MINIREVIEWS

The Yin and Yang of traditional Chinese and Western medicine

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Abstract
The success of Western Scientific approaches to medicine, over the last 150 years, can be measured by substantial increases in life expectancy, reductions in infant mortality and the virtual elimination of many infectious diseases accompanied by development of effective management practices for noncommunicable diseases. However, major challenges remain in the form of infectious diseases that evolve resistance to pharmaceuticals rapidly, new diseases, particularly those caused by viruses and effective long-term treatments for chronic, noncommunicable diseases. Traditional Chinese Medicine (TCM) can offer complementary treatments based on personalised interventions, informed by knowledge accumulated from empirical observations gathered over centuries of practice, that address the impact of disease on the whole body.

We provide examples of both infectious and noncommunicable diseases where the combination of Western Scientific Medicine (WSM) and TCM can benefit patients in terms of the speed and efficacy of recovery or disease management. TCM is a healing skill based on practice, while WSM is scientific, based on experiments. Against this background, an understanding of the mechanisms of action...
Traditional medical practices, particularly Traditional Chinese Medicine (TCM) have often been portrayed as philosophically distinct from Western Scientific Medicine (WSM), fuelled by the absence of hard evidence for efficacy of traditional practices involving the WSM gold standard; randomized, double-blind, placebo-controlled clinical trials. Additionally, western pharmaceutical companies have often declined to develop therapies based on traditional medicines, because of the lack of opportunities for patenting. However, views of TCM as “unreliable, fanciful, false, and irrelevant”\(^1\) were refuted effectively by the award of the Nobel Prize for medicine in 2015 to three scientists for identifying natural products for treatment of human diseases caused by parasites, one of whom was Youyou Tu, who led the team that identified artemisinin from *Artemisia annua* (Qinghao), an effective treatment for the malarial parasite *Plasmodium falciparum*.

Despite the excitement surrounding the award of the 2015 Nobel Prize, there remains considerable scepticism surrounding TCM, typically because of the absence of data that meet US Food and Drug Administration standards for efficacy and lack of side effects. Ironically, TCM is the product of accumulated clinical observations gathered over centuries of practice.

Of course, there are fundamental differences between the philosophies of TCM and WSM as well as the ways in which they are applied. Although these differences have often led to the dismissal of TCM, based on criteria established for WSM, the two approaches may, like Yin and Yang (阴和阳), be complementary, interconnected and interdependent in terms of disease outcomes and consequently may offer hope in the form of combination therapies that allow more effective management and treatment of the most challenging of human diseases.

WSM takes a technocentric approach. Disease is seen as something “going wrong” with the body. Starting in earnest more than 150 years ago methods based on surgery and drugs have been used to repair the body and get things working again. WSM is evidence-based and its methodology is fundamentally analytical and reductive.

In contrast, TCM is an empirical discipline developed over more than 2000 years. Consequently, TCM is a product of accumulated observations gathered over centuries of practice. It looks at the behaviour of the human body as a whole during the course of a disease. TCM defines a healthy individual as having balance within themselves and with their natural environment. A diseased condition represents a deviation from that balance and the role of TCM is to restore balance.

One of the most important and fundamental theories of TCM is prevention of disease; prevention before disease onset, prevention from exacerbation of disease and prevention of recurrence.\(^2\) Prevention is increasingly being emphasised by modern western medicine, and advocated by the WHO in its annual reports since 1996.\(^3\) In TCM, prescriptions are personalized, according to the physical condition and personal habits of the patient and the
development of the disease, reflecting an emphasis on individualised treatment, more recently also adopted by western medicine.

The advances that have come from WSM have improved the quality of human life enormously, particularly in reducing infant mortality and because of this success, WSM has become the predominant medical system in the world. Even in China surveys suggest that less than 30% of the population use TCM and, when they do, their use is predominantly as a complement to WSM, although use is also very dependent on the age of the patient, their geographic location and the nature of the complaint. However, the methodology of western medicine does not always address disease completely, for three main reasons.

(1) No two individuals are the same, and ideally medication should be individualized.
(2) The human body is an open, large, and complex system and cannot be understood by analysing subsystems in isolation.
(3) The human body’s role in pathogenesis is often forgotten in WSM. Diseases consist of two components, the cause of the disease (infection, cancer etc.) and the body’s responses to the cause of the disease.

In this mini-review we consider TCM treatments for three diseases, (two infectious and one chronic) of current relevance to societies globally and compare these to WSM treatments. The benefits of TCM are specific to each example, due to the different mechanisms of action of traditional interventions, but collectively they support arguments for the wider adoption of combined therapies. We assess the benefits of harnessing the complementarity of TCM and WSM approaches, and how western approaches to understanding how TCM works may augment the benefits of combined therapies.

