Radix et Rhizoma Rubiae*) is a perennial grass with red and yellow pigments in its roots. It has been used since ancient times for fabric dyeing and painting, and it's the oldest red dye in both Europe and China. Xi Yang Qian (*Rubia tirctorum* L.) spread from the East to the West, while Zhong Guo Qian (*Rubia cordifolia* L.) spread from the West to the East. Both were integral in the development of Chinese and Western color cultures. Nowadays, although it is no longer commonly used in dyes and paints, Qian Cao is still used in clinical medicine as a medicinal herb.

Keywords: Xi Yang Qian (*Rubia tirctorum* L.); Turkey red; Zhong Guo Qian (*Rubia cordifolia* L.); Qian Cao (*Radix et Rhizoma Rubiae*)

1 Introduction

During the development of human society, *Rubia* and *Coffea* are the two most important genera in the *Rubiaceae* family. Since the Arabian physician Razes[1] first wrote about coffee in the 10th century, this dark beverage has spread around the world and has become an indispensable part of people's daily life. The fate of Qian Cao (茜草 *Radix et Rhizoma Rubiae*), however, differed from that of coffee. Qian Cao is one of the most ancient red dyes, but it has been gradually replaced by other natural red dyes such as Yan Zhi Chong (胭脂虫 *Dactylopius confusus*), Hong Hua (红花 *Flos Carthami*), and Su Mu (苏木 *Lignum Sappan*). It has become largely obsolete after the introduction of synthetic and chemical dyes. Although it is still used as a medicinal herb and natural dyestuff, it has lost much of its former glory.

Qian Cao is a perennial herb with red and yellow pigments in its roots, and because of this, it can be used in fabric dyes and paints. After drying, the pigments are preserved in the roots, which is conducive for transportation and storage. Qian Cao is widely distributed around the world and contains diverse species. There are three main species of Qian Cao used in traditional dyeing, that is, Xi Yang Qian (西洋茜 *Rubia tirctorum* L.), Zhong Guo Qian (中国茜 *Rubia cordifolia* L.), and Yin Du Qian (印度茜 *Rubia cordifolia* Linn.) (Fig. 1), all of which produce slightly different shades of red.

Figure 1 Dried root of Yin Du Qian (印度茜 *Rubia cordifolia* Linn.)

Xi Yang Qian is characterized by whorls of six leaves. Its traditional origin is the Mediterranean coast of Eastern Europe, close to Western Asia, where Turkey is the most famous producer. Therefore, the red dye from Xi Yang Qian is known as "Turkey red."[2] Zhong Guo Qian has whorls of four leaves. Li Shizhen (李时珍) once quoted Tao Hongjing's (陶弘景) view in *Bencao Gangmu* (《本草纲目》*The Grand Compendium of Materia Medica*) that "it can be found in many places in the East, but the yield is less than that in the West." Therefore, there are the names "Xi Tian Wang Cao (西天王草)" and "Qian Cao (茜草)."[3] Yin Du Qian is similar in shape to Zhong Guo Qian and also has whorls of four leaves. As early as the Indus Valley Civilization, ancient Indians dyed

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cotton fabrics with Qian Cao and transported them to ancient Mesopotamia as well as ancient Egypt for trade.[4]

The vast area from southeast Europe to southwest China was an important region for the cultivation and use of Qian Cao in ancient times. As a traditional dye-yielding plant, Qian Cao was involved in the development of color cultures of ancient civilizations.

2 Xi Yang Qian: The secret of Turkey red

The main origins of Xi Yang Qian (Fig. 2) are Southern Europe and Western Asia along the Mediterranean coast. People in these regions had been using Qian Cao for making a red dye for a long time; however, the details of the process remained a trade secret in Turkey and Greece. Because of its property of imparting a red color to the bones of animals[5] that fed on the roots, Qian Cao was considered to have mysterious powers. European aristocrats became infatuated with it. For centuries, red pigments and exotic fabrics were continuously imported from Turkey to Europe, and their high cost meant that red was a luxury color in Europe affordable only to nobles.

Figure 2 Xi Yang Qian (西洋茜 *Rubia tirctorum* L.) with whorls of six leaves

Because of its very high value, Xi Yang Qian was introduced and cultivated in the Netherlands on a large scale from the 14th century. By the 17th century, the Netherlands had acquired a monopoly over Xi Yang Qian.[6] Due to the great success in the cultivation of Xi Yang Qian in the Netherlands, imports from Turkey to Western European countries decreased, and this reduced the price of Qian Cao. From then on, red-colored clothes began to be worn by common people, and were no longer a privilege of nobility.

In the 18th century, France joined the trade war over red pigments. In addition to the large-scale cultivation of Xi Yang Qian, skilled dyers from Turkey and Greece were recruited to start a new exploration of the Turkey red dyeing industry. In 1756, the Society of Arts established an award to encourage innovations in red-dyeing technology.[7] Through trades, field visits, experiments, and improvements, France gradually replaced the Netherlands as the new production and trade center of Qian Cao. It retained this core position until the middle of the 19th century. Fabre, a famous French entomologist, studied the extraction of alizarine and finally obtained a patent[8]. This demonstrates the great commercial and economic value of the technology of producing red dyes with Qian Cao in France at that time.

Since the middle and late 19th century, the booming chemical industry has begun to impose an impact on the research of natural pigments. Studies on the topics of pigment analysis and pigment synthesis have made substantial achievements. Edward Schunck published a series of papers called "Notes on madder coloring matters" in the *Journal of the Chemical Society* in 1860, 1877, 1878, 1893, and 1894.[9-13] Under the powerful driving force of scientific research, artificial alizarine was successfully invented. In the short period between 1871 and 1886, the price of artificial alizarine fell from 270 to 9 marks per kilogram.[14] As the main supplier of natural alizarin at that time, French growers of Qian Cao ultimately could not compete with chemically synthesized alizarin. The market for Qian Cao shrank rapidly and almost disappeared.

