Statistical Evaluation of Dissolution of Solid Pharmaceutical Preparations in Vitro

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Abstract: Objective to Investigate the in Vitro Dissolution Calculation Method of Solid Pharmaceutical Preparations. Methods There Are Five Methods for Dissolution Evaluation: Probability Unit Method, Weibull Method and Gompertz Method, Logarithmic Curve Method and Exponential Mode Method. in This Study, Three Different Prescriptions Were Calculated during the Development of Corrosion Inhibitors, and the Foreign Preparations of the Same Variety Were Selected as Control Drugs to Complete the in Vitro Dissolution Calculation. Results No. 1 Drug Similarity Factor Was Below 50; No. 2 Drug and No. 3 Drug Were between 50 and 100. Conclusion the in Vitro Dissolution Can Accurately Reflect the Pharmacokinetics of the Drug and the Bioavailability of the Drug, Which Can Provide a Basis for Clinical Rational Drug Use, and It is Worthy of Popularization and Application.

1. Introduction

The Dissolution Data of Solid Drugs in Vitro is the General Evaluation Index of Drugs, Which Plays an Important Role in the Production of Drugs, the Types of Drugs, the Quality Control of Batches and So on. However, Due to the Different Medical Priorities of Each Country, the Standards of Each Drug Are Different. in Order to Improve the Safety of Drugs, Fda of the United States Believes That in Vitro Elution Test Can Be Used Instead of in Vivo Test, Which Has the Advantage of Simple and Reliable Results. Clinical Research Shows That the Dissolution in Vitro is Affected by Many Factors and Closely Related to the Bioavailability in Vivo[1]. the Dissolution Rate of a Given Dose is Related to the Absorption Rate in Vivo. Mean in Vitro Cleavage Was Correlated with Mean Residence Time. Dissolution and Solubility Are Related to the Pharmacokinetic Parameters Tmax, Cmax, Ka and Auc. Compared with Bioavailability, Extracorporeal Pyrolysis Has Many Advantages, Such as Simple Operation, High Accuracy and Good Repeatability. Therefore, Fda Completed a Study on Bioavailability and Biological Disinfection of Solid Drugs in 1999, and Found That the Similarity Coefficient of F2 > 50 Was Equal. This Paper Reports the in Vitro Elution of Solid Drugs and the Comprehensive Analysis of Statistical Methods.

2. Derivation of Macro Dynamic Model

In Vitro Dissolution of Solid Preparations is a Basic Method for Investigating the Effects on the Composition of Preparations, Excipients and the Quality of Solid Preparations. the Process Consists of Two Stages: Destruction of Solid Preparation and Dissolution of Active Components. through the Real-Time Measurement of the Dissolution of the Active Ingredients, the Absorption Effect of the Agents in Vivo Can Be Inferred, and the Quality of the Formulation Can Also Be Evaluated. he Also Developed a Mathematical Model Describing the Dissolution Process of Western Medicine Solid Preparations in Vitro. Many of Them Are Empirical Models[2]. the Equations Derived from Gucci's Law Are Based on Theoretical Research, But the Mechanism of This Process Has Not Been Determined. the Dissolution Process of Solid Preparation of Traditional Chinese Medicine in Vitro is Quite Different from That of the Model. on the Basis of Reasonable Analysis and Process

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Hypothesis, a New Mathematical Model is Established by Using the Theory of Material Movement, and It is Applied to the Analysis of Solubility Data of Propylene Bismuth Table.

2.1 Basic Analysis of Dissolution Process

In the process of dissolution in vitro, the solid preparation first decomposes and produces a large number of drug particles. Then, the small particles in the drug are continuously dissolved on a specific medium, and the active ingredients are gradually dissolved. The small particles in the drug continue to shrink until they disappear completely. When the decay rate is much higher than the dissolution rate of active components, the influence of decay can be ignored. The macro dynamic mathematical model of the process under these conditions is studied[3]. (1) the solvent molecules move from the liquid phase to the solid surface through the solid-phase liquid membrane. (2) solvent and (water and reaction, acid and water decomposition reaction, alkali and water decomposition reaction) are carried out on the solid surface and the effective component B in the solvent. (3) liquid product f (water and substance, acid decomposition product, alkali water decomposition product) enters the liquid from the solid phase through the liquid surface.

Process (3) only explains the macro motion model of step (1) and step (2), because the control of process rate is less. In order to simplify the derivation process, the following two hypotheses are proposed: the dissolution process is a metastable process. In other words, the moving speed of solvent A is equal to the consumption rate of reaction, and there is no material accumulation at the liquid interface; then the internal temperature of the whole particle is uniform[4]. To sum up, the dissolution process in vitro should be regarded as a series of generalized reaction process and mass transfer process, and the total reaction formula can be expressed as

$$A_{(l)} + bB_{(s)} \longrightarrow fF_{(l)} \tag{1}$$

2.2 Identification of Control Steps in Drug Dissolution Process

According to the mathematical model derived from different control steps, the control steps of the process can be distinguished from the cumulative release and dissolution time of the effective components of the drug. This provides a theoretical basis for drug research[5]. Although the hypothesis of the model proposed in this paper is very small, the dissolution process of solid system is affected by the decay rate, the type of excipients, the amount of excipients, the surface morphology of particles and other factors. If necessary, you must analyze according to certain conditions.

