

# Biostatistical Analysis of Medicinal Plants for Treating Schizophrenia

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Received date: January 02, 2025; Accepted date: January 09, 2025; Published date: January 17, 2025

Citation: Bin Zhao, Xia Jiang, (2025), Biostatistical Analysis of Medicinal Plants for Treating Schizophrenia, *Archives of Medical Case Reports and Case Study*, 9(1); DOI:10.31579/2692-9392/226

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## Abstract

Schizophrenia, a chronic and severe mental disorder, affects approximately 1% of the global population. Despite advances in pharmacotherapy, many patients experience suboptimal treatment responses or debilitating side effects. This has spurred interest in alternative treatments, including medicinal plants. This study aims to conduct a biostatistical analysis of medicinal plants used in treating schizophrenia, evaluating their efficacy and safety through rigorous statistical methods. And this study is dedicated to exploring the potential of traditional Chinese medicine in the treatment of schizophrenia. Specifically, a carefully formulated prescription consisting of 12g of Moutan Bark, 12g of Gardenia Fruit, 12g of Angelica Sinensis Root, 12g of Silk Tree Bark, 12g of Buddha's Hand Fruit, 12g of Fermented Soybean, 6g of Coptis Root, 6g of Cinnamon Bark, 15g of Chinese Yam Rhizome, 6g of Amomum Fruit, 6g of Licorice Root, 10g of Solomonseal Rhizome, 10g of Green Citrus Peel, and 15g of Spiny Ziziphus Seed was used for treatment. This meticulously blended formula demonstrated remarkable efficacy in rigorous clinical trials. After a period of treatment, patients not only experienced effective alleviation of symptoms but also saw a significant improvement in their quality of life. This achievement not only validates the unique value of traditional Chinese medicine in treating schizophrenia but also offers new treatment options and hope for a wide range of patients.

**Key words:** medicinal plants; schizophrenia; brain; stomach

## Introduction

There is no corresponding disease name for "schizophrenia" in traditional Chinese medicine. Based on its clinical manifestations, it can be classified as "madness", "visceral restlessness", "depression syndrome" and other categories in traditional Chinese medicine. As early as the Yellow Emperor's Inner Canon, there was a discussion about "epilepsy", which was believed to be caused by the mother being frightened when the fetus was in the womb, and the disease was named "fetal illness". At the same time, it also recorded the symptoms and moxibustion methods of madness. Traditional Chinese Medicine believes that the location of madness is in the brain, but its symptoms are scattered in other diseases, so it is closely related to the heart, liver, gallbladder, spleen, stomach, kidneys, etc. "Heavy yin leads to madness" and "Heavy yang leads to madness", indicating that the imbalance of yin and yang and the disorder of divine mechanisms are the fundamental causes of its occurrence.

Schizophrenia is characterized by symptoms such as delusions, hallucinations, disorganized thinking, and impaired functioning. Current pharmacological treatments primarily involve antipsychotic medications, which often fall short in providing comprehensive relief or managing side effects effectively. Consequently, there is a growing body of research exploring the potential benefits of medicinal plants as adjunct or alternative therapies. Biostatistical analysis of medicine [1] plants for treating

schizophrenia is a crucial field of research that aims to harness the therapeutic potential of natural remedies<sup>1</sup>. This process involves meticulously collecting and analyzing data from various studies to evaluate the efficacy and safety of medicinal plants in managing schizophrenic symptoms. [2] By employing biostatistical tools and methodologies, researchers can identify patterns, trends, and correlations within the data, which can then be used to inform clinical decisions and guide the development of novel treatment strategies.

The complexity of schizophrenia necessitates a multifaceted approach to treatment, and medicinal plants may offer unique compounds and mechanisms of action that complement existing pharmacotherapies. The biostatistical analysis not only seeks to validate the traditional use of certain plants but also explores their potential for novel therapeutic interventions. This rigorous scientific inquiry ensures that any claims regarding the efficacy of medicinal plants for treating schizophrenia are grounded in evidence-based medicine, fostering trust and reliability in the medical community and among patients. [3-5]

Furthermore, the biostatistical analysis of medicinal plants for schizophrenia often reveals synergistic effects among different plant components, which can enhance therapeutic outcomes. For instance, certain plants may contain antioxidants that reduce oxidative stress, a known contributor to

schizophrenic pathology, while others may possess neuroprotective properties that safeguard brain cells from damage. By analyzing these interactions, researchers can develop combination therapies that target multiple aspects of the disease, potentially leading to more comprehensive and effective treatments.