Today, although the root of Xi Yang Qian (Fig. 3) is only rarely used as a source of red dye, it is still used as a medicinal herb in clinical medicine for the prevention and treatment of kidney disease.[15]

Figure 3 Dried root of Xi Yang Qian

3 Zhong Guo Qian: Medicinal herb and source of Chinese red

Qian Cao, Hong Hua, and Su Mu are the three most important traditional red dyes in China. According to

Bencao Gangmu, Qian Cao, the source of a traditional red dye, is a trailing plant distributed in the central and western regions of China. Hong Hua, referred to as Xi Grass (隰草) in *Bencao Gangmu*, grows in wetlands. It originated in Egypt and India, and was imported from western regions into the central plains along the Silk Road as an important trade commodity. Su Mu is listed as arbor in *Bencao Gangmu*. It was originally distributed between East India and the Malay Peninsula, and spread as an important trade commodity from southern regions to central plains along the Maritime Silk Road. As Chinese herbal medicines, they all have the effect of activating blood and removing blood stasis. As traditional Chinese herbal dyes, the terracotta shade of Qian Cao, the true red color of Hong Hua, and the wood-like red hue of Su Mu were interwoven together to constitute the landscape of traditional Chinese red.

Qian Cao is the oldest red-dye yielding plant in China. Before the introduction and popularization of other natural red-dye yielding plants such as Hong Hua and Su Mu, Qian Cao has been the most important and main source of red dye in China for a very long time. The color from Qian Cao has been recorded in detail in *Kao Gong Ji* (《考工记》 *Record of Handicrafts*) of the Zhou dynasty: "when Qian Cao is first used for dyeing, the color is Quan (縓 orange pink); the second time is Cheng (赬 light red); the third time is Xun (纁 red)."[16] It shows the color change from orange pink to red in the dyeing process with Qian Cao.

Zhong Guo Qian (Figs. 4 and 5) is widely distributed and has various alternative names. According to Zeng Qixiong (曾启雄)'s research, Qian Cao was recorded in more than 30 ancient Chinese classics under 85 different names.[17] The ancient name of Qian Cao is Mao Sou (茅蒐). Crimson leather dyed with Mao Sou is known as Mei Ge (韎韐), a clothing of ancient Chinese warrior mainly used to cover the knees. Mei Ge, as a formal dress of the coming-of-age ceremony for men, was recorded in the literature *Yi Li* (《仪礼》 *Compilation of Etiquette*) from the Zhou dynasty.[18] Women's crimson clothing dyed with Mao Sou, known as Ru Lyu (茹藘), was mentioned twice in *Shi Jing* (《诗经》 *Classic of Poetry*) of the pre-Qin period.[19] The records of Ru Lyu and Mei Ge prove that Qian Cao has been used as a dye since ancient times in China. In the Han dynasty, Xu Shen (许慎) used the character "茜" (Qian) to refer to Mao Sou in *Shuowen Jiezi* (《说文解字》 *Elucidations of Script and Explications of Characters*).[20] In the Wei and Jin dynasties, Wu Pu (吴普) referred to the herb Mao Sou as Qian Gen (茜根) in *Shen Nong Bencao Jing* (《神农本草经》 *Shen Nong's Classic of the Materia Medica*).[21] Since then, Qian Cao has gradually replaced Mao Sou and become the standard name. According to the ancient literature, Qian Cao was first used as a dye and then as a medicinal herb.

4 Color from Qian Cao: The red color obtained by complex mordant dyeing

With the development of traditional Chinese red dyes, Qian Cao was gradually replaced by Hong Hua with its richer color and Su Mu with its simpler dyeing process. The reduced use of Qian Cao for dyeing led to the rapid shrinkage of its cultivation area, and the gradual disappearance of complex dyeing technology. In modern times, a number of reformers and practitioners of traditional dyeing methods have emerged in China, such as Du Yansun (杜燕孙), the author of *Guochan Zhiwu Ranliao Ranse Fa* (《国产植物染料染色法》 *Dyeing Method with Chinese Plants*), and Meng Xinru (孟心如), the author of *Zhiwu Sesu* (《植物色素》 *Plant Pigments*). They followed the lead of Western chemical research, and explored the possibility of industrializing plant pig-

Figure 4 Zhong Guo Qian (中国茜 *Rubia cordifolia* L.) with whorls of four leaves

Figure 5 Fresh root of Zhong Guo Qian produced in Henan Province of China

Figure 6 Fermentation of Qian Cao root (left: fermentation of Zhong Guo Qian, day 1; right: fermentation of Yin Du Qian, day 7)

Figure 7 Red foam produced when boiling Yin Du Qian root at a high temperature

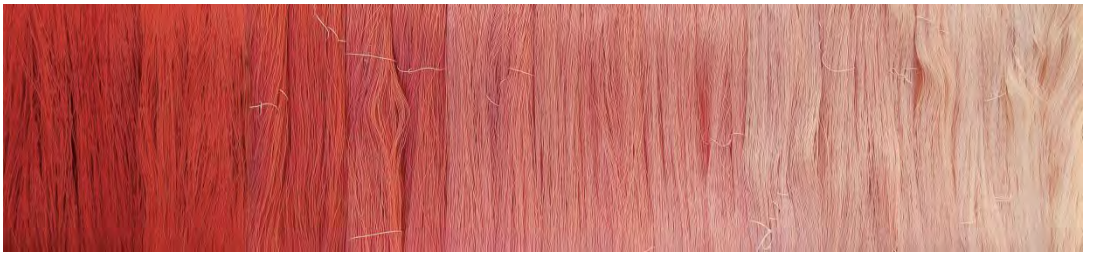

Figure 8 Silk threads dyed with red from Yin Du Qian

ments. They also reviewed ancient extraction technologies of pigments from Qian Cao with the help of new chemical methods. As a result of these incremental improvements, Qian Cao can now be used to produce a pure red pigment.

