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

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The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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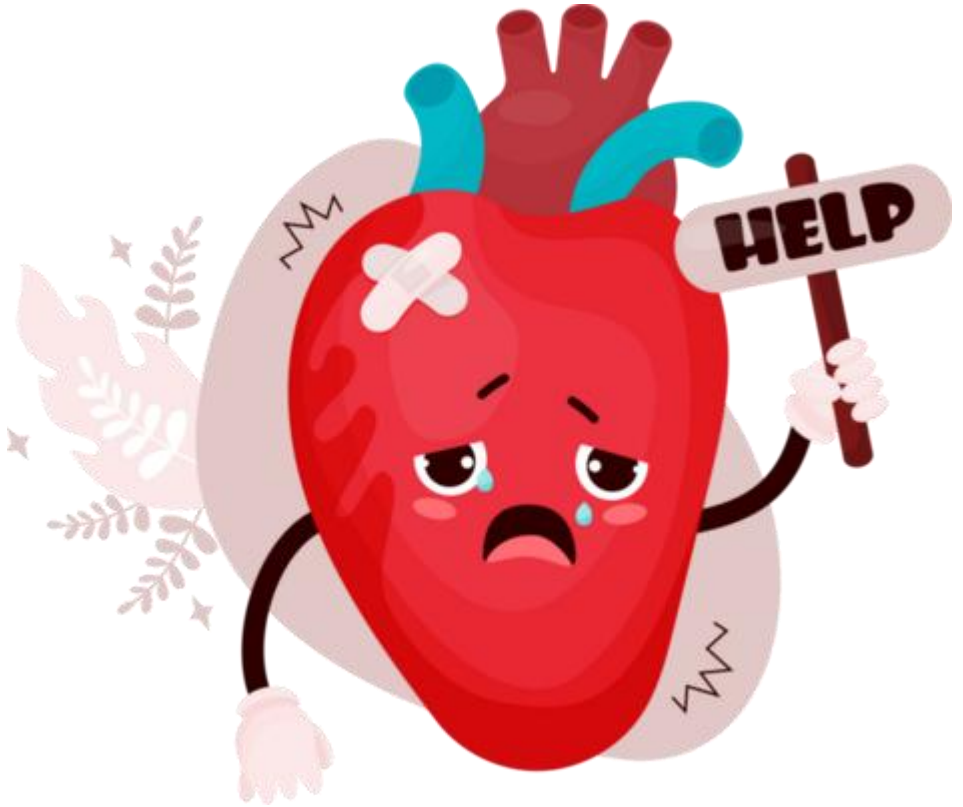
Background – HIV and Cardiovascular Risk

- ART has greatly improved survival in people with HIV
- Cardiovascular disease (CVD) risk remains higher, even with viral suppression[1]
- Risk factors include both traditional and HIV-related drivers: especially inflammation and immune activation[2]



1: Ruamtawee, W. et al. (2023). BMC Public Health. 23(1), 477.
2: Jaworowski, A. et al. (2019). Frontiers in Immunology. 10.