3. Data and Methods

3.1 Clinical Data

In this study, three different formulations were calculated in the process of inhibitor development, and the same kind of foreign preparation was selected as the control drug to complete the in vitro dissolution calculation.

3.2 Method

The similarity factor method was used in this experiment to compare the dissolution of experimental drugs and control substances in vitro, and to analyze the bioavailability similarity of the two drugs[6].

So far, the evaluation methods of clinical co dissolution include logarithmic curve method, probability single frame method, Gompertz method, exponential mode method and Weibull method. In terms of data statistics, multivariate factor method, regression analysis method, similarity factor method, variance method, splitpollr method, Chow method, etc. are mainly used. Through clinical trials, it has been proved that the similar factor method plays an important role in evaluating the dissolution relationship between the test drug and the in vitro control drug. The specificity of the similarity factor method is the sum of the difference between the cumulative dissolution of the experimental and control drugs.

Calculate correlation factors f2[7].

$$f2 = 50 \times \lg[(1 + Q/n - 0.5 \times 100] \quad (2)$$

If F2 is between 50 and 100, it is confirmed that the dissolution of the two preparations is the same.

3.3 Statistical Analysis

SPSS 18.0 software was used for processing, x 2 test was used for counting data, n (%), t test was used for measuring data, X ± s was used, P < 0.05.

4. Result

Drug 1 similarity factor is below 50; drug 2 and drug 3 are between 50 and 100. See Table 1 and table 2 for specific test results.

4.1 In Vitro Dissolution Test Results

See Table 1 for the details of the dissolution test of the drug and control sample prepared by the three prescription schemes.

Table 1 Test Results Of Dissolution in Vitro

Measurement data time	No. 1 drug	No. 2 drug	No. 3 drug	No. 4 drug
1h	14.35±2.35	28.44±.357	26.47±4.22	34.78±3.11
3h	50.43±4.16	65.33±2.77	63.3±3.12	66.58±2.24
6h	71.25±3.16	82.32±3.33	82.31±3.74	81.42±2.47
12h	85.59±3.62	98.62±3.42	97.31±2.16	94.33±2.68

4.2 In Vitro Dissolution Test Results

See Table 2 for the details of the dissolution test of the drug and control sample prepared by the three prescription schemes.

Table 2 Details of Research on Q-Value and Similar Factors of Three Drug Prescriptions

Category	No. 1 drug	No. 2 drug	No. 3 drug
Similarity factor	49.3	68.5	81.5
Qvalue	723.6	1130	329

5. Conclusion

Equivalent limit method and similarity factor method are usually used to detect the dissolution of solid drugs, but similar factor method is widely used in clinical practice. This method is easy to operate and has a short detection period. It can correctly reflect the control drugs and experimental drugs. The solubility is different. At the same time, the similarity coefficient method can make up for the defects of the equivalent limit method. Since the limit of quantity method is used to determine the limit of quantity method, it is necessary to first complete the calculation of Q value to reflect the dissolution of the comparison sample[8]. Domestic scholars say that the similarity coefficient method can also be used to determine the biological identity of drugs. In the case of measurement > 50, the drugs were almost the same after oral administration. The drug utilization rate of those 50 patients was relatively low, so it was necessary to adjust the treatment plan. This study measured the dissolution rates of three solid drugs. The results showed that the drug similarity factor 1 was less than 50. No. 2 and No. 3 are between 50 and 100, and the similarity between No. 2 and No. 3 is very high. The similarity of drugs is very high. In a word, the irresistible dissolution rate can accurately reflect the drug dynamic and biological function of the drug, provide a reasonable basis for clinical drug use, and is worthy of promotion and application.

In vitro elution test can be used to evaluate the preparation, bioavailability and pharmacokinetics of drugs, and it is of great significance to compare the bioavailability of domestic and imported

drugs. The specificity of the similarity coefficient method is the sum of the difference between the cumulative dissolution of the test and the control.

It is pointed out in the literature that the equivalent calculation method is simpler than the similarity coefficient method and can determine the difference of dissolution between the control drug and the experimental drug. Equivalent limit method can not calculate equivalent limit[9]. On this basis, the Q value is calculated first, and then the similarity limit is calculated. This can indicate the similar dissolution conditions of the experimental sample and the control sample.

Similar factor method can also be used as an in vitro evaluation method to study the biological adaptation and equivalence of drugs. Most of the drugs in F 2 > 50 can be compared with the evaluation in vitro, but for the evaluation of bioequivalence in vitro, it is very important in practicality.

In this experiment, the method was used to compare the dissolution of three solid preparations in vitro. It was found that the drug like factor I was less than 50, which was different from the control drug. The similarity factor of drug III was 50-100, and the two drugs were similar to the control drug.

Through the statistical analysis of the dissolution of solid drugs in vitro, the similarity factor method is more accurate and simpler than other methods, which can be used to determine and determine the differences between the experimental samples and the control samples[10]. It is of great significance to evaluate the difference between Chinese medicine and original medicine in clinical practice, which is worthy of clinical application.

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