Retraction

Retraction: Study on Hypoglycemic Effect of Mulberry Leaf Extract Based on Big Data analysis (J. Phys.: Conf. Ser. 1744 022105)

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Study on Hypoglycemic Effect of Mulberry Leaf Extract Based on Big Data analysis

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Abstract: With the improvement of people's living standards and the emergence of aging society, the incidence of diabetes is increasing year by year, and diabetes and its complications have become the third killer threatening human health. There are many drugs for treating diabetes, but their toxic and side effects are all great. Therefore, using big data analysis to find and develop natural products with hypoglycemic effect has high practical value. Therefore, the purpose of this paper is to study the hypoglycemic effect of mulberry leaf extract based on big data analysis. Firstly, this paper studies the medicinal value of mulberry leaves and related application methods by consulting relevant data. Through big data analysis, it is found that mulberry leaves are rich in alkaloid component 1-deoxynojirimycin (DNJ), accounting for more than 50% of alkaloid content. Therefore, this paper takes mulberry leaf extract DNJ as the research object, and firstly prepares mulberry leaf extract. Mulberry leaf water extract was perfused into stomach for 15 consecutive days, and fasting blood glucose of diabetic mice was measured 2 hours after eating by glucose oxidase method at specified time. The hypoglycemic effect of mulberry leaf water extract was analyzed by big data. The results showed that mulberry leaf extract could effectively inhibit the enzyme activity of decomposing sugar and prevent glucose absorption. Therefore, it can significantly reduce the blood sugar level of diabetic mice by about 50%. And the higher the dose of mulberry leaf extract, the better the hypoglycemic effect, showing a dose effect.

Key Words: Big Data analysis, Mulberry Leaf Extract, Hypoglycemic Effect, Diabetic Model in Mice

1. Introduction

Mulberry leaves are medicinal and edible plant resources, which were used to treat diabetes in ancient times. Mulberry leaves are used to treat diabetes in many Asian countries. Many scholars at home and
abroad have reported on the treatment of diabetes with mulberry leaves, mostly focusing on the hypoglycemic effect of polysaccharides and flavonoids in mulberry leaves. However, the hypoglycemic effect of these ingredients is not particularly good, and even some ingredients have toxic and side effects. Therefore, it is of great value to find and develop natural products with hypoglycemic effect. This has high practical value for the treatment and health care of diabetic patients.

At present, with the continuous development of big data analysis technology, there are many researches on using big data and other related technologies to find the treatment of diabetes. In foreign countries, Mbaka suggested that silkworm larvae and mulberry leaves as silkworm food should be taken as hypoglycemic foods for diabetics [1]. In China, many similar studies have been reported. Zhang, Jin used the crude extract of mulberry leaves to test some common enzymes that break down sugars in diabetes and found that the crude extract of mulberry leaves could effectively inhibit the activity of enzymes that break down sugars, prevent glucose absorption and reduce blood glucose levels [2].

In this paper, aiming at the research of hypoglycemic effect of mulberry leaf extract based on big data analysis, the medicinal value and related application methods of mulberry leaf were analyzed from the actual situation of mulberry leaf as medicine. Through big data analysis, we found that mulberry leaves are rich in alkaloid DNJ. Therefore, DNJ, an extract from mulberry leaves, was taken as the research object, and a mouse model of diabetes was established. It was found that mulberry leaf extract can significantly reduce the blood sugar level of diabetic mice, and the higher the dose of mulberry leaf extract, the better the blood sugar lowering effect, showing a dose effect. This meets the needs of diabetes treatment in hospitals, and has important reference significance for further exploring effective drugs for diabetes treatment.

2. Technical research on Hypoglycemic Effect of Mulberry Leaf Extract Based on Big Data analysis

2.1 Big Data analysis Theory
(1) Data acquisition
For any data analysis, the primary thing is data collection, so the first technology of big data analysis software is data collection technology. This tool can collect data distributed on the Internet and data in some mobile clients quickly and widely. At the same time, it can quickly import data from data sources in some other platforms into this tool, and clean, transform and integrate the data, thus forming it in the database or data mart of this tool for contact analysis and processing [3].