2 | MALARIA

Malaria is caused by *Plasmodium falciparum* infection and has probably been around for more than 50,000 years. Despite substantial scientific progress in the modern era, malaria remains a worldwide problem and causes hundreds of thousands of deaths every year. In 2018, an estimated 228 million cases occurred worldwide and caused approximately 405,000 deaths, among which, two thirds were deaths of children under 5 years old. Natural medicines from plants have made significant contributions to the treatment of malaria, including quinine from *Cinchona ledgeriana* and artemisinin (qinghaosu) from *Artemisia annua* (*Qinghao*).

In China, qinghao has been recommended traditionally for the treatment of malaria, reported originally in *Zhouhou Beiji Fang* (*The Handbook of Prescriptions for Emergencies, 肘後備急方*) edited by Ge Hong in the 4th Century AD. Following structural identification and the report on the use of artemisinin to treat malaria, many research groups systematically purified and analyzed artemisinin using WSM strategies. Due to the rapidity with which it can clear the parasite from the human body and reduce fever, artemisinin became the frontline drug for treatment of malaria from the late 1990s until 2012, but the production of combination therapies and the development of resistance to artemisinin particularly in South East Asia, saw the World Health Organisation then advise against use of artemisinin alone. Currently, artemisinin-based combination therapies comprise semisynthetic artemisinin derivatives paired with distinct chemical classes of longer acting drugs, including quinine derivatives, which are recommended for the treatment of uncomplicated malaria by the World Health Organization. Consequently, the success of artemisinin has been built on both TCM and, more recently, refinement by WSM.

Several western scientific strategies have been adopted to increase the activity and production of artemisinin. To increase the efficacy of artemisinin, its solubility in oil and water has been improved through the development of several artemisinin derivatives, including dihydroartemisinin, artemether, and artesunate, which have been shown to have enhanced anti-malarial activities.
In practice, artemisinin is usually extracted from *A. annua* leaves and used for further modification. Consequently, a major limitation on production has been the low content of artemisinin in *A. annua* leaves. Many accessions of *A. annua* contain artemisinin below 0.2% and cannot be used for commercial production.\(^{14}\)
To maintain a stable supply of artemisinin, different western production strategies have been employed. Chemical synthesis began shortly after the discovery of artemisinin and the total synthesis of artemisinin from (-)-isoeugenol was first reported in 1983. At the same time, conversion of artemisinic acid to artemisinin was reported providing the theoretical ground-work for semi-synthetic production. The need for high levels of investment, and low yields have limited chemical synthesis for industrial-scale applications.

The pursuit of high artemisinin varieties of *A. annua* by plant breeders has also been ongoing since artemisinin was first discovered. Massive breeding programs have created high content varieties. Varieties with artemisinin contents of over 1% have been cultivated by farmers in China and now represent the major source for the world supply of artemisinin (Figure 2). More advanced approaches including metabolic engineering by breeding, marker-assisted selection and mutation breeding have also been used to select higher content varieties, with many now awaiting field trials and regulatory approval.

Production of artemisinin in other plant chassis has been reported but the maximum production attainable, so far, has been 120 mg kg\(^{-1}\) fresh weight of tobacco leaves, which translates to a yield of 0.12% from the leaves. When the costs for transformation, plant cultivation and regulatory approval are also taken into consideration, it seems unlikely that this production route will be competitive, economically.

Identification of the partial biosynthetic pathway of artemisinin from acyl CoA to artemisinic acid offered the opportunity for engineering artemisinic acid production in yeast by introducing the *A. annua* genes encoding the enzymes of the pathway, blocking competing pathways and building synthetic metabolons to improve flux. Although the best strains can now achieve yields of 25 g L\(^{-1}\) in combination with semi-synthetic conversion of artemisic acid to artemisinin, this route is still more expensive (350–400 US$ per kg) than growing *A. annua* plants and extracting artemisinin from the leaves directly (<250 US$ per kg) and production in yeast has been limited since 2015.

Consequently, economics still dictates that the most cost-effective means of producing artemisinin is the traditional way from leaves of *A. annua* plants. Thus, the most effective treatment for malaria was identified from TCM and is still produced in a close-to-traditional fashion (Figure 2), although WSM has contributed substantially through the development of combination therapies which reflect TCM philosophy by combining anti-malarial bioactivities.

