A new understanding of prescription

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**Abstract**
To promote the development of Traditional Chinese Medicine (TCM), it is necessary to innovate the traditional prescription. It is feasible to use one or several components to substitute TCM, which can be regarded as a process of discarding the dregs and preserving the essential components. In this way, traditional prescription can be converted into various combinations of pharmacological ingredients deriving from several TCMs. Furthermore, some of pharmacological ingredients should be modified to increase their efficacy. It is practical to select the main structural unit with specific substituents having strong pharmacological activity. After the innovation mentioned above, the prescription will evolve into a variety of modified components having distinct pharmacological activity, and this is the novel integration of active ingredients.

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Traditional Chinese Medicine (TCM) is the gem of Chinese culture, while TCM culture the root and driving force for its development. For thousands of years, it has made an indelible contribution to health care services and to the prosperity of China. The prescription, known as “Fang” in Chinese, consists of appropriate substances combined together properly according to the TCM principle. Dose and usage are established by Chinese medical practitioners under the guidance of Chinese medicine theory, and followed syndrome differentiation, pathogenic examination and therapeutic determination. Prescription dosage forms include decoctions, powders, pills and ointments. In addition, other formulations such as granules, oral solutions and injections are often used in modern times. Prescriptions are derived from the Chinese Materia Medica,
Under the influence of the world trend of "returning to nature", many countries have increasing interest in natural medicines. TCM has attracted the attention of pharmaceutical researchers worldwide due to its rich resources, unique therapeutic effects and lack of side effects. Systems biology has significantly increased in recent years, which will help to understand Chinese medicine syndromes (CMS) and modernize TCM. It is a great opportunity to modernize Chinese medicine but also challenges of the position of prescriptions in the domestic market. In order to rejuvenate TCM and increase the international competitiveness of our prescription industry, we must rely on modern science and technology to further explore and realize the modernization of TCMs.

It is undeniable that tradition and innovation will integrate. There will also be concern that the fundamental constituents of traditional prescriptions will erode during prescription development. It has always been our goal to find a way for TCM to be developed, and to be identified by patients, domestic pharmaceutical colleagues and international pharmaceutical communities. As prescriptions are composed of many TCMs that are selected according to the principle of "assist and guide", traditional formulation principles need to be followed during the process of making TCMs more contemporary. So, some adaptations of the traditional prescription are clearly needed. There will need to be a balance between the heritage, theory and practice of TCM prescriptions, and development, innovation and modification of content and form.

Prescription studies is described in the following sections:

(a) Separation of TCM/prescription

TCM has a high reputation globally, but the theories and principles of Chinese medicine have not been accepted outside of Chinese communities, nor has it been recognized by Western Medicine. The mechanism of TCM and prescriptions is reinvestigated by modern pharmacology and/or molecular biology. This brings them closer to the international standards and help to bring Chinese medicine to the world.

(b) Identification of the active ingredients of TCM and prescription (simplification principle)

Compared with Western Medicine (chemical medicine), the composition of TCM and prescriptions are extremely complex, ranging from dozens to tens of thousands of constituents. However, the active ingredients with pharmacodynamic effects are basically determined. Moreover, the types of the active ingredients are generally few, but the content is relatively high. Therefore, it is feasible to use one or several active ingredients on behalf of certain herbs or TCM. Liu et al. reported that the column containing co-immobilized receptors has potential for screening bioactive compounds with multi-targets from complex matrices including TCMs.

That is to say, a blend of a few active ingredients can be developed from a combination of several TCMs. As a result, the prescription is equivalent to an integration of active ingredients (IAI). IAI is different from the traditional prescription, but it is derived from the prescription without deviating from the theory of TCM. Compared with the traditional prescription, IAI is easier to receive the western world recognition. Zhou et al. have found the best pharmacodynamically active ingredients of Qingdai according to the binding interactions of the inhibitors at the catalytic site performed in best docking combinations. Recently, TCM integrative database has been facilitated the study of combination therapy and understanding of the underlying mechanisms for TCM at molecular level.

(c) Structural modification of the active ingredients

The practice has showed that that the natural compound is not necessarily the best. Some compounds require modification to improve therapeutic effect, and this also applies to the active ingredients of TCM. Take the active ingredients of the drug as small chemical molecules, remain the scaffolds unchanged, modify and improve different substituents at low cost, select appropriate constituents with better activity, we will achieve the IAI of reducing toxicity and increasing efficacy. Chemical spatial analysis can be applied in this field. According to the principle that two similar compounds have comparable biological activity: two compounds have 85%"similarity" and one compound has biological activity, and the other has the biological activity is 80% (Figure 1). Similar bioactivities (increased or decreased) were observed before and after modification of active ingredients. By researching the structure-activity relationships, we reconstructed the spatial structure for each active ingredient to increase their activity and reduce toxicity. We also optimized the best compatibility and proportion of active ingredients so as to develop new "TCMs" or "prescriptions".

(d) Docking of Chinese medicine and Western Medicine

After the above modifications, the prescription (the "IAI" or the "new prescription") becomes a combination of a variety of modified "new" active ingredients with better therapeutic effects. In principle, the new prescription does not deviate from the theory of TCM. It is both traditional and innovative. The new prescription has characteristics of defined composition, low toxicity and good curative effect. This makes it easier to be accepted by medical practitioners both at home and abroad. It not only expands the world influence of "TCM", but also promotes its underlying theory, which is beneficial to promote Chinese medicine to the world and set up a cultural bridge between China and the west.
In summary, traditional prescription can be converted into various combinations of pharmacological ingredients deriving from several TCMs. Furthermore, some of pharmacological ingredients should be modified to increase their efficacy. It is practical to select the main structural unit with specific substituents having strong pharmacological activity. After the innovation mentioned above, the prescription will evolve into a variety of modified components having distinct pharmacological activity, this is the novel IAI.

REFERENCES