(2) Data access
After the data is collected, another technology of big data analysis, data access, will continue to play a role. It can relate the database, make it convenient for users to store the original data in use, and collect and use it quickly. Then there is the basic architecture, such as transportation and storage and distributed file storage, which are common.

(3) Data processing
Data processing can be said to be one of the core technologies of the software. Facing the huge and complex data, the tool can use some calculation methods or statistical methods to process the data, including its statistics, induction, classification, etc., so that users can deeply understand the deep value of the data [4].

2.2 Mulberry Leaf Extract
(1) Types of mulberry leaf extracts
1) Alkaloid
Most of the alkaloids in mulberry leaves are mainly polyhydroxy alkaloids. Three compounds can be obtained from the water extract of mulberry leaves: betaine, buckwheat alkali and 1-DNJ; Five
Polyhydroxy alkaloids were isolated and identified from mulberry leaves, which were 1-DNJ, N-methyl-1-deoxynojirimycin, 2-oxo-a-D-galactopyranoside-1-deoxynojirimycin and buckwheat alkali.

2) Polysaccharides
Poly saccharide components, Mucopolysaccharide I, Mucopolysaccharide II and Mucopolysaccharide III, were identified from mulberry leaves by boiling water extraction and gel chromatography. Mulberry leaves were extracted with hot water, precipitated with more than 95% ethanol, decolorized, put on the treated DEAE column, and purified by gel column chromatography to obtain uniform polysaccharide components. Many polysaccharide compounds were identified by sugar composition analysis, methylation analysis, 1H-NMR, 13C-NMR and IR[5].

3) Amino acids and organic acids
The basic components of protein are mainly amino acids. In recent years, the contents and types of proteins in mulberry leaves have been systematically studied in China. Studies have shown that mulberry leaves are rich in protein resources, containing about 18 kinds of amino acids, such as alanine, proline, leucine and tryptophan, among which human essential amino acids account for more than 50% of the total, and their contents will decrease with the growth of leaves.

(2) Extraction and detection methods of DNJ
The extraction methods of 1-deoxynojirimycin (DNJ) from Moraceae plants mainly include hydrochloric acid extraction, distilled water extraction, ethanol extraction, microwave-assisted extraction and deionized water extraction. In terms of purification, cation exchange resin and reverse chromatography are the most widely used technologies. At present, the commonly used detection methods of DNJ include gas phase detection, reversed-phase high performance liquid chromatography, reversed-phase high performance liquid chromatography, fluorescence derivatization, pre-column derivatization high performance liquid chromatography, gas chromatography-mass spectrometry, high performance liquid chromatography-differential refraction detection, etc[6].

2.3 Relevant Theories in Experiments
(1) Determination of inhibitory activity of DNJ on α-glucosidase
When determining its inhibition, centrifugation is needed, and then the enzyme in each hole of the enzyme label plate is mixed with the drug evenly, and incubated in a water bath at 37°C for 20 minutes; After incubation, add 50uL of PNPG reaction solution into the above enzyme labeled well, and put it in a water bath to react for 15 minutes. At the end of the reaction, add 200uL Sodium carbonate solution to each enzyme labeled well to terminate the reaction. The activity value was read with a microplate reader at 400nm wavelength [7]. Use the following formula to calculate the inhibition rate of enzyme activity by samples:

\[
P = 1 - \frac{x - z}{y - z} * 100% \tag{1}
\]

In which \( p \) is the inhibition rate, \( x \) is the sample group, \( y \) is the control group and \( z \) is the blank group.