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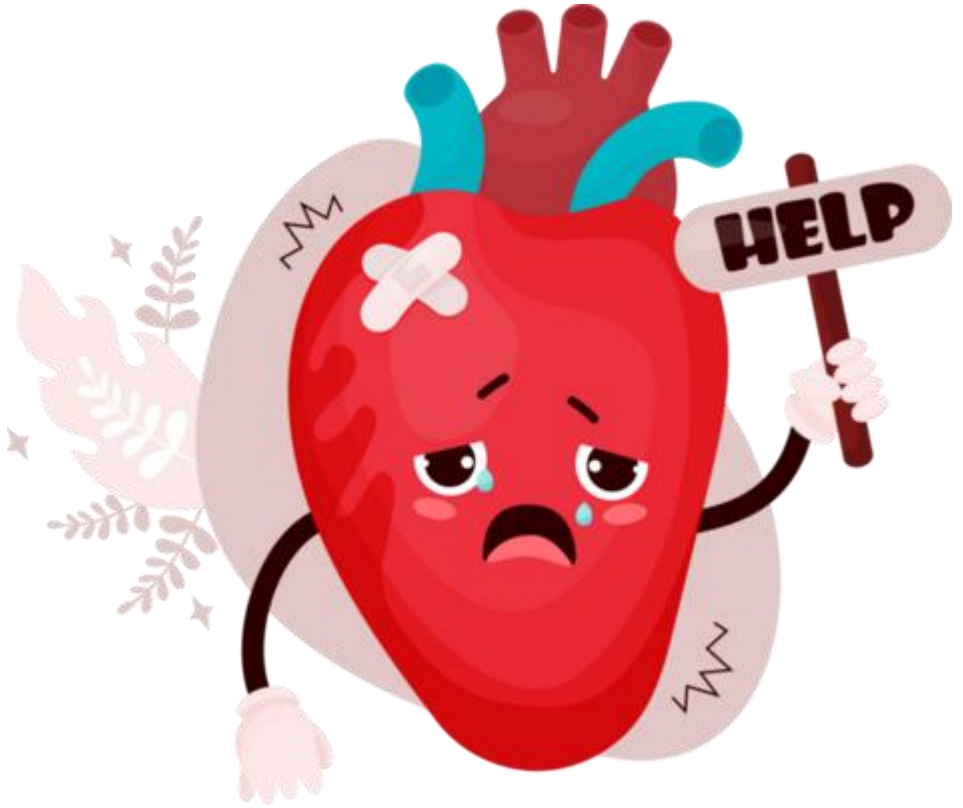
Background – HIV and Cardiovascular Risk



- **Statins are helpful, but tolerance issues highlight the need for alternatives**

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Principles of Herbal Formula Design

Role in Formula	Chinese Medicine Function	Western Medicine Analogy
Jun, 君 (Emperor)	Main herb, **treats the primary disorder** Defines the formula's therapeutic intent	Like the **main therapeutic agent** or core treatment
Chen, 臣 (Minister)	**Supports Jun** to strengthen main effect Treats **secondary or coexisting patterns**	Like a **co-therapy or add-on drug** that broadens scope
Zuo, 佐 (Assistant)	**Reinforces** Jun/Chen if needed **Moderates harshness/toxicity** Treats **minor accompanying symptoms**	Like an **adjuvant** (enhancer), **side-effect moderator**, or **symptom reliever**
Shi, 使 (Envoy)	**Guides action** to specific meridians/organs **Harmonizes** the whole formula for synergy	Like a **drug delivery guide** or **synergistic stabilizer**

CVD1 Formula: Bridging Classical JCZS Principles with Modern Evidence - Li et al (2022) Front Cardiovascular Med

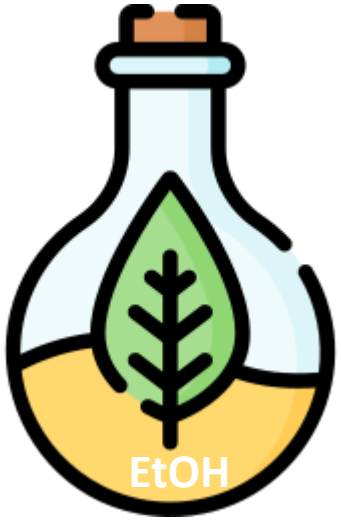
Role		Herb (Latin)	main Bioactive ingredients	Biomedical Relevance
Jun (Emperor)		dan shen (*S. miltiorrhiza*)	Tanshinone IIA, Tanshinone I, Cryptotanshinone, Salvianolic Acid B	Anti-inflammatory, endothelial protection, anti-thrombotic, vasodilatory
Chen (Minister)		huang qi *(A. membranaceus)*	Astragaloside IV, Calycosin-7-O-beta-D-glucoside	Immune modulation, gut barrier repair, metabolic regulation
		bai zhu (*A. macrocephala*)	Atractylone	Regulates gut microbiota, improves metabolic balance, reduces systemic inflammation
Zuo (Assistant)		chuan Xiong (*L. chuanxiong*)	Ferulic Acid	Improves circulation, vasodilation, anti-platelet, prevents atherosclerosis
		dang gui (*A. sinensis*)	Ferulic Acid	Vascular protection, hematopoietic support, antioxidant effects
Shi (Envoy)		gan cao (*G. uralensis*)	Glycyrrhizic Acid, Liquiritin	Enhances tolerability, protects gut/liver, anti-inflammatory, pharmacokinetic modulation