**FIGURE 2** Cultivation of *Artemisia annua* in Southwest China for artemisinin production. Photograph was provided by Dr. Chunxia Yang and Dr. Zhihua Liao from Southwest University, China [Color figure can be viewed at wileyonlinelibrary.com]
3 | COVID-19

In December 2019, coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), appeared and spread rapidly. By October 20th 2020 there had been 40,251,950 confirmed infections and 1,116,131 deaths around the world. At the time of preparing this review, no specific medicine or vaccines had been officially approved for effective prevention or treatment. Despite the projected availability of vaccines, effective treatment regimens are likely to be required for some time to come. During the past 9 months, integrated TCM and WSM were employed systematically for the treatment of COVID-19 in China, in accordance with the guidelines for diagnosis and treatment of COVID-19, and from experience in China of treating other infections caused by viruses, such as Middle East respiratory syndrome and severe acute respiratory syndrome (SARS) which are both caused by coronaviruses.29–34

So far, eight versions of the guidelines for diagnosis and treatment of COVID-19 have been issued in China. In the latest version, guidelines for treatments by both TCM and WSM were included.29 For WSM, recommendations depend on the stage of the disease. Supportive care, oxygen therapy, antiviral therapy, and antibiotic therapy were all recommended for conventional (WSM) treatment of COVID-19 and recommended antiviral drugs included interferon-α, lopinavir/ritonavir, ribavirin, chloroquine phosphate, and arbidol. For severe and critical cases, respiratory support, circulatory support, anticoagulation therapy, continuous renal replacement therapy, blood purification therapy, and immunotherapy were recommended. Glucocorticoids can be used in selected situations.

TCM guidelines, on the other hand, recommend an initial medical observation and then clinical treatment. During the period of medical observation, treatment with Chinese patented medicines was recommended; Huoxiang Zhengqi Capsules (藿香正气胶囊, as pills, liquid or oral liquid) for fatigue with accompanying gastrointestinal discomfort, and Jinhua Qinggan Granules (金花清感颗粒), Lianhua Qingwen Capsules (连花清瘟胶囊, granules), Shufeng Jiedu Capsules (疏风解毒胶囊, granules) for fatigue with accompanying fever. During the clinical treatment period, recommended treatments were for mild (cold-damp constraints in the lung or damp-heat accumulation in the lung), moderate (damp-toxin constraints in the lung or cold-damp obstructions in the lung), severe (epidemic toxin blocking the lung or blazing of both qi and ying), critical (internal blockages and external desertion) and convalescence (lung-spleen deficiency in qi or deficiency of both qi and yin) stages, and subtypes of each stage (see Table 1 for the definition of TCM terms). TCM formulas have been recommended for mild and moderate cases of COVID-19 infection as well as for convalescence (Figure 3). Combinations of TCM formulas and Chinese patented medicines have been recommended for treating severe and critical cases. Qingfei Paidu Decoction (清肺排毒汤) was recommended for mild, moderate, and severe cases, and could also be used for critical patients, according to their specific conditions (Figure 4).

The basic formula of Qingfei Paidu Decoction, which includes 20 herbs and one chemical constituent, is shown in Table 2. Analysis suggests it contains 45% flavonoids (including 4′-deoxyflavones from roots of Scutellaria baicalensis [Huang Qin]), 15% glycosides, 10% carboxylic acids and 5% saponins. A component of particular importance is the Ma Xing Shi Gan decoction (麻杏石甘汤), of which glycyrrhizic acid, a saponin from liquorice roots (Figure 5) appears to play a pivotal role in suppressing pulmonary inflammation and the cytokinin storm that accompanies COVID-19 infection.33 Glycyrrhizic acid has been recognised for a long time as an effective anti-inflammatory and an antioxidant, although at high doses it may also show toxicity. Consequently its delivery within a therapeutic window is important for its efficacy and its composition in the Ma Xing Shi Gan decoction seems to fit well within this dosage window. The ephedrine (Ma Huang) in the Qingfei Paidu Decoction inhibits platelet aggregation and may serve to suppress blood clotting in severe cases of COVID-19 infection (Figure 6).33

TCM showed considerable power in the prevention and treatment of SARS in 2003.34,40 This demonstrated the efficacy of TCM against infectious diseases. However, integration of TCM and WSM has shown even better outcomes in the treatment of COVID-19 than WSM alone.30,41 Compared to WSM, integrated medicine had a better overall response rate, higher cure rate, lower severity of illness rate, lower mortality rate, and shorter
hospital stays in the treatment of COVID-19. The integrated approach also improved the disappearance rate of symptoms including fever, fatigue, coughing and expectoration and reduced the duration of fever and fatigue.

Outcomes from an example of 51 moderate cases treated by the Chinese patented medicine, Lianhua Qingwen Granule, combined with conventional treatment as the treatment group and 51 moderate cases with only conventional treatment as the control group\(^4\) are shown in Table 3.

