Benefit Clarification of Longxuetongluo Capsule Towards Ischemic Stroke Rats by ischemic stroke rats by LC MS/MS Based Metabolomics

Sun Jing  
Beijing University of Chinese Medicine

Xianyang Chen  
Bao Feng Biotech

Bei Fan  
Chinese Academy of Agricultural Sciences

Bo Pan  
Beijing University of Chinese Medicine

Jiani Liu  
Chinese Academy of Agricultural Sciences

Xiaonan Chen  
Beijing University of Chinese Medicine

Jiao Zheng  
Beijing University of Chinese Medicine

Pengfei Tu  
Beijing University of Chinese Medicine

Jiarui Han  
Bao Feng Biotech

Yuelin Song  
Beijing University of Chinese Medicine

Li Jun (📧 drlj666@163.com)  
Modern Research Center for Traditional Chinese Medicine, School of Chinese Materia Medica, Beijing University of Chinese Medicine, Beijing 100029, China

Research

Keywords: Longxuetongluo Capsule, UHPLC-Q Exactive MS, Phenolic compounds, Metabolomics, Middle cerebral artery occlusion

DOI: https://doi.org/10.21203/rs.3.rs-141958/v1
Abstract

Background:

Longxuetongluo Capsule (LTC) that was prepared from the phenolic compound cluster of Chinese dragon's blood, has been clinically utilized for years towards ischemic stroke. However, its therapeutic mechanisms remain unclear. The present study aimed to evaluate the therapeutic effect and to explore the underlying mechanisms of LTC on ischemic stroke rats characterized by cerebral ischemia reperfusion injury.

Method:

Ischemic stroke rats were simulated by middle cerebral artery occlusion and validated by the assays in terms of histological and behavioral assessments. The plasma metabolome comparisons amongst different groups were conducted by UHPLC Q Executive MS in combination with subsequent multivariate statistical analysis, aiming to finding the molecules in respond to the surgery or LTC treatment.

Result:

Intragastric administration of LTC significantly decreased not only the neurobehavioral abnormality scores but also the cerebral infarct area of MCAO rats. A total of 21 potential biomarkers related to ischemic stroke were observed, and 18 biomarkers (such as LysoPC, PE, SM, N1-Methyl-4-pyridone-3-carboxamide, PE (24:1/18:3 etc.) were selected after Youden index >0.7. The results showed that LTC was beneficial to ischemic stroke rats induced by ischemia reperfusion injury by Glycerophospholipid metabolism, Glycosylphosphatidylinositol (GPI) anchor biosynthesis, Nicotinate and nicotinamide metabolism and Sphingolipid metabolism.

Conclusion:

The present study could provide evidence that metabolomics, as a systematic approach, revealed its capacity to evaluate the holistic efficacy of TCM, and investigate the molecular mechanism underlying the clinical treatment of LTC on ischemic stroke.

Full-text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.

Figures
Figure 1

HE, Neun and Tunel observed the anti inflammatory effects of LTC a) shows HE staining; (b) shows NeuN labeled neurons(brown); TUNEL reaction(c). The arrows show TUNEL positive cells (brown).
Figure 2

Infarct regions and neurobehavioral disability restored by LTC treatment, revealed by TTC (2,3,5 triphenyltetrazoliumchloride) staining and neurological scores: TTC staining of brain (a), infarct area (b), neurological deficit score measurement on day 2 after MCAO (c), neurological deficit score measurement on day 7 after MCAO (d).
Figure 3

Representative total ion current chromatograms (TICs) of plasma samples derived from the different groups in RPLC -(+) ion
Figure 4

Scores plot from PCA 353 model for sham, sham+LTC, MCAO, and MCAO+LTC groups in RPLC -(+) ion mode.
Figure 5

Scores plot (a) a), permutation test (b), and S plot (c) from OPLS DA analysis of LC MS data in RPLC -(+) ion mode for MCAO and MCAO+LTC groups.
Figure 6

Ingenuity pathway analysis based on the 18 lipid metabolites with higher diagnostic performance (AUC 0.70). The p value (y axis) was represented by the color of the circle and the pathway impact (x axis) was indicated by the size of the circle. The involved pathways of the circles are indicated.
Figure 7

Network of the remarkably perturbed metabolic pathways by MetScape analysis. The red hexagons represent different lipid metabolites identified in our study. Pink is an unidentified metabolite in our study. The purple circle represents related genes. Green squares represent the enzymes participating in the reaction.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile120210103.pdf