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Synergistic antidepressant effect of Schisandra lignans and Schisandra polysaccharides

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Abstract: The CUMS（Chronic unpredictable mild stress） method was used to establish a depression model，and the combination of schisandra lignans and schisandra polysaccharides was used for drug treatment, and its effect on the depressive behavior of mice was observed through behavioral indicators, and then the synergistic anti-inflammatory effects of schisandra lignans and schisandra polysaccharides were explored. The study found that the food intake of the CUMS-induced model mice decreased significantly after depression, and major symptoms such as depression, anxiety, loss of libido, and weight loss appeared. After 28 days of administration, the depression symptoms of the positive control group, Schisandra lignan group, Schisandra polysaccharide group, Schisandra lignan and polysaccharide group gradually improved, while the model group showed obvious depression. Schisandra lignans and Schisandra polysaccharides have synergistic antidepressant effects.

Keywords: Schisandra lignans; Schisandra polysaccharides; Synergistic antidepressant effect; Behavioral indicators.

1. Introduction

Depression, as a common mood disorder syndrome, is characterized by low mood, often accompanied by anxiety, physical discomfort, sleep disturbance, loss of appetite and libido and other main symptoms [1]. It was found that the factors that lead to depression are complex, including congenital physiological factors, social psychological factors and acquired environmental factors [2]. At present, there are mainly two methods of Western medicine treatment and Chinese medicine treatment to the drug treatment of depression. There are many disadvantages in the treatment of western medicine, which has the disadvantages of slow onset of effect, easy to cause recurrence of disease, and large side effects [3]. More people have shifted the research focus of antidepressants to the direction of natural medicines. Therefore, this experiment is to study the effect of the combination of Schisandra lignans and Schisandra polysaccharides on the process.

2. Experimental methods

2.1. Establishment and administration of mouse CUMS model

After reviewing the literature [3], this experiment decided to establish a mouse model of chronic unpredictable mild stress (CUMS). The stimulating factors used in this experiment are: tail clamping for 1 min, fasting for 24 h, water deprivation for 24 h, squirrel cage tilted at 45° for 24 h, wet litter for 24 h, day and night reversal for 24 h, swimming in hot water at 45°C for 5 min, Swim in ice water at 4°C for 5 minutes, and shake the mouse cage horizontally at a frequency of 1 time/s for 15 minutes. This experiment adopts the experimental method of drug administration while making the model. After 28 days of the experiment, the behavioral experiment is compared, and the depression state of the mice in each group is judged through the behavioral experiment to analyze the effect of the combination of Schisandra lignans and Schisandra polysaccharides on mice.

After the mice were randomly grouped, they were given adaptive feeding for 7 days. During these 7 days, no stimulation was given to the mice, and the mice in the same group were marked. The blank group mice (the mice given While feeding with common feed, the same volume of normal saline was administered into the stomach), the model group (the mouse was given CUMS to build the model ; the corresponding volume of normal saline was given to the stomach), the positive control group 1 was fluoxetine hydrochloride (given Simultaneously with mouse CUMS modeling; fluoxetine hydrochloride was administered orally at a dose of 8 mg/kg/d for 28 days), the positive control group 2 was the Livzon Changle group (while mice were given CUMS model; Livzon Changle was orally administered at a dose of 90 mg/kg/d for 28 days), Schisandra lignan group (while giving CUMS to mice for modeling; Schisandra lignan at a dose of 800 mg/kg/d intragastric administration for 28 days), Schisandra polysaccharide group (administered CUMS to mice at the same time; Schisandra polysaccharides were intragastrically administered at a dose of 800 mg/kg/d for 28 days), Schisandra combined group (administered to mice Simultaneously with CUMS modeling; Schisandra lignans + Schisandra polysaccharides were administered in a ratio of 1:1, administered orally at a dose of 800 mg/kg/d for 28 days).

2.2. General situation observation

The body weight of the mice during modeling and treatment was weighed and recorded every 7 days, and the water intake and food intake of the mice were recorded. It will be used as an important reference for judging the physical condition of mice.

2.3. Appearance observation of mice

On the 7th day and the 28th day of the experiment, the changes in the color and luster of the fur of the mice were observed.

2.4. Sugar water preference experiment

Experimental principle: Normal mice usually have a preference for sugar water after training with sugar water, while depressed mice will show anhedonia and consume less

sugar water. Therefore, the consumption rate of sugar water can be used to reflect the anhedonia of mice.