### TABLE 1  Glossary of TCM terms used\(^35,36\)

| Term | Definition |
|------|------------|
| Yin (阴) | A term from ancient Chinese philosophy referring to things or natures which are cold, downward, inert, dim, internal, material, declining, and inhibitory. |
| Yang (阳) | Things or natures opposite to yin. |
| Yin and Yang  | A concept of dualism, describing how opposite or contrary forces may actually be complementary, interconnected, and interdependent in the natural world. |
| Qi (气) | Flowing refined nutritive materials in the body or functional activities of the body. |
| Ying (营) | One substance from the digested food which circulates to nourish the body. |
| Blazing of both qi and ying (气营两燔) | A disease characterized by high fever, dysphoria, thirst, epistaxis, irregular or fast pulse, etc. |
| Cold (寒) | An exogenous pathogenic factor which hinders the dispersion of yang and obstructs the activities of qi and blood. It's also a term used to describe decreased functioning of an organ system which presents as any of the following: body aches, chills, poor circulation, fatigue, lack of appetite, loose stools or diarrhea, poor digestion, pain in the joints. It pertains to all "hypo" conditions such as hypoadrenalism, hypoglycemia and hypothyroidism. |
| Damp (湿) | A pathogenic factor, whose nature is heavy, sticky and greasy, obstructing the activities of qi and spleen. It's also a term describing excessive fluids in the body with symptoms of abdominal bloating, loss of appetite, nausea, vomiting, lack of thirst, sluggishness, and stiff, aching, or sore joints. |
| Cold-damp (寒湿) | A pathogenic factor causing obstruction of yang and blood activities, pain of skin, less flexibility of joints, etc. |
| Damp-toxin (湿毒) | Accumulated damp, causing diseases which are chronic, long-lasting, and with copious exudations. |
| Heat (热) | A pathogenic factor with the same nature as fire or a symptom characterized as excess yang. |
| Damp-heat (湿热) | Combination of damp and heat, causing diseases to the spleen, liver, large intestine, bladder, skin, such as jaundice, hepatitis, urinary problems, or eczema due to damp-heat. |
| Decoction (汤剂) | A medicinal soup or tea obtained by brewing herbs in boiling water and then removing the herbs from the mixture. |
| Deficiency (虚, 虚症) | Any weakness or insufficiency of qi, blood, yin, yang or essence. |

Abbreviation: TCM, Traditional Chinese Medicine.
FIGURE 3  (A) Preparation of herbs for formulation of a TCM decoction. (B) Drawers containing dried herbs for preparation of TCM prescriptions. The photographs were provided by Dr. Xin Zhou and Dr. Guangwei Zhu. TCM, Traditional Chinese Medicine [Color figure can be viewed at wileyonlinelibrary.com]

FIGURE 4  The number of chemical constituents of each herb and structures of representative constituents identified from Qingfei Paidu Decoction. Reproduced with permission from Pharmacological Research[33] [Color figure can be viewed at wileyonlinelibrary.com]
| Chinese name | Pinyin name | Dose  | TCM name | Scientific name | Tissue used                  |
|--------------|-------------|-------|----------|-----------------|------------------------------|
| 麻黄         | Ma Huang    | 9 g   | Ephedra Herba | Ephedra sinica Stapf | Herbaceous stem               |
|              |             |       |          | Ephedra intermedia Schrenk et C. A. Mey. |                             |
|              |             |       |          | Ephedra equisetina Bge. |                             |
| 炙甘草       | Zhi Gan Cao | 6 g   | Glycyrrhiza Radix | Glycyrrhiza uralensis Fisch. | Roots and rhizome            |
|              |             |       |          | Glycyrrhiza inflata Bat. |                             |
|              |             |       |          | Glycyrrhiza glabra L. |                             |
| 苦杏仁       | Ku Xing Ren | 9 g   | Armeniaceae Semen Amarum | Prunus armeniaca L. var. ansu Maxim. | Seed                         |
|              |             |       |          | Prunus sibirica L. |                             |
|              |             |       |          | Prunus mandshurica (Maxim.) Koehne |                             |
|              |             |       |          | Prunus armeniaca L. |                             |
| 生石膏 (先煎) | Sheng Shi Gao | 15-30 g | Gypsum fibrosum | CaSO₄·2H₂O |                             |
| 桂枝         | Gui Zhi     | 9 g   | Cinnamomi Ramulus | Cinnamomum cassia Presl | Young shoot                  |
| 泽泻         | Ze Xie      | 9 g   | Alismatis Rhizoma | Alisma orientale (Sam.) Juzep | Tuber                        |
|              |             |       |          | Alisma plantago-aquatica Linn. |                             |
| 猪苓         | Zhu Ling    | 9 g   | Polyporus | Polyporus umbellatus (Pers.) Fries | Sclerotium                   |
| 白术         | Bai Zhu     | 9 g   | Atractylodis macrocephalae Rhizoma | Atractylodes macrocephala Koidz. | Rhizome                      |
|              |             |       |          | |                             |
| 茯苓         | Fu Ling     | 15 g  | Poria    | Poria cocos (Schw.) Wolf | Sclerotium                   |
| 柴胡         | Chai Hu     | 16 g  | Bupleuri Radix | Bupleurum chinense DC. | Roots                        |
|              |             |       |          | Bupleurum scorzonerifolium Wild. |                             |
| 黄芩         | Huang Qin   | 6 g   | Scutellariae Radix | Scutellaria baicalensis Georgi | Roots                       |
| 姜半夏       | Jiang Ban Xia | 9 g  | Pinellinae Rhizoma Praeparatum cum Zingibere | Pinellia ternatae (Thunb.) Breit | Tuber                       |
| 生姜         | Sheng Jiang | 9 g   | Zingiberis Rhizoma recens | Zingiber officinale Rosc. | Rhizome                      |
| 紫菀         | Zi Wan      | 9 g   | Asteris Radix | Aster tataricus L. f. | Roots                        |
| 散冬花       | Kuan Dong Hua | 9 g  | Farfarae Flos | Tussilago farfara L. | Flower                       |
| 射干         | She Gan     | 9 g   | Belamcandae Rhizoma | Belamcanda chinensis (L.) DC. | Rhizome                      |