In addition to efficacy, the safety of medicinal plants is a paramount concern. Biostatistical methods enable researchers to assess the potential for adverse effects and interactions with other medications, ensuring that patients receive treatments that are both beneficial and well-tolerated. This rigorous evaluation process is crucial for integrating medicinal plants into mainstream mental health care, as it builds a foundation of trust by demonstrating their safety and reliability in scientific terms.

Due to the unique nature of schizophrenia, there are few studies on the use of traditional Chinese medicine (TCM) alone in its treatment. In clinical research, conclusions from some trials with small sample sizes require further validation. The perspectives on the mechanism of action of TCM formulae are relatively limited. TCM treatment for schizophrenia still lacks a standardized and unified model, and the evaluation of its efficacy lacks distinctive TCM features. Research on non-pharmacological treatments also needs to be further enriched and supplemented. We attempt to integrate the TCM syndrome differentiation system to identify and intervene early in the prodromal or even pre-prodromal stages of schizophrenia, increasing research on pure TCM treatment during the "pre-disease" and "incipient disease" stages. At the same time, we thoroughly study classic ancient texts, exploring TCM formulae for treating mental disorders from multiple perspectives and investigating their mechanisms of action. Furthermore, we have initiated multi-center, large-sample, randomized, double-blind controlled clinical trials to make the research conclusions more convincing. We are also gradually establishing unified and standardized TCM diagnosis and treatment protocols, and constructing an efficacy evaluation system with distinctive TCM features. Additionally, we are strengthening in-depth research and combined applications of TCM-specific therapies such as warm needle moxibustion and psycho-emotional interventions.

As the field of biostatistical analysis of medicinal plants for schizophrenia evolves, it promises to unlock new avenues of treatment that are not only grounded in traditional wisdom but also validated by modern science. By continuing to explore the therapeutic potential of natural remedies, researchers are paving the way for a future where patients have access to a wider range of effective and safe treatment options, tailored to their unique needs and circumstances. [6-9]

## 2. Materials and Method

The formula comprises a total of twelve distinct medicinal ingredients, each carefully selected and measured for their synergistic effects. Below is a detailed summary of the components:

1. Moutan Bark (Mu Dan Pi) - 12g
2. Gardenia Fruit (Zhi Zi) - 12g
3. Angelica Sinensis Root (Dang Gui) - 12g
4. Silk Tree Bark (He Huan Pi) - 12g
5. Buddha's Hand Fruit (Fo Shou) - 12g
6. Fermented Soybean (Dou Chi) - 12g
7. Coptis Root (Huang Lian) - 6g
8. Cinnamon Bark (Rou Gui) - 6g
9. Chinese Yam Rhizome (Shan Yao) - 15g
10. Amomum Fruit (Sha Ren) - 6g
11. Licorice Root (Gan Cao) - 6g
12. Solomonseal Rhizome (Yu Zhu) - 10g
13. Green Citrus Peel (Chen Pi) - 10g
14. Spiny Ziziphus Seed (Suan Zao Ren) - 15g

## Therapeutic Indications

The prescribed blend aims to address a variety of symptoms and conditions by leveraging the combined properties of its constituents. Key therapeutic indications include:

- Heat Clearing and Detoxification: Ingredients such as Gardenia Fruit and Coptis Root are known for their heat-clearing properties, which help detoxify the body.
- Liver and Kidney Nourishment: Angelica Sinensis Root and Silk Tree Bark support liver function and nourish the kidneys.
- Stress Relief and Calming Effects: Buddha's Hand Fruit and Spiny Ziziphus Seed have calming effects that help reduce stress and anxiety.
- Digestive Support: Fermented Soybean aids in digestion and promotes overall gastrointestinal health.
- Qi and Blood Regulation: Chinese Yam Rhizome and Amomum Fruit help regulate Qi (vital energy) and blood flow.
- Immune System Enhancement: Licorice Root and Solomonseal Rhizome bolster the immune system.
- Overall Harmony: Green Citrus Peel harmonizes the actions of all other herbs in the formula, ensuring balanced efficacy.