Qian Cao contains a variety of pigments. According to the author's experience, it is necessary to use the acid-alkali method and control the temperature appropriately to separate various pigments and eliminate interference from impurities. In addition, alum must be used as a pre-mordant for wool or silk fabrics to deepen the color of the dye. The following points are important when dyeing:

First, selection of Qian Cao. Qian Cao is commercially available in dry and fresh forms. When choosing dry Qian Cao, it is difficult to distinguish between stems (aboveground) and roots (belowground). The two different parts greatly differ in their dyeing effect. The solution is to purchase the Qian Cao with a high degree of traceability. Fresh Qian Cao needs to be washed, trimmed, sliced or halved, and then fermented or dried in the sun before use.

Second, acidic environment. Alizarin is only released effectively under acidic conditions, which can be achieved either by fermenting and acidifying fresh Qian Cao (Fig. 6), or by adding vinegar or smoked plum when boiling dry Qian Cao.

Third, pre-mordanting dyeing with alum and high-temperature. The silk threads or fabrics to be dyed should be soaked in alum solution for 15 to 20 minutes before adding Qian Cao. Simultaneous-mordanting or post-mordanting dye methods can greatly reduce the dyeing effect. To optimize the release of alizarin, the temperature of the dye liquor should be maintained at 80°C to 90°C. Continuous heating is required during the dyeing process (Fig. 7) to prevent the temperature of dye liquor from being too high or too low and to avoid producing a fancy shade.

5 Conclusions

Qian Cao is widely distributed around the world. It originated in the area between Eastern Europe and Western Asia, and witnessed the development of color culture in ancient civilizations. There is a very long history of using Qian Cao, which was first used as a dye and then as a medicinal herb. Qian Cao was once a prized red dye, but it has gradually been replaced by other natural red dyes and chemical pigments. Currently, it is mainly used as a medicinal herb, and only rarely used as a plant dye. Qian Cao can be used with pre-mordants in a complicated dyeing process to produce a bright red color (Fig. 8).

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Ethical approval

This study does not contain any studies with human or animal subjects performed by the author.

Author contributions

Min Shao wrote and reviewed the article.

Conflicts of interest

The author declares no financial or other conflicts of interest.

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Use of Non-Verbal Representations to Define Concept of Pulse Conditions in Traditional Chinese Medicine Standards

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Abstract

The standardization of terms and definitions is fundamental to all activities in the domain of traditional Chinese medicine (TCM). For decades, definitions of TCM terminology relied on conventional verbal representations to differentiate between related concepts. However, the ancient Chinese is obscure and comprises a massive volume of information, making it difficult to convey the definition accurately in other languages. This article proposes a potential solution that the definition for pulse terminology can be supplemented by modern means of non-verbal representation, i.e., using pulse waveform graphs and parameters to complete the definition of each pulse. A discussion of the challenges of obtaining reliable data is also included.

Keywords: Non-verbal representation; Pulse condition; Standard; Terminology of traditional Chinese medicine

1 Introduction

The standardization of traditional Chinese medicine (TCM) terminology is fundamental to the dissemination of TCM culture and the global trade of TCM products.[1] There are specific requirements when defining a concept,[2] including accuracy, conciseness, and avoidance of circular definitions. However, over the long history of TCM, medical terms have been deeply influenced by ancient Chinese culture, regional characteristics, ethnomedicine, and foreign cultures. TCM practitioners tend to use descriptive language to express and define terms. However, this language can sometimes be obscure and ambiguous and has a high information density,[3-4] leading to confusion and loss of information. The use of modern informatics and sensor technology in the TCM sector is expected to make terms more scientific and easier to be understood. Taking the terminology of TCM pulse conditions as an example, the present study used non-verbal representations, such as figures and parameters, to complement the terminological entries. Describing the characteristics of pulse waveforms and computing pulse parameters can help reconceptualize the definitions of pulse conditions.

2 Examples of existing standards on TCM pulse conditions

From the earliest days in China, metaphors and descriptive languages have been used to describe the characteristics of various pulse conditions in treatises. For example, a Fu Mai (浮脉 floating pulse) is presented as being like wood floating on water, a Kou Mai (芤脉 hollow pulse) is described as the feeling of pressing a scallion stalk, and a Ge Mai (革脉 drumskin pulse) is described as resembling the beating of a drum. These descriptions are incomplete and conceptually unclear, without specific data references.

Two international standards including terminology of pulse conditions have been developed: *International Standard Chinese-English Basic Nomenclature of Chinese Medicine* (ISN) by the World Federation of Chinese Medicine Societies (WFCMS) and the *WHO International Standard Terminologies on Traditional Medicine in the Western Pacific Region* (WHO IST) published by the World Health Organization (WHO). The terminological entries of pulse conditions in ISN[5] include Chinese names, pinyin, and English names, such as "弦脉 (xian mai, wiry pulse)." While, in WHO IST,[6] the term "弦脉" not only has an English equivalent term "string-like pulse," but a further description of "a straight, long, and taut pulse, like a musical string to the touch" is added to complement the definition. The different English names in the two publications indicate different under-

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standings of some pulse conditions.[7-8] Moreover, the definitions of pulses in the WHO IST are literal descriptions of the pulse concepts, which are difficult to understand.

How can we convey TCM concepts with minimal misunderstanding? As non-verbal representation is semantically significant, definitions in terminology standards should be complemented or supplemented by non-verbal clarification, such as figures, tables, and mathematical expressions derived from new technologies and devices.