(Continues)
| Chinese name | Pinyin name | Dose | TCM name | Scientific name | Tissue used |
|--------------|-------------|------|----------|-----------------|-------------|
| 细辛         | Xi Xin      | 6 g  | Asari Radix et Rhizoma | Asarum heterotropoides Fr. Schmidt var. mandshuricum (Maxim.) Kitag. | Roots and rhizome |
| 山药         | Shan Yao    | 12 g | Dioscoreae Rhizoma | Dioscorea opposita Thunb. | Rhizome |
| 杭实         | Zhi Shi     | 6 g  | Aurantii Fructus immaturus | Citrus aurantium L. | Immature fruit |
| 陈皮         | Chen Pi     | 6 g  | Citri reticulatae Pericarpium | Citrus reticulata Blanco | Fruit peel |
| 广藿香       | Guang Huo Xiang | 9 g  | Pogostemonis Herba | Pogostemon cablin (Blanco) Benth. | Aerial part |

**FIGURE 5** (A) Glycyrrhiza glabra, English liquorice whose roots are a rich source of glycyrrhizin from Bentley and Trimen, 1880. (B and C) Glycyrrhiza ursensis Fisch. and its radix and rhizome preparation used in TCM. The photographs were provided by Guiqing Liu and Zhaolong Liu from Plant Photo Bank of China. (D) The structure of glycyrrhizin. TCM, Traditional Chinese Medicine [Color figure can be viewed at wileyonlinelibrary.com]
A second example involved 40 patients with COVID-19 (30 severe cases and 10 critical cases) were subjected to Integrated TCM and WSM (26 cases) or WSM alone (14 cases). In the WSM group, antiviral drugs (arbidol), antibiotics, drugs for coughing, asthma and phlegm-resolution, nutritional support drugs, and hormone drugs (methylprednisolone) were used for treatment. In the integrated medicine group, TCM treatment was added to WSM treatment. TCM was used mainly in the decoction form. Qingfei Paidu Decoction (Table 2), Huashi Jiedu Decoction (化湿解毒汤, a herbal mixture with immuno-enhancing, detoxifying and antineoplastic activities), Huayu Jiedu Decoction (化瘀解毒汤, a herbal mixture with antitumor and antimetastasis activity), and Huifu Formula (恢复方) were used according to the details available for individual patients. Outcomes are shown in Table 4. There were two deaths (14.29%) in the WSM group, but no deaths in the group receiving integrated TCM and WSM (Table 4).

A third example referred to 52 patients including moderate (76.9%), severe (19.2%), and critical cases (3.8%). 18 cases were treated with WSM alone including antivirals, antibiotics, and auxiliary supportive drugs. Thirty-four cases were treated with Integrated TCM and WSM by applying TCM decoctions, Chinese patent medicines, and

### TABLE 3 Study one: moderate cases treated by Lianhua Qingwen Granule (LQG) combined with conventional treatment or conventional treatment only

| Symptom                        | LQG + conventional | Conventional |
|--------------------------------|--------------------|--------------|
|                                | Disappearance rate | Treatment time (days) | Disappearance rate | Treatment time (days) |
| Fever                          | 83.70%             | 2.9 ± 1.7     | 61.00%             | 3.9 ± 1.3             |
| Fatigue                        | 61.30%             | 3.5 ± 1.5     | 34.30%             | 4.8 ± 1.5             |
| Cough                          | 62.20%             | 3.9 ± 2.0     | 35.90%             | 5.2 ± 1.8             |
| Cases converted to severe stage| 4 (7.8%)           | 11 (21.6%)    |                 |                    |
| Overall efficacy               | 86.30%             | 68.60%        |                 |                    |

*Fifty-one cases for each treatment.
TCM injections in addition to WSM treatments. Outcomes for the integrated medicine group were better than those for the WSM group (Table 5).