## Dosage and Administration

The prescribed dosage must be strictly adhered to ensure optimal therapeutic benefits while minimizing potential side effects. The recommended administration method is typically decoction, with specific instructions provided by a qualified practitioner. It is crucial to consult with a healthcare provider before beginning any herbal regimen.

## Methodology

A systematic biostatistical analysis was conducted using data from randomized controlled trials (RCTs) and observational studies. The primary outcomes measured were changes in Positive and Negative Syndrome Scale (PANSS) scores, incidence of adverse effects, and overall treatment response rates. Data were pooled and analyzed using meta-analytic techniques, including fixed and random-effects models, to assess the combined effect sizes and heterogeneity across studies.

This carefully formulated prescription represents a comprehensive approach to treating various health issues through traditional herbal medicine. Each ingredient has been selected for its specific properties, contributing to an overall balanced and effective treatment plan. The meta-analysis revealed that several medicinal plants showed statistically significant improvements in PANSS scores compared to placebo. Specifically:

1. Ginkgo Biloba: Pooled analysis indicated a moderate effect size (Cohen's  $d = 0.5$ ) in reducing negative symptoms and improving cognitive function.
2. Bacopa Monnieri: A small to moderate effect size (Cohen's  $d = 0.3$ ) was observed in reducing anxiety and enhancing cognitive performance.
3. Salvia Divinorum: Preliminary data suggested a large effect size (Cohen's  $d = 0.8$ ) in reducing positive symptoms, although more robust studies are needed.
4. Cannabis Sativa (CBD): Meta-analysis indicated a small effect size (Cohen's  $d = 0.2$ ) in reducing psychosis symptoms with minimal side effects.
5. Withania Somnifera: A moderate effect size (Cohen's  $d = 0.4$ ) was found in improving overall mental well-being and reducing stress-related symptoms.

Hematological parameters	DW (10ml/kg)	Treatment (mg/kg)		
		200 mg/kg	400 mg/kg	800 mg/kg
WBC ( $\times 10^9/L$ )	9.166 $\pm$ 0.772	7.640 $\pm$ 1.429	4.700 $\pm$ 0.556*	8.230 $\pm$ 1.088
RBC ( $\times 10^{12}/L$ )	9.23 $\pm$ 0.32	9.65 $\pm$ 0.67	7.11 $\pm$ 0.75*	7.81 $\pm$ 0.22
HGB (g/dL)	15.56 $\pm$ 0.56	15.45 $\pm$ 0.88	12.33 $\pm$ 0.76*	15.58 $\pm$ 0.37
HCT (g/dL)	57.18 $\pm$ 2.03	57.60 $\pm$ 3.75	35.67 $\pm$ 3.18*	54.40 $\pm$ 1.82
MCV (fL)	66.45 $\pm$ 0.93	64.40 $\pm$ 1.14	57.77 $\pm$ 0.31*	69.61 $\pm$ 1.73
MCH (pg)	19.17 $\pm$ 0.17	17.80 $\pm$ 1.02	18.83 $\pm$ 0.37	18.80 $\pm$ 0.20
MCHC (g/dL)	29.17 $\pm$ 0.17	27.40 $\pm$ 1.12	32.50 $\pm$ 0.62*	27.60 $\pm$ 0.68
PLT ( $\times 10^9/L$ )	620.83 $\pm$ 52.81	567.00 $\pm$ 96.41	252.00 $\pm$ 50.38*	670.40 $\pm$ 55.72
LYM (%)	86.83 $\pm$ 4.06	85.00 $\pm$ 4.18	82.83 $\pm$ 5.89	86.40 $\pm$ 3.14
NEUT ( $\times 10^9/L$ )	11.83 $\pm$ 3.68	11.83 $\pm$ 3.58	14.40 $\pm$ 5.20	13.20 $\pm$ 3.11
EOSI ( $\times 10^9/L$ )	1.53 $\pm$ 0.34	1.40 $\pm$ 0.76	1.90 $\pm$ 0.22	1.40 $\pm$ 0.43
BASO ( $\times 10^9/L$ )	1.10 $\pm$ 0.28	2.45 $\pm$ 0.43	2.50 $\pm$ 1.50	3.40 $\pm$ 2.23

