Anti-depression effect and mechanism of Suanzaoren Decoction on mice with depression

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Abstract. Objective: To study the therapeutic effect and mechanism of Suanzaoren Decoction on mice with depression. Methods: A model of depression was prepared by chronic unpredictable stimulation and reserpine induction. Behavioral tests, determination of norepinephrine and dopamine were performed. Results: The behavioral indicators of the model group were reduced, and the expression of norepinephrine and dopamine was decreased. Conclusion: Suanzaoren Decoction has an effect on the increase of serum norepinephrine and dopamine content, indicating that the jujube seed Soup has a certain effect on depression.

Keywords: Suanzaoren Decoction, Reserpine, Depression, Norepinephrine, Dopamine.

1. Introduction
Depression is a common mental and emotional disorder. The main clinical manifestations are: depression, decreased interest, loss of pleasure, sleep disorders, and serious suicidal tendencies. As the pace of life accelerates and continues to strain, the number of people with depression continues to rise [1].

The etiology of depression is complicated, and there are many hypotheses about the pathogenesis. Modern medical treatment is not ideal, and there are many adverse reactions. The treatment of depression in the motherland has the advantages of small side effects, which can significantly reduce the side effects caused by taking western medicine alone, and exert unique advantages in the prevention and treatment of depression [2]. Suanzaoren soup is contained in the "Golden Dragonfly", its effect is to nourish blood and soothe the nerves, clear heart and trouble. It has good curative effect on improving animal behavior and biochemical indicators. Its mechanism mainly involves regulating monoamine neurotransmitters and their receptors in the brain, improving hypothalamic-pituitary-adrenal (HPA) axis function, anti-free radicals, Anti-inflammatory and other effects, this experiment explored the effect of Suanzaoren Decoction on mice with depression by establishing a chronic unpredictable stimulus and a model of depression induced by reserpine [3].
2. Experimental material

2.1. Experimental animals
Kunming rat, SPF grade and weight (18-22) g [4], were housed in a temperature and humidity-controlled environment (20°C-24°C, 50%-60%).

2.2. Experimental drugs
Experimental reagent fluoxetine dispersible tablets (Changzhou Si Yao Pharmaceutical Co., Ltd.); sodium chloride injection (Henan Kelun Pharmaceutical Co., Ltd.); compound reserpine triamterene tablets (Specification: 0.1mg reserpine) (China Resources Shuanghe Pharmaceutical Co., Ltd.) Suanzaoren Decoction (Jiangyin Tianjiang Frying Granules): Suanzaoren (fried) 15g, licorice 3g, Zhimu, Poria, Chuanxiong 6g each.

2.3. Experimental instruments and reagents
ELISA kits (and Nantianchi Biotechnology Co., Ltd.); TD5K low-speed centrifuge; micropipette (2-20 uL) × 1, micropipette (20-200 uL) × 1.

3. Preparation model

3.1. Animal grouping
Twenty-five male Kunming rats were stochastically divided into 5 groups, 5 in each group, normal control group, model group, fluoxetine hydrochloride group (0.069 mg/kg/d), Suanzaoren decoction high-dose group (12.4g/kg/d), and Suanzaoren decoction low-dose group (3.2g/kg/d).

3.2. Model preparation
The model of depression was built by the method of chronic unpredictable mild stimulation (CUMS): each model mouse was raised in a single cage, and the stimulating factors included 10 kinds of fasting for 24 hours, water for 24 hours, and 4 °C ice water for 5 minutes. 2-3 kinds of stimuli were randomly given daily, and each stimuli were used 2-3 times in total for 7 days.

The investigator used the method of intraperitoneal injection when using reserpine. In this experiment, the model of depression was prepared by intragastric administration of reserpine 0.171 mg/kg. [5]

3.3. Observation indicators

3.3.1. Effect on body temperature of reserpine model mice. The thermometer probe was inserted into the anus 2 cm of the mouse 1 and 2 h after the injection of reserpine, and the anus temperature of the mouse was measured [6].

3.3.2. NE and DA. blood was collected by eyeball extraction, centrifuged at 3000r/min for 15min, supernatant was taken, and the content of norepinephrine and dopamine was determined strictly according to the ELISA kit instructions. [7].

