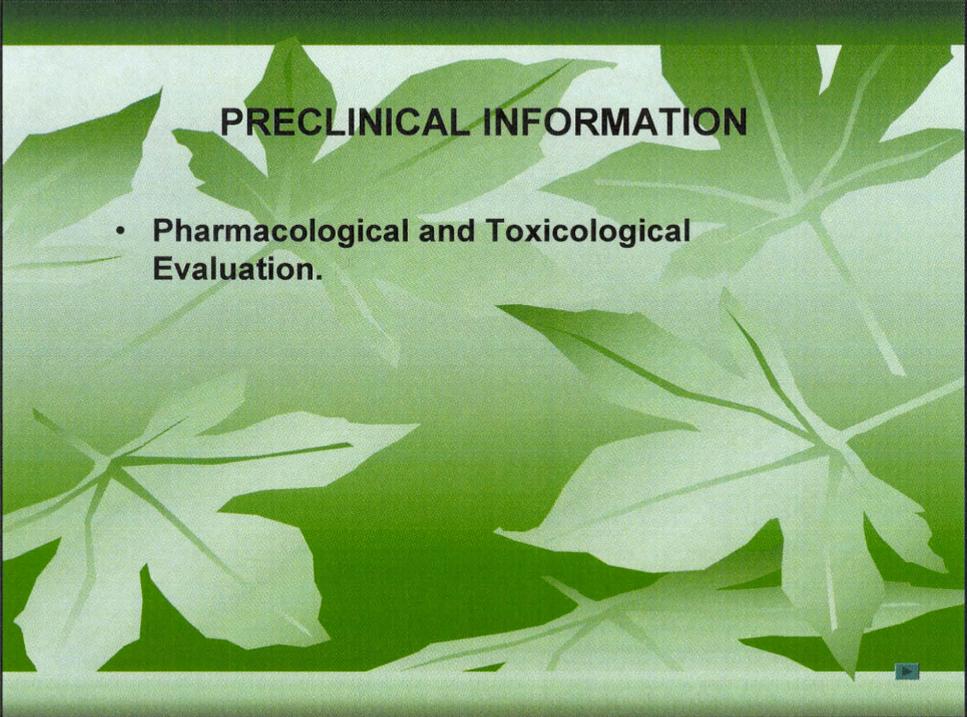


ADMINISTRATIVE INFORMATION

- **Name of the Company. GMP Certificate.**
- **General information about the product. Trade name, of finished medicinal product, strength, pharmaceutical form, route of administration. Category of the product in Cuba.**
- **Samples of the product.**

CHEMICAL PHARMACEUTICAL AND BIOLOGICAL INFORMATION

- **Qualitative and quantitative Composition of herbal medicines. Specification about the quality of plant materials and herbal medicines.**
- **Description of analysis method.**
- **Brief description of manufacturing process**
- **Stability Studies.**



PRECLINICAL INFORMATION

- **Pharmacological and Toxicological Evaluation.**



CLINICAL INFORMATION

- **Clinical Trials**
- **Ethnomedical information.**
- **Post-marketing experience**



International Symposium on Standardization of Traditional Medicine

Studies on Pharmacodynamic Evaluation in Complicate System of Traditional Chinese Formula

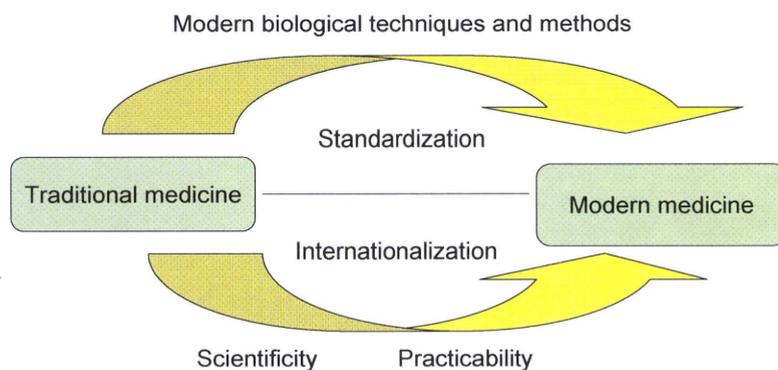
「藥者上而」
子牙為升記是
古河心湖雖水
為而打蓮聲
學如堂
即是此為此為
能了五味透來
藥作水眼富
湯清性

Xiao-Bo SUN
IMPLAD, CAMS & PUMC.

Contents

-  Present studies and future tendency
-  Research ideas
-  Techniques and methods

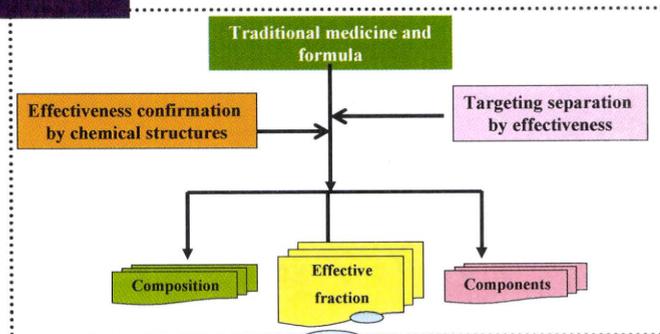
- Traditional medicines in clinic is usually used in the form of formula, which is difficult to be understood and accepted by western medical experts. However, the effectiveness of traditional medicine has been objectively proven by the long history of clinical use.
- It is important to figure out how to explain the mechanisms of traditional medicine in a way that western experts can take in.



