

EVIDENCE-BASED STUDY

Herbal compatibility of Traditional Chinese Medical formulas for acquired immunodeficiency syndrome

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Abstract

OBJECTIVE: Because herbal compatibility is one of the most important reasons why Traditional Chinese Medicine (TCM) formulas are effective for acquired immunodeficiency syndrome (AIDS), our study aimed to determine the compatibility of herbs based on published AIDS clinical research in Chinese periodicals. To achieve this aim, we designed a new data-mining algorithm according to TCM data characteristics.

METHODS: We found 25 clinical AIDS studies, all using Chinese herbs for treatment, in the Traditional Chinese Medicine Database System, and information on diagnosis and treatment was extracted. To find out herbal compatibility, especially the formulae for herbal combinations, we proposed an im-

proved association rule algorithm based on the frequency of combinations. In this algorithm, all the compatibility relationships were displayed in a tree structure, by which the relationship between formulas and their derivation could be clearly inferred.

RESULTS: Data analysis showed that approximately 100 herbs have been used for treating AIDS. Based on the whole herb compatibility tree, we calculated a basic formula for AIDS: Huang Qi combined with Ren Shen, Fu Ling, Bai Zhu, Bai Zhu, Dang Gui, and Bai Shao. This formula, deriving from most of clinical prescriptions, and was chosen by most of clinicians for AIDS treatment. From data mining we found that *Qi* replenishment and detoxification were the main treatment principles, which coincided with the AIDS pathological mechanism in which immune function is destroyed by human immunodeficiency virus (HIV).

CONCLUSIONS: Our data-mining results suggest that the core TCM treatment of AIDS is replenishing *Qi* and detoxification, by which AIDS patients' immune system may be enhanced. Compatibility of Huang Qi with some frequently-used herbs have shown real efficacy in clinical practice, which warrants pharmacological research in the future.

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Key words: Acquired immunodeficiency syndrome; Drugs; Chinese herbal; Chinese medical formula; Data mining

INTRODUCTION

Chinese herbs are becoming increasingly promising in

acquired immune deficiency syndrome (AIDS) treatment, and many clinical studies have been carried out to confirm their efficacy. Because herbal compatibility is one of the most important reasons why TCM formulas are effective for AIDS, our study aimed to determine the compatibility of herbs based on published AIDS clinical research in Chinese periodicals. We designed a data-mining algorithm according to TCM data characteristics. This will be discussed below.

In China, up to the end of 2009 there were approximately 740 thousand people living with HIV or AIDS. Among them, 105,000 were AIDS patients, and the number of newly-diagnosed HIV-infected patients in 2009 was 48,000.¹ The treatment of AIDS with Chinese herbs has been widely adopted. Research has shown that traditional Chinese medicine (TCM) may significantly improve the clinical symptoms of AIDS patients, improve and stabilize immune function, improve the quality of life, and reduce toxicity and side effects of antiviral drugs.^{2,4} A systematic evaluation has also shown that the combined use of antiviral drugs and Chinese herbal medicines may enhance the efficacy of antiviral drugs.⁵ By 2010, the State Administration of TCM had provided free herbal medicine treatment for 10,000 newly-diagnosed AIDS patients (including HIV-infected individuals) in 19 provinces of China, costing a total of approximately 160 million Yuan.⁶

In TCM, the pathogenesis of AIDS consists of two aspects: 1) the external aspect is that the latent pathogen or epidemic toxin injures the original *Qi* (Yuan *Qi*) of the body; and 2) the internal aspect is that the attack of AIDS depends on waxing or waning of the healthy *Qi*.

AIDS in the acute phase or early stage is categorized as pestilence (Wen Yi), with heat toxins or damp-heat turbidity as the pathogenic characteristics. AIDS may show signs and symptoms, such as fever, scrofuloderma and scrofula, throat pain, skin lesions, diarrhea or dry stool, yellow urine, and a red tongue with thick and greasy coating. However, in the late stage or severe cases of AIDS, with the original *Qi* depletion and essence insufficiency as the pathogenic characteristics, it may show signs and symptoms, such as general fatigue, progressive emaciation, spontaneous sweating and/or night sweating, frequent common colds, a tender tongue, and a soft or deep, weak pulse.⁷⁻⁹

The superiority of modern medicine treatment for AIDS is inhibition of virus replication, while Chinese medicine places emphasis on individual assessment, overall regulation, and syndrome differentiation, to promote recovery of immune function, improve clinical symptoms, and control the opportunistic infection. Drug tolerance is relatively low in use of Chinese herbal medicines, which may have fewer side effects, and are available in remote rural areas. Chinese medicinal herbs may improve non-CD4+ cell immunity and extend the asymptomatic period of AIDS, and can also

enhance the efficacy of antiviral drugs, or provide treatment for those patients who cannot receive antiretroviral therapy. In addition, Chinese medicine may reduce the high cost for public health care in China.¹⁰