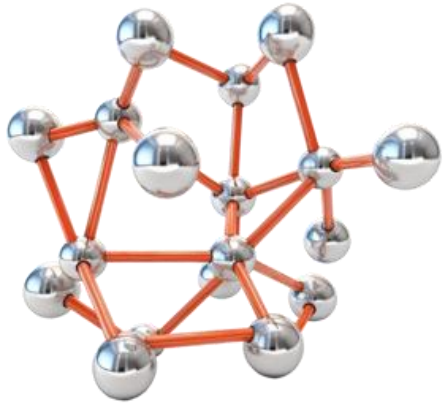
Why CVD1?

- Safe to use in people with HIV ❓
- Herb–drug interactions between CVD1 components and ART ❓

Forms of Herbs in Research

- Aqueous extracts – similar to traditional decoctions; closest to clinical practice
- Organic solvent extracts – concentrate selected active compounds
- Isolated single compounds – used for research, not taken directly by patients





Why Herb–Drug Interactions Matter

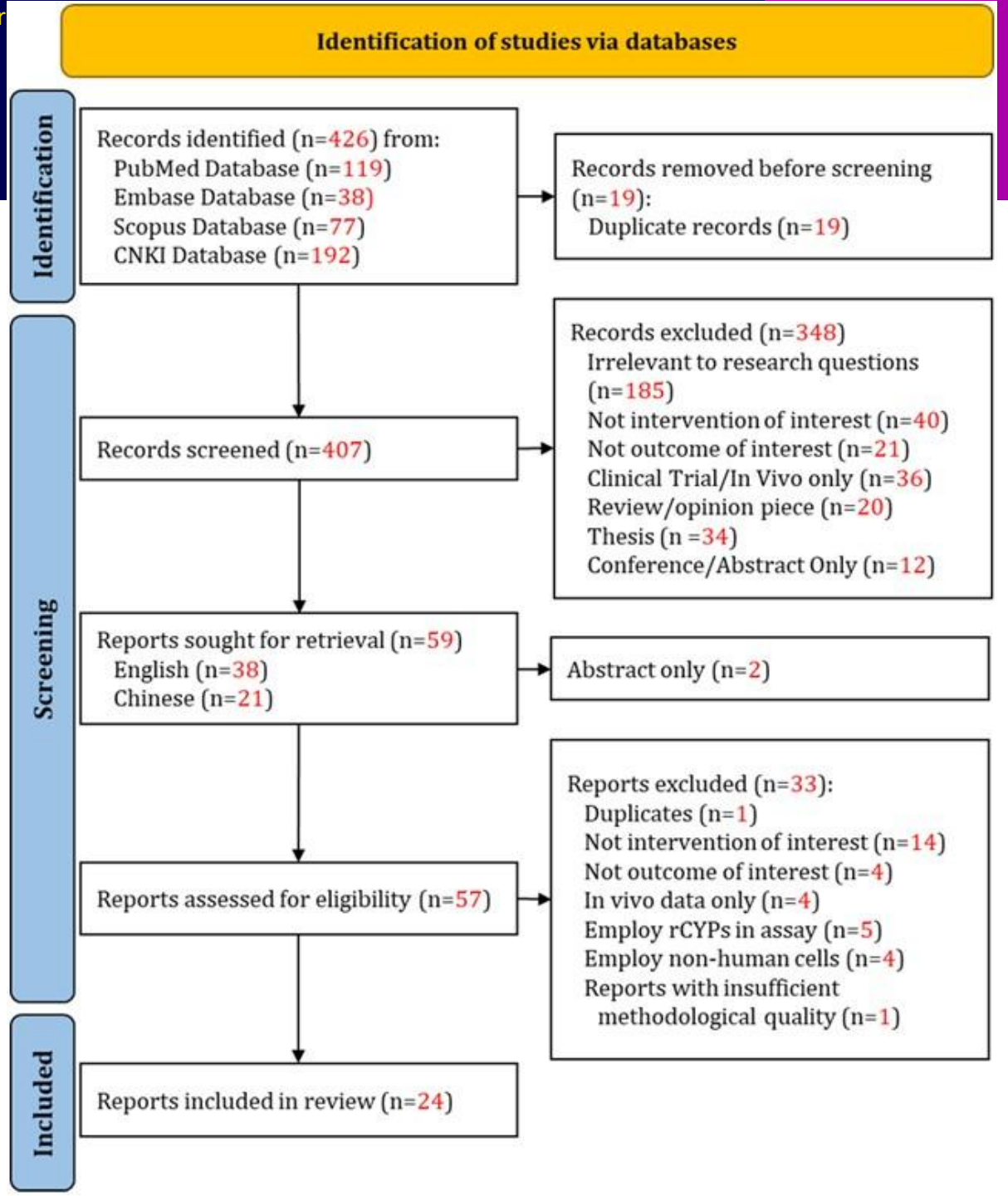
- Most ART drugs are broken down in the liver by CYP enzymes
- Chinese herbs can affect these enzymes—either slowing them down or speeding them up—which can change drug levels
- Nuclear receptors (PXR, CAR)

