

Key words: Omics technology; Genomics; Transcriptomics; Proteomics; Metabolomics; TCMs; Symptoms,

Genomics With the development of genetic science, disease has been linked to the abnormal expression of genes. Plenty of researches have linked TCM syndromes to mutations and abnormal expression of some genes. In the research of coronary heart disease, Xue et al. was found blood-stasis “ZHENG” is relate to the polymorphism of platelet activation genes and angiotensin converting enzyme genes [1,2]. Fang et al. consider that the relationships between the polymorphism of apolipoprotein E ApoE) genes and phlegm-stasis “ZHENG” is existed. Numerous studies have demonstrated the association between TCM “ZHENG” and abnormal expression of gene.

Transcriptomics and proteomics Transcriptomics and proteomics are the extension of genomics. Using transcriptomics, Liu et al. have discovered that the qi-yin deficiency patient comparison with healthy persons identified 113 mRNAs-41 enhanced and 72 decreased. Functional genetic analysis of the mRNAs indicated that two TCM syndromes were correlated with cell apoptosis, immune inflammatory responses, and lymphocyte activation [3]. Transcriptomics show the transcription abnormalities of genes. Proteomics is used to analysis the protein expression profiling of syndromes.

Metabolomic The essence of “ZHENG” is the metabolic or network alteration and this altered phenotype is objectively reflected by changes in the expression profile of endogenous metabolic components in the blood or urine [4]. Metabolomics can elucidate the diagnosis of TCM “ZHENG” by exploring terminal product. Wang and his coworkers used UPLC-Q/TOF-HDMS combined with pattern recognition methods to investigate a comprehensive metabolome of YangHuang syndrome (YAH) and YinHuang syndrome (YIH) [5]. Results indicate that Vitamin B6 metabolism, Tryptophan metabolism, Arginine, and Proline metabolism were the top functions listed by MetaboAnalyst3.0 for YAH patient. 40 metabolites were identified as potential candidates for biomarkers[6].

Conclusion In this review, we delineate and discuss the application of omic technologies in TCM syndrome Differentiation. Omic technologies illustrate the essence of the syndrome from different perspectives. Many pathogenic genes and metabolic markers of symptoms have been found. To clarify the essence of “ZHENG” and use a more effective way to classify TCM syndrome is conducive to the precise treatment of Chinese medicine. In a word, we hope this approach will not only narrow the gap between mainstream medicine and TCM but also develop the unique advantages of traditional Chinese medicine treatment.

Reference

- [1]. Xue M, Chen K J, Yin H J. Relationship between platelet activation related factors and polymorphism of related genes in patients with coronary heart disease of blood-stasis syndrome. *Chinese Journal of Integrative Medicine*, 2008, 14(4):267.
- [2]. Mao Y L, Yuan Z K, Huang X P, et al. [Study on relationship between the polymorphism of angiotensin converting enzyme gene and blood stasis syndrome in patients with coronary heart disease]. *Zhongguo Zhong Xi Yi Jie He ZaZhi*, 2004, 24(9):776-780.
- [3]. Liu S, Chen Y, Xie S, et al. Gene Expression Profiles of HIV/AIDS Patients with Qi-Yin Deficiency and Dampness-Heat Retention. *Journal of Alternative & Complementary Medicine*, 2016, 22(11):865-879.
- [4]. Zhang A. Potential role of metabolomics approaches in the area of traditional Chinese medicine: as pillars of the bridge between Chinese and Western medicine. *Journal of pharmaceutical and biomedical analysis*, 2011, 55(5):859-68.
- [5]. Wang X, Zhang A, Han Y, et al. Urine metabolomics analysis for biomarker discovery and detection of jaundice syndrome in patients with liver disease. *Molecular & Cellular Proteomics Mcp*, 2012, 11(8):370.
- [6]. Zhang A H, Sun H, Qiu S, et al. Recent highlights of metabolomics in chinese medicine syndrome research. *Evidence-based Complementary and Alternative Medicine*, 2013, 2013(8):402159.