3 Examples of illustrations of TCM pulse conditions from ancient times

Given the obscurity and incomprehensibility of pulse terminology, visual aids have been sought to define pulse conditions since ancient times. The earliest published book that uses drawings to illustrate the characteristics of pulse conditions is *Chabing Zhinan* (《察病指南》*A Guide to Disease Examination*)[9-10] (Fig. 1). *Tuzhu Maijue Bianzhen* (《图注脉诀辨真》*Pulse Discrimination by Figure*) published in the Ming dynasty and *Renyuan Maiying Guizhi Tushuo* (《人元脉影归指图说》*Condensed Pulse illustration*) published in the Western Jin dynasty (Fig. 2),[10-11] also used drawings to illustrate the distinct characteristics of pulse conditions.

Drawings in these ancient books were simply dots and lines or a combination of pictograms in one circular area. This intuitive approach is helpful for learners and inspires us to use non-verbal representations to achieve greater consensus on how to define a TCM concept accurately, completely and intuitively.

4 Examples of using figures and parameters to define pulse conditions

According to the *Shuyu Gongzuo: Yuanze Yu Fangfa* (《术语工作—原则与方法》*Terminology Work: Principles and Methods*),[2] non-verbal representations can illustrate and exemplify a concept. In general, they should not replace a definition but complement it. Non-verbal representations include visual representations, such as figures, and mathematical expressions. Modern science and technology provide tools for visual representation and quantification of pulse conditions that can help present precise definition of pulses.

In the 1950s, Chinese scholar Zhu Yan (朱颜) introduced a lever-type pulse descriptor to research TCM pulse conditions.[12] Since then, most studies have focused on pulse measuring devices and analysis methods of pulse, and have formed a unified understanding on the typical pulse figures of common pulses such as the slippery pulse and the string-like pulse. Therefore, we can draw on the

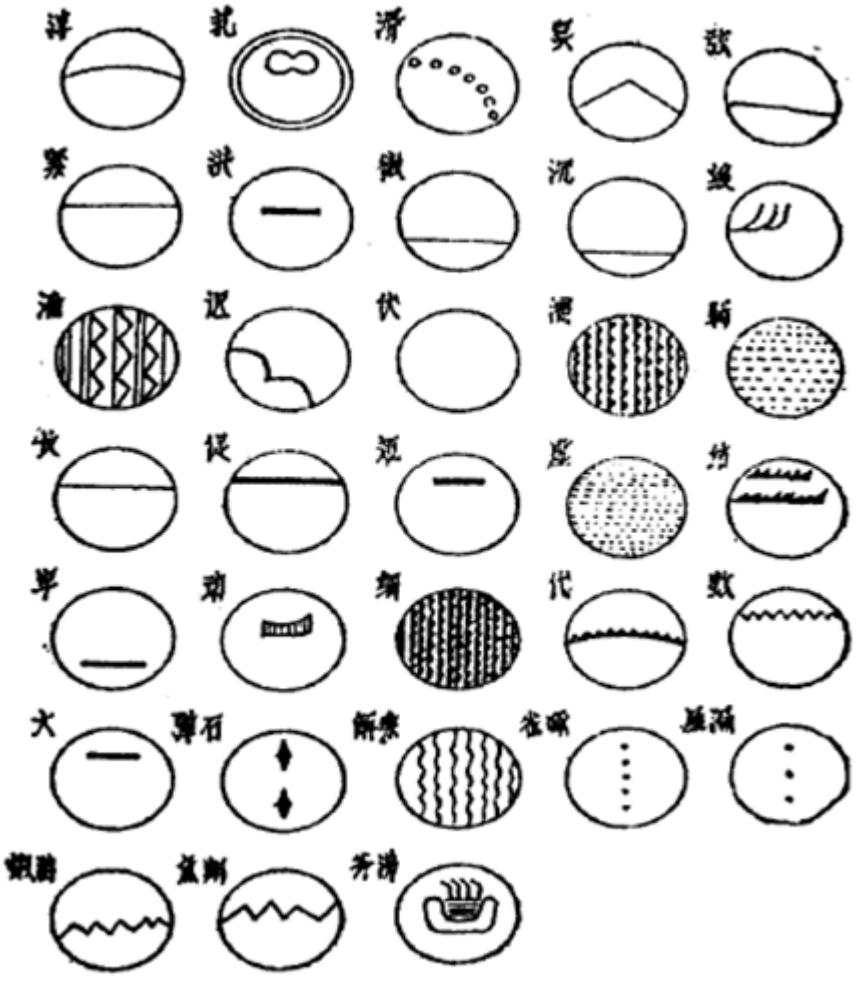


Figure 1 Thirty-three pulse types in the *Chabing Zhinan* (《察病指南》*A Guide to Disease Examination*)[10]

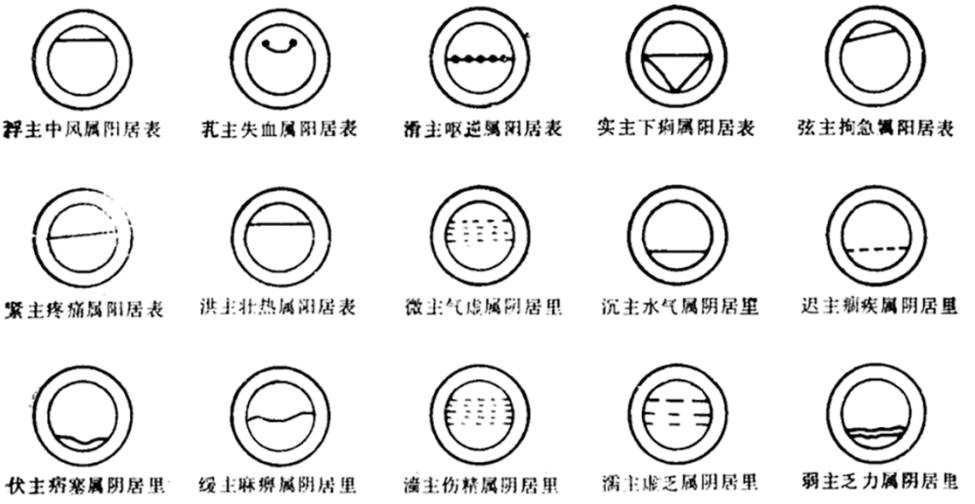


Figure 2 Schematic diagram in *Renyuan Maiying Guizhi Tushuo* (《人元脉影归指图说》 *Condensed Pulse illustration*)[10]

outcomes of pulse objectification research to supplement the definition of pulse terminology. In this paper, we, taking slippery pulse and string-like pulse as examples, use pulse waveforms and parameters to define pulse terminology.