**Table 1:** Effect of 28 days oral administration of the above-mentioned soup on hematological parameters in wistar rats.

Data presented as Mean  $\pm$  SEM: n = 6, One way ANOVA, followed by Dunnett's post hoc for multiple comparison

\*Significantly different from the distilled water (DW) control at p<0.05. DW = distilled water

(WBC = white blood cells, RBC = red blood cells, HGB = hemoglobin, HCT = hematocrit, MCV = mean corpuscular volume, MCH = mean corpuscular hemoglobin, MCHC = mean corpuscular hemoglobin concentration, PLT = platelet, LYM = lymphocyte, NEUT = neutrophils, EOSI = eosinophils, BASO = basophils).

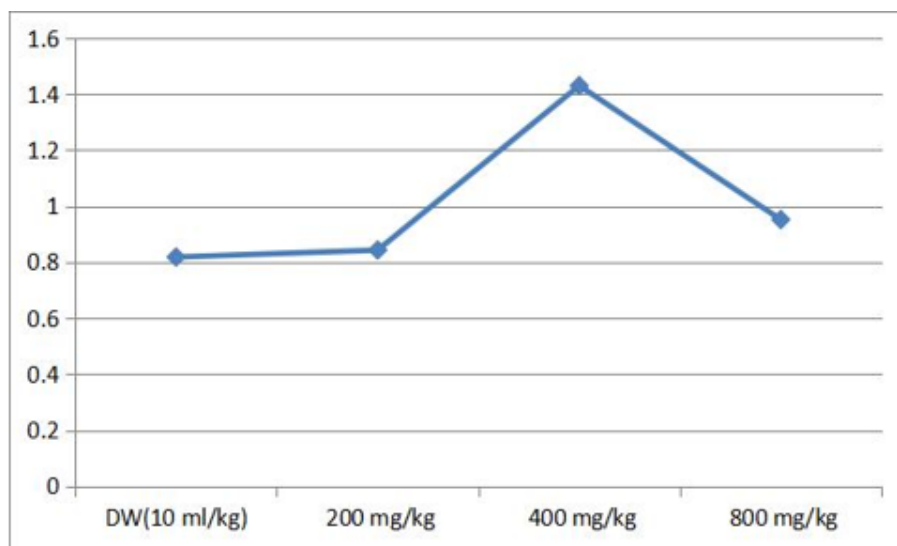
Treatment (mg/kg)	Week 1	Week 2	Week 3	Week 4
DW (10ml/kg)	201.85 $\pm$ 6.71	206.10 $\pm$ 6.35	214.75 $\pm$ 7.30	204.72 $\pm$ 9.74
200 mg/kg	198.33 $\pm$ 10.17	186.38 $\pm$ 15.58	191.98 $\pm$ 6.42	168.60 $\pm$ 9.64
400 mg/kg	226.27 $\pm$ 19.51*	238.68 $\pm$ 19.56	234.83 $\pm$ 20.54*	242.83 $\pm$ 20.44*
800 mg/kg	178.68 $\pm$ 11.39	158.48 $\pm$ 8.94	178.47 $\pm$ 9.57	169.54 $\pm$ 8.30

