

# Thoughts on the Dose-effect Correlation of Chinese Medicine

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**Abstract—Objective:** To explore the relationship between dose and efficacy of traditional Chinese medicine, to provide reference for the study of Chinese medicine dose and toxic medicine attenuated efficiency. **Methods:** Through the study on Chinese medicine dose effect relationship and access to the previous use of traditional Chinese medicine to grasp the dose, summed up the Chinese medicine dose effect relationship law. **Results:** The dose-effect relationship of different Chinese medicines varied greatly. Some Chinese medicines showed good linear relationship within a certain dose range, while others had no obvious dose-effect relationship. **Conclusion:** The relationship between dosage and effect of traditional Chinese medicine should be carefully grasped, especially toxic traditional Chinese medicine, which has narrow safety range and should be monitored in real time.

**Keywords—***toxic Chinese medicine; dose effect relationship; attenuated and synergistic effects*

## I. INTRODUCTION

The use of Chinese medicine has a long history. The ancient ancestors have accumulated rich experience in the practice of using Chinese medicine to prevent and treat diseases. The drug dosage has been deeply explored, and the complexity of traditional Chinese medicine ingredients has caused the complexity of the dose-effect relationship of traditional Chinese medicine. Summarizing the rule of Chinese medicine, it can provide guidance for the clinical use of modern toxic Chinese medicine. Nowadays, many traditional toxic Chinese medicines are used less and less in clinical practice, which has an impact on the use of some traditional medicines. Therefore, it is necessary to summarize the medication rules of traditional medicines, and to ensure the efficacy of drugs, while using new technologies and new methods to ensure the clinical use of drugs safety.

## II. THE MEANING OF THE TOXICITY OF TRADITIONAL CHINESE MEDICINE

The concept of the toxicity of traditional Chinese medicine can be summarized into three kinds of understandings: 1) poison is a medicine, and all medicines for treating diseases are poisons. This recognition juxtaposes drug and toxicity, collectively referred to as "poison." 2) refers to the bias of the drug. 3) refers to the toxic side effects of the drug. Modern research believes that the understanding of the toxicity of traditional Chinese medicine should be understood from the following aspects: 1) Whether it contains toxic components. Generally, the toxic traditional Chinese medicine contains a

highly toxic component [1], such as strychnine containing alkaloid, aconite containing aconitine, vermiculite containing arsenic trioxide, etc., while non-toxic Chinese medicine does not contain toxic components or However, the amount is small. 2) Whether the whole is toxic. Traditional Chinese medicines are mostly natural medicines containing multiple components, but the components are mutually restricted and mutually influential. Of course, the toxic components are no exception. This causes some Chinese medicines to contain toxic components but does not show toxicity as a whole, such as ginseng Hemolysis is due to the hemolysis of ginsenosides b and c, while ginsenoside a has an antihemolytic effect [2]. Therefore, the overall toxicity and toxic components of traditional Chinese medicine are both intrinsically linked and different. 3) Is the dosage appropriate? The key to determining whether a Chinese medicine is toxic is whether the dose is appropriate, including the length of time [3]. Treating with traditional Chinese medicine, as long as the appropriate dosage is selected, it does not exceed the maximum tolerance of the body, and it will not cause obvious toxic effects on the body, that is, it is non-toxic; if the dose used exceeds the maximum human body can withstand the dose will cause poisoning, and this Chinese medicine becomes a toxic drug. If the dose is small and the disease is not enough, it will not help. If the medicine is too sick, it will cause him to suffer from the injury. For example, the poisoning reaction of bitter almond is more than the dosage [4].

## III. TOXIC CHINESE MEDICINE DRUG CHARACTERISTICS

### A. The Dose of Some Toxic Chinese Medicines Shows a Clear Dose-effect Relationship within a Certain Range

In the discussion of the dose-effect relationship of single-component chemical drugs, it is often possible to accurately describe the dose-effect relationship of drugs by establishing mathematical models. Although the study of the dose-effect relationship of traditional Chinese medicines cannot be as accurate as Western medicine, the large-scale dose and effect are Experimental studies have found that some Chinese medicines can still show a good linear relationship. For example, Deng Jiagang, Fan Lili et al. [5] verified the dose-effect relationship of aconites by in vitro frog heart test and classic analgesia test. The effect is dose dependent, as shown in Table 1:

TABLE I. THE DOSE-EFFECT RELATIONSHIP EQUATION OF TOXIC CHINESE MEDICINE ACONITE IN THE RANGE OF DOSE RANGE TO THE ISOLATED FROG HEART TEST AND CLASSIC ANALGESIA TEST.

