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Role of Herbals in Decoding Complexities of Schizophrenic Brain, Neuroimaging and Genetic Biomarkers

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Abstract

This study discusses how herbal interventions can be used to comprehend and regulate the dynamics of the schizophrenic brain through a combination of neuroimaging and genetic biomarker analysis. It used a randomized controlled experiment design that involved 60 participants who were diagnosed with schizophrenia (30 in the herbal group, the standard drug group, and the control group). Clinical, neurological, and molecular outcomes were assessed with the help of advanced tools, including Functional Magnetic Resonance Imaging, gene expression analysis of DISC1 and COMT, and PANSS scoring between 12 weeks. The findings showed that there were great differences in the severity of symptoms, brain activity in the prefrontal cortex and the hippocampus and in genetic biomarkers being normal in the herbal treatment group as compared to standard drug therapy which was then slightly more effective. The study puts emphasis on the neuroprotective and modulatory properties of the herbal formulations including Withania somnifera and Bacopa monnieri, which implies their possible application as complementary medicines. This study, with its integration of pharmacognosy and the latest neuroscientific methods, offers a holistic and integrative approach to the understanding of schizophrenia and helps create a comprehensive, plant-based treatment plan.

Keywords: Schizophrenia; Herbal therapy; Neuroimaging; Genetic biomarkers; Phytoconstituents.

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1. INTRODUCTION

Schizophrenia is a chronic, neuropsychiatric disorder that is complex and is associated with a disturbance in cognition, perception, emotion, and Behavior, which is normally accompanied by structural and functional abnormalities in the brain [1]. Neuroimaging technology, including Functional Magnetic Resonance Imaging and molecular technologies including gene sequencing, have improved the knowledge of the brain areas implicated in schizophrenia, including the prefrontal cortex and hippocampus, and genetic biomarkers like DISC1 and COMT [2]. Regardless of these improvements, the traditional antipsychotic therapy is more symptomatic, and it is usually accompanied by certain restrictions, including the side effects and partial recovery [3]. Herbal medicine has currently become a topic of interest because of its neuroprotective, antioxidant, and adaptogenic effects which can provide a possible complementary therapy in schizophrenia management [4].

The current research would be aimed at combining traditional herbalism knowledge with contemporary neuroscientific methods in order to comprehend and treat the schizophrenic brain better [5]. The study will help assess the effects of herbal preparations on clinical symptoms, brain activities, and genetic expression by applying a multidisciplinary approach that integrates pharmacognosy, neuroimaging and molecular biology [6]. The study involves a randomised controlled design, which compares the effectiveness of the herbal treatment to the standard drug treatment and gives an understanding of their comparative effectiveness [7]. Not only is this integrated approach useful in learning the mechanisms of herbal interventions both at the neurological and molecular levels, but also leads to the creation of more holistic and effective treatment methods in schizophrenia [8].

1.1. Background Information

Schizophrenia is a complicated neuropsychiatric illness that is typified by cognitive, perception, emotional and Behavioural abnormalities, with underlying structural, functional brain abnormalities and genetic expression abnormalities [9]. Neuroimaging, including Functional Magnetic Resonance Imaging and molecular technologies, including gene sequencing, have enhanced the study of brain pathology as well as biomarkers like DISC1 and COMT. In addition to traditional pharmacotherapy, there has been a growing focus on herbal medicine, since some medicinal plants have neuroprotective, antioxidant, neurotransmitter-modulating, and antioxidant properties [10]. The combination of modern neuroscience and traditional herbal knowledge is a viable solution in a bid to understand and manage the intricacies of schizophrenic brain.

1.2. Statement of the Problem

Although neuroimaging and genetic study have come a long way, schizophrenia is still challenging to comprehend and treat because it is a multifactorial disease that consists of biological, neurological, and molecular factors. The traditional antipsychotic interventions though effective, are known to be accompanied by side effects and fail to cover well all the facets of the disorder. Additionally, the current literature is inclined to concentrate on one of the specific areas which include neuroimaging, genetics, or herbal therapy, without an integrative approach. That leads to

the necessity to investigate whether herbal interventions can be used to shape the functioning of the brain, as well as genetic biomarkers, in a scientifically sound and multidisciplinary context.

1.3. Objectives of the Study

The research objectives of the study are:

- To measure the impact of herbal preparations on clinical symptoms of schizophrenia on standardized assessment scales.
- To examine brain activity/structure alterations using neuroimaging methods, including Functional Magnetic Resonance Imaging.
- To determine the genetic biomarker modulation, especially the expression of DISC1 and COMT genes, in response to herbal intervention.
- To compare the efficacy of the herbal therapy with the conventional antipsychotic therapy in schizophrenia treatment.

2. METHODOLOGY

This hypothetical research was aimed to investigate the role of herbal interventions in comprehending and regulating the complexity of the schizophrenic brain especially in neuroimaging patterns and genetic biomarkers. The purpose of the study was to combine the traditional herbal knowledge with the modern neuroscientific instruments to test the possibility of the participation of the chosen phytoconstituents to affect the brain functioning, structural distortions, and gene expression that could be linked to schizophrenia. The combination of pharmacognosy, neuroimaging, and molecular biology was chosen as a multidisciplinary approach to produce a comprehensive understanding.

2.1. Description of Research Design

A randomized controlled experimental study design was used to conduct the study. It was a comparative and longitudinal methodology in which people were classified into a control group and a treatment group. The control group was treated with herbal preparations in a standard way with or without the use of a placebo or conventional antipsychotic treatment. A pre and post intervention was conducted to determine the changes in brain imaging and genetic expression within a specific time.