CYP Enzymes in ARV Metabolism

- **CYP3A4**: protease inhibitors (PI), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and some integrase inhibitors.
- **CYP2B6**: certain NNRTIs and other (tenofovir).
- **CYP2C9**: nevirapine.
- **CYP2D6**: certain PI and NNRTIs.
- **CYP2C19**: some NNRTIs.

Does CVD1 affect CYP activity?

- **426** reports screened (Medline, Embase, Scopus, and CNKI)
- → **24** studies (Human liver microsomes/cell lines; recombinant CYPs excluded)
- Overall risk of bias (SciRAP): **low**



Induction assay using organic extract:
Induction assay using aqueous extract:
Induction assay using reference compounds:

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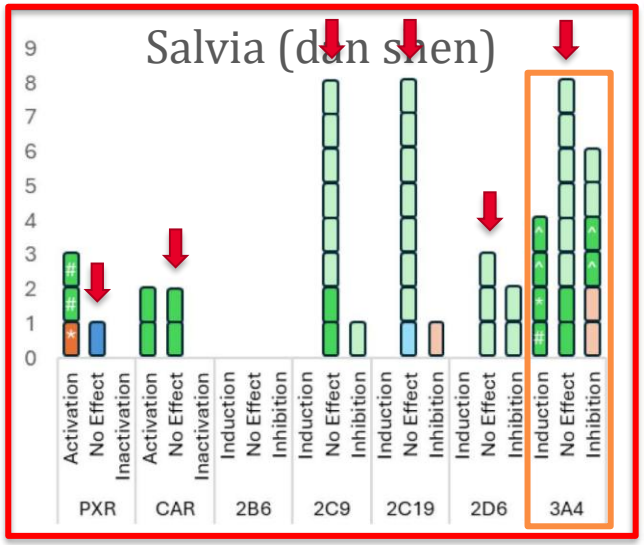
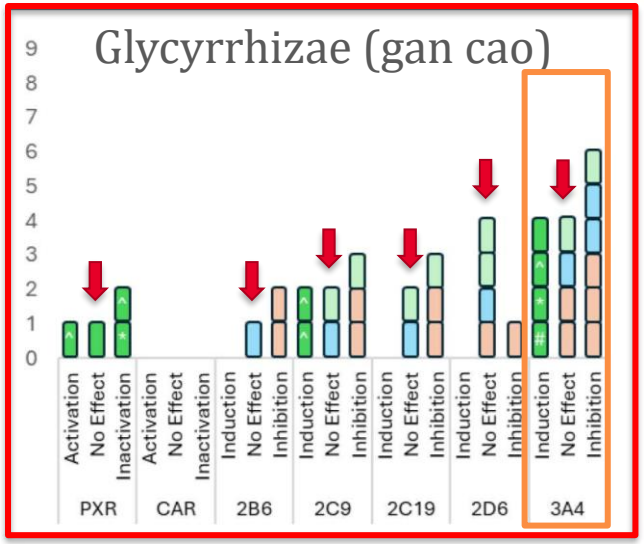
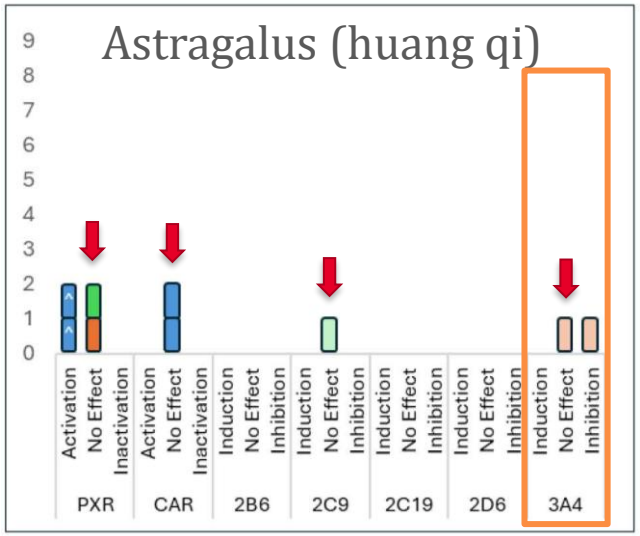
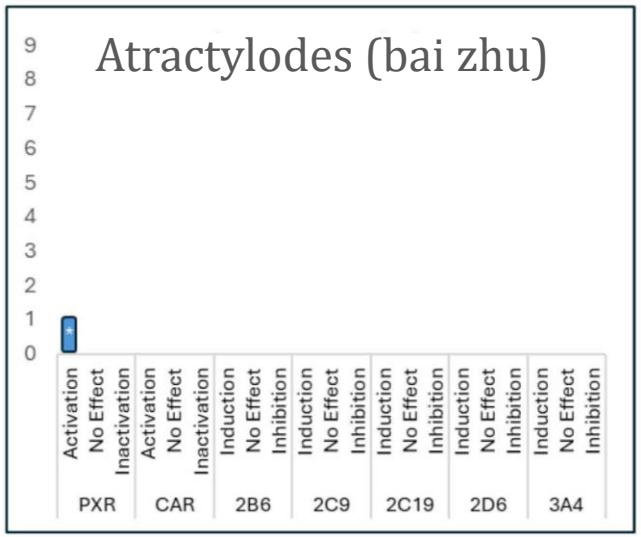
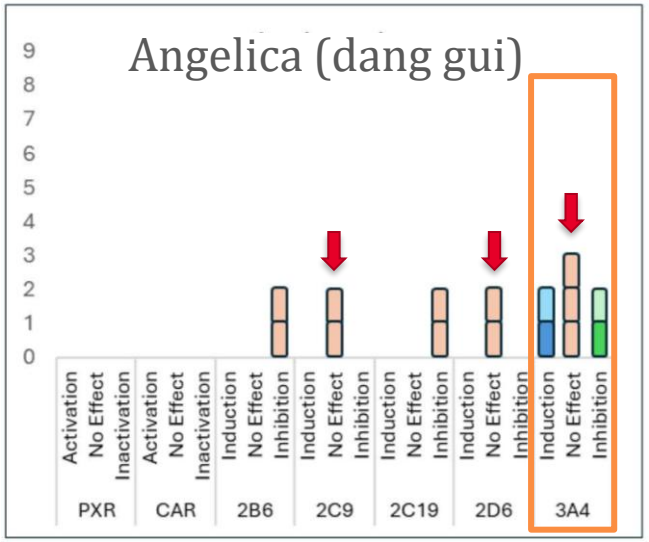
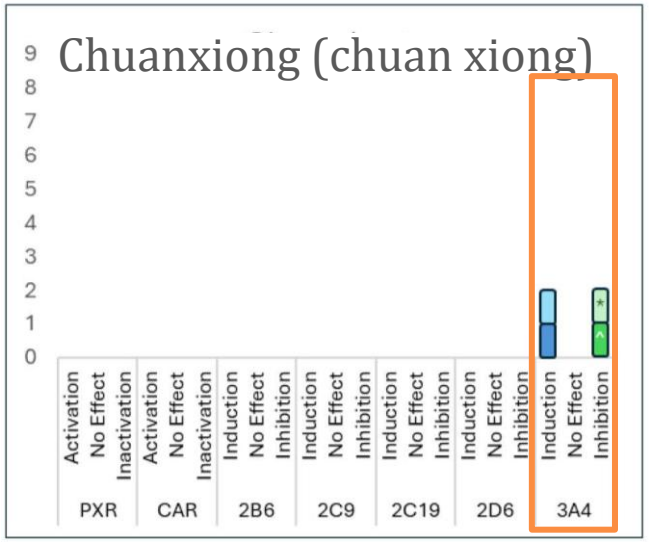