	Dose range	Dose-effect relationship equation
Isolated frog heart test	0.625 ~ 40 mg/ml	$Y=0.0254x+0.2$ 265, R=0.933 (normal)
Analemia test	0.625 ~ 70 mg/ml 0.75 ~ 6 g/kg	$Y=0.026x+0.6768$ , R=0.9641 (heart failure) $Y=0.0696x+0.2222$ , R=0.8301

#### B. Some Toxic Chinese Medicines Have no Obvious Dose-effect Relationship

Statistical analysis of toxic traditional Chinese medicines in ancient literatures shows that the dosage of the same medicines varies from Dynasty to dynasty, sometimes with great differences. According to Dong Zhenfei's research [6] on the dose-effect relationship of Arapaima in different dynasties, and Pei Xingjian's research [7] on the clinical dose-effect relationship of Evodia radiocarpal, it is found that the dosage of arapaima radiocarpal and Evodia urticaria varies from Dynasty to dynasty.

##### ● Different doses of different effects

The relationship between the amount of toxic drug and the therapeutic effect has been known in ancient times. For example, the application of the dose of Pinellia ternata in the "Treatise on Febrile Diseases"[8], in the prescription, the dose of 4g of Pinellia can promote blood circulation, softening and stasis. 7~13g can be used for relieving cough and dispersing sputum. The maximum dose is 64g, and the dose-effect relationship is very obvious. In different prescriptions, the different doses of Pinellia ternata showed different effects, as shown in Table 2[8]:

TABLE II. EFFECT OF PINELLIA TERNATA CONTENT ON FUNCTIONAL INDICATIONS IN DIFFERENT PRESCRIPTIONS

Jing Fang	Pinellia content (g)	Indication
Chaihu Guizhi Soup	32	Indications of vomiting, fever, slightly aversion
Xiao Chai Hu Tang	64	Indications, vomiting, cold and hot
Da Chai Hu Tang	64	Indications and vomiting
Small pinellia soup	128	Indications
Big half summer soup	256	Indications for stomach vomiting

##### ● Some toxic Chinese medicines show great differences

Some researchers [9] combed the application dose regularity and characteristics of 48 traditional Chinese medicine ancient books from the Eastern Han Dynasty to the Qing Dynasty. It was found that the dosage application of Chinese medicine such as aconite and aconite was very different, as shown in Table 3:

TABLE III. COMPARISON OF THE MINIMUM AND MAXIMUM DOSAGE OF ACONITE, ACONITE AND TIANXIONG

Drug name	Minimum dose	Maximum dose
Aconitum	0.03g	112.50g
aconite	0.0033g	111.90g
Tianxiong	0.03g	37.30g

Traditional Chinese medicine has a long history of application. In the absence of accurate measurement tools and research methods in ancient times, ancient medicines relied on long-term accumulated medication experience, and the use of toxic Chinese medicines was often cautious.

#### IV. THE METHOD OF REDUCING TOXICITY AND INCREASING EFFICIENCY OF TOXIC CHINESE MEDICINE

Traditional Chinese medicine practitioners have taken various effective measures to reduce the toxicity of drugs, while preserving the effectiveness of drugs, thus changing the dose-effect relationship of toxic drugs. The common methods of attenuation and synergy of toxic Chinese medicines, such as various processing methods, the medicine is compatible with the dosage form. In addition, with the improvement of science and technology, Chinese medicine has made great progress in various aspects. For example, the use of technologies such as broken wall tablets, micronized powder, and ultrafine powder can significantly reduce the dosage of drugs, thereby reducing the toxicity of drugs. The research on the efficacy of traditional Chinese medicine broken-wall pieces and traditional decoction pieces[10], the dose of broken-wall pieces is often much lower than the traditional consumption of tablets, and in addition to the micro-powdering, ultra-micronized horses The study of the dose-effect relationship of Qianzi found that the minimum effective dose and the pharmacological action were significantly increased after micronized, but at the same time, the lethal toxicity of micronized powder was significantly enhanced[11].