- Traditional medicine with long history of clinical practice contributes enormously to human health.
- The standardization and internationalization of traditional medicine is essential for its approval and acceptance world widely.
- Modern biological techniques and methods provide fundamental basis for the standardization and internationalization of traditional medicine, which may objectively clarify the scientificity and practicability of traditional medicine.

- We use **Traditional Chinese Medicine (TCM)** as an example to explain the application of modern biological techniques and methods in standardization and internationalization of traditional medicine.
- With the development of “biological network”, the relationship between drugs’ targets and biological network has been studied thoroughly.
- Interestingly, chemical drug acting on definite single target appears to act on multiple targets from the point of biological regulation system.
- Therefore, the conception of network pharmacology and polypharmacology has been suggested. (PNAS and NATURE have reported).
- In fact, Traditional Chinese Medicine formula achieved its effectiveness by network effects.

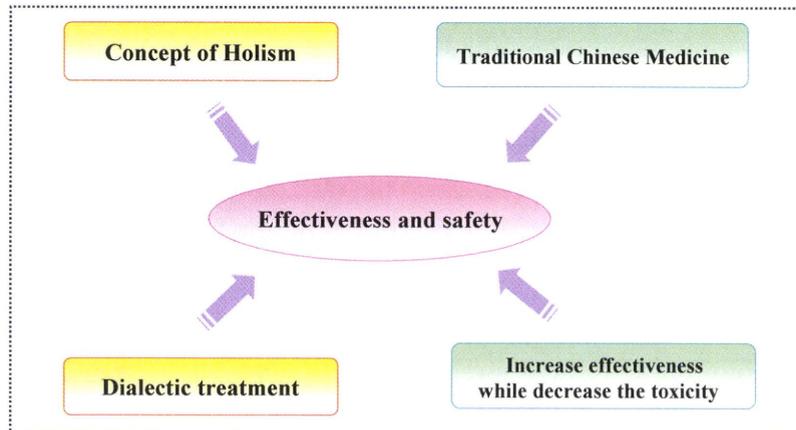
Present studies



- ◆ It is difficult to reflect on the characters of traditional Chinese medicine .
- ◆ It has a weak correlation with clinical diseases in traditional Chinese medicine
- ◆ It has a weak correlation with the effectiveness of traditional Chinese medicine