4.1 Typical waveform representing the slippery pulse and string-like pulse

A pulse waveform graph records the trajectories of vascular pulsation of the radial artery at the wrist and contains data regarding the cardiac ejection and the process which the pulse wave travels along the vascular system.[10] Different physiological and pathological states produce pulse conditions with different waveforms. The typical pulse waveform graphs of the slippery pulse and string-like pulse which consensus has been reached are presented in Figure 3.

The pulse waveforms only support a qualitative understanding of pulse conditions,thus quantitative analysis of the waveforms is needed to obtain pulse parameters.

4.2 Methods for extraction and anaylysis of pulse parameters

Zhou Xuehai (周学海), a physician in the late Qing dynasty, wrote that[13] "location, rate, shape, and force

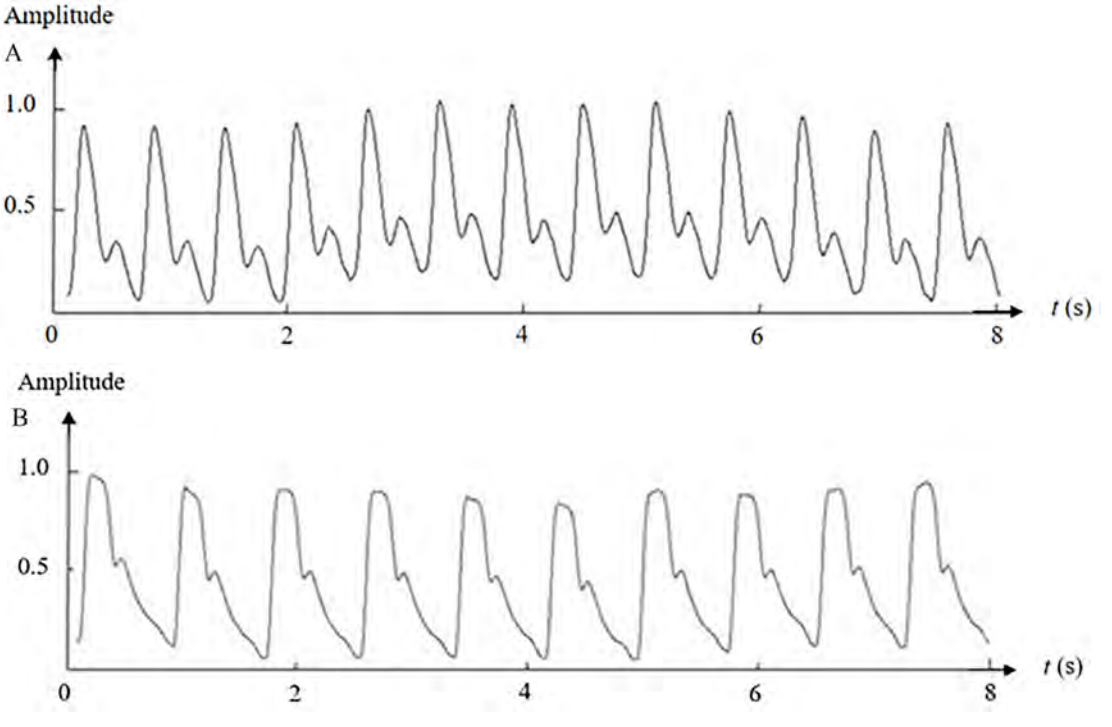


Figure 3 The pulse waveforms visualizing the characteristics of pulse conditions through a two-dimension representation with X-axis and Y-axis representing time and amplitude, respectively: (A) A slippery pulse with obvious double-peak waveform and a narrow percussion wave; (B) A string-like pulse with a broad and high percussion wave

must be clarified to understand all pulse conditions." This classical quotation means that the identification of pulse conditions is mainly made through four aspects: location, rate, shape, and force. Pulse parameters should be extracted to reflect the four aspects of pulse conditions using different analytical methods. Of the four aspects, the pulse shape can be quantified by the time-domain analysis method and the hemodynamic method.[14-16] We, therefore, used these approaches to extract the parameters of the string-like pulse and the slippery pulse.

The time-domain method[17] is an intuitive method that mainly quantifies the characteristics of the pulse waveform in a single cardiac cycle (Fig. 4). The pulse waveform parameters, including *h*2/*h*1, *h*3/*h*1, *h*4/*h*1, *h*5/*h*1, *As*/*Ad*, *t*1/*t*, *t*1/*t*4, and *t*5/*t*4, can reflect the morphology of different waveforms, and have different physiological significances (Table 1).