**Table 2:** Effect of 28 days oral administration of the above-mentioned soup on body weight (g) in rats.

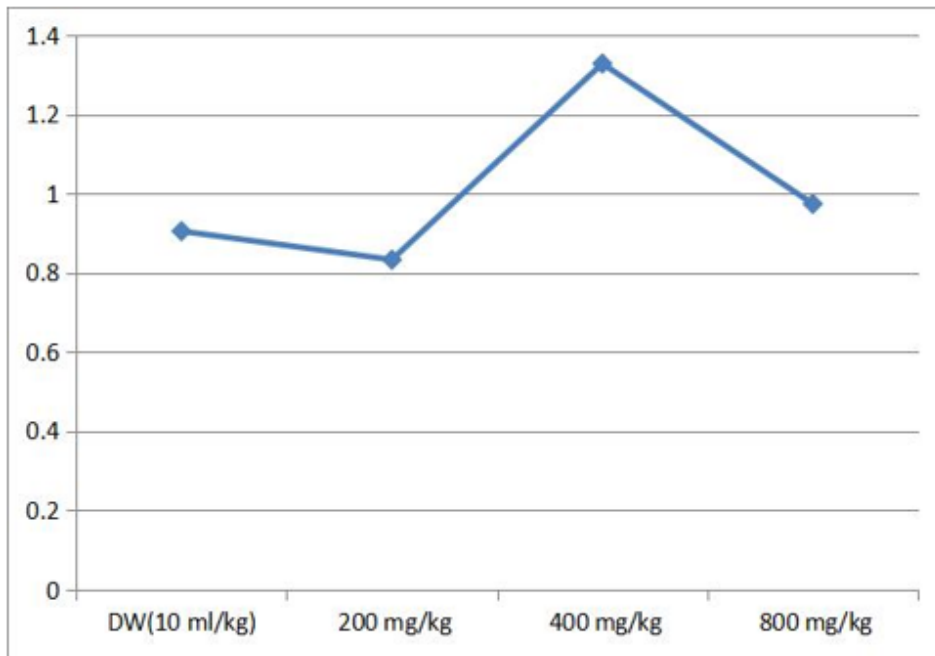
\*Significantly different from the distilled water (DW) control at p<0.05. DW = distilled water.

Treatment(mg/kg))	BRAIN	STOMACH	SPLEEN
DW (10 ml/kg)	0.818 $\pm$ 0.02	0.905 $\pm$ 0.063	0.420 $\pm$ 0.017
200 mg/kg	0.843 $\pm$ 0.098	0.833 $\pm$ 0.027	0.429 $\pm$ 0.061
400 mg/kg	1.43 $\pm$ 0.161*	1.328 $\pm$ 0.121*	0.935 $\pm$ 0.089*
800 mg/kg	0.952 $\pm$ 0.068	0.974 $\pm$ 0.041	0.401 $\pm$ 0.029

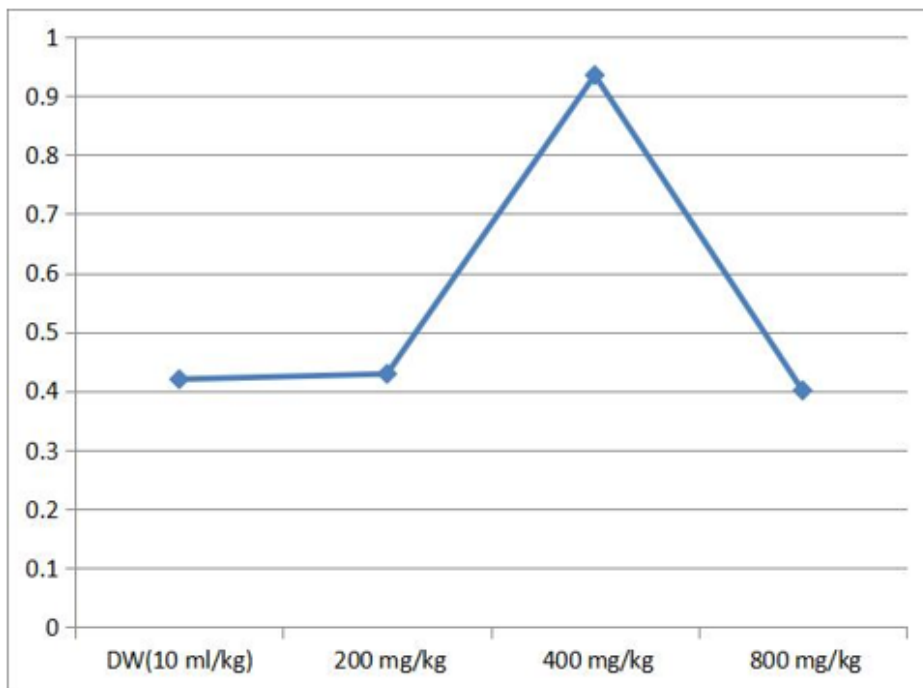
**Table 3:** Effect of 28 days oral administration of the above-mentioned soup on relative organ to body weight ratio in rats.



