POTENTIAL INTERACTIONS OF CARDIOPROTECTIVE CHINESE HERBS WITH ANTIRETROVIRAL DRUGS: A SYSTEMATIC REVIEW OF IN VITRO STUDIES

Authors:
Cheng WJ[1], Jaworowski A[1,2], Trevillyan JM[3,4], Hearps AC[2,4,5], Xue CC[1,6], Zhang AL[1]

Affiliations:
[1] School of Health and Biomedical Sciences, Royal Melbourne Institute of Technology (RMIT) University, Bundoora, Australia
[2] Life Sciences Discipline, Burnet Institute, Melbourne, Australia
[3] Department of Infectious Diseases & Immunology; Clinical Virology and HIV Services, Austin Health, Melbourne, Australia
[4] Department of Infectious Diseases, University of Melbourne, at the Peter Doherty Institute of Infection and Immunity, Melbourne, Australia
[5] Department of Infectious Diseases, Alfred Hospital, Monash University, Melbourne, Australia
[6] Guangdong Provincial Academy of Chinese Medical Sciences, Guangzhou, China

Background:
People with HIV (PWH) remain at increased risk of cardiovascular disease (CVD) despite successful antiretroviral therapy (ART). Chinese herbal medicine offers potential as an alternative to statins for reducing CVD risk, but interactions of specific herbs with ART, particularly drug metabolism, are not well understood. We conducted a systematic review to evaluate preclinical evidence on these interactions.

Methods:
A Chinese herbal formula, CVD1, has been designed based on demonstrated anti-inflammatory and cardioprotective properties of selected herbs. We conducted a systematic review to evaluate the safety of CVD1 in PWH receiving ART, focusing on potential herb-drug interactions with cytochrome P450 (CYP) enzymes involved in antiretroviral drug metabolism. Peer-reviewed studies in English or Chinese were included, focusing on CVD1's component herbs *Salvia miltiorrhiza*, *Astragalus*, *Atractylodes macrocephala*, *Angelica sinensis*, *Chuanxiong*, and *Glycyrrhizae*. Searches were performed on Medline, Embase, Scopus, and CNKI databases. Risk of bias was assessed using SciRAP2.1, and studies were categorized by methodology, focusing on enzyme induction or inhibition in human cell lines and liver microsomes.

Results:
From 426 reports, 24 studies met our eligibility criteria. Most studies adhered to best methodological practices, though reporting details could be improved. Overall risk of bias was low. *Salvia miltiorrhiza* and *Glycyrrhizae* were the most frequently studied herbs. "No effect" was the most common outcome (61% for *Salvia miltiorrhiza*, 37% for *Glycyrrhizae*, 47% for *Angelica sinensis*, and 67% for *Astragalus*). *Salvia miltiorrhiza* had minimal impact on CYP3A4 activity, while *Glycyrrhizae* may inhibit CYP3A4 activity. Other herbs showed tendencies toward CYP3A4 induction.

Conclusion:
Data suggests co-prescribing *Salvia miltiorrhiza* with ART is safe, particularly with non-nucleoside reverse transcriptase inhibitors, pharmacokinetic enhancers, and

protease inhibitors. Caution is advised with other herbs. Further research is needed on whole formula extracts to clarify herb-drug interactions. This review provides insights into evaluating the safety of herbal products with ART.
(300words)

Disclosure of Interest Statement:
The project is funded by RMIT University and the OpalGate Foundation for a PhD scholarship to Cheng WJ. The authors declare no conflicts of interest.