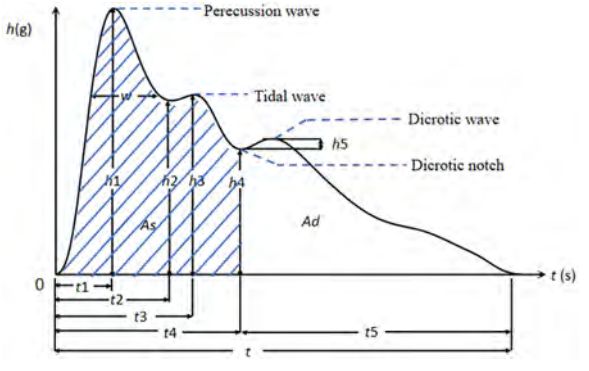


Figure 4 The pulse waveform graph in a single cardiac cycle with *X*-axis and *Y*-axis representing time and amplitude, respectively.
*h*1: the height of percussion wave; *h*2: the height of canyon between percussion wave and tidal wave; *h*3: the height of tidal wave; *h*4: the height of dicrotic notch; *h*5: the height of dicrotic wave; *t*1: the time distance between the start point of pulse chart and percussion wave; *t*4: the time distance between the start point of pulse chart and dicrotic notch; *t*5: the time distance between dicrotic notch and the endpoint of pulse waveform; *t*: the time distance between the start point and the endpoint; *w*: the width of percussion wave in its 1/3 height position

Table 1 Physiological significance of pulse parameters

Parameter	Physiological significance
*h*2/*h*1	Reflects the compliance and peripheral resistance of vascular wall
*h*3/*h*1	Reflects the compliance and peripheral resistance of vascular wall
*h*4/*h*1	Reflects peripheral resistance
*h*5/*h*1	Reflects aortic compliance or aortic valve function
As/ *Ad*	Relates to cardiac output
*t*1/*t*	Reflects the ejection function of the heart
*t*1/*t*4	Reflects the rapid ejection of the heart
*t*5/*t*4	Relates to the heart rate
w/*t*	Reflects the duration of elevated aortic pressure

The purpose of pulse analysis in the hemodynamic method is to analyze the factors influencing pulse waveforms. According to the hemodynamic principle, pulse waves can be decomposed into forward and reflected components. The pulse wave recorded in the radial artery is the synthesis of forward and reflected traveling waves.[18-19] Therefore, the pulse wave velocity (PWV) and the reflection coefficient (R_f), which represent properties of transmission and reflection of the pulse wave, respectively, are parameters that can be used to explain morphological changes of the different pulse waveforms. The formation graphs of a string-like pulse and a slippery pulse waveforms are presented in Figures 5 and 6.[19]

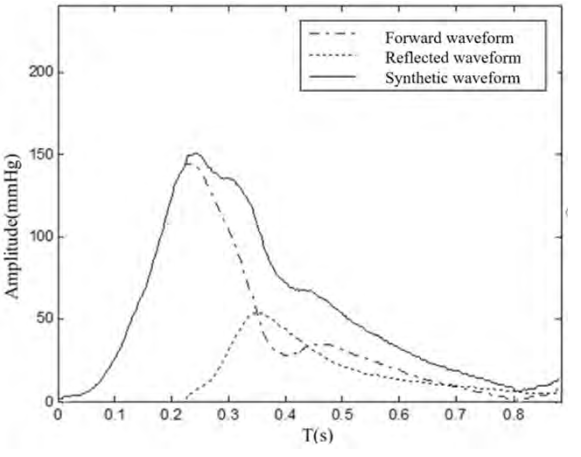


Figure 5 The formation graph of a string-like pulse waveform.[19] For example, in older individuals, arterial stiffening causes increased pulse wave velocity. Thus, the early return of the reflected wave affects the systolic rather than the diastolic part of the wave, augmenting the percussion wave with a secondary rise in late systole after an early systolic peak that creates the waveform of a string-like pulse.

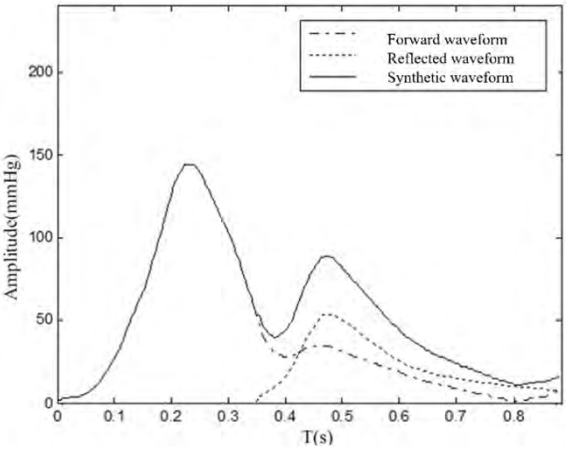


Figure 6 The formation graph of a slippery pulse waveform.[19] For example, in youth, good arterial compliance causes decreased pulse wave velocity. Thus, the reflected wave affects the diastolic rather than the systolic part of the wave, causing secondary fluctuations in diastole, and forming the double-peak wave of a slippery pulse.

Figures 5 and 6 show that PWV and Rf are the factors affecting the formation of pulse waveforms, which help interpret the waveform differences between a slippery pulse and a string-like pulse. Using the hemodynamic method for extracting physiological information from TCM pulse conditions,[20] we obtained the values of PWV and R_f of the slippery pulses and the string-like pulses.

4.3 Complementing definitions of the two pulses

The experimental data in this paper are from the pulse database provided by the Key Laboratory of Health Identification and Assessment of Shanghai. We used the

time-domain and hemodynamic methods to analyze 247 samples of slippery pulse and 622 samples of string-like pulse, and calculated the time-domain parameters (*h*2/*h*1, *h*3/*h*1, *h*4/*h*1, *h*5/*h*1, *As*/*Ad*, *t*1/*t*, *t*1/*t*4, *t*5/*t*4, and *w*/*t*), PWV and R_f of these pulses. SPSS 25.0 (IBM Corp, Armonk, NY) was used to analyze the pulse parameters. The Mann-Whitney *U* test for non-parametric method was applied to compare pulse parameters that are not normally distributed, and distributions of pulse parameters are described by median, the highest and lowest quartile, as *M* (Q_L, Q_H). The results are presented in Tables 2–4.