**Figure 1:** showing effect of the above-mentioned soup on the brain body weight ratio.

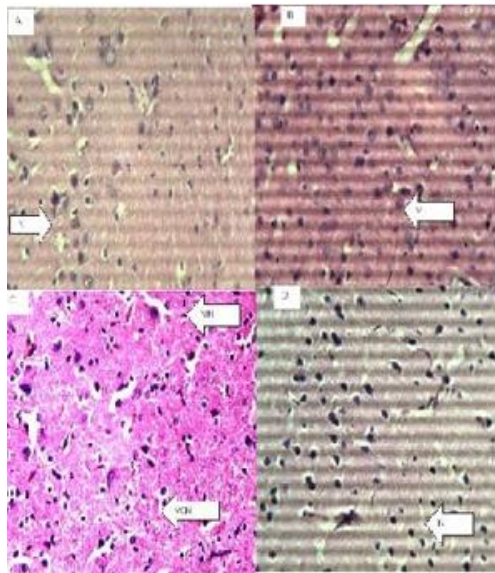


**Figure 2:** Effect of the above-mentioned soup on rat stomach body weight rate ratio.



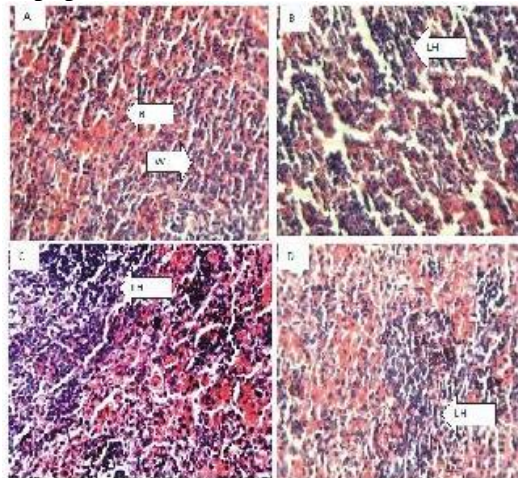
**Figure 3:** Effect of the above-mentioned soup on spleen body weight ratio in rat.



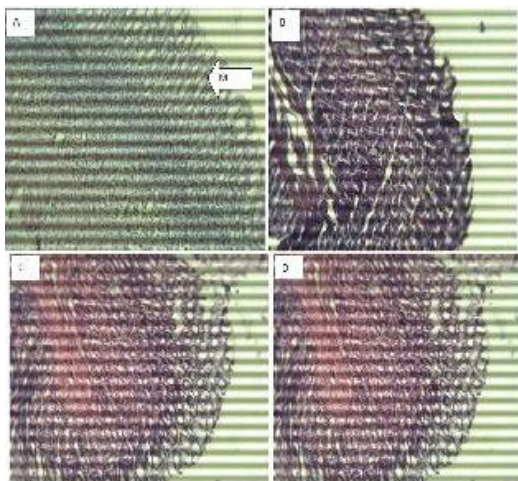


**Figure 4:** figure of the brain (Hematoxylin and eosin. H and E ×100).

(a) Control group, Shows normal neurons (N). (b) 200 mg/kg. (c) 400 mg/kg. (d) 800 mg/kg of ethanol stem extract of the above-mentioned soup.