(2) Determination of fluorescence quenching mechanism
There is an interaction between DNJ and α-glucosidase, and energy transfer takes place. It can be seen that DNJ has fluorescence quenching effect on α-glucosidase. The types of fluorescence quenching are divided into dynamic quenching and static quenching. Whether for energy or electron, its transfer has no significant effect on physiological activity or structure of protein in static state. While the secondary structure of protein is affected by dynamic quenching. The fluorescence quenching accords with Stern-Volmer equation:

\[
\frac{F_0}{F} = 1 + k_v \tau_o[Q] = 1 + k_v[Q] \tag{2}
\]
Where $F_0$ is fluorescence intensity without quencher, $F$ is fluorescence intensity after quencher is added, $k_q$ is apparent quenching constant, $k_w$ is Stern-Volmer quenching constant, which means the competition between two decay paths, which is the ratio of bimolecular quenching constant to monomolecular decay rate constant, $\tau_0$ is the average lifetime of fluorescent molecules without quencher, and the fluorescence lifetime of biological macromolecules is generally about $10^{-8}$ s. Is the quencher concentration, $[Q]$ that is, the concentration of DNJ [8].

(3) Determination of binding constant and number of binding sites

Binding constant ($k$) and number of binding sites ($n$) are important quantitative data of interaction between small molecules and macromolecular proteins. In the process of static quenching of biological macromolecules by small molecules, assuming that small molecules have multiple similar and independent binding sites on biological macromolecules, the binding constant and the number of binding sites in the interaction reaction system between DNJ and α-glucosidase can be obtained by double logarithmic equation [9].

$$\lg \frac{F_0 - F}{F} = \lg k + n \lg [Q]$$

(3)

(4) Judgment of thermodynamic properties and acting forces

Small molecules are combined with biological macromolecules such as enzymes through hydrophobic interaction, hydrogen bonding force, Van der Waals force and electrostatic attraction. It can determine whether the binding reaction between small molecules and enzymes can proceed spontaneously. When the reaction proceeds spontaneously, $\Delta G < 0$. The type of interaction between the above-mentioned small molecules and proteins can also be judged by the positive and negative of or [10]. The free energy change can be obtained by the following formula:

$$\Delta G = \Delta H - T \Delta S$$

(4)

$$k = \frac{\Delta H}{2.303RT} + \frac{\Delta S}{2.303R}$$

(5)

Where $\Delta H$ enthalpy change, $\Delta S$ entropy change, $\Delta G$ free energy change and $T$ temperature.

3. Experimental Study on Hypoglycemic Effect of Mulberry Leaf Extract Based on Big Data analysis

3.1 Experimental Data

In this paper, 50 healthy adult mouses were selected and divided into 5 groups with 10 mice in each group. Ten mice were selected as healthy control group, and the other 40 mice were used to establish diabetes model. These 50 mice were divided into five groups: healthy control group, high, medium and low dose group of mulberry leaf water extract, and model control group.

3.2 Experimental Process

(1) preparing mulberry leaf extract

Firstly, mulberry leaf extract was prepared, and its technological process was as follows: mulberry leaf was picked, cleaned, dried, crushed, mulberry leaf powder was extracted with water ($80^\circ C, 3h$), centrifuged and concentrated, and finally mulberry leaf extract was obtained. The content of DNJ in mulberry leaf extract was determined by RP-HPLC-fluorescence detection.
(2) Establishment and grouping of diabetic mouse model

Ten mice were randomly selected as normal control group, and the rest were diabetic mice. All mice were fasted for 6 hours, and alloxan was injected intraperitoneally according to the body weight of 150mg/kg, while normal control mice were injected with the same dose of normal saline. After fasting for 72 hours, blood was collected from tail vein, serum was separated, fasting blood glucose (FBG) was measured by glucose oxidase-peroxidase method, and those with fasting blood glucose higher than 11.1mmol/L were selected as experimental diabetic mice. Model mice were randomly divided into model control group, high, medium and low dose groups of mulberry leaf extract, with 10 mice in each group.