In these experimental pulse samples, the values of time-domain parameters *h*2/*h*1, *h*3/*h*1, *h*4/*h*1, *h*5/*h*1, *t*1/*t*, *t*1/*t*4 and *w*/*t* in the string-like pulses were higher than those in the slippery pulses ($P<0.001$), and the *t*5/*t*4 value was lower than that in the slippery pulses ($P<0.001$). The PWV and R_f of string-like pulses were higher than those of slippery pulses ($P<0.001$). These differences between the two groups of pulses were statistically significant. The experimental results show that pulse parameters can distinguish the waveforms of slippery pulses and string-like pulses.

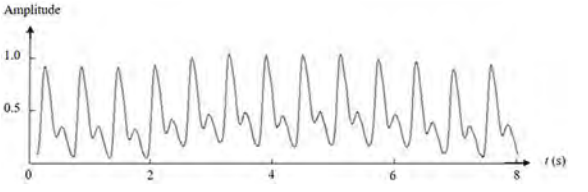
The hemodynamic principle indicates that arterial stiffening and peripheral resistance can be reflected from the waveform of pulse, and arterial stiffening and peripheral resistance can be characterized by PWV and R_f. Our study shows that the string-like pulse with higher PWV and R_f indicates high arterial tension, and corresponds to the description that "a string-like pulse is like the musical strings, and stiff under the force of the fingers."[21] The slippery pulse with a lower PWV and R_f represents good arterial compliance, and corresponds to the description[21] "a slippery pulse arrives and departs smoothly. Its form is like pearls rolling on a plate." Therefore, the time-domain parameters, PWV, and R_f of the pulse conditions can quantify the waveform differences of string-like pulse and slippery pulse from the aspects of morphology and formation mechanism of waveforms. As exemplified in the above examples, these parameters are used to complement the definition of two types of pulses. By referring to the terminological entries of pulse conditions in the WHO IST, we now propose a new presentation for defining slippery pulse and string-like pulse as follows:

The first example:

Hua Mai (滑脉 slippery pulse)

Definition: a pulse coming and going smoothly like beads rolling on a plate

Note 1 to entry:



Note 2 to entry: Pulse parameters described as *M* (Q_L, Q_H)

*h*2/*h*1: 0.631(0.564, 0.735)
*h*3/*h*1: 0.503(0.414, 0.592)
*h*4/*h*1: 0.323(0.257, 0.375)
*h*5/*h*1: 0.413(0.354, 0.464)
As/*Ad*: 1.935(1.618, 2.352)
*t*1/*t*: 0.138(0.120, 0.155)
*t*1/*t*4: 0.343(0.318, 0.368)
*t*5/*t*4: 1.297(1.238, 1.353)
w/*t*: 0.170(0.147, 0.196)
PWV: 8.502(6.919, 12.920)
R_f: 0.736(0.653, 0.813)

The second example:

Xian Mai (弦脉 string-like pulse)

Conception: a straight, long and taut pulse, like a musical string to the touch

Note 1 to entry:

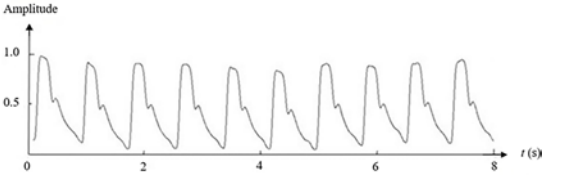


Table 2 Comparison of time-domain parameters of the two groups of the pulses *M* (Q_L, Q_H)

Group	*n*	*h*2/*h*1	*h*3/*h*1	*h*4/*h*1	*h*5/*h*1	*As*/*Ad*
Slippery pulse	247	0.631(0.564, 0.735)	0.503(0.414, 0.592)	0.323(0.257, 0.375)	0.413(0.354, 0.464)	1.935(1.618, 2.352)
String-like pulse	622	0.955(0.889, 0.982)*	0.836(0.774, 0.881) *	0.485(0.425, 0.549) *	0.458(0.392, 0.511) *	2.094(1.782, 2.526)*

* represents a significant difference compared with a slippery pulse, $P < 0.001$.

Table 3 Comparison of time-domain parameters of the two groups of the pulses *M* (Q_L, Q_H)

Group	*n*	*t*1/*t*	*t*1/*t*4	*t*5/*t*4	*w*/*t*
Slippery pulse	247	0.138(0.120, 0.155)	0.343(0.318, 0.368)	1.297(1.238, 1.353)	0.170(0.147, 0.196)
String-like pulse	622	0.146(0.125, 0.177) *	0.359(0.312, 0.431)	1.193(1.129, 1.249) *	0.259(0.238, 0.280) *

* represents a significant difference compared with a slippery pulse, $P < 0.001$

Table 4 Comparison of PWV and Rf of the two groups of the pulses *M* (Q_L, Q_H)

Group	*n*	PWV	R_f
Slippery pulse	247	8.502(6.919, 12.920)	0.736(0.653, 0.813)
String-like pulse	622	11.646(10.091, 13.147) *	0.811(0.742, 0.886) *

* represents a significant difference compared with a slippery pulse, $P < 0.001$.

Note 2 to entry: Pulse parameters described as *M* (Q_L, Q_H)

*h*2/*h*1: 0.955(0.889, 0.982)
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As/*Ad*: 2.094(1.782, 2.526)
*t*1/*t*: 0.146(0.125, 0.177)
*t*1/*t*4: 0.359(0.312, 0.431)
*t*5/*t*4: 1.193(1.129, 1.249)
w/*t*: 0.259(0.238, 0.280)
PWV: 11.646(10.091, 13.147)
R_f: 0.811(0.742, 0.886)

5 Conclusions and further suggestions

Terminology of pulse conditions is fundamental to the subject of pulse diagnosis, which is an important tool for TCM practitioners. The following are three major challenges in obtaining reliable non-verbal representations which would assist in defining the terminology of TCM pulse conditions.