There are a huge number of components in TCM decoctions and formulas. Network pharmacology and integrative pharmacology studies undertaken on Qinfei Paidu Decoction (Table 2 and Figure 4) treatment for COVID-19 showed it impacts COVID-19 by altering multiple signalling pathways, including a series of ACE2 (receptor of SARS-CoV-2) coexpressed proteins and COVID-19-related pathways to balance the immune responses and eliminate inflammation.45,46 It may also target ribosomal proteins needed for viral replication so acting as an antiviral agent that inhibits translation of viral messenger RNA and inhibits the impact of viral proteins on host processes.

Xuebijing Injection (血必净注射液) is a Chinese patented medicine which has been recommended for treating severe and critical cases of COVID-19.29 Network pharmacological investigations of Xuebijing Injection in COVID-19 treatment found that its common targets with COVID-19 included fourteen critical targets involved in the regulation of

### Table 4

Study two: 40 cases treated by integrated treatment (TCM combined with WM) or WM only

|                           | Integrated treatment | WM treatment |
|---------------------------|----------------------|--------------|
| Clinical symptoms         | 92.31%               | 57.14%       |
| Body temperature          | 96.15%               | 64.29%       |
| Accompanying symptoms     | 88.46%               | 50.00%       |
| CT image improvement      | 84.62%               | 50.00%       |
| Nucleic acid testing negative | 88.46%             | 50.00%       |
| Death rate                | 0.00%                | 14.29%       |

Abbreviations: TCM, Traditional Chinese Medicine; WSM, Western Scientific Medicine.

*Thirty severe cases and 10 critical cases. Twenty-six cases for Integrated treatment and 14 cases for WM treatment.

*Combined with WSM treatment, Qingfei Paidu Decoction, Huashi Jiedu Decoction, Huayu Jiedu Decoction, and Huifu Formula were used according to the details of patients.

*Antiviral drug (arbidol), antibiotics, drugs for cough, asthma and phlegm-resolving, nutritional support drugs, and hormone drug (methylprednisolone) were used.

### Table 5

Study three: 52 cases treated by integrated treatment or WSM only

|                           | Integrated treatment | WM treatment |
|---------------------------|----------------------|--------------|
| Body temperature          | 2.64 ± 1.31          | 4.38 ± 1.90  |
| Clinical symptoms         | 5.15 ± 1.68          | 7.15 ± 2.12  |
| Hospital stay             | 7.38 ± 2.06          | 9.59 ± 3.59  |
| Accompanying symptoms     | 87.90%               | 38.90%       |
| Clinical cure             | 91.20%               | 61.10%       |
| Cases converted to severe stage | 5.90%              | 33.30%       |

Abbreviations: TCM, Traditional Chinese Medicine; WSM, Western Scientific Medicine.

*The percentages of moderate, severe, and critical cases are 76.9%, 19.2%, and 3.8%, respectively.

*TCM decoctions, Chinese patent medicines and TCM injections were added to WSM treatment.

*Antiviral, antibiotics, and auxiliary supportive drugs were used.
Toll-like receptors, T cell receptors, and other signaling pathways involved in immune responses. These indicated Xuebijing Injection functions mainly in protecting vital organs through modulating inflammation triggered by the immune response to the virus. Molecular docking showed good affinity of the main components of Xuebijing Injection with ACE2 and SARS-CoV-2 3CL hydrolase, supporting the antiviral effects of the Xuebijing injection.

The multiple components of TCM decoctions, formulas and injections offer advantages in treatment targeting multiple pathways affected by the virus, and their impact on these broad targets may result in benefits through synergy in treating the disease, explaining the efficacy of TCM as a complement to WSM in COVID-19 treatment.

Due to the effectiveness of Integrated Traditional Chinese and Western Medicine, integrated medicine has been used widely for the treatment of COVID-19 in China. More than 90% of the confirmed COVID-19 cases received TCM treatment. Although these data are very recent, the use of integrated traditional Chinese and western medicine would appear to be particularly effective in the treatment of COVID-19 and recommended for more widespread adoption, since COVID-19 infection remains severe around the world.

4 | TYPE 2 DIABETES

Type 2 diabetes (T2D) is a chronic disease involving raised glucose levels in the blood as a result of reduced sensitivity to insulin (insulin resistance) and/or inadequate insulin production. Elevated blood glucose levels can cause serious complications including damage to eyes, kidneys, heart, blood vessels, and nerves, leading to retinopathy and sight loss, kidney failure, heart failure and increased risk of cardiovascular disease as well as amputations. There were an estimated 463 million cases of diabetes worldwide in 2019, 90% of which were T2D. Because of its association with obesity, the number of people in the world suffering from T2D is predicted to rise to 700 million by 2045.