4. Experimental analysis of Auxiliary Drug Management and Control Platform Based on Big Data

4.1 Changes of Blood Sugar and Body Weight in Mice

Within 15 days of the experiment, the blood glucose content and body weight of each mouse were tested within the specified time. The experimental result are shown in table 1 and figure 1.

| Table 1. Changes of body weight in mice |
|----------------------------------------|
| Time | Initial | Day 2 | Day 4 | Day 6 | Day 8 | Day 10 | Day 12 | Day 14 |
|------|---------|-------|-------|-------|-------|--------|--------|--------|
| Normal control group(g) | 230 | 234 | 231 | 233 | 240 | 241 | 244 | 247 |
| Model control group(g) | 212 | 210 | 211 | 205 | 201 | 198 | 194 | 190 |
| High concentration group(g) | 213 | 215 | 217 | 220 | 223 | 222 | 225 | 231 |
| Medium concentration group(g) | 211 | 212 | 215 | 216 | 218 | 219 | 222 | 226 |
| Low concentration group(g) | 214 | 213 | 214 | 215 | 215 | 217 | 220 | 223 |

It can be seen from the record results of body weight that there is a huge difference between healthy control group and diabetes group at the beginning, and the weight of mice in healthy control group is obviously higher than that in diabetes group. Through big data analysis, after 15 days' supplementation with mulberry leaf extract, the weight of three groups of mice supplemented with different concentrations increased, and the symptoms of diabetes improved to varying degrees. At the beginning, the blood sugar content of the five groups is also very different, and the mice in the normal group are about twice as large as those in the diabetes group. After 15 days' supplementation with
mulberry leaf extract, the blood sugar content of mice in high and medium concentration groups decreased obviously, but the effect in low concentration group was not obvious. However, the blood sugar content of the model control group did not change. This shows that mulberry leaf extract has obvious hypoglycemic effect on diabetic mice, and has obvious effects on body weight and blood sugar.

4.2 Effects of Different Concentrations of Mulberry Leaf Extract on Blood Sugar

In the 15th day of the experiment, the blood sugar content of each group of mice was measured within the specified time. Visualize it, and analyze the law between different concentrations of mulberry leaf extract and blood sugar content. In this paper, the blood sugar content of each group of mice at each time point was fitted by the mean value, and the blood sugar content change graph of mice was obtained. As shown in Figure 2.

![Figure 2. Effect of different concentrations of mulberry leaf extract on blood sugar](image)

It can be seen from the experimental results that at the beginning, the blood sugar content of the three groups of mice was about 16 mmol/L. However, due to the different concentrations of mulberry leaf extract added to the three groups, the difference of blood sugar content among the three groups gradually increased with the passage of time. The concentration of mulberry leaf extract supplemented by these three groups is the best experimental concentration based on big data analysis. Among them, the blood sugar content of high concentration group decreased the fastest, followed by medium concentration group. Then, the blood glucose concentration of mice in low concentration group decreased only a little. This shows that the therapeutic effect of mulberry leaf extract on diabetes is closely related to its concentration, that is, the higher the concentration of mulberry leaf extract, the better the hypoglycemic effect, showing a dose effect. According to the analysis of big data, the experimental results obtained by supplementing different concentrations of mulberry leaf extract to diabetic mice are also different, which has an important reference for selecting the most suitable concentration of mulberry leaf extract to treat diabetes.

5. Conclusions

Based on big data analysis, this paper studies the hypoglycemic effect of mulberry leaf extract. According to the actual situation of mulberry leaves used as medicine, this paper analyzes the medicinal value and related application methods of mulberry leaves. Through big data analysis, it is found that mulberry leaves are rich in alkaloid DNJ. Therefore, taking mulberry leaf extract DNJ as the research object, the mouse diabetes model was established. It is found that mulberry leaf extract can significantly reduce the blood sugar level of diabetic mice, and the higher the dose of mulberry leaf extract, the better the hypoglycemic effect, showing a dose effect. This can not only realize the choice of the best drug for treating diabetes, but also analyze the dosage of the drug, which is
convenient for clinical control of diabetes drugs. This is in line with the needs of hospital diabetes treatment, and has important reference significance for further exploring effective drugs for treating diabetes.

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