First, pulse measuring device with a single-probe pressure sensor is most commonly used in clinical settings to obtain pulse information and display the dynamic pulse waveforms of a patient's radial artery. Researchers have made progress in obtaining objective pulse conditions through extraction and analysis of pulse parameters.[17,22] However, information obtained from device using the single-probe pressure sensor is far from comprehensive in reflecting the four aspects of a pulse condition. Therefore, multi-point sensing instruments were later developed and expected to collect much more complete information, reflecting "location, rate, shape, force" of the pulse conditions.

Second, the positioning mode of current pulse measuring devices produced by some companies still relies on manual positioning. The sensor must be manually moved to the position of the radial artery and pressure needs to be manually adjusted to obtain an optimal pulse waveform. These manual operations result in unreliable data, affecting the accurate acquisition of pulse waveforms and parameters. Thus, automatic positioning and pressurization techniques are important issues to be resolved in the future.

Nevertheless, the traditional approach to pulse diagnosis relies on the sensitive palpation of a physician's fingers, through which the physician obtains 3D pulse information. New sensors and digital signal processing technology should be applied in pulse measuring devices to obtain 3D waveforms of pulse conditions. Using 3D pulse waveforms could maximize the simulation of the TCM pulse diagnosis process and obtain more reliable pulse information. We can make a clear and rigorous definition of pulse terms by analyzing pulse information.

The development of sensor technology, artificial intelligence and big data may support the informatization and digitization of TCM pulse diagnosis, ultimately ensuring that the theoretical system of pulse diagnosis can be improved for future generations. Future TCM practitioners may have a clearer understanding of pulse conditions through the intuitive and quantitative description of pulse conditions, which can be acquired and visualized by AI robotic fingers fully mimcing TCM practitioners' skills of pulse taking.

In conclusion, standardized methods on digitalization and quantification of pulse conditions based on AI can provide objective data for subjective definition of TCM pulses, thus improving the disease diagnosis and treatment of TCM, as well as teaching and training of TCM.

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Ethical approval

The Scientific Research Section and Moral and Ethical Committee of Shanghai University of Traditional Chinese Medicine approved the study. Also, following acquisition of informed consent, they approved all of the volunteers taking part in this research project.

Author contributions

Chun-Ke Zhang wrote the whole manuscript text, which was revised by Yi-Qin Wang, Rui Guo, Hai-Xia Yan, and Jing Li. Jing Li and Rui Guo provided the idea and the structure of this manuscript. Jian-Jun Yan analyzed the data in the paper. Chun-Ke Zhang and Wen-Ji Wu collected and collated the data in the paper. All authors reviewed the manuscript.

Conflicts of interest

The authors declare no financial or other conflicts of interest.

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The First Terminology International Standard of Traditional Chinese Medicine Diagnosis ISO 23961-2: 2021 Traditional Chinese Medicine - Vocabulary for Diagnostics - Part 2: Pulse

With the policy of one belt, one road, traditional Chinese medicine (TCM) is rapidly spreading in more and more countries and regions. Driven by market demand, TCM is gradually opening up the international market through the construction of standardization system. In the process of integrating TCM with international practice, the embedding and docking of TCM information system determines the internationalization of TCM. However, terminology standards are the foundation of TCM information standardization. Only with the standardized terminology, the standardized expression and effective dissemination of information can be realized, and then in-depth sharing and comprehensive utilization of information be realized.

It is exciting that the International Organization for Standardization (ISO) officially released the international standard "ISO 23961-1" and "ISO 23961-2" on November 5, 2021. It is the first time for ISO/TC249 to publish the standard of TCM diagnostic terms. The terminology standard, "ISO 23961-2:2021 Traditional Chinese Medicine - Vocabulary for Diagnostics - Part 2: Pulse", was formulated by the team of Professor Wang Yiqin, School of Basic Medicine of Shanghai University of TCM and Shanghai Key Laboratory of Health Identification and Evaluation. In order to serve the national strategy of TCM internationalization, Professor Wang Yiqin led her team to submit a standard proposal to ISO/TC249 in 2016. After several rounds of discussion with ISO/TC249 experts and corresponding revision, ISO 23961-2 was approved unanimously by the Committee and 7 countries committed to participate in the joint development of standards, and ISO 23961-2 was finally officially adopted in March 2018.

ISO 23961-2 is formulated in accordance with ISO international standards specification. It adopts the method of combining analysis of ancient texts, literature tracing, and literature collation to determine the classification framework for terms. By comparing with pulse terms in other international standards such as WHO and seeking common ground while reserving difference, ISO 23961-2 identifies and interprets pulse terms that meet ISO requirements. The project team has considered the idioms of terminology in different countries and regions and the needs of different fields such as scientific research, education and trade, therefore, its documents includes English, pinyin, classical and simplified Chinese characters, Japanese name and Korean names, which greatly expands the applicability of standard.

ISO 23961-2 help the international trade and technical cooperation of pulse-equipment-related enterprises and the standardized information construction of traditional Chinese medicine, which will bring benefits to scholars, governments and enterprises all over the world. Firstly, standardized pulse terminology helps to encourage improvement of pulse-equipment-related industrial and research field. With standardized terminology, the versatility of pulse-equipment-related products or service can be improved to benefit international technical cooperation. Secondly, the use of standardized pulse terminology in diagnosis helps to avoid confusion among researchers in the field of pulse diagnosis. Thirdly, the internet-based medicine is developing very quickly. The standardized terminology is not only important for the computerized information, but also very useful and necessary for the successful communication between physicians and patients from different countries. With advances in artificial Intelligence, Medical AI doctors also need standardized terminology.

(Shanghai Key Laboratory of Health Identification and Assessment)