The basic treatments for T2D are management through education and maintenance of a healthy lifestyle; adopting a healthy diet (low in refined fats and sugars), undertaking suitable physical exercise, cessation of smoking, control of alcohol intake and, most importantly, control of body weight. Indeed, recent reports suggest that adopting a healthy diet including decreased intake of added sugars and processed foods, swapping out refined grains for whole grains, increasing fiber intake, increasing intake of fruit and vegetables, avoiding processed red meat and eating healthier fats in the form of oils such as olive oil, walnut oil, flax seed oil and oils from marine fish can improve outcomes and life expectancy of patients with T2D. One example is based on results from the DIRECT project where 149 prediabetic individuals undertook antidiabetic and antihypertensive drug withdrawal, total diet replacement (825–853 kcal/day formula diet for 3–5 months), then stepped food reintroduction (2–8 weeks), and structured support for long-term weight loss maintenance, compared to 149 prediabetic individuals treated with best practice care according to the National Health Service (UK) guidelines as the control group. At 12 months, almost half of participants in the treatment group had achieved remission to a nondiabetic state and were off antidiabetic drugs.

However, when adoption of a healthier lifestyle is not enough for the control of blood glucose levels, pharmacologic treatment is needed. In WSM, metformin is recommended universally as the frontline drug in pharmacological therapy. When metformin is insufficient, as tends to happen over time from first diagnosis, a combination of metformin and other glucose-lowering drugs is used for dual or triple therapy, including sulfonylureas, dipeptidyl peptidase 4 inhibitors, sodium-dependent glucose transporters 2, glucagon-like peptide 1 (GLP-1) receptor agonists, and alpha-glucosidase inhibitors. When such combined therapies are ineffective for the control of hyperglycemia, insulin injections become necessary, usually slow-release insulin. Beyond the control of blood glucose levels, the blood pressure and blood lipid levels of T2D patients also need to be managed.

TCM has been used to treat diabetes for thousands of years with relatively good efficacy. Diabetes-related symptoms were referred to as “Xiaoke” (消渴, meaning consumptive thirst) disease in ancient China.
Four pathological stages of T2D have been defined by the International TCM guidelines for diagnostic and treatment principles of T2D: the stagnation stage, the heat stage, the deficiency stage and the injuring stage, corresponding to the prediabetic or early stage of diabetes, the stage of diabetic attack, the diabetic deterioration stage (the most common stage), and end stage of diabetes (chronic complications). TCM has shown considerable power in treatment of T2D. For example, Tianqi Capsule (天芪降糖胶囊) reduced T2D incidence by 32.1% in the treatment of prediabetes. The principle component of Tian Qi capsule is the root of Panax ginseng and ginsenosides are believed to be the principle bioactives operating to reduce insulin insensitivity (Figure 7). Jinlida Granule (津力达颗粒) significantly improved control of hyperglycemia in T2D patients and again ginsenosides are major constituents of this TCM prescription. Gegen Qinlian Decoction (葛根芩连汤, the principal ingredients of which are glycyrrhizic acid and 4′-deoxyflavones) and Dachaihu Decoction (大柴胡汤) both showed significant anti-hyperglycemic effects in treatment of T2D. The Compound Danshen Dripping Pill (复方丹参滴丸), which contains three medicinal herbs, Salvia miltiorrhiza roots with salvianolic acids U and T as characteristic bioactive ingredients, Panax notoginseng with saponin ginsenosides, and borneol from Heterotheca or Artemisia, has been reported to be effective in the treatment of diabetic retinopathy which is a severe complication of T2D.

Integration of TCM and WSM has shown advantages in treatment of T2D. In an integrated treatment, the Chinese patent medicine, Jinlida Granule, or a placebo were given to two groups of T2D patients who were already taking metformin. After 12 weeks, levels of HbA1c, fasting plasma glucose (FPG), and 2 h postprandial glucose (2-h PG) in the Jinlida Granule plus metformin group were significantly lower than those in the placebo plus metformin group. This indicated that the integrated treatment of Jinlida Granule and metformin was more efficient in the control of blood glucose levels than the monotherapy of metformin. In another study, an integrated treatment of Xiaoxianxiong Decoction (小陷胸汤, principally Gua Lou; Trichosanthes kirilowii fruit also known as Chinese cucumber) and metformin was used to treat phlegm-heat T2D patients for 12 weeks. Metformin alone was used for the control group. The efficacy rate of the treatment group was significantly higher (92.31%) than that of control group (76.92%). Symptom scores, FPG, 2-h PG, total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were significantly lower in the treatment group than in the control group.

