Scholar Publishing Group
International Journal of Multimedia Computing
https://doi.org/10.38007/IJMC.2022.030103
ISSN 2789-7168 Vol. 3, Issue 1: 15-22

Computer Prediction Model in Prediction of Toxic Components of Traditional Chinese Medicine

Ryo Kawachi

University of Tsukuba, Japan

Keywords: Computer Toxicology, Prediction Model, Traditional Chinese Medicine, Toxicity

Abstract: More and more attention has been paid to the toxicity study of traditional Chinese medicine. With the accumulation of toxicity knowledge of a large number of compounds, it provides a reliable basis for toxicity prediction. The method of computational toxicology will be more widely used in elucidating the material basis and mechanism of toxicity of traditional Chinese medicine. In order to understand and master the application of computer prediction model in toxicology research and toxicity component prediction of traditional Chinese medicine, the concept of computer toxicology was introduced briefly, the challenges faced by computer prediction model in toxicity component prediction of traditional Chinese medicine were analyzed, and the application of computer prediction model in toxicity component prediction of traditional Chinese medicine was also discussed.

1. Introduction

Each herbal medicine contains many chemical components, so it is time-consuming and heavy workload to find potential toxic components of traditional Chinese medicine by traditional methods. Moreover, due to the low content of chemical components, it is difficult to obtain enough quantities for in vivo and in vitro experiments to explore the application of computer prediction model in the prediction of toxic components of traditional Chinese medicine [1-3]. The computer prediction model only predicts the toxicity based on the molecular structure of compounds. When determining the chemical structure of traditional Chinese medicine components, the early toxic components can be screened, which provides guidance for further in vivo and in vitro experiments [4-7]. However, with the further study of toxicity mechanism, molecular mechanism model can not only discover the potential toxic components of traditional Chinese medicine, but also explore the possible toxic mechanism of traditional Chinese medicine components [7-10]. Moreover, each Chinese herbal medicine contains many chemical components, and the toxicity of a single compound cannot represent the toxicity of the mixture. Prediction of combined toxicity of various compounds is also a difficult problem in computational toxicology [11-12]. Therefore, to apply the prediction model to

risk assessment of traditional Chinese medicine, it is necessary to establish a model to predict the combined toxicity of mixtures.

2. Computer Toxicology

2.1. Development of Computational Toxicology

Computational toxicology is a discipline that studies the relationship between chemical structure and toxicity. Its method can be used to predict the toxicity of compounds. The EPA defines computational toxicology as the application of mathematical and computer models to predict and elucidate the toxic and side effects of compounds and their mechanisms of action. Computational toxicology began in the early 1980s. The main reason for its emergence is the high cost of animal toxicity testing and social opposition, and the number of compounds to be screened has increased dramatically. At the same time, the rapid growth of chemical toxicology research provides a large number of chemical structure and toxicity data, which provides a reliable basis for the calculation and prediction of drug toxicity. That is to say, at present, many compounds have been tested toxicologically, and the relationship between structure and toxicity of compounds has been studied extensively. A large amount of data has been accumulated. Based on these data, data mining has been carried out through computer science and artificial intelligence technology to find out certain rules, establish computer prediction model of toxicity, and then, according to the model under study or the possible toxicity and toxic target organs of new compounds were predicted.

2.2. Current Status of Computational Toxicology

At present, computational toxicology is widely used in toxicity evaluation of new drugs. In foreign countries, toxicity of drugs is one of the main reasons for clinical failure of newly developed drugs. Computational toxicology is used to predict the possible metabolites and toxicity of drugs in human body. Even in the early stage of drug screening, computational toxicology is used to evaluate or predict the toxicity of lead compounds and candidate drugs, eliminate toxic compounds from lead compounds as early as possible, help shorten the development cycle, reduce development costs and improve the success rate of new drug development. The importance of toxicity identification in the early stage of compound design has been recognized, and computer toxicity prediction is considered to be one of the effective ways to shorten the time of drug and pesticide development and reduce the cost. In recent years, computational toxicology has been used more and more in toxicity prediction of new drugs and safety evaluation of environmental compounds. Some studies abroad show that quantitative structure-activity relationship can be used to predict toxicity of natural chemical components, which provides a basis for computational toxicology research of traditional Chinese medicine. However, the application of computational toxicology in the field of traditional Chinese medicine has not been carried out in China. Because of the complex chemical composition of traditional Chinese medicine, it is difficult to extract and separate most of its components. Traditional toxicological methods in vitro and in vivo have their limitations in evaluating the toxicity of traditional Chinese medicine. Computational toxicological methods can be used to study and predict the toxicity of traditional Chinese medicine quickly and effectively. However, it is also the complexity of the components of traditional Chinese medicine that makes the toxicity prediction of traditional Chinese medicine more challenging. Therefore, domestic toxicity prediction is still in its infancy, and computational toxicology has not been used in the study of traditional Chinese medicine and its compounds.