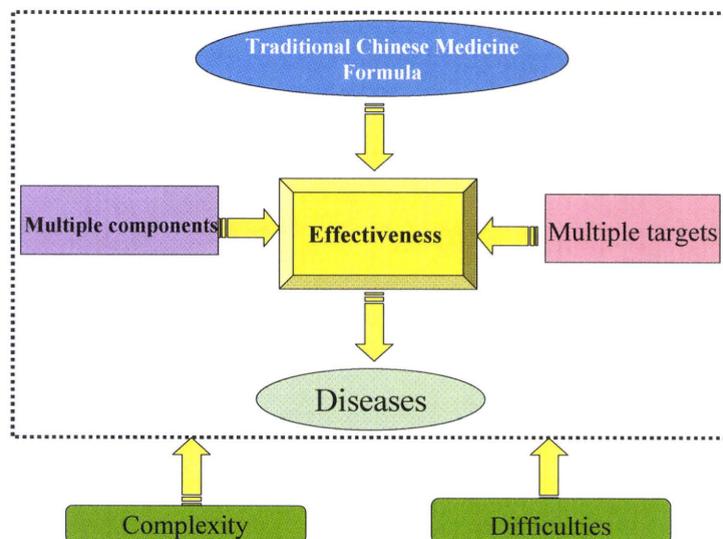
Present studies

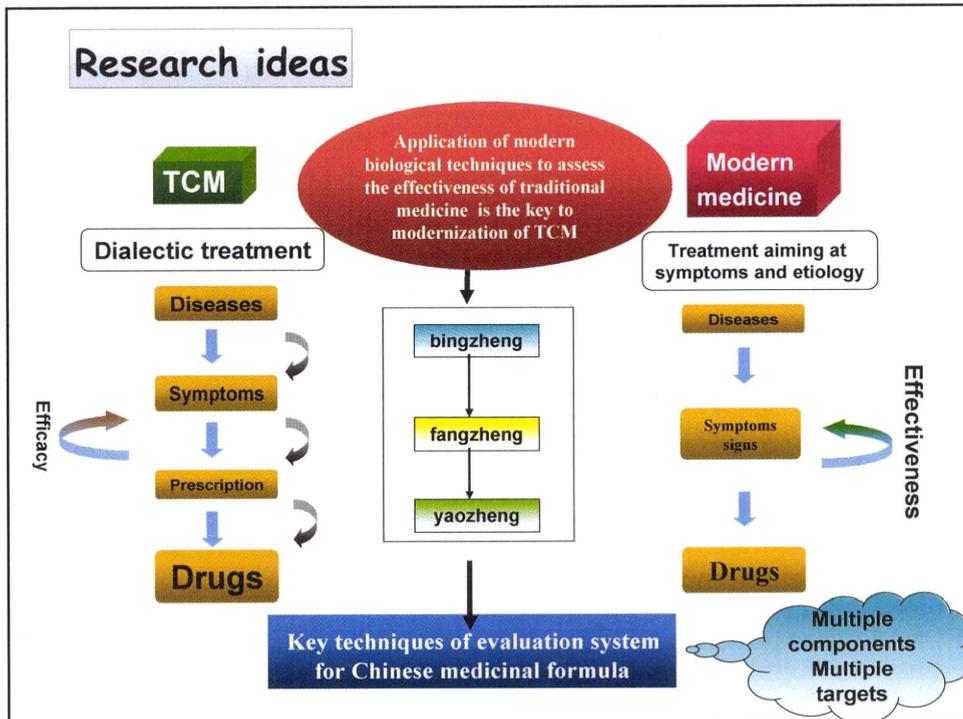
Traditional Chinese Medicine (TCM) emphasize on the concept of holism. Traditional Chinese Medicine is characterized by the use of formula to achieve the purpose of increasing effectiveness while decreasing toxicity.



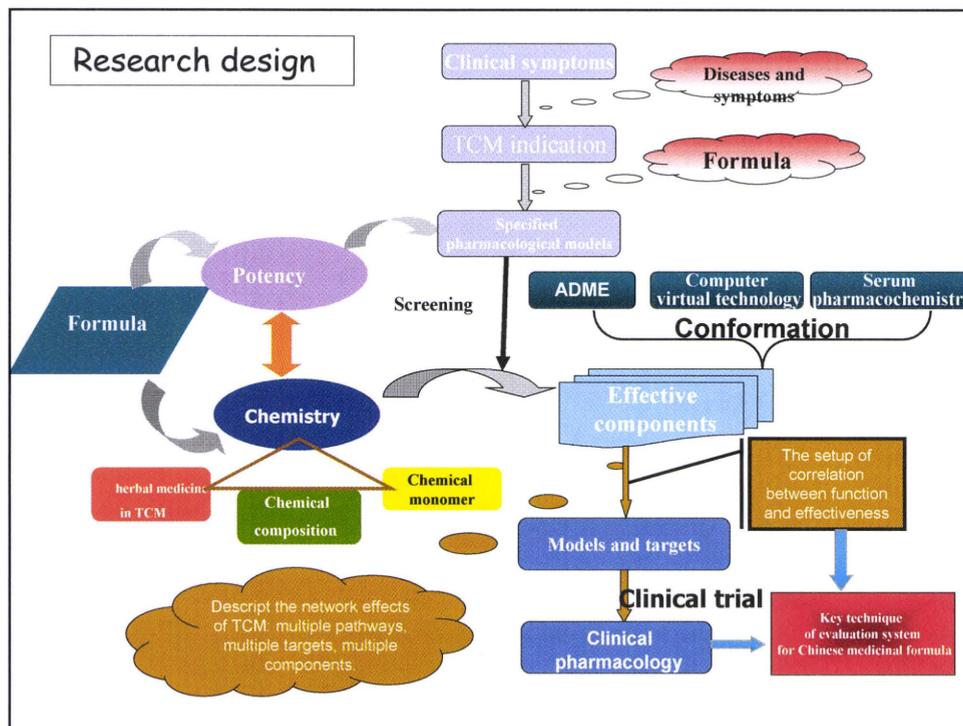
Present studies

Traditional Chinese Medicine (TCM) achieve its effectiveness by multiple components acting on multiple targets, which causes great difficulties to researches.





- TCM and western medicine shares basic principles and purposes.
- To explain the mechanisms of TCM by modern biological techniques is very important to the formation of Key techniques of evaluation system for Chinese medicinal formula.
- The selection of proper biological markers related to the disease and reflecting the effectiveness of drugs and the correlation between effective component and biological markers are important to the research of traditional Chinese medicine. Modern biological technique will be one of the effective methods to study on TCM.

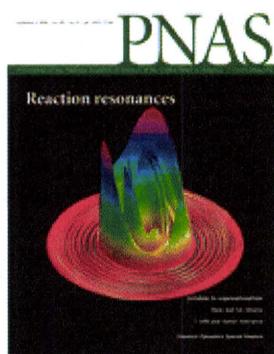


- This is the design of research.
- From formula to components and effectiveness...
- It objectively decrypts the network effects of multiple components acting on multiple targets of TCM.