MATERIALS AND METHODS

Retrieval of literature and data extraction

The on-line Traditional Chinese Medicine Database System was developed by the Institute of Information on Traditional Chinese Medicine, China Academy of Chinese Medical Sciences. This system has information from 1949 up to the present date, consisting of over 100 categories of Chinese Medicine databases and more than 1,100,000 items of data.¹¹ The on-line Traditional Chinese Medicine Database System was used to identify the keywords "AIDS" or "acquired immunodeficiency syndrome". The documents searched included clinical trials, controlled clinical trials, randomized controlled trials, clinical literature, and multi-center studies, but did not include experimental research, meat analysis, historical documents, evaluation studies, review literature, and symposiums. We found a total of 28 documents,¹²⁻³⁹ among which 3 were repeated publications. A final total of 25 clinical studies were retrieved. All of these studies involved treatment for AIDS, and all of them included the use of Chinese herbs and the therapeutic results all proved effective.

To analyze herbal compatibility, information on the diagnosis and treatment was extracted from the literature, such as research title, case number, therapeutic results, TCM syndrome, symptoms, therapy strategy, and herbs, which were collected to establish a database for further data analysis.

Herbal Compatibility

Approximately 2000 years ago, TCM began using formulas (combinations of herbs) to treat diseases, and got gradually improved curative effects with herbal compatibility improvement. Herbal compatibility that has a curative effect for certain diseases or syndromes is recorded as a formula. Currently, there are more than 10,000 TCM formulas, and an increasing amount of formulas are developed in clinical practice.¹¹

For commonly-used herbal combinations usually have a close connection with the essence of the disease, therefore, they can be regarded as basic formulas, and they are effective in most cases. An increasing amount of target-specific prescriptions have been developed for different patients. We hypothesize that if a basic formula exists, consensus on effective therapy exists in clinical practice. This suggests that a basic formula may be recommended in the treatment of disease in most cases.⁴⁰

Algorithm

The composition of herbs into formulas is based on the following rules: 1) several important herbs are chosen as the basic formula according to the essence of the disease; and 2) modifications (additions and subtractions) are made depending on the individual specific signs and symptoms, and different stage of the disease. To find out herbal compatibility, we proposed an improved association rule algorithm, which was designed mainly according to the frequency of the herbs and their combinations. All the combinations formed a matrix of herbs, and the most frequently appearing herb was calculated out as a root of all herbal combinations.

The other herbs were continuously calculated in the same way to select the next root, until no repeated herb was present at the end of calculations. Therefore, the compatibility relationships were displayed in a tree structure, by which the relationship of the formulas and their derivation was able to be determined.⁴⁰

RESULTS

Herbal Compatibility for AIDS

The tree structure of the herbs for the 25 AIDS formulas is shown in Figure 1.