#### V. THE OUTLOOK

Compared with traditional Chinese medicine, the dose-effect relationship of western medicine is relatively clear. Mathematical models such as one-compartment model and two-compartment model can be established, so that the dose application of drugs can reach the quantitative standard. Due to the complex characteristics of traditional Chinese medicine compounds, the dose-effectiveness of traditional Chinese medicine is difficult. Achieve the degree of quantification. As a reference for the current clinical doses, in addition to reviewing the dosages of the ancient physicians from the ancient books, it is necessary to apply the results of contemporary Chinese medicine research, combined with modern medical technology, to carry out scientific and detailed animal experiments, clinical experiments, and comprehensive consideration of drugs for the human body. The overall impact is to explore the effects of toxic drugs on cells and organisms at the molecular level. With the advancement of science and technology, the research on traditional Chinese medicine has gradually deepened. The evaluation of the effects of toxic drugs on human functions in terms of toxicity and efficacy in a deep and multi-faceted

manner, and then the formulation of drug use strategies is the inevitable result of Chinese medicine going international and moving toward the future trend.

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#### REFERENCE

- [1] Wang Yuguang, Ma Zengchun, Liang Gande, et al. Thoughts and methods of toxicity research of traditional Chinese medicine [j]. Chinese herbal medicine, 2012, 43 (10): 1875-1879.
- [2] Ni Li, Zhang Bing. Theoretical study on toxicity of traditional Chinese medicine based on body state [j]. Chinese Journal of Traditional Chinese Medicine, 2009, 24 (5): 549-551.
- [3] Peng Li, Zhang Lin, Li Pin, et al. Discussion on potential toxic Chinese medicine [j]. Chinese Journal of Experimental Formulaology, 2017, 23 (02): 227-234.
- [4] Tang Qingfa, Xie Ying, Chen Feilong, et al. The existence form of amygdalin in bitter almond and its influencing factors [j]. Chinese Journal of Experimental Traditional Chinese Medicine, 2013, 19 (08): 107-109.
- [5] Fan Lili, Zheng Zuowen, Yang Ke, Deng Jiagang, Hao Erwei. Experimental study on the dose-effect relationship of toxic Chinese medicine aconite [j]. Sichuan Traditional Chinese Medicine, 2011, 29 (05): 53-57.
- [6] Dong Zhenfei. Study on the rule of drug use of Tiannanxing based on the association of "toxicity-effect-proof" [d]. Shandong University of Traditional Chinese Medicine, 2017.
- [7] Pei Xiangjun. Study on the clinical dose-effect relationship and application characteristics of Wu Yu [d]. Beijing University of Chinese Medicine, 2018.
- [8] Huang Jitang. Study on the dose-effect relationship and application characteristics of Pinellia ternata in "Treatise on Febrile Diseases" [j]. Inner Mongolia Traditional Chinese Medicine, 2017, 36(16): 91-92.
- [9] Zhang Xiaotong, Lin Zhijian, Li Fan, et al. Study on the dose rule of internal treatment of Chinese medicine based on effect-toxicity [J]. Chinese Journal of Traditional Chinese Medicine, 2018, 43 (02): 205-210.
- [10] Cheng Jinle, Peng Lihua, Deng Wen. A preliminary study on the dose-effect relationship of Chinese medicine Chinese medicine broken wall pieces [j]. World Chinese Medicine, 2016, 11 (03): 529-532.
- [11] Yang Wei, Wang Yuhong, Zhang Xiuli, Han Yuanshan, Ding Zhiping. Study on the dose-effect relationship parameters of the ultrafine powder of Maqinzi on rheumatoid arthritis model rats[J]. Journal of Emergency in Traditional Chinese Medicine, 2012, 21(12): 1942-1944.