Example 1: a new breakthrough in the studies on Chinese medicinal formula

PNAS 2008 105 : 4826-4831
Doi:10.1073/pnas.0712365105



Dissection of mechanisms of Chinese medicinal formula Realgar-Indigo naturalis as an effective treatment for promyelocytic leukemia

Lan Wang^{*1}, Guang-Biao Zhou^{*1}, Ping Liu^{*1}, Jun-Hong Song^{*}, Yang Liang^{*}, Xiao-Jing Yan^{*}, Fang Xu⁵, Bing-Shun Wang⁶, Jian-Hua Mao^{*}, Zhi-Xiang Shen^{*}, Sai-Juan Chen^{*6}, and Zhu Chen^{*1}

^{*}State Key Laboratory of Medical Genomics and Shanghai Institute of Hematology, Rui Jin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, 197 Rui Jin Road II, Shanghai 200025, China; ¹Guangzhou Institute of Biomedicine and Health, Chinese Academy of Sciences, Guangzhou Science Park, Guangzhou 510663, China; ²Shanghai Center for Systems Biomedicine, ³School of Environmental Science and Engineering, Shanghai Jiao Tong University, 800 Dong Chuan Road, Shanghai 200240, China; and ⁴Department of Biostatistics, Shanghai Jiao Tong University School of Medicine, 227 South Chongqing Road, Shanghai 200025, China

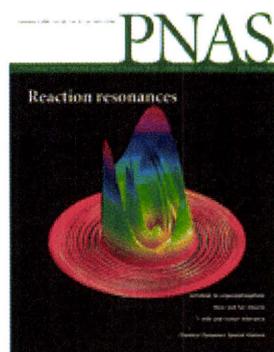
Contributed by Zhu Chen, December 31, 2007 (sent for review December 8, 2007)

Zhu Chen, the minister of Chinese Ministry of Public Health, reported “*Dissection of mechanisms of Chinese medicinal formula Realgar-Indigo naturalis as an effective treatment for promyelocytic leukemia*” in PNAS.



Example 1: a new breakthrough in the studies on Chinese medicinal formula

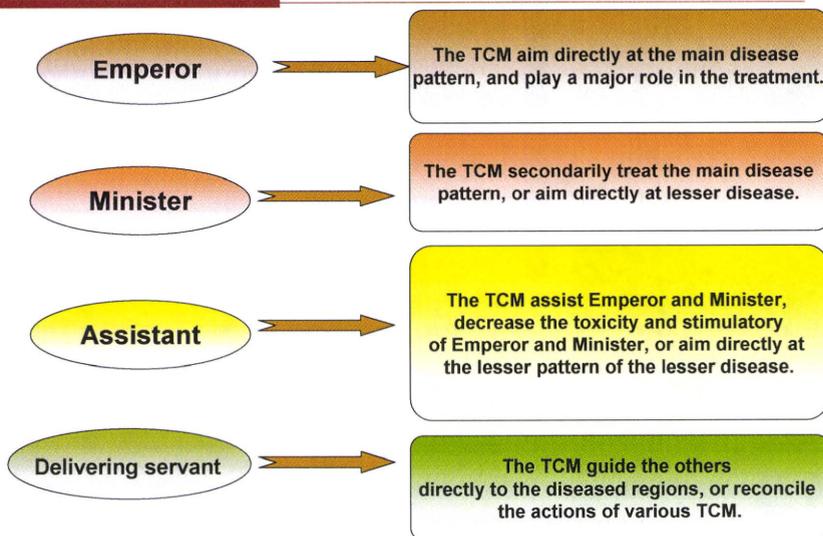
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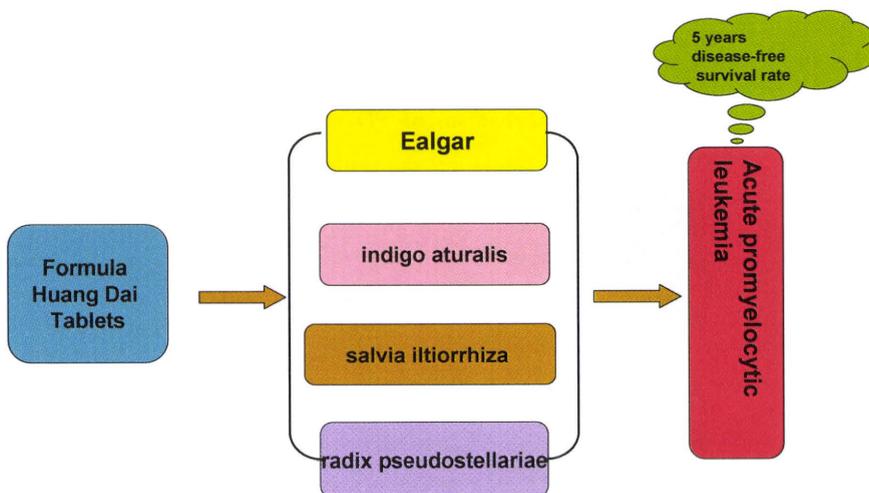
This research paper clarified the multi-target mechanism of PD action in Chinese medicinal formula on molecular level. Simultaneously, it indicated the compatibility principle, “Emperor, Minister, Assistant and Delivering servant”, is with not only the scientific meaning but also the strong vitality.