Experimental method: While stimulating the mice, conduct a sugar water preference experiment every 7 days. Before the start of the experiment, all mice are trained to drink sugar water with a concentration of 1%, and two jars of sucrose solution are placed in each cage 24 h, and then replace a bottle of sucrose solution with water for 24 h. Start the experiment after acclimatization. First, the mice were deprived of water and food 24 hours before the experiment, and each group of mice was locked in a separate cage. After the experiment began, each group of mice would freely get two bottles containing sucrose solution and water. After h, record the volumes of sucrose solution and water consumed.

$$W = \frac{W_1}{W_{1+}W_2} \times 100\% \quad (1)$$

In the formula, W1 --consumption of sucrose water; W2--Consumption of purified water.

3. Results

3.1. Analysis of Schisandra lignans and Schisandra polysaccharides

200 g Schisandra chinensis was used to obtain 17.76 g Schisandra lignans, and the yield of Schisandra lignans was 8.88%. The determination results of the detection wavelength are as Figure 1,(y=5. 3899 x +0. 3314, R2 =0.99 92). The content of lignans is 51.73% as determined by the colorimetric method of color-changing acid .

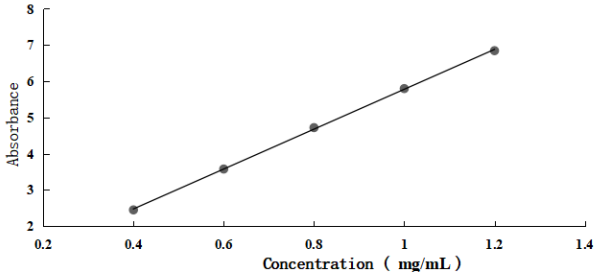

Figure 1. Standard curve of absorbance measurement

200 g schisandra were used to obtain 15.96 g schisandra polysaccharides, and the yield of schisandra polysaccharides was 7.98%. The results of detection wavelength are as Figure 2. (y=7. 1632 x+0.0 252, R2 =0.999 3). The polysaccharide content is 53.31% as determined by the phenol-sulfuric acid method.

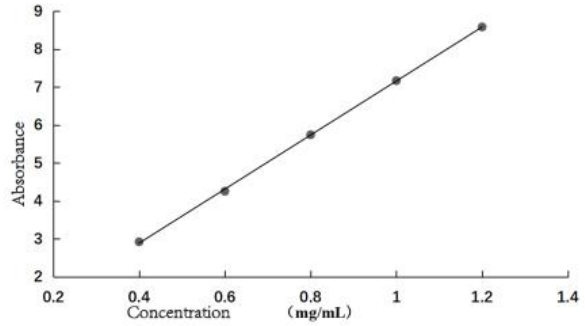

Figure 2. Absorbance detection value standard curve

3.2. Comparison of mouse body weight gain

The specific values of body weight are shown in Table 1.

Table 1. Body weight results of mice (n=10)

group	weight (g)			
	7 days	14 days	21 days	28 days
blank group	27.23±1.96	28.34±1.51	32.17±1.91	32.57±2.31
model group	26.89±1.74	24.31±1.56	26.61±1.82	27.88±2.21 ##
Fluoxetine hydrochloride group	27.20±1.36	24.85±2.30	27.82±0.71	31.17±2.30 **
Livzon intestinal music group	27.23±1.54	24.23±1.36	25.32±1.63	30.86±2.50 **
Lignans	28.32±1.36	25.85±2.10	29.23±1.96	29.45±2.30 *
polysaccharide group	28.12±0.96	25.32±1.32	27.23±1.56	29.34±2.50 *
combination group	27.80±0.96	24.32±0.87	30.13±1.34	30.12±2.60 *

*p ≤0.05, ** p ≤0.01, # p ≤0.05, ##p ≤0.01

3.3. Observation results of mouse appearance and morphology

Changes in mouse coat color can be seen from Table 2.

Table 2. Changes in mouse coat color (n=10)

group	Number of samples	day 7	day 28
blank group	10	smooth and shiny fur	smooth and shiny fur
model group	10	smooth and shiny fur	matted, dull fur
Fluoxetine group	10	smooth and shiny fur	smooth and shiny fur
Livzon intestinal music group	10	smooth and shiny fur	smooth and shiny fur
Lignans	10	smooth and shiny fur	smooth and shiny fur
polysaccharide group	10	smooth and shiny fur	smooth and shiny fur
combination group	10	smooth and shiny fur	smooth and shiny fur

3.4. Experimental results of sugar water preference in mice

The sugar water preference rate of the mice in the blank group was higher than that of the other 6 groups of mice. The specific values are shown in Table 3.