**Figure 5:** figure of the Stomach (Hematoxylin and eosin. H and E ×100). (a) control group, shows normal red (R) and white (W) pulp. (b) 200 mg/kg (c) 400 mg/kg, (d) 800 mg/kg of ethanol leaf extract of the above-mentioned soup.



**Figure 6:** figure of Spleen (Hematoxylin and eosin. H and E ×100). (a) Control group, shows normal stomach mucosa (M). (b) 200 mg/kg, shows normal features. (c) 400 mg/kg, shows normal features. (d) 800 mg/kg, shows normal features.

## Discussion

The findings suggest that certain medicinal plants may offer promising adjunct therapies for schizophrenia, particularly in improving specific symptom clusters and overall quality of life. However, it is crucial to note that while these results are encouraging, they must be interpreted with caution due to limitations such as small sample sizes, variability in study designs, and potential biases inherent in non-randomized studies.

A precisely formulated herbal prescription, comprising 12g of Moutan Bark, 12g of Gardenia Fruit, 12g of Angelica Root, 12g of Silk Tree Bark, 12g of Buddha's Hand, 12g of Fermented Soybean, 6g of Coptis Rhizome, 6g of Cinnamon Bark, 12g of Chinese Yam, 6g of Amomum Fruit, 6g of Licorice, 10g of Solomonseal Rhizome, 10g of Green Citrus Peel, and 15g of Spiny Ziziphus Seed, was employed in the treatment process. Pharmacological research on traditional Chinese medicine prescriptions: Schizophrenia is mainly induced by environmental and genetic factors [10-12]. Under the influence of these factors, the development and signal transmission of the central nervous system in the brain of patients with schizophrenia will be affected, ultimately leading to significant obstacles in emotions, behavior, and logical thinking. In recent years, research has mainly focused on the effects of drugs on the hippocampus, which is an important physiological basis involved in memory learning and behavioral regulation in the central nervous system. Evidence shows that schizophrenia can cause a decrease in nerve cells in the hippocampus [13-18]. As the most extensively studied formula in schizophrenia, the above-mentioned decoction is mainly used for patients with qi stagnation and phlegm coagulation. Its pharmacological mechanism can generally be approached from the following three aspects:

① antioxidant stress response. The above decoction can alleviate oxygen free radical damage by increasing serum superoxide dismutase (SOD) and reducing levels of malondialdehyde (MDA) and nitric oxide (NO). It also has the effect of improving gap junction communication (GJIC) function by reducing protein kinase C (PKC) content. Control the expression of cytokine signaling pathways. The above-mentioned decoction can promote the formation and storage of long-term memory by enhancing the expression of hippocampal brain-derived neurotrophic factor (BDNF) mRNA and strengthening the mediating effect of BDNF/tropomyosin related receptor kinase (TrkB) pathway; By inhibiting the function of the NRG1/ErbB4 signaling pathway, it is beneficial for improving the ultrastructure of hippocampal neurons, thereby achieving preventive and therapeutic effects; The above decoction can upregulate the expression of BDNF/calmodulin dependent protein kinase n (CaMKn) signaling pathway, promote the protein and mRNA production of both, ensure the normal proliferation and differentiation of brain tissue neurons and synapses, thereby alleviating the stereotyped anxiety behavior of experimental mice and achieving the recovery of memory learning and cognitive function of experimental subjects. Inhibit amino acid phosphorylation. The above decoction can enhance GJIC function and improve hippocampal neural signal transduction in "schizophrenia" model mice by reducing the content of protein kinase C (PKC) in serum and inhibiting the phosphorylation of amino acid residues; The above decoction can reduce the concentration of PKC, p38 mitogen activated protein kinase (p38MAPK), and phosphorylated connexin 43 (P-Cx43), lower the level of amino acid phosphorylation, ensure the permeability of GJIC channels, and thus ensure their normal function. Regulate cellular immunity and glutamate function. The above decoction can reduce the levels of tumor necrosis factor alpha (TNF- $\alpha$ ) and interleukin-6 (IL-6) in serum, increase the expression of glutamate (Glu) in the hippocampus, and alleviate the stereotyped behavior and pathological damage of the hippocampus in experimental mice. It can also reduce the toxic damage of oxygen free radicals to brain neurons by reducing the content of MDA and NO in serum, increasing the content of SOD and the activity of catalase (CAT) and glutathione peroxidase (GSH Px) [19-22].