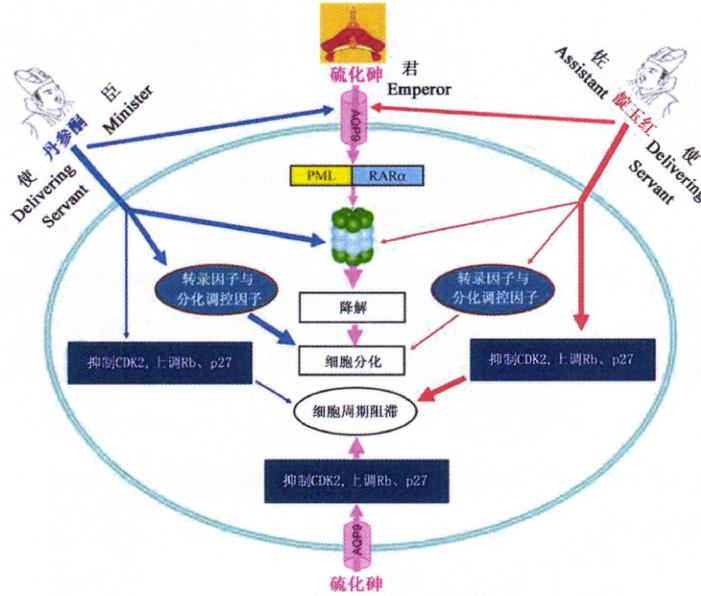


Example 1: a new breakthrough in the studies on Chinese medicinal formula



Example 1: a new breakthrough in the studies on Chinese medicinal formula





a new breakthrough in the studies on Chinese medicinal formula



"Nature" magazine Commentary:
A novel modern interpretation of the
ancient Chinese medicinal formula.

It is significant for the communication of
TCM and modern western medicine.



a new breakthrough in the studies on Chinese medicinal formula

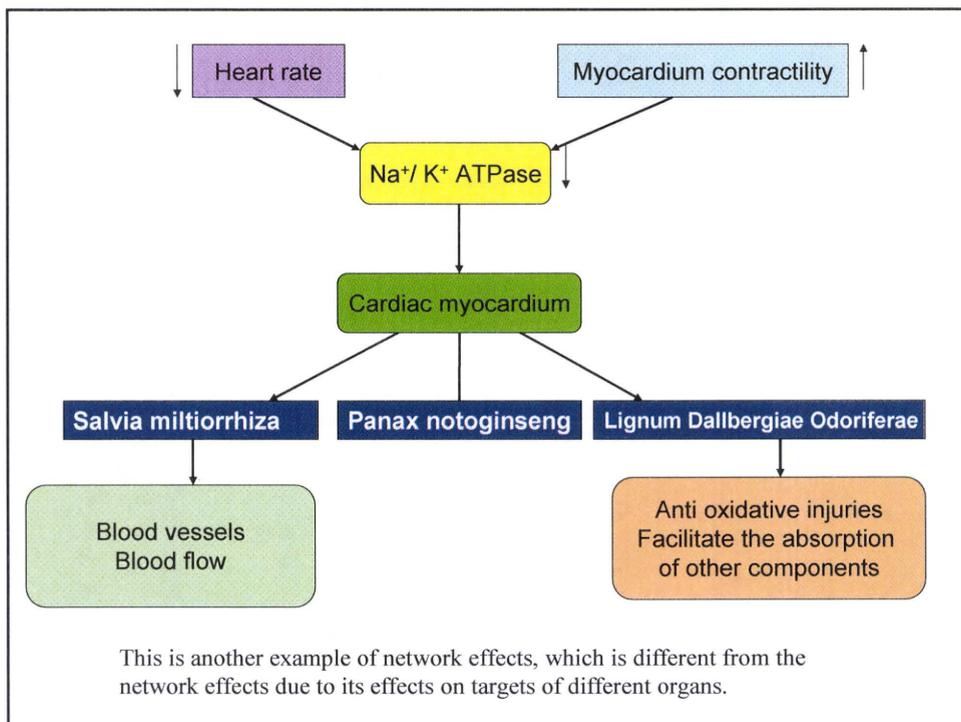
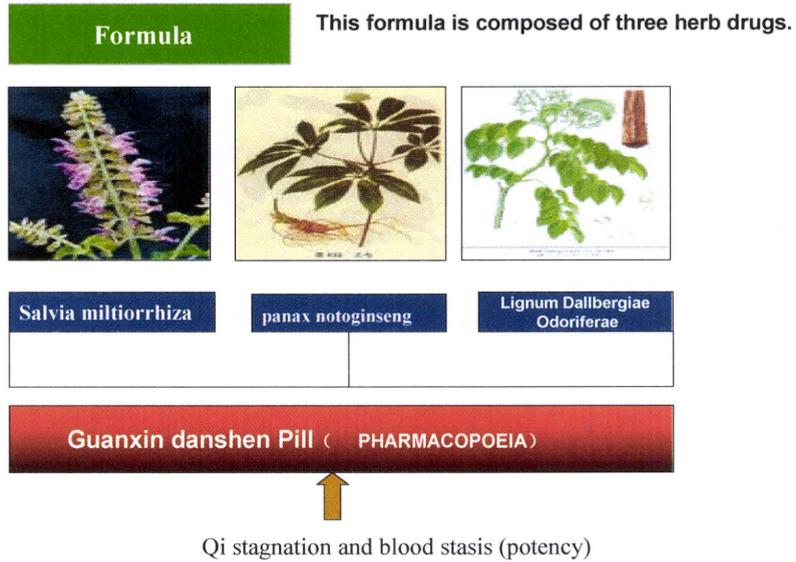
- ◆ **The study on Formula Huang Dai Tablets clarified the multi-component and multi-target mechanism of PD action in Chinese medicinal formula at the molecular level, and indicated the rationality of the TCM compatibility principles for the first time.**
- ◆ **The research shows that it is feasible to interpret the mechanisms of Chinese medicinal formula at the molecular level.**

