

**Different approaches in Pharmacological Research**

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**Introduction**

In recent global health politics, the increasing number of diseases that are difficult to control or treat using only mono-therapy approach has drawn the concerns of worldwide scientists. The availability of current drugs in the market is apparently insufficient to handle the unceasingly increase of diseases in this era. Therefore, scientists have started to search for alternatives instead of solely defending typical reductionism approach of Western medicine. In fact, there is a promising alternative avenue that has been practiced widely in human population since ancient time, and that is the traditional Chinese medicine (TCM). Although many diseases are not described in TCM term, but the physicians who practice TCM in China attempt to treat these diseases using TCM principles have proved to be clinically effective [1].

Based on the fundamental concept of TCM, an individual is considered as “healthy” only when all the five elements (fire, wood, metal, water and earth) and the Yin, which refers to “negative” and Yang which represents “positive” are in balance [2]. An individual will be sick once there is imbalance in Yin-Yang and the five elements in the body, while different kinds of syndromes would occur according to the types of disease adhered to the body. Typically, a disease can cause different types of syndromes that eventually cause different types of symptoms in the human body. According to the principles of TCM, all human diseases will be treated according to the syndromes observed, and TCM prescriptions are the most frequently used method to treat different kinds of diseases via oral administration. According to the Shen Nong’s herbal classic, the TCM prescription is formulated according to the capability of TCM herbs to counter different syndromes caused by diseases which includes at least four different roles played by TCM herbs which are sovereign, minister, assistant and envoy drugs [3].

Thus, rather than explaining varied kinds of diseases the human race faces today, this present review looks at specifically the globally concerning multi-syndromic disease, the hypertension. It is frequently being reported as having poor controllability using existing antihypertensive drugs in current market via mono-therapy approach as well as these drugs’ association with undesired adverse effects would also be a topic of discussion in this review and elaborated based on the principles of TCM along with scientific evidences. This could be one of the most persuading examples to prove the feasibility of TCM in treating diseases based on its principles as well as the formulation of combination of herbs using the new scientific-based orthogonal stimulus-response compatibility approach.

**Hypertension in the View of TCM**

Hypertension is a well-known “silent killer” and a symptomatic disease that can cause various concomitant diseases after years of adherence in human body. According to the evolution of antihypertensive drugs, the classes of the antihypertensive drugs that are preferred to be used clinically often changes from time-to-time, and combination drugs therapy is more often used than single drug therapy in majority of hypertension patients in order to achieve the targeted blood pressure range [4,5]. However, the chronic adverse effects caused by the antihypertensive drugs in patients’ bodies that are being reported frequently have drawn the concerns of worldwide scientists. For this reason, researchers have started to employ the principles of TCM in the antihypertensive drugs researches in recent years.

According to the principles of TCM, hypertension is a multi- syndromic disease which can cause three major syndromes. The first syndrome is the “fire” syndrome that could be further divided into 4 types such as heart, stomach, intestine and liver fire. Secondly, there are “phlegm-fluid retention” syndrome, and “deficiency” syndrome that could occur in kidney and spleen [1,6]. There are some common symptoms caused by the hypertension including

dizziness, headache, neck stiffness, and fatigue. According to literatures, one of the most frequently used approach to formulate a TCM prescription is the orthogonal stimulus-response compatibility group studies.

For instances, there was a TCM prescription (known as BPAid) successfully formulated by combining four TCM herbs such as *Uncaria rhynchophylla*, *Pueraria thomsonii*, *Panax notoginseng*, and *Alisma orientale* which were selected according to their ability to counter three major syndromes caused by hypertension, with the use of orthogonal stimulus-response  $L(5^5)$  formulation, the resulting vasodilatory effects of the 50% ethanolic crude extract of these combined TCM herbs at ratio of 5.32:2.44:9.24:1 was better than those exerted by any of its single drug [7,8]. Besides, there was another article which showed promising vasodilatory effects exerted by the 50% ethanolic crude extract of five combined TCM herbs (known as Banxia Baizhu Tianma Tang) such as *Glycyrrhiza uralensis* Fisch., *Gastrodia elata* Bl., *Atractylodes macrocephala* Koidz, *Poria cocos* (Schw.) Wolf, and *Citri reticulatae* Blanco at ratio 2.71:1.14:1:5.57:7.14 formulated by using similar approach, the orthogonal stimulus-response  $L(6^6)$  formulation (Tan et al., 2017b). The antihypertensive effects of both of these TCM prescriptions were further tested in vivo by orally administrating spontaneous hypertensive rats (SHRs) for 28-days consecutively, and the resulting systolic (SBP), diastolic (DBP), and mean arterial pressure (MAP) were significantly decreased, whilst there has no adverse effect shown in the biochemical and hematological tests on the SHRs blood [9,10]. These proved the reliability and safeness of the use of combined TCM herbs in treating disease, the hypertension in particular.

There was another example regarding the antihypertensive drugs research, the authors combined the vasoactive compounds such as gastrodin, baicalin, tetramethylpyrazine, and puerarin, and the best ratio for the combination of these four vasoactive compounds was determined by using the orthogonal stimulus-response compatibility studies with  $L(5^5)$  formula<sub>3</sub>, and the best combination ratio was found at 5.33:1:2.67:5.33 [11]. In fact, the crude extracts of TCM herb are more preferable to be used in pharmacological research of antihypertensive drugs due to its holistic effect in the signalling mechanism pathways employed for exerting the vasodilatory effect as well as being cost-effective from industrial viewpoint compared to the use of fractionated or pure vasoactive compounds [12-14].

## **Conclusion**

In fact, TCM was dominant before the rise of western medicine, but the limited scientific support and evidences regarding their therapeutic effects in human have repressed its development. However, in recent years, the increasing number of scientists that has started to apply TCM principles as well as the combination of TCM herbs has gradually returned to its fame that it deserved. Furthermore, the examples shown above proved the feasibility of TCM principles at least in the case of treating hypertension, whereby formulating the TCM prescription using the orthogonal stimulus-response compatibility approach and the use of crude extract could provide better therapeutic effect over single compound via its holistic mechanisms of actions. This could be the trend for future pharmaceutical research and may as well solve the greatest problem in human history, curing diseases that were previously impossible to cure and without adverse effects.

## **References**

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