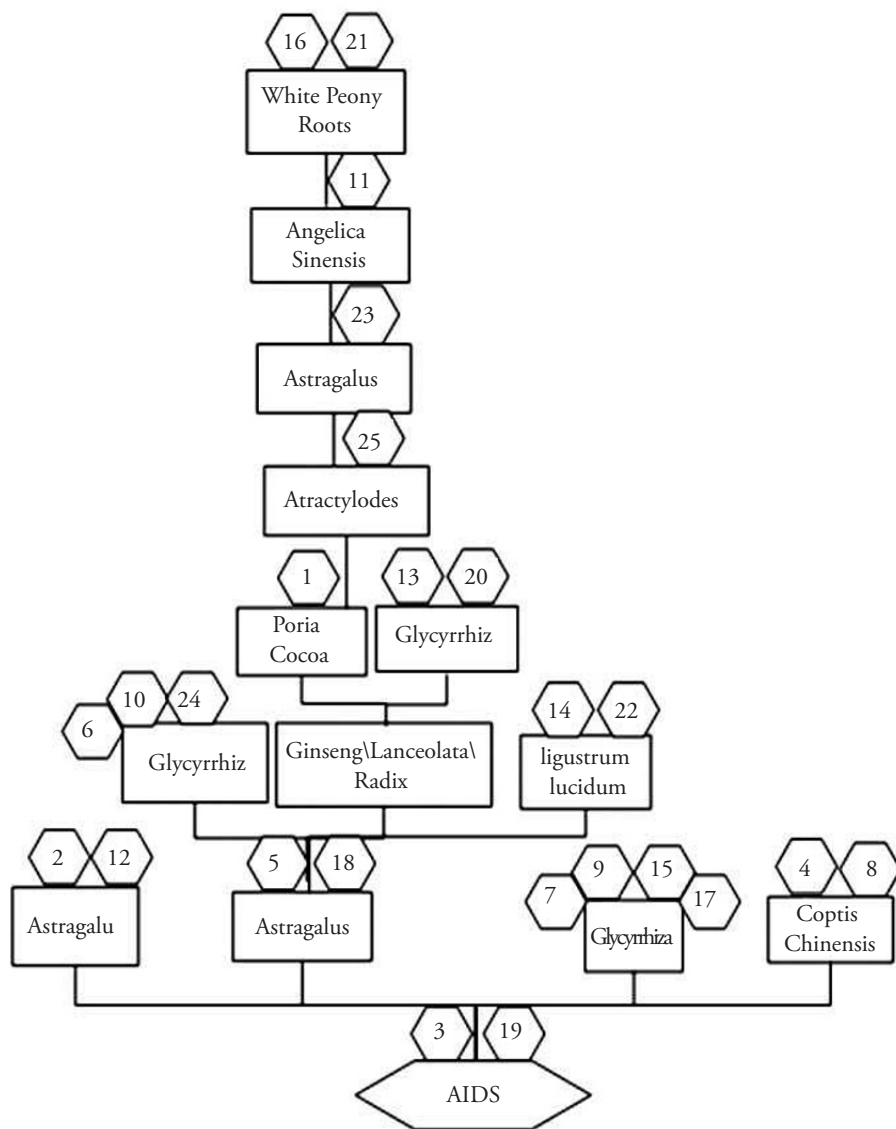


Figure 1 Herbal Compatibility of TCM Formulas for AIDS

The numbers 1 to 25 represent different formulas

The tree structure diagram displays the main compatibility relations of TCM formulas for treating AIDS. The figure shows the following trunk: Huang Qi (Radix Astragali) → Ren Shen (Radix et Rhizoma Ginseng) → Fu Ling (Poria) → Bai Zhu (Rhizoma Atractylodis Macrocephalae) → Bai Zhu (Radix Scutellariae) → Dang Gui (Radix Angelicae Sinensis) → Bai Shao (Radix Paeoniae Alba). Six branches were as follows: Huang Qi → Gan Cao (Radix et Rhizoma Glycyrrhizae), Huang Qi → Nv Zhen Zi (Fructus Ligustri Lu-

cidii), Huang Qi → Ren Shen → Gan Cao, Bai Zhu, Gan Cao, and Huang Lian.

As shown in Figure 1, on the Huang Qi node, there were 15 formulas, while 10 other formulas lay on branches beside the truck. The concentrated distribution of formulas suggested some consensus on the treatment of AIDS with Chinese herbs. With this formula tree, we were able to identify all of the compatibility relationships located at the trunk, and they were all related to Huang Qi (Table 1).

Table 1 Main herbs in AIDS formulas and their compatibility

No.	Compatibility and Combination	Support
1	Huang Qi, Ren Shen	8/25
2	Huang Qi, Ren Shen	6/25
3	Huang Qi, Ren Shen, Fu Ling, Bai Zhu	5/25
4	Huang Qi, Ren Shen, Fu Ling, Bai Zhu, Huang Qin	4/25
5	Huang Qi, Ren Shen, Fu Ling, Bai Zhu, Huang Qin, Dang Gui	3/25
6	Huang Qi, Gan Cao	3/25
7	Huang Qi, Ren Shen, Gan Cao	2/25
8	Huang Qi, Nv Zhen Zi	2/25
9	Huang Qi, Ren Shen, Fu Ling, Bai Zhu, Huang Qin, Dang Gui, Bai Shao	2/25

Notes: The most frequently used herb in the 25 formulas was Huang Qi (15/25 = 60%). Compatibility with Huang Qi led to a basic skeleton formula, and all the clinical formulas for AIDS originated from it.

Treatment strategy compatibility

Although we identified the basic skeleton formula for AIDS, some different herbs are used for the same treatment strategy, so they should be analysed in strategy level for getting more synthetical conclusion,. In the tree diagram shown in Figure 2, herbs are replaced by

treatment strategies based on the same algorithms.

The tree diagram showing the treatment principles for AIDS, being more nodes concentrated, forming two trunks, derived from detoxification and replenishing Qi as the starting node. The supportability of every strategy and their compatibility is shown in Table 2.