2.3. Challenges in Computational Toxicology of Traditional Chinese Medicine

The study of computational toxicology has been gradually carried out in China. For example, the Institute of Organic Chemistry has developed a Carcinogenic Toxicity Prediction System for Compounds (PSCT). PSCT can predict the carcinogenic toxicity of compounds provided by users, and provide information on carcinogenic toxicity of new drugs or new materials for users. For example, the biological and ecological effects produced by the mixture are different from the biological activities of each single component. Even when the single component of the mixture system is at an invalid concentration, the component still contributes to the total toxicity effect of the mixture. Therefore, extrapolating the risk assessment criteria of a single compound to the assessment of the actual environment may lead to unreliable conclusions. Establishing an effective method for evaluating and predicting the combined toxicity of mixtures is of great significance for risk management of organic pollutants. Despite the rapid development of computational toxicology and its preliminary success in predicting the toxicity of natural products, the toxicity prediction of traditional Chinese medicine still faces many challenges.

3. Theory of Toxicity Prediction

3.1. Toxicity Prediction Tool

In the research of traditional Chinese medicine, it is often necessary to analyze the toxicity of traditional Chinese medicine. The traditional toxicity prediction method needs a lot of time, material resources and complicated steps. The computer prediction model provides a simple, fast and reliable tool for preliminary screening of toxic substances. The development and application of related databases and new bioinformatics tools of computer prediction model is one of the most important aspects of toxicology research. It will help to explain and study the large amount of bioinformatics produced in the field of toxicology of traditional Chinese medicine. At present, many toxicity prediction tools have been developed and used in different situations, such as the development of Virtual ToxLab. In order to predict a toxicity prediction tool based on molecular docking, virtual ToxLab was validated by estrogen receptor effect and CYP isoenzyme inhibition. Or the development of ToxSYS to predict the mutagenicity and acute toxicity of exogenous substances. In addition, in the detection of organophosphorus pesticides, biosensors based on nanotechnology are used to detect organophosphorus pesticides, and combined with computer technology, computational models (such as Auto Dock software) are used to predict receptor-ligand interactions. The computer software INVDOCK can be used to automatically identify the potential toxicity of several bioactive substances separated from traditional Chinese medicine.

3.2. Fundamental

The gray prediction model first identifies the difference degree of the development trends among the system factors, then generates the raw data, explores the change law of each system factors and generates a strong regular data sequence, and finally establishes a differential equation model for the sequence to predict the future development trend and amplitude of the sequence.Among them, the core model of the grey prediction method is the GM(1,1) model, which essentially consists of a first order differential equation containing an univariate, a gray model of first order one variable. Among the influencing factors of CPI total CPI, some information is known, some information is unknown, and it has developed exponentially to meet the modeling conditions of the gray model. For which, the gray model GM(1,1) can be selected for description.

Assuming $X^{(0)} = (X^{(0)}(1), X^{(0)}(2), L)$, the original data of an index to be predicted, in most cases the sequence is a non-stationary random sequence. If such a random sequence fluctuates too much, it would be impossible to explore the regularity of its development trend. The random original sequence can be generated, namely:

The first step, to construct the cumulative generation sequence:

$$X^{(1)} = (X^{(1)}(1), X^{(1)}(2), LX^{(1)}(N)) \tag{1}$$

$X^{(1)}(K) = \sum_{i=2}^{k} x^{(0)}(i)$

Its , xn is the 1-AGO sequence of x(0). Through this evolution, a new sequence can be obtained, and the change trend of the new sequence can be approximately described by the following differential equation:

$$\frac{dx^{(1)}}{dt} + ax^{(1)} = b \tag{2}$$

The above formula can be fitted using the following least squares method to obtain the values of a and b:

$$a = \begin{bmatrix} a \\ b \end{bmatrix} = (b, c) - 1 \tag{3}$$

3.3. Establishment of Toxicity Prediction and Calculation Model of Traditional Chinese Medicine

When dealing with computational toxicity models, methods for solving general toxicity phenomena can be distinguished, such as carcinogenicity and methods, which involve factors that contribute to the process of toxicity manifestations. Therefore, some models address systemic toxicity, while others focus on organ-specific toxicity. There are a lot of computational models for toxicity phenomena. Although these genotoxicity and carcinogenicity are very complex, they are the most widely studied. However, the availability of the model is different from the reliability of the model prediction. In addition, the possibility of applying the model satisfactorily to interested drugs depends on the availability of molecular toxicological data related to the solid chemistry. In contrast, models of developmental or reproductive toxicity are lacking. Comparing with the above models, the calculation models of organ-specific effects usually focus on drugs, because data availability is the most abundant for drug-like compounds. Among them, hepatotoxicity is often studied, and now more and more interest is focused on cardiotoxicity and nephrotoxicity. Limited models can be used for neurotoxicity or other effects. Some studies involve the use of adverse impact databases or the use of comprehensive risk indices to assess the impact combinations of several receptor targets.

3.4. Computer Prediction of Toxicity of Traditional Chinese Medicine

Computational studies are more time-saving and cheaper than experiments, so a large number of computational methods can be evaluated to predict toxicity, including quantitative structure-activity relationship (QSAR) model, expert system, 3D-QSAR and molecular docking. The QSAR method is used to find a mathematical relationship between a set of molecular descriptors describing each molecule in a group of chemicals and their toxicity values. It is very important to verify the

predictive performance of the model by using appropriate statistical methods. These methods include internal and external validation. In the case of external validation, a set of new chemicals was applied that had never been used in model development. A recent book describes the theory and application of computer models, focusing on "expert systems", where software programs compile a series of rules that experts determine in areas of interest. A typical example is when there is a known set of toxic debris, the software identifies their presence in the target chemical. A problem associated with this method is that the toxic fragments may not be complete, which may lead to false negativity, i.e. false predictions of chemical safety. However, 3D-QSAR is based on the concept of "molecular interaction field". The changes in the space and electrostatic interaction energy calculated by this technique between each molecule and probe are related to the changes in the properties studied. 3D-QSAR usually concentrates on a group of compounds with similar structures with relevant toxicity data, while docking simulation combines with biological macromolecules. In general, docking is not often used for toxicity estimation, because most common toxicity phenomena involve complex sequence of events, and binding to specific receptors is only a possible component of the sequence. On the contrary, docking research is more often used in drug design processes, where therapeutic targets are known, and the reasons for toxicological phenomena are often not clarified at the biochemical level. Estimate a large number of compounds.

4. Application of Computer Prediction Model in Prediction of Toxic Components of Traditional Chinese Medicine

4.1. Application of Computer Prediction Model in Prediction of Hepatotoxic Components of Traditional Chinese Medicine

The liver is mainly responsible for biosynthesis, metabolism and excretion. Drug metabolism mainly occurs in the liver. Therefore, the liver is one of the main target organs of drug-induced injury, and most of the drug-induced liver injury is caused by Chinese herbal medicine.

Table 1. Information on TCM toxic target organs

Common evaluation model of liver toxicity	Representative of liver toxicity plants
Primary hepatocyte	Pseudo-ginseng
Human embryonic stem cell model	Polygonum multiflorum
Subcell model	Semen psoraleae
Zebra ish Model	Rheum officinale
3 D training model	Folium sennae

After research, Panax notoginseng, Polygonum multiflorum, Psoralea corylifolia, Rhubarb, Senna leaf and other traditional Chinese medicines have been proved to have certain hepatotoxicity by clinical practice, so the study of hepatotoxicity is essential. Common hepatotoxicity assessment models include primary hepatocytes, human embryonic stem cell models, subcellular models,

zebrafish models, three-dimensional culture models, etc. The complex mechanism of multi-target and multi-channel of TCM hepatotoxicity fits well with the advantages of computer prediction model. The computer prediction model can extract the information of toxic target organs of TCM from the database and construct a toxic TCM-target network with the help of relevant tools.