FIGURE 7: Extracts of the root of American ginseng represent cooling yin qualities, while Asian ginseng (Panax ginseng) embodies the warmer aspects of yang. (A) Panax quinquefolius—American ginseng (B and C) Asian ginseng (Panax ginseng C. A. Mey) and its root. The photographs were provided by Qiang Wang from the Plant Photo Bank of China (B) and Dr. Linlin Dong from China Academy of Chinese Medical Sciences, China (C). (D) The structure of Ginsenoside Rg1 [Color figure can be viewed at wileyonlinelibrary.com]
lipoprotein cholesterol, and low-density lipoprotein cholesterol (LDL-C) values of plasma were all better in the treatment group than those values in the control group. Therefore, integrated treatment of Xiaoxianxiong Decoction with metformin can improve the control of blood glucose levels and the metabolism of blood lipids for improved therapeutic effects on phlegm-heat in T2D patients.

In the treatment for T2D patients with obesity, a combination of Xiaoshi Zhuyun Decoction (消食助运方) and liraglutide (a GLP-1 receptor agonist) injection was applied in a treatment group, and liraglutide injection alone was used in the control group. After 3 months, improvements in plasma FPG, 2-h PG, and HbA1c levels, and T2D syndrome scores were observed in the treatment group compared to the control group. Adverse reaction rates were lower in the treatment group than in the control group, indicating that the combination of Xiaoshi Zhuyun Decoction and liraglutide had better effects in the treatment of T2D patients with obesity than the monotherapy of liraglutide. The integrated treatment also reduced adverse reactions to liraglutide.

In treatment of T2D patients the effects of Buzhong Shengqing Xieyinhuo compound prescription (补中升清泻阴火复方) combined with insulin injections have been assessed. Buzhong Shengqing Xieyinhuo compound prescription and premixed insulin were given to the treatment group, while a placebo and premixed insulin were given to the control group. After treatment for 12 weeks, plasma FPG, 2-h PG, HbA1c, TG, and LDL-C levels were all lower in the treatment group than those in the control group. The degree of hypoglycemia resulting from overactivity of the injected insulin was also lower in the treatment group than the control group. Fasting insulin levels, the insulin acuity index, and the homeostatic model assessment index for β cell function were all higher in the treatment group than in the control group. Therefore, a combination of Buzhong Shengqing Xieyinhuo compound prescription and insulin could improve the control of blood glucose levels, lipid metabolism, reduce the risk of hypoglycemia, and help in the recovery of β cell function in treatment of more advanced T2D patients. In conclusion, these examples suggest strongly that the integration of TCM and WSM treatments can improve the management and control of T2D.

5 | OUTLOOK

There is mounting evidence that treating human diseases, both infectious and noncommunicable, with therapies that integrate western medicine with TCM can substantially improve outcomes, compared to western medicine alone. It is true that we do not yet know many of the mechanisms by which TCM affects disease and recovery from disease, but this does not mean that we should ignore the benefits of traditional medicine, particularly when integrated with western medicine. Acupuncture carried a stigma similar to that bourn by TCM in the West in the 1970s, before the discovery that acupuncture needles could stimulate the release of β-endorphins and reduce pain. Now use of acupuncture to treat pain is far more widely endorsed.

Although current scientific studies have not established all the mechanisms underlying the beneficial effects of TCM, the methodologies of WSM can shed light on some of the existing problems in the use of TCM. TCM emphasises specific medical materials, which are more widely known as “Daodi” (道地) in Chinese. Genuine or “daodi” medical material is material which has been grown in a specific geographical region and screened for efficacy in accordance with long-term traditional medical practice, usually associated with unique cultivation conditions. These guidelines are reasonable from the perspective of plant science, because most of the bioactive compounds used in TCM are specialised metabolites, and the accumulation of these compounds can be influenced hugely by the environment and cultivation management practices. Therefore, quality control of medical herbs has been a significant issue in the application of TCM, and failures in QC can lead to inefficacy and sometimes, toxicity. To address QC issues, DNA barcoding and chemical fingerprinting are now being used to facilitate compound identification, traceability, and standardisation of medicinal herbs. More recently, machine learning has been shown to be very effective in facilitating compound identification.
introduction of conventional breeding as well as marker-assisted selection and clonal propagation, has improved quality control and availability of medicinal herbs, especially those derived from endangered species.75,76

Similarly, once the mechanisms of action of TCM are better defined, together with greater quality control of prescriptions, it is highly likely that the benefits of TCM will become more widely accepted. Because TCM is an empirical discipline, it is not necessary to believe in its efficacy, to derive benefits. However, if the benefits of integrated TCM and WSM are to be disseminated more widely, there will be an inevitable increase in the demand for TCM practitioners as well as the herbs that are used to make the decoctions, formulas, capsules, granules, and patented medicines.

Consequently far more research is required into the bioactives in TCM prescriptions, their synergies, their dosage windows, any side effects and their mechanisms of action in the human body. Greater research and understanding will lead to more widespread adoption and acceptance of TCM. Further development of Chinese patent medicines, and their integration with WSM will undoubtedly lead to better health outcomes and lower cost burdens on health services across the world.

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