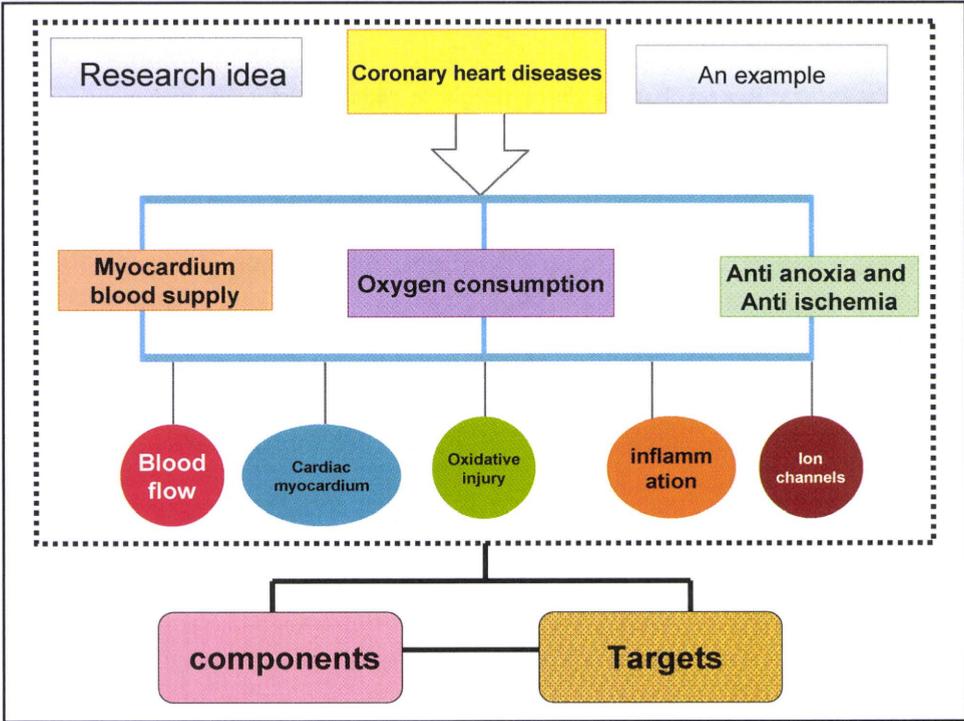


a new breakthrough in the studies on Chinese medicinal formula

- ◆ **The suitable animal models and cell models are very important. These models should be consistent with human disease.**
- ◆ **The methods and techniques of modern molecular biology are the common platform and tools for the research of TCM and western MED.**
- ◆ **The clinical efficacy of Chinese medicinal formula must be proved by multi-center clinical studies.**

Example 2: Our Researches on the synergistic reaction of TCM formula

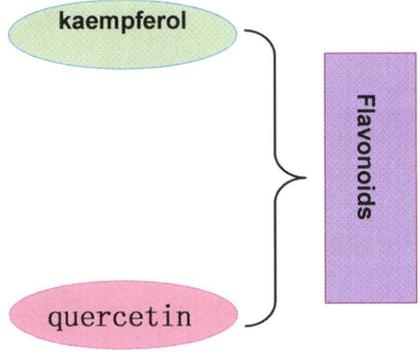
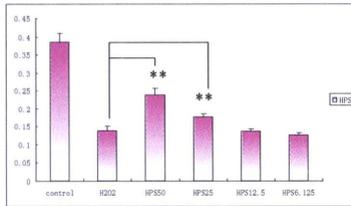
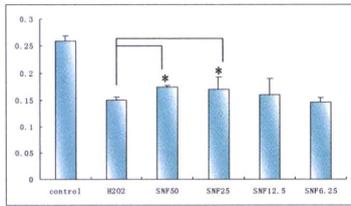




