



# Characterizing Approaches and Research Methods for Traditional Chinese Medicine Syndrome Differentiation and Treatment in Chronic Liver Diseases

Jasmine Ma<sup>1</sup>, Yiyu Lu<sup>2</sup> and Shi-Bing Su<sup>2\*</sup>

<sup>1</sup>Rehabilitation College, Fujian University of Traditional Chinese Medicine, Fuzhou, Fujian, 350122, China

<sup>2</sup>Institute of Interdisciplinary Integrative Medicine Research, Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China

\*Corresponding author: Shi-Bing Su, Institute of Interdisciplinary Integrative Medicine Research, Shanghai University of Traditional Chinese Medicine, Shanghai, 201203, China; shibingsu07@163.com.

Received: 📅 September 24, 2021

Published: 📅 October 07, 2021

## Abstract

TCM syndrome (a.k.a., ZHENG or Zheng-Hou) is the foundation of clinical diagnoses and treatments for chronic liver diseases (CLDs) in traditional Chinese medicine (TCM). This Mini-Review introduces research approaches and methods for TCM syndrome differentiation and treatment, including Top-Down, Bottom-Up and Integration approaches. It then summarizes a variety of applications of these methods to help guide the development of more accurate and advanced TCM diagnosis and treatment in CLDs.

**keywords:** TCM syndrome differentiation and treatment; Research approaches; Methods; Chronic liver diseases

## Abbreviations

TCM: traditional Chinese medicine

CLD: chronic liver diseases

AI: artificial intelligence

## Introduction

Traditional Chinese medicine (TCM) syndrome (a.k.a., ZHENG or Zheng-Hou), "in essence, is a characteristic profile of all clinical manifestations that can be identified by a TCM practitioner." TCM syndrome is the differentiation of the symptoms and signs of patients, reflecting the overall pathological state including the etiology, disease location and pathogenesis of a certain stage of the body during the disease process [1]. As TCM syndrome is the external manifestation of the internal changes associated with the disease, it reflects the overall state of the body and has its own integrity, while the external symptoms and signs are constantly changing with the disease's occurrence and development, reflecting the complex characteristics of uncertainty and human-made factors.

TCM syndrome differentiation is the process of recognizing syndromes, which then guides the practitioner to determine the corresponding treatment method. Considering the limits to the

rational understanding and behavior of both doctors and patients, TCM syndrome differentiation and treatment is a complex, dynamic, nonlinear system. This review aims to summarize three primary approaches to TCM syndrome in the chronic liver diseases (CLDs), including research needs in these areas, as follows:

### "Top-Down" Approach Based on Holism, System Theory and Cybernetics

The human brain can make reasonable decisions through limited rationality and some information. This kind of approach is known as "control" or "expert system", it has been applied in research of TCM, called "TCM expert system" [2,3]. With the rapid development and popularization of big data, artificial intelligence (AI) and modern engineering technologies such as highly sensitive sensors, wearable equipment, drug release and intervention systems, etc., a new generation of "TCM expert system" as the

intelligent system with human-machine combinations of TCM diagnosis and treatment can be expected. This new approach will be characterized by the application of reliable means of information collection and processing, recognition of the human body's functional states, and automatic knowledge acquisition ability, combined with deep model and deep reasoning mechanisms.

### “Bottom-Up” Approach Based on Reductionism And Systematic Combination

By clarifying various elements of the complex system of TCM, system integration can be carried out “from bottom to top” by using reductionist methods. These methods could include systems biology [4-6], network pharmacology [7], system pharmacology [8] and clinical TCM syndrome pharmacology [9] including high-throughput detection of omics such as genomics, transcriptomics, proteomics, metabolomics, and metagenomics, bioinformation analysis and integration, modeling, system simulation and system dynamics research.

### “Integration” Approach Based on The Integration of Reductionism, Holism, and System Theory

The two approaches of “Top-down” and “Bottom-up” can also be combined, leading to a third approach of “Integration” of the methods of reductionism, holism, and system theory. The concept here is that the study of TCM syndrome differentiation and treatment should not only cover system integration and its impact on the whole system's dynamic evolution, but also investigate the relationship among each element in its impact overall. That includes searching within the complex system for “sensitive points” or “targets” which can lead the practitioner to “characteristic” or “key points”, or simple rules or heuristics to clarify or change the status of the system [10]. Applications of the three categories above can lead to a rich variety of approaches and technologies, yielding promising new research methods for TCM syndrome differentiation and treatment in CLDs including.

- a) TCM syndrome diagnosis and/or treatment methods based on AI-based TCM assistive diagnostic system [11], and TCM expert system in chronic hepatitis [12].
- b) TCM syndrome identification methods based on omics technologies [13], including proteomic, transcriptomic, metabolomic and bioinformatic analysis in hepatitis B and hepatitis B-caused cirrhosis [14-17], and dynamic network biomarkers in chronic hepatitis B [18].
- c) Efficacy evaluation methods of TCM individualization treatment based on molecular classification of “Disease-Syndrome” in hepatitis B-caused cirrhosis [16].
- d) Evaluation methods of clinical TCM syndrome pharmacology in hepatitis B-caused cirrhosis based on genomic [16], transcriptomic [17] and metabolomic analysis [18].
- e) Comprehensive analysis methods for Chinese herbal formulae with multi-compounds, multi-targets and multi-effects in the

treatment of liver fibrosis [19, 20] and chronic liver disease [21] based on system or network pharmacology.

- f) Methods for the composition and compatibility of Chinese herbal medicine or formulae in liver cancer [22].
- g) The overall evaluation method of TCM syndrome differentiation and treatment based on biological big data mining in hepatitis B-caused cirrhosis [23], etc.

This compilation of methods provides new approaches for the further development of accurate TCM diagnosis and treatment using biological big data and TCM information. Particularly, with the rapid development of AI-assisted system as a non-invasive diagnostic test in the prediction, diagnosis and treatment of CLDs [24-26], which were used to predict liver fibrosis, cirrhosis, non-alcoholic fatty liver disease, and differentiation of benign tumors from hepatocellular carcinoma etc., it provides the valuable references for developing the TCM intelligent diagnosis and treatment methods in CLDs.

### Declarations

### Author contributions

SBS contributed conception and design of the review; JM wrote the first draft of the manuscript; All authors contributed to manuscript revision, read and approved the submitted version.

### Conflicts of interest

The authors declare that they have no conflicts of interest.

### Ethical Approval

Not applicable.

### Consent To Participate

Not applicable.

### Consent To Publication

Informed consent to publication was obtained from relevant participants.

### Availability of data and materials

Not applicable.

### Funding

Not applicable.

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DOI: [10.32474/OAJCAM.2021.03.000167](https://doi.org/10.32474/OAJCAM.2021.03.000167)



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