4. Statistical methods
The experimental data were indicated as mean ± standard deviation and all data were statistically processed by SPSS 21.0 software. First of all, the data in each group is tested for normal distribution, and a One-way ANOVA is used for normal distribution, and non-parameter test is used for that does not conform to normal distribution. P<0.05 was accounted to be statistically significant.
5. Result

5.1. Effect of Suanzaoren Decoction on body weight of insomnia mice

On the first day of experiment, there was no great difference in weight of mice between the groups. On the seventh day of the experiment, the body weight of the model group was extremely lower than that of the normal group (P<0.01 Opposing to the model group, the weight of the positive, high, and low dose mice Significantly elevated, the database analysis was obvious(P <0.01).

![Figure 1](image1.png)

**Figure 1.** Effect of Suanzaoren Decoction on body weight of first-day depression mice

Note: Being opposed to the normal group, ** indicates P<0.01, and *indicates P<0.05; Opposing to the model group, ## indicates P<0.01, and # indicates P<0.05.

![Figure 2](image2.png)

**Figure 2.** Effect of Suanzaoren Decoction on body weight of mice in depression model on the seventh day

Note: Opposing to the normal group, ** indicates P<0.01, and *indicates P<0.05; Opposing to the model group, ## indicates P<0.01, and # indicates P<0.05.
5.2. Effect of Suanzaoren Decoction on body temperature of depressed mice

Opposing to the normal group, the body temperature of the model group declined greatly, and there was a statistically great variation (P<0.01). Opposing to the model group, the body temperature of the positive drug group was extremely added (P<0.01), Suanzaoren Decoction. The body temperature of the mice in the low-dose group was greatly aggrandized, and the body temperature of the high-dose mice was greatly higher (P<0.05).

![Figure 3. Changes in body temperature in depressed mice within 5 days](image)

Note: Opposing to the normal group, ** indicates P<0.01, and *indicates P<0.05; Opposing to the model group, ## indicates P<0.01, and # indicates P<0.05.

5.3. Effect of Suanzaoren Decoction on serum norepinephrine in depressed mice

Opposing to the normal group of mice, the concentration of mice in the model group was significantly lower (P<0.01). Opposing to the model group, the concentration of the positive drug group and the low dose group of Suanzaoren Decoction increased. Statistically significant (P < 0.05).

![Figure 4. Effect of Suanzaoren Decoction on serum norepinephrine content in depressed mice](image)

Note: Opposing to the normal group, ** indicates P<0.01, and *indicates P<0.05; Opposing to the model group, ## indicates P<0.01, and # indicates P<0.05.
5.4. Effect of Suanzaoren Decoction on serum dopamine concentration in depressed mice

Opposing to the normal group of mice, the concentration of mice in the model group was significantly lower (P<0.01). Opposing to the model group of mice, the concentration of dopamine was significantly increased in the positive drug group (P<0.01), and the concentration of high and low dose mice was increased, which was statistically significant (P<0.05).

Figure 5. Effect of Suanzaoren Decoction on serum dopamine content in depressed mice

Note: Opposing to the normal group, ** indicates P<0.01, and * indicates P<0.05; Opposing to the model group, ## indicates P<0.01, and # indicates P<0.05.

6. Conclusion

In this experiment, the mouse model of depression was established by chronic stress and drug (reserpine), and the mechanism of Suanzaoren decoction in the treatment of depression and the incidence of depression were discussed. The mechanism of disease. Reserpine can exhaust the behavior and endocrine system of 5-HT and DA. When chronic unpredictable stimulation exceeds the range of self-regulation, its behavior and endocrine system will change accordingly. In the later stage of the experiment, compare to the blank group, the mice in the model group lost weight, significantly reduced the scores of vertical and horizontal tests, and appeared symptoms similar to depression, which shows that the model of depression is ideal.

Animals will appear depression when subjected to unpredictable stimulation, which directly leads to animal eating loss and weight loss; reserpine can lead to body temperature decrease in depressed mice [8]; Comparing to the model group, the autonomic activity of depressed mice was significantly improved after administration of Suanzaoren decoction, and gradually returned to the active state of blank group with the increase of drug dose. Norepinephrine (norepinephrine, NE) and dopamine (dopamine, A) and their receptor theory suggest that depression is due to the deficiency of NE in the central nervous system of the brain and the decrease of DA function[9,10]. This indicates that Zaojugren decoction has a remission effect on depression.

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