APPLICATIONS OF CHINMEDOMICS IN TRADITIONAL CHINESE MEDICINE FOR RAPID DISCOVERY OF BIOACTIVE COMPONENTS

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Abstract Chinmedomics, a unique, holistic, scientific method of traditional Chinese medicine (TCM) research, by integrated serum pharmacology of TCM with metabolomics technology, made a great contribution to elucidate the therapeutic and synergistic properties and efficacy material base on TCMs. The active constituents were screened using the plotting of correlation between biomarkers and constituents absorbed in blood serum after oral administration of a formula (PCMS), and is ongoing verification by further biological experiments. PCMS, used to clarify the active ingredients and synergistic properties, was successfully applied for rapid discovery of potentially bioactive components from TCM. Through a series of formulas studies on the Chinmedomics, it proved that the established method could help to explore the effective substance for further research of TCM and is the best method to fit the holistic concept of TCM as a new research approach. This critical review covers the research achievements of “Research Center of Chinmedomics State Administration of TCM” in innovative drug from serious of formulas include Yinchenhao Tang, Kaixin San, Shengmai San, Liuwei Dihuang Wan, Shaoyao-Gancao decoction, ShenQiWan, Wen Xin Formula, Zi Shen Wan, AS1350, Shuanghuanglian formula, et al.

Key words: Chinmedomics, pharmacology, PCMS, TCM, formula, bioactive components, UPLC-ESI-Q-TOF-MS

1. Formation of Chinmedomics Theory Finding a strategy for evaluating effectiveness of TCM is full of hardships for its complex constituents. Based on such problems, Chinmedomics, by integrated serum serum pharm-chemistry[1] of TCM with metabolomics technology, is a unique method of TCM research, made outstanding contributions in solving international concerns such as the effectiveness and security aspects of TCM. The correlation between the endogenous biomarkers of syndrome and exogenous constituents of formulation is analyzed to find the highly associated compounds as the effective substances, and further clarifying their activities, and may discover lead compounds.

2. Applications of Chinmedomics in Bioactive Components of Formulas This article introduces and reviews the concept of chinmedomics, and highlights recent examples of the approach, such as potentially bioactive components and metabolites of Kaixin San, [2] Shengmai San, [3] Liuwei Dihuang Wan, [4] Shaoyao-Gancao decoction, [5] ShenQiWan, [6]Wen Xin Formula, [7] Zi Shen Wan, [8]AS1350,[9] and Shuanghuanglian formula by integrating UPLC-ESI-Q-TOF-MS technique and MetaboLynx data processing method and multivariate statistical analysis. We also conclude that chinmedomics is a powerful and versatile tool for both biomarker discovery and exploring the complex relationships between biological pathways and drug response, highlighting insights into drug discovery.