Table 3. Experimental results of sugar water preference in mice (n=10)

group	Sugar water preference rate%			
	7 days	14 days	21 days	28 days
blank group	70.6±2.66	64.7±2.12	76.7±2.71	77.1±2.78
model group	71.2±2.36	50.0±2.34	45.6±3.12	45.2±3.12 ##
Fluoxetine hydrochloride group	69.5±2.34	62.9±2.98	65.9±2.88	67.4±3.45**
Livzon intestinal music group	68.2±3.12	60.0±3.01	62.3±2.76	59.0±3.21*
Lignans	70.0±1.18	59.9±3.11	61.0±2.50	60.8±2.45*
polysaccharide group	68.8±2.14	58.9±2.86	58.6±3.21	59.8±3.24*
combination group	69.0±2.13	63.7±2.68	64.5±3.26	67.2±2.56**

* p ≤0.05, ** p ≤0.01, # p ≤0.05, ## p ≤0.01

3.5. Results of forced swimming experiment on mice

The immobility time of the mice see Table 4 for specific values.

Table 4. The immobility time of mice forced to swim (n=10)

group	Swimming immobility time (s)			
	7 days	14 days	21 days	28 days
blank group	100±5.68	102 ±5.76	101 ±5.01	103 ±5.99
model group	96±5.63	120 ±5.63	132 ±5.36	140 ±5.66 ##
Fluoxetine hydrochloride group	103±5.66	103 ±5.77	106 ±5.46	110 ±5.67 **
Livzon intestinal music group	100±4.98	115 ±5.13	123 ±5.41	113±5.34 **
Lignans	99±6.01	113 ±5.14	117 ±5.38	122 ±5.45 *
polysaccharide group	101±4.23	110 ±5.21	120 ±5.87	124 ±5.87 *
combination group	98±4.35	115 ±5.23	110 ±5.32	115 ±5.03 **

* p ≤0.05, **p ≤0.01, #p ≤0.05, ## p ≤0.01

3.6. Results of open field experiments on mice

The number of horizontal grid crossings and upright times of mice see Table 5.

Table 5. Results of open field experiment on mice: (a)horizontal crossing; (b)vertical crossing; (c) immobility time (n=10)

(a)

group	Number of grids traversed horizontally			
	7 days	14 days	21 days	28 days
blank group	148 ±4.35	151 ±4.32	148 ±4.32	147± 4.69
model group	150 ±5.32	135 ±5.32	126 ±4.32	102± 4.68 ##
Fluoxetine hydrochloride group	146 ±4.63	140 ±3.98	132 ±4.65	133± 4.75 **
Livzon intestinal music group	148 ±4.25	122 ±4.23	119 ±4.39	116± 3.68 *
Lignans	150 ±4.36	129 ±4.32	130 ±5.03	126± 4.65 *
polysaccharide group	148 ±4.23	120 ±4.52	128 ±3.97	123± 5.03 *
combination group	149 ±5.32	139 ±4.36	132 ±3.86	130± 4.3 **

(b)

group	Upright times			
	7 days	14 days	21 days	28 days
blank group	42± 2.32	46± 3.12	43± 2.36	45± 2.65
model group	41± 2.63	37± 2.45	34± 2.54	30± 3.11 ##
Fluoxetine hydrochloride group	42± 3.42	40± 2.69	37± 2.98	40± 2.39 **
Livzon intestinal music group	41± 1.98	39± 2.57	35± 2.87	33± 3.14 **
Lignans	41± 3.21	40± 3.01	33± 2.39	35± 2.95 *
polysaccharide group	40± 2.63	38± 2.69	35± 1.98	33± 3.87 *
combination group	40± 2.65	42± 2.14	36± 1.39	38± 2.32 **

(c)

group	Open field accumulative immobility time (s)			
	7 days	14 days	21 days	28 days
blank group	25.9 ±1.2	24.1± 1.36	26.1± 1.01	24.3± 1.35
model group	24.2 ±1.3	34.2± 1.36	38.3± 1.21	42.6± 1.45##
Fluoxetine hydrochloride group	26.4 ±1.3	30.2± 1.23	34.5± 1.32	32.5± 2.36**
Livzon intestinal music group	26.9 ±1.4	35.2± 0.96	36.4± 1.36	35.4± 1.23 *
Lignans	24.4 ±1.3	32.3± 0.98	33.6± 0.96	30.3± 2.32**
polysaccharide group	25.4 ±1.5	35.3± 1.30	30.4± 2.11	28.6± 1.65**
combination group	25.3 ±1.3	33.2±. 1.34	30.4± 2.32	27.6± 1.36**

*p ≤0.05, **p ≤0.01, # p ≤0.05, ## p ≤0.01

3.7. Results of mouse tail suspension experiment

Tail suspension time of mice see Table 6 for details.