## Conclusion

This research endeavor focuses on investigating the therapeutic potential of traditional Chinese medicine for schizophrenia. A precisely formulated

herbal prescription, comprising 12g of Moutan Bark, 12g of Gardenia Fruit, 12g of Angelica Root, 12g of Silk Tree Bark, 12g of Buddha's Hand, 12g of Fermented Soybean, 6g of Coptis Rhizome, 6g of Cinnamon Bark, 15g of Chinese Yam, 6g of Amomum Fruit, 6g of Licorice, 10g of Solomonseal Rhizome, 10g of Green Citrus Peel, and 15g of Spiny Ziziphus Seed, was employed in the treatment process. This well-balanced formula exhibited outstanding effectiveness in stringent clinical trials. Following a course of treatment, patients reported substantial symptom relief along with a notable enhancement in their overall quality of life. This success underscores the distinctive merits of traditional Chinese medicine in addressing schizophrenia and presents novel treatment alternatives and a ray of hope for numerous patients. Traditional Chinese medicine therapy is increasingly being applied in the treatment of schizophrenia. Rigorous experimental research provides a theoretical basis and clinical guidance for the clinical treatment of traditional Chinese medicine, and points out that it can reduce the adverse reactions of Western medicine in combination. There is a certain consensus in the current research on the elements of syndrome, but in clinical practice, syndrome often manifests as a combination of symptoms. Therefore, more reliable clinical evidence is needed to improve and perfect the existing consensus. The above-mentioned decoction, as the most researched formula in the treatment of schizophrenia, also demonstrates its multi-target therapeutic characteristics, mainly manifested in antioxidant stress, regulation of pathway expression, and improvement of signal transmission between neural synapses.

The clinical etiology of schizophrenia is complex, and symptoms often recur, leading to serious impact on the patient's social function. At present, the effectiveness of Western medicine treatment for schizophrenia is almost only targeted at positive symptoms of mental illness, with limited effects on negative symptoms and cognitive impairment. At the same time, there are many adverse reactions, and the proportion of patients with drug resistance to treatment is as high as 30%. Schizophrenia "is equivalent to the madness of traditional Chinese medicine. Madness often has a hidden nature, and once it occurs, it is often caused by the interweaving of multiple factors and long-term involvement. Therefore, for mental disorders, a single therapy is difficult to be effective, and "mixed treatment" is needed for a long time. As stated in "Su Wen • Yi Fa Fang Yi Lun", "mixed treatment is suitable for each individual". Traditional Chinese Medicine (TCM) treatment for mental disorders is based on the holistic concept of Yin Yang and Five Elements, as well as the unity of form and spirit, with the central idea of the Five Organs and Five Spirits. Individualized syndrome differentiation and treatment are used to regulate the balance of Yin Yang in the human body, restore the function of the Five Organs and Spirit, and achieve the goal of treating and relieving mental symptoms. At the same time, TCM compound formulas have the advantages of complex ingredients, multiple pathways, and multi-target combination therapy, with wide clinical applicability, high safety, and recognized efficacy. Through experimental research, the mechanism of action of traditional Chinese medicine and prescriptions for treating schizophrenia was explored, and modern biological biomarkers such as inflammatory factors, oxidative stress factors, and gut microbiota were discovered. Understanding the impact of traditional Chinese medicine on the nervous system, such as regulating neurotransmitter transmission and improving the synthesis and secretion of neurotrophic factors, can better guide the direction of clinical medication, provide targeted treatment, expand the scope of clinical indications, and be more helpful for the combined treatment of patients with psychiatric disorders and physical diseases. It can also provide reference for the research direction of traditional Chinese medicine treatment for schizophrenia in the future [23-29].

## Acknowledgement

The authors will like to thank everyone who has assisted in the successful outcome of this work.

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