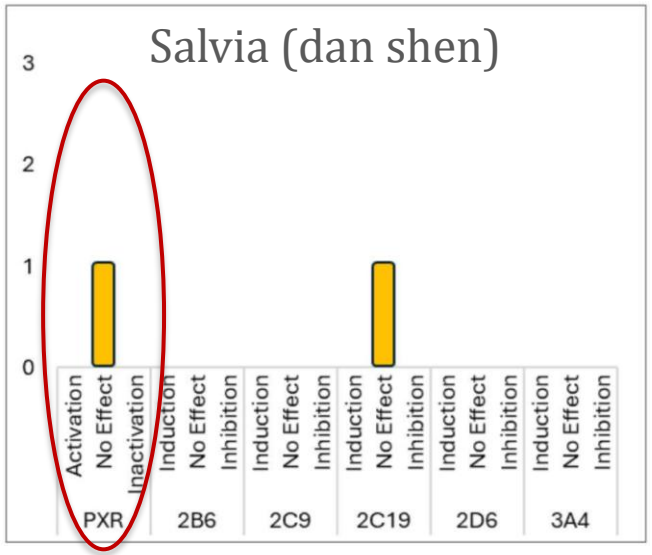


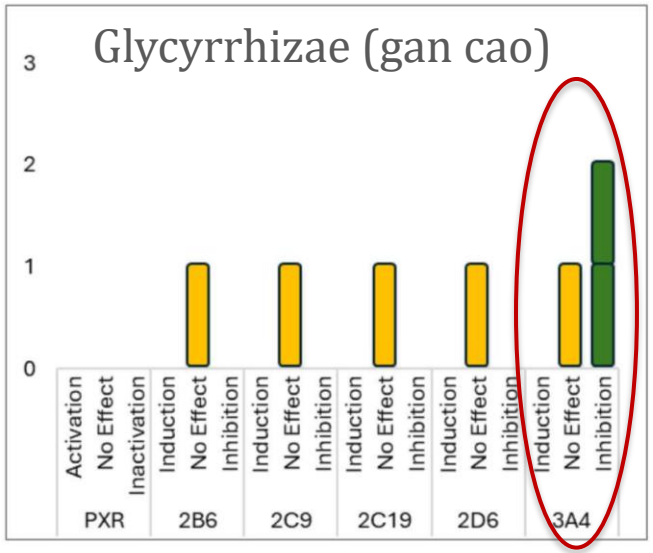


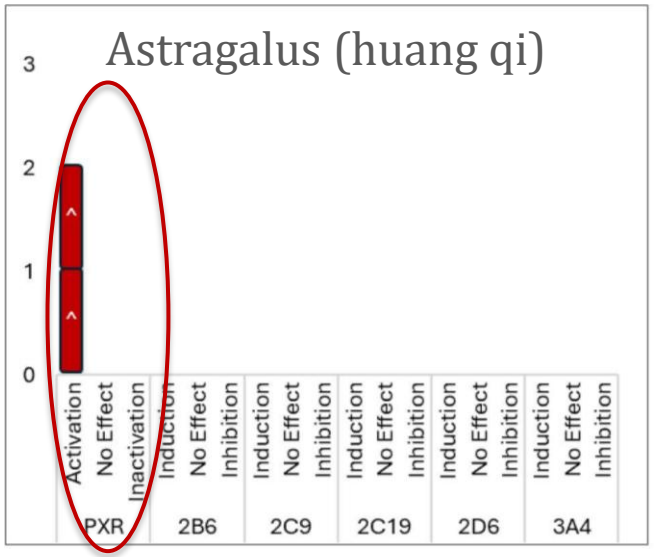


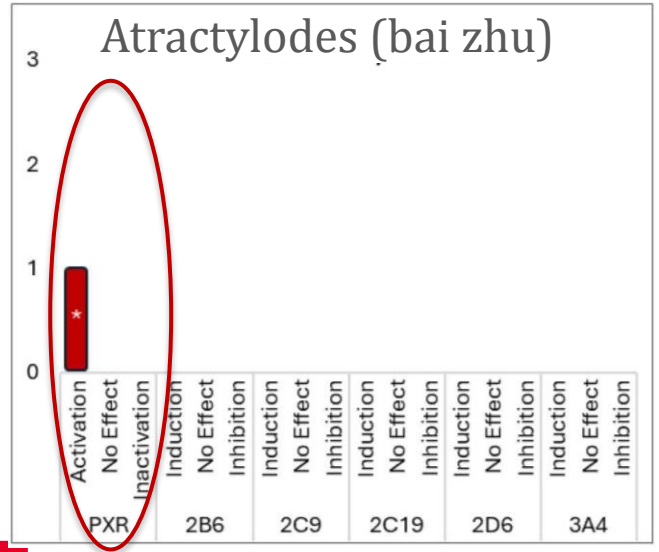


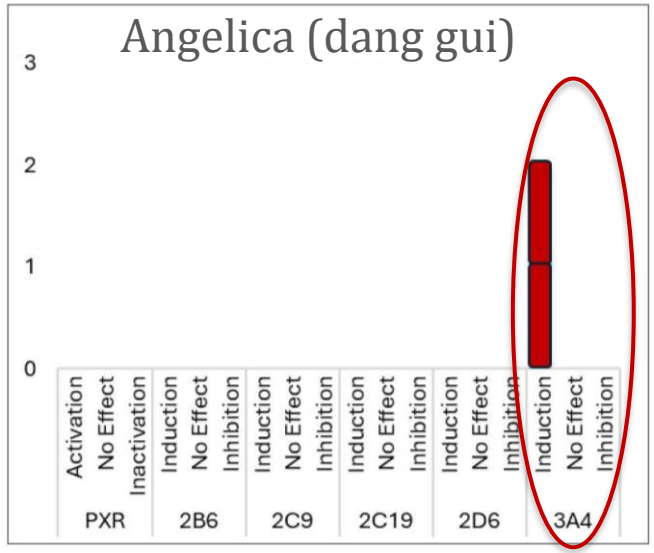
Assay showing Induction effect:
Assay showing no effect:
Assay showing inhibition effect:

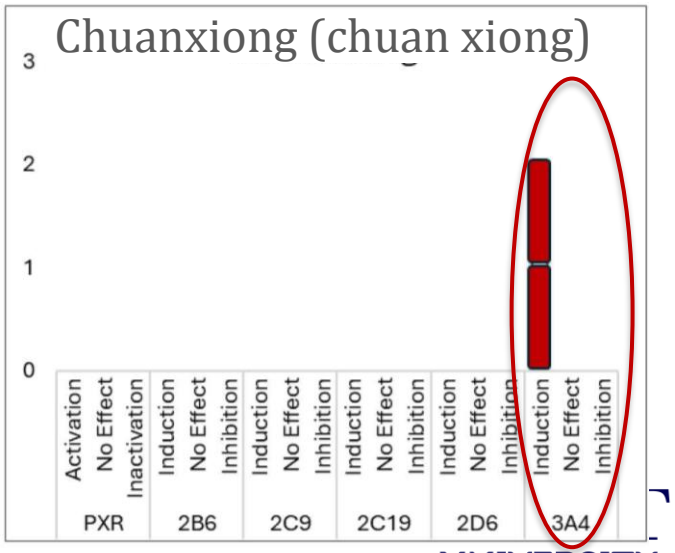












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Key Takeaways

- *Dan shen (Salvia)* appears safest for cardiovascular use alongside ART
- Findings support gan cao (*Glycyrrhizae)* as a harmonizing herb in formulas
- Herbs contain multiple active compounds, which can have opposing effects on CYPs, explaining variation across extracts or isolated components
- Studying whole formulas is essential, as combined effects can differ from single herbs

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