Example 2: Our Researches on the synergistic reaction of TCM formula

Anti oxidative effects

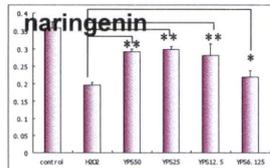
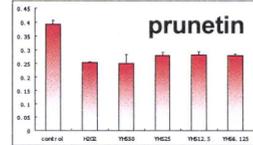
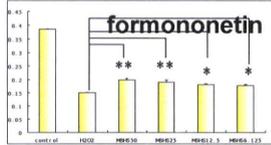
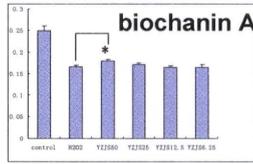
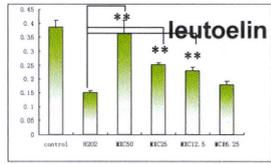
Flavonoids from Panax Notoginseng show protective effects on H₂O₂ induced H9c2 cardiomyoblasts injuries



Example 2: Our Researches on the synergistic reaction of TCM formula

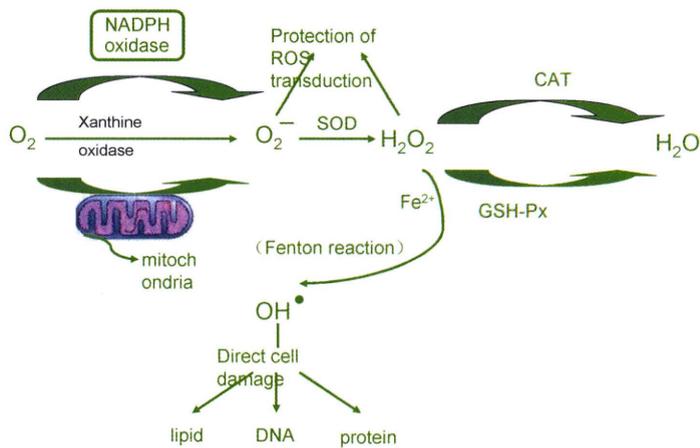
Anti oxidative effects

Flavonoids from *Lignum Dallbergiae Odoriferae* show protective effects on H₂O₂ induced H9c2 cardiomyoblasts injuries

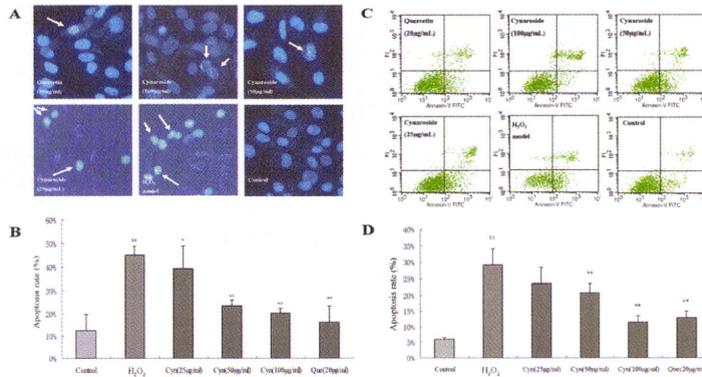


Flavonoids

Mechanisms of anti oxidative effects

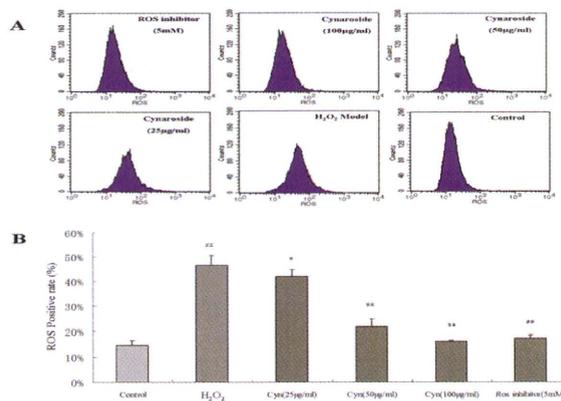


Researches on mechanisms of anti cardiac myocyte apoptosis



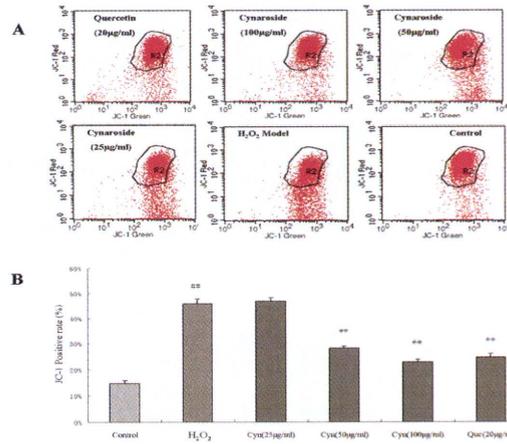
Effects of flavonoid (cynaroside) from Lignum Dallbergiae Odoriferae on H₂O₂-induced apoptosis in H9c2 cells.