Table 6. Tail suspension time of mice (n=10)

group	Tail suspension immobility time (s)			
	7 days	14 days	21 days	28 days
blank group	65± 2.25	66± 2.52	67± 2.35	65± 1.89
model group	64± 2.32	69± 2.65	82± 2.63	90± 2.32 ##
Fluoxetine hydrochloride group	67± 2.02	70± 2.23	66± 2.62	75± 2.35 **
Livzon intestinal music group	64± 2.32	71± 2.65	74± 2.56	75± 2.69 **
Lignans	65± 2.13	69± 2.56	73± 2.36	78± 2.68*
polysaccharide group	66± 2.23	68± 2.89	78± 2.65	80± 1.75*
combination group	63± 2.65	68± 2.56	72± 2.25	75± 2.12**

*p ≤0.05, **p ≤0.01, # p ≤0.05, ## p ≤0.01

4. Discussion

The common extraction methods of Schisandra polysaccharides include ultrasonic extraction, enzymatic extraction, aqueous two-phase system extraction, flash extraction, ultrasonic-assisted enzymatic extraction, etc. [6] . Integrating laboratory conditions and other objective environmental requirements, this experiment chose the water extraction and alcohol precipitation method to extract Schisandra polysaccharides [7,8]. During the pharmacological experiment of this topic, it is better to prepare more polysaccharides than expected, because it is inevitable that some will be lost during the experiment, and more preparations can avoid the loss of polysaccharides due to experimental errors and can be replenished in time.

The mouse Chronic unpredictable mild stress (CUMS) model adopted in this experiment is recognized as a classic animal model of depression. Through the study, it was found that after chronic unpredictable mild stress (CUMS) induced depression in the mice of the model, compared with the mice in the blank group, the mice in the model group showed a significant decrease in food intake, depression, anxiety, loss of libido, and weight loss. Decline and other main symptoms. After 28 days of administration, the mice in the Schisandra polysaccharide group, the Schisandra lignan group, and the combination group could alleviate the depression-like behavior of the mice to varying degrees, and the combination group had the best therapeutic effect in a dose-dependent manner. The antidepressant effect of the fluoxetine group was better than that of the schisandra combined group, and the effect of the Livzon Changle group was not obvious. The former is currently recognized as an antidepressant drug on the market, while the non-administered group had obvious depression. The weight of the mice in each group was basically normal on the first day, and the weight of the mice in each group decreased significantly after depression. In the later period, after administration, the weight gain of the mice increased, which widened the gap with the model group; the sugar preference rate of the model group was significantly higher than that of the Schisandra polysaccharide group, The Schisandra lignan group and the combination group were lower; the immobility time of the forced swimming model group was longer than that of the Schisandra polysaccharide group, the Schisandra lignan group, and the combination group; The mice in the polysaccharide group, Schisandra lignan group, and combination group were longer; in the open field experiment, the Schisandra polysaccharide group, Schisandra lignan group, and combination group also had significant antidepressant effects compared with the model group . Among them, the Schisandra combined group has more effect than the sugar group and lignan group. The data analysis of this experiment shows that the combination of schisandra lignans and polysaccharides can play a synergistic antidepressant effect. It will play a huge role, and it is believed that the combination of schisandra lignans and schisandra polysaccharides will certainly bring benefits to patients with depression in the future.

5. Conclusion

This experiment studies the synergistic antidepressant effect of schisandra lignans and schisandra polysaccharides. Through mouse pharmacological experiments, CUMS models are made on mice. The combination of adiposide and Schisandra polysaccharides was administered to mice, and the depression of the mice was observed through behavioral experiments. The data obtained through behavioral experiments showed that although Schisandra lignans, Schisandra polysaccharides, Schisandra lignans and Schisandra polysaccharides combined The effect is slightly worse than that of fluoxetine, but the combination of Schisandra lignans, Schisandra polysaccharides, Schisandra lignans and Schisandra polysaccharides can also improve the depression of mice to a certain extent, and the combined administration of Schisandra lignans and polysaccharides It is better than the effect of single administration of schisandra lignans and schisandra polysaccharides, so the combination of schisandra lignans and schisandra polysaccharides can play a synergistic antidepressant effect.

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