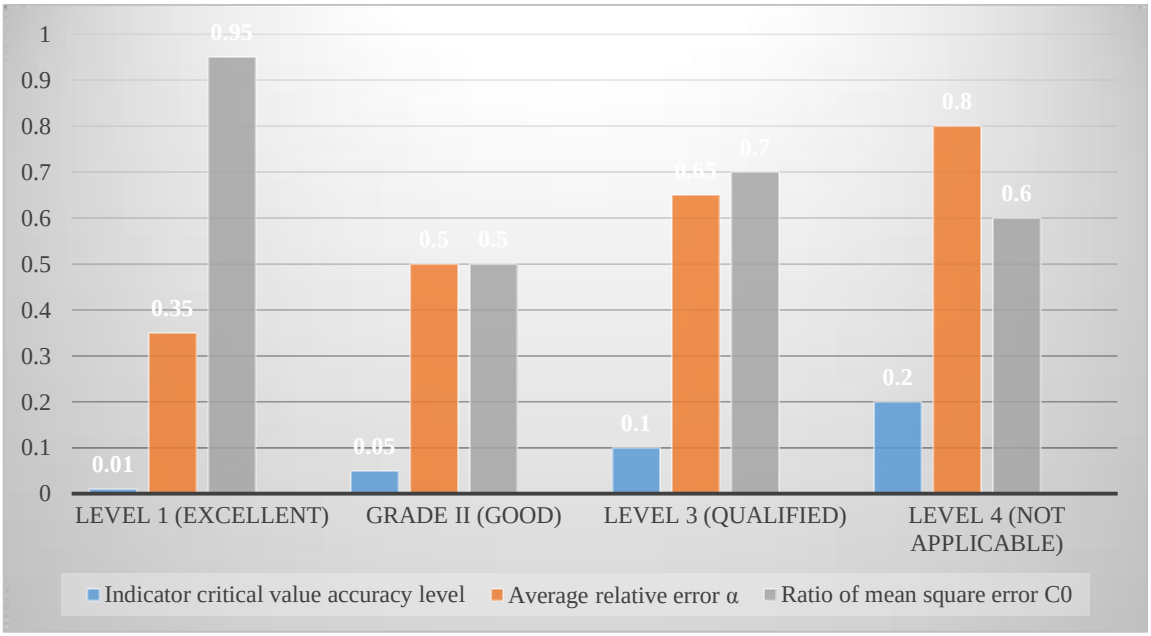

Figure 1. Refer to the precision test grade

The grey prediction model established based on the above steps must perform a series of grey prediction tests to verify that it has high accuracy for predicting the commonly used accuracy level Figure given below, this data is for reference only.

4.2 Application of Computer Prediction Model in Prediction of Nephrotoxic Components of Traditional Chinese Medicine

Kidney is an important excretory organ of human body, which is used to maintain the balance of water and electrolyte. It is also the most common target organ of drug toxicity, second only to liver. In the study of kidney, there are many reports of nephrotoxicity caused by traditional Chinese medicine. It is difficult to detect the damage of renal function caused by drugs in the early stage of taking drugs. Therefore, predicting drug nephrotoxicity has become an important part of the safety evaluation of traditional Chinese medicine, and can also promote the development of new drugs. Traditional Chinese medicine nephrotoxicity research methods generally use in vivo and in vitro test models, which have the advantages of reliable and comprehensive results. However, cell line-based nephrotoxicity evaluation model in vitro lacks the specificity of target organ toxicity, and cannot distinguish the cytotoxic effects and nephrotoxicity of compounds. When using this method for high-throughput screening, it usually costs a lot of money and takes a long time. When using computer prediction model to study nephrotoxicity, the application of quantitative structure-activity relationship can help optimize animal experimental design, reduce the use of experimental animals, reduce experimental costs, and realize the prediction of toxicity of large quantities of compounds in a short time.

4.3 Application of Computer Prediction Model in Prediction of Cardiac Toxicity Components of Traditional Chinese Medicine

Cardiac toxicity refers to drug reactions that affect cardiac function and myocardial damage in relatively small doses and relatively short time. It is one of the main causes of adverse drug reactions. Heart damage caused by drug toxicity is also a matter of great concern to the pharmaceutical industry and drug regulatory agencies. Relevant reports indicate that aconitum, Tripterygium wilfordii, oleander containing glycosides, traditional Chinese medicine containing polypeptide amino acids and scorpion venom protein can cause cardiovascular toxicity. Traditional animal experimental methods for screening cardiotoxic components of traditional Chinese medicines are time-consuming and costly, while computer prediction model overcomes the above shortcomings. Using computer-aided new drug screening method to construct quantitative structure-activity relationship model and predict cardiotoxic components of traditional Chinese medicines can not only predict the toxicity of chemicals, but also provide priority for subsequent toxicity experiments. Guidance. For example, the toxic components and toxic mechanism of aconite are well known. Strong cardiotoxicity and neurotoxicity are mainly attributed to hypertoxic diester diterpenoid alkaloids and their effects on voltage-sensitive sodium channels in myocardium, nerve and other cell membranes.