Researches on mechanisms of anti cardiac myocyte apoptosis



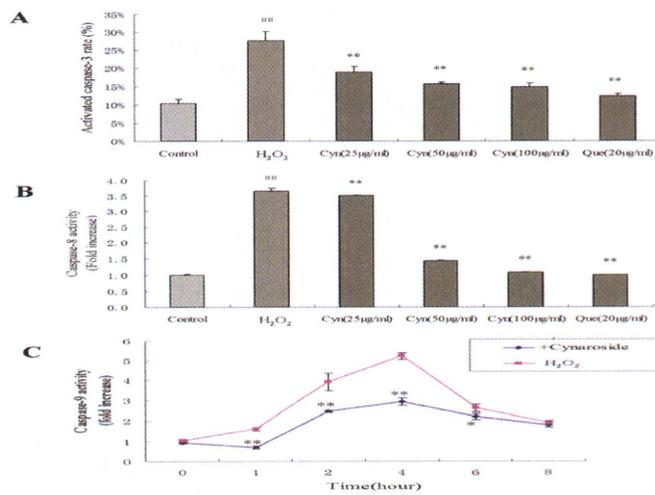
Favonoid from Lignum Dallbergiae Odoriferae lower intracellular ROS concentration dose-dependently.

Researches on mechanisms of anti cardiac myocyte apoptosis



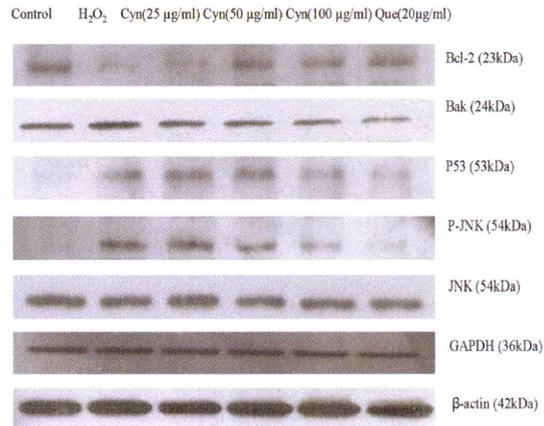
Effects of flavonoid from *Lignum Dallbergiae Odoriferae* on mitochondrial potential

Researches on mechanisms of anti cardiac myocyte apoptosis



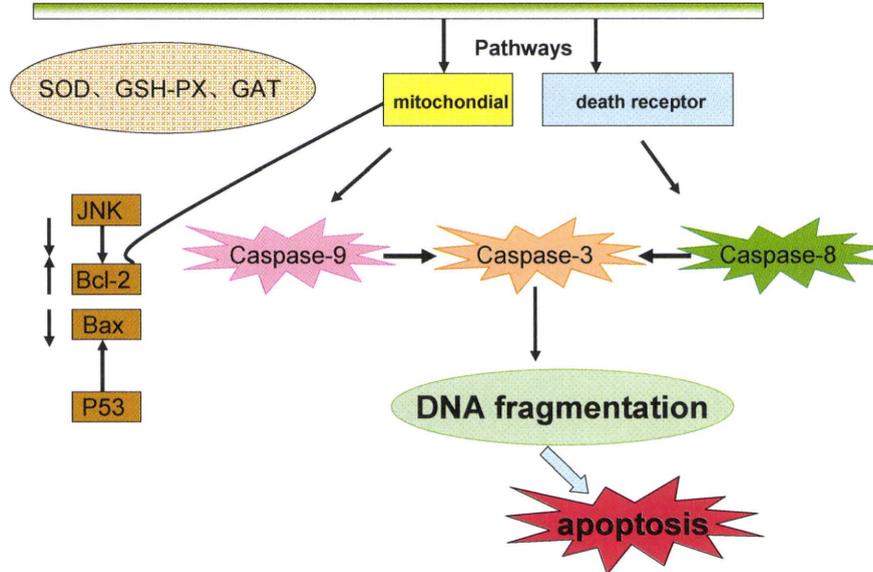
Effects of flavonoid from *Lignum Dallbergiae Odoriferae* on caspase-3, 8, 9 activities

Researches on mechanisms of anti cardiac myocyte apoptosis



Effects of flavonoid from Lignum Dallbergiae Odoriferae on the expression of apoptotic related proteins.

Flavonoids—mechanisms of anti oxidative effects



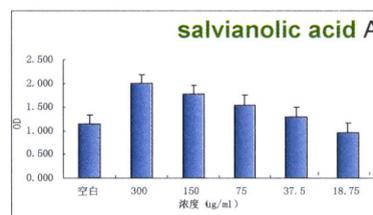
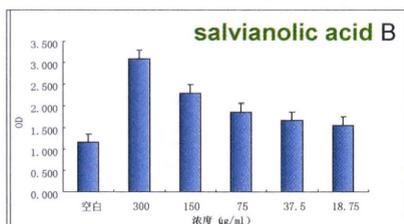
- These results should provide explanation for microcosmic network pharmacology mentioned above.
- In fact, TCM compound prescription is a much higher level of network pharmacological effects and each effective component shows a microcosmic network pharmacological effect.

Researches on mechanisms of anti cardiac myocyte apoptosis

cell proliferation effects



Cell proliferation effects of salvianolic acid A, B on H9C2 Cells



Cell proliferation effects of salvianolic acid A, B on H9C2 Cells