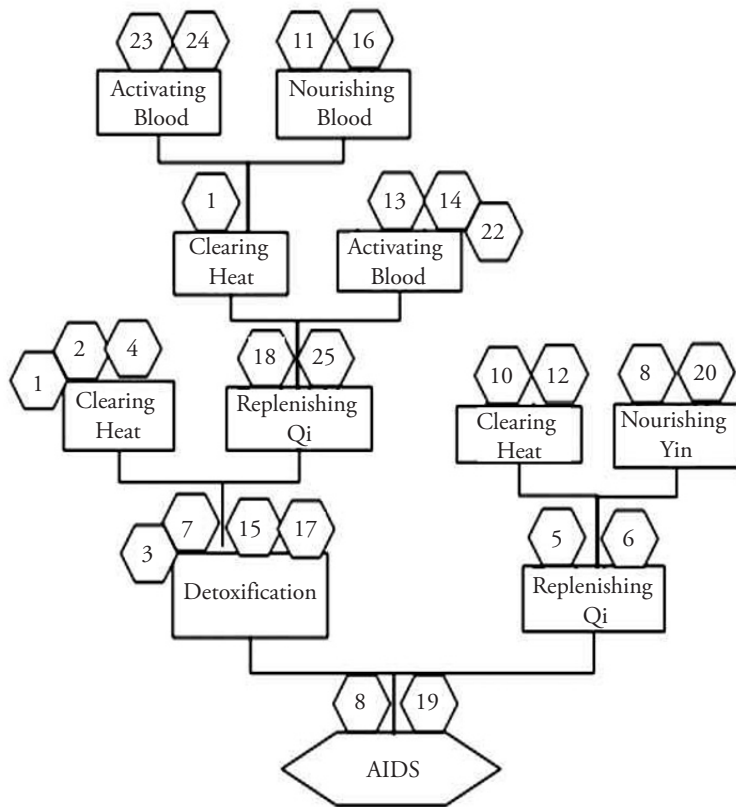


Figure 2 Tree chart of Chinese herbal treatment strategies for AIDS

Table 2 The compatibility of strategies for treating AIDS

No.	Compatibility and Combination	Support
1	Detoxification	17/25
2	Replenishing Qi	16/25
3	Detoxification and Replenishing Qi	10/25
4	Detoxification and clearing heat	8/25
5	Replenishing Qi and clearing heat	7/25
6	Detoxification, Replenishing Qi, and clearing heat	5/25
7	Replenishing Qi and nourishing yin	5/25
8	Detoxification, replenishing Qi, and activation of blood	3/25
9	Detoxification, Replenishing Qi, clearing heat, and activation of blood	2/25
10	Detoxification, Replenishing Qi, clearing heat, and nourishing blood	2/25

DISCUSSION

Currently, although modern medicine has made great progress in AIDS basic research and clinical treatment, AIDS still threatens human health. TCM, as an ancient medical science, may be effective for immune regulation and whole-body function improvement for AIDS patients. Over the past 20 years of TCM treatment for AIDS, treatment has progressed for individual patients to large-scale clinical trials, as well as TCM clinical knowledge and experience in AIDS treatment, and its therapeutic effects, have gradually been recognized worldwide.

The efficacy of single-herb treatment for AIDS is much lower than that of western medicine, but through herbal compatibility, TCM formulas may significantly enhance the effectiveness and increase the range of applications. Therefore, herbal compatibility is important for treatment. The current study used a new method of analysis for TCM data, and determined how TCM should be used to treat AIDS.

Qi, an invisible substance within the body, applies to normal physiological functions, including immunity. Toxin, generally referring to a strong pathological substance, severely affects the body, especially in time of *Qi* insufficiency. For AIDS patients, an opportunistic infection (toxin) occurs after the immune system (*Qi*) deteriorates. In the current study, from data mining, we found that replenishing *Qi* and detoxification were the main treatment principles, which coincided with the AIDS pathological mechanism that immune function is destroyed by HIV.

The current study also found in calculating that the basic formula for AIDS that Huang Qi combined with Ren Shen, Fu Ling, Bai Zhu, Bai Zhu, Dang Gui and Bai Shao yielded most of the clinical prescriptions, which represents most clinicians' consensus for AIDS treatment. This basic formula functions by activating *Qi* of the lung and spleen, nourishing *yin* and blood, and detoxification. In the future, more pharmacological research maybe is required to confirm the mechanism of basic formula coming from clinical trials, and new drug development also needs to take into consideration herbal compatibility and treatment strategies, because TCM theory and practices are still the foundation of TCM resource mining.

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