5. Conclusion

Toxicity of traditional Chinese medicine is an important part of modern research of traditional Chinese medicine. Traditional methods of toxicity prediction often need a lot of energy and material resources, and the steps are complex. The computer prediction model provides a simple, accurate and reliable tool for preliminary screening of toxic substances, which plays an important role in the prediction of toxic components of traditional Chinese medicine. Prediction models based on synthetic compounds have limited applicability. In some studies, synthetic drugs and components of traditional Chinese medicine are used as training sets to build models. The prediction performance of these models is better than that of using synthetic drugs only as training sets. Establishing prediction model of Chinese herbal components can be more suitable for toxicity prediction of Chinese herbal components, but there are fewer studies on toxicity of Chinese herbal components, and fewer data can be used to establish the model.

Funding

This article is not supported by any foundation.

Data Availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

Conflict of Interest

The author states that this article has no conflict of interest.

References

[1]Xia C, Fu L, Liu Z, et al. Aquatic Toxic Analysis by Monitoring Fish Behavior Using Computer Vision: A Recent Progress. Journal of Toxicology, 2018,(2018-4-3), 2018, 2018:1-11.

https://doi.org/10.1155/2018/2591924

[2] Pradeep, Prachi. Hybrid Computational Toxicology Models for Regulatory Risk Assessment. Dissertations & Theses - Gradworks, 2015.

[3] Bailey S A, Li D, Potter D M. General Toxicology, Safety Pharmacology, Reproductive Toxicology, and Juvenile Toxicology Studies// Nonclinical Statistics for Pharmaceutical and Biotechnology Industries. 2016. https://doi.org/10.1007/978-3-319-23558-5_10

[4] Potkrajac D M, Rakic B, Apic G, et al. Data Sources for Signature Discovery in Toxicology. Methods in Pharmacology & Toxicology, 2015, 54:95-108. https://doi.org/10.1007/978-1-4939-2778-4_4

[5] Kaufman J J, Koski W S, Hariharan P C, et al. Prediction of toxicology and pharmacology based on model toxicophores and pharmacophores using the new TOX‐MATCH–PHARM‐MATCH program. International Journal of Quantum Chemistry, 2015, 24(S10):375-415. https://doi.org/10.1002/qua.560240736

[6] Setio A A A, Jacobs C, Ciompi F, et al. Computer-aided detection of lung cancer: combining pulmonary nodule detection systems with a tumor risk prediction model. 2015. https://doi.org/10.1117/12.2080955

[7] Moon W K, Chen I L, Yi A, et al. Computer-aided Prediction Model for Axillary Lymph Node Metastasis in Breast Cancer using Tumor Morphological and Textural Features on Ultrasound. Computer Methods & Programs in Biomedicine, 2018, 162:129-137. https://doi.org/10.1016/j.cmpb.2018.05.011

[8] Borhani S, Kilmarx J, Saffo D, et al. Optimizing Prediction Model for a Noninvasive Brain Computer Interface Platform using Channel Selection, Classification and Regression. IEEE Journal of Biomedical and Health Informatics, 2019, PP(99):1-1.

[9] Kleandrova V V, Luan F, Speck-Planche A, et al. In Silico Modeling of Acute Toxicity of Chemicals: Recent Advances and New Model for Multitasking Prediction of Toxicity. Mini Rev Med Chem, 2015, 15(8):677. https://doi.org/10.2174/1389557515666150219143604

[10] Purser D A. Chapter 7:Application of Animal Models and Human Studies to Prediction of Combustion Toxicity in Humans// Toxicology, Survival and Helath Hazards of Combustion Products. 2015. https://doi.org/10.1039/9781849737487-00173

[11] Shi S Z, Wang Q, Toxicology D O. Validation of two predictive softwares for the toxicity prediction of chemical ingredients in traditional Chinese medicine. Chinese Journal of New Drugs, 2016.

[12] Liu H, Li T, Chen L, et al. To Set Up a Logistic Regression Prediction Model for Hepatotoxicity of Chinese Herbal Medicines Based on Traditional Chinese Medicine Theory. Evidence-Based Complementary and Alternative Medicine, 2016, 2016(6):1-9 https://doi.org/10.1155/2016/7273940