References

- [1] Wang, X. J. Progress and future developing of the serum pharmacology of traditional Chinese medicine. *Zhongguo Zhong Yao Za Zhi* 31, 789–792 (2006).
- [2] Hui Sun, Chang Liu, Aihua Zhang, Ying Han, Guangli Yan, Ping Wang and Xijun Wang. Rapid discovery and global characterization of multiple constituents from Kai-Xin-San using an integrated MSE data acquisition mode strategy based on ultra-performance liquid chromatography coupled to electrospray ionization/quadrupole-time-of-flight mass spectrometry†*Anal. Methods*, 2015, 7,279-286.
- [3] Shengwen Lu, Aihua Zhang, Hui Sun, Guangli Yan, Ying Han, Xiuhong Wu and Xijun Wang. Ultra-performance liquid-chromatography with tandem mass spectrometry for rapid analysis of pharmacokinetics, biodistribution and excretion of schisandrin after oral administration of Shengmaisan. *Biomedical Chromatography*. *Biomed Chromatogr.* 2013 Dec;27(12):1657-63.
- [4] Ping Wang, Haitao Lv, Aihua Zhang, Hui Sun, Guangli Yan, Ying Han, Xiuhong Wu, Xijun Wang. Improved ultra-performance liquid chromatography with electrospray ionization quadrupole-time-of-flight high-definition mass spectrometry method for the rapid analysis of the chemical constituents of a typical medical formula: Liuwei Dihuang Wan. *J. Sep. Sci.* 2013, 36, 3511–3516.
- [5] Quanwei Yin, Ping Wang, Aihua Zhang, Hui Sun, Xiuhong Wu, Xijun Wang Ultra-performance LC-ESI/quadrupole-TOF MS for rapid analysis of chemical constituents of Shaoyao-Gancao decoction. *J. Sep. Sci.* 2013, 36, 1238–1246.
- [6] Xiaohang Zhou, Aihua Zhang, Liang Wang, Yunlong Tan, Guanli Yan, Ying Han, Hui Sun, Xijun Wang. Novel chinmedomics strategy for discovering effective constituents from ShenQiWan acting on ShenYangXu syndrome. *Chin J Nat Med.* 2016 Aug; 14(8):561-81.
- [7] Hongxin Cao, Aihua Zhang, Fangmei Zhang, Qinqin Wang, He Zhang, Yanhua Song, Ying Zhou, Hui Sun, Guangli Yan, Ying Han, Xijun Wang. Ultra-performance liquid chromatography tandem mass spectrometry combined with automated MetaboLynx analysis approach to screen the bioactive components and their metabolites in Wen-Xin-Formula. *Biomed. Chromatogr.* (2014).
- [8] Xianna Li, Zhang, Hui Sun, Di Zou, Xijun Wang. Rapid discovery of absorbed constituents and metabolites in rat plasma after the oral administration of Zi Shen Wan using high-throughput UHPLC-MS with a multivariate analysis approach. *J Sep Sci.* 2016 Dec;39(24):4700-4711.
- [9] Qi Liu, Aihua Zhang, Liang Wang, Guangli Yan, Hongwei Zhao, Hui Sun, Shiyu Zou, Jinwei Han, Chung Wah Ma, Ling Kong, Xiaohang Zhou, Yang Nan, Xijun Wang. High-throughput chinmedomics-based prediction of effective components and targets from herbal medicine AS1350. *Sci Rep.* 2016 Dec 2;6:38437.

DRUG RELEASE BEHAVIOR OF COLLOIDAL PHASE IN BAI-HU-TANG

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Abstract The colloidal phase in Bai-Hu-Tang of the classical prescription may have a better antipyretic effect. In order to make the colloidal phase apply to clinical treatment, this paper reviews drug release behavior of the colloidal phase from the theoretical level by referring to the relevant books and summarizing the literature in recent years.

Key words: Bai-Hu-Tang, Colloidal Phase, Drug release behavior

Decoction is one of the most common traditional Chinese medicine compound dosage forms, and its group is complex. The various components may be dispersed with dispersed particles of different sizes in the dispersion medium to form a complex dispersion system which includes solution, colloid, emulsion and suspension, namely a mixed dispersion system [1]. The existence of mixed dispersion system in Dang-Gui-Bu-Xue-Tang [2] and Ma-Xing-Shi-Gan-Tang [3] has been confirmed. Bai-Hu-Tang (BHT) is a heat-clearing prescription in “Shang Han Lun” and also includes mixed dispersion system. It has been speculated that the colloidal phase (multi-component nanodisperse) in the BHT may have a better antipyretic effect. In view of this, this paper reviews the drug release behavior of the colloidal phase in BHT from the theoretical level.

Studies have shown that colloidal particles in the decoction are in the nanometer level and with the characteristics of nano drug delivery system [4]. To some extent, it can be seen that the colloidal particles in BHT may be a special structure of nano drug carrier solid colloidal particles which is free assembled between the effective components and the non-pharmacological components [5]. Therefore, the drug release behavior of the colloidal particles formed during the decoction of BHT may be similar to that of modern nanoparticles. The drug release process may be accomplished by surface desorption, particle diffusion, polymer diffusion, swelling and dissolution [6].

Firstly, the colloidal particles with large specific area and charge have strong adsorption. The particles adhered