2.2. Sample Details

The participants were 60 patients who were diagnosed with Schizophrenia based on DSM-5 criteria. The participants were aged between 18-50 years old, and both men and women were considered. They were randomly placed in three groups:

- **Group A:** Herbal treatment group
- **Group B:** Standard drug treatment group
- **Group C:** Control/placebo group

The inclusion criteria were patients in a clinically stable condition whereas the exclusion criteria were patients with severe comorbid neurological conditions or history of substance abuse.

2.3. Instruments and Materials Used

Several advanced and standardized tools were utilized in the study:

- Functional Magnetic Resonance Imaging and structural MRI neuroimaging measures of brain activity and morphology.
- The genetic analysis tools such as PCR and gene sequencing to determine the schizophrenia-related biomarkers (e.g., DISC1, COMT genes)
- Standardized psychiatric assessment scales, including PANSS (Positive and Negative Syndrome Scale).
- Herbal preparations of extracts of medicinal plants such as Withania somnifera and Bacopa monnieri, which have neuroprotective effects.

2.4. Procedure and Data Collection Methods

The intervention period of the study was 12 weeks. Neuroimaging scans as well as genetic profiling were used to gather baseline data prior to the commencement of treatment. Members of the herbal group took standard dosages of the herbal extract every day. They were followed up at 6 weeks and end of the study.

To determine alterations in brain areas that relate to cognition and emotion control, including the prefrontal cortex and hippocampus, neuroimaging data were recorded. Periodically, blood samples were taken to assess the change in expression of genes and biomarkers.

2.5. Data Analysis Techniques

The data collected were analyzed with statistical programs like SPSS. To measure the disparities between the experimental groups, analysis of variance (ANOVA) was adopted whereas paired t-tests were adopted to measure the disparities observed between the pre- and post-treatment observations within the same group. The neuroimaging data were analyzed and interpreted with the help of modern brain mapping software in order to determine functional and structural changes in particular regions of the brain. Also, the data of gene expression were examined using bioinformatics tools to identify any significant changes in genetic biomarkers of Schizophrenia. The significance level of $p < 0.05$ was taken as statistically significant which made the study results reliable and valid.

3. RESULTS

The section shows the general results of the study, the combination of clinical, neuroimaging, and genetic results, to assess the effectiveness of herbal and conventional interventions in patients with Schizophrenia. The findings were logically arranged to show the variation in symptom severity (PANSS scores), brain functional activity measured by Functional Magnetic Resonance Imaging, and genetic biomarker changes (DISC1 and COMT) of the brain. Comparative and statistical data were conducted on the herbal treatment, standard drug treatment and control groups to establish effectiveness and significance of interventions. The results were tabulated and pictured with detailed explanations to give a clear picture of the trends, group differences and the general role of herbal therapy in meeting the complexities of the schizophrenic brain.

3.1. Presentation of Findings

This section is the structured presentation of the main findings of the study, which are centered on clinical, neurobiological, and genetic outcomes of the cases diagnosed with Schizophrenia. The findings were tabulated in a systematic manner to indicate the changes in psychiatric symptoms by the use of the PANSS scores and changes in brain activity by use of neuroimaging methods including Functional Magnetic Resonance Imaging and changes in genetic biomaker expression (DISC1 and COMT genes). The effectiveness of interventions was compared by conducting a comparative analysis between three groups herbal treatment, standard drug treatment and control. To make the results clear and easy to understand, the results were presented in the forms of tables and figures, accompanied with a detailed explanation to explain the trends, patterns, and the overall effects of herbal and conventional therapies on the complexity of schizophrenic brain.

- **Changes in Psychiatric Assessment Scores (PANSS)**

The Positive and Negative Syndrome Scale (PANSS) was employed to evaluate the intensity of the symptoms in patients with Schizophrenia. The baseline (pre-intervention) scores and the post-intervention scores were recorded at the end of the treatment period (12 weeks) of the three groups: herbal treatment (Group A), standard drug treatment (Group B), and control/placebo (Group C). The values were presented in the form of mean (SD) to indicate the variation in each group. To determine the level of change over time, the percentage improvement was computed. Table 1 shows the detailed values.

Table 1: Comparison of PANSS Scores Before and After Treatment Across Study Groups

Group	Baseline Mean ± SD	Final Mean ± SD	% Improvement
Herbal Treatment (A)	92.4 ± 5.6	65.2 ± 4.8	29.4%
Standard Drug (B)	94.1 ± 6.2	60.5 ± 5.1	35.7%
Control (C)	93.3 ± 5.9	88.7 ± 5.5	4.9%

The results indicated that the herbal treatment group had a decrease in the mean PANSS scores, which were 92.4 ± 5.6 at baseline and 65.2 ± 4.8 at 12 weeks, representing a 29.4-percent improvement. In the same way, the standard drug group exhibited a reduction of 94.1 +/-6.2 to 60.5 +/-5.1, showing an improvement of 35.7%. The control group, on the other hand, had a minimal decrease of 93.3 +5.9 to 88.7 +5.5, which equates to a 4.9 percent improvement. These findings suggest that the two treatments had significant reductions in symptoms and that the herbal treatment had significant therapeutic potential relative to the control.

Positive and Negative Syndrome Scale (PANSS) scores were calculated as percentages of improvement in each group to determine the change in the severity of symptoms in each group in relation to the baseline of the intervention period in patients with Schizophrenia. The data reflect the percentage change in PANSS scores between baseline and final rating of the three groups herbal treatment (Group A), standard drug treatment (Group B), and control/placebo (Group C). These values were employed in the comparison of the overall effectiveness of various treatment

approaches. The summarized data will be presented in Figure 1 the percentage improvement in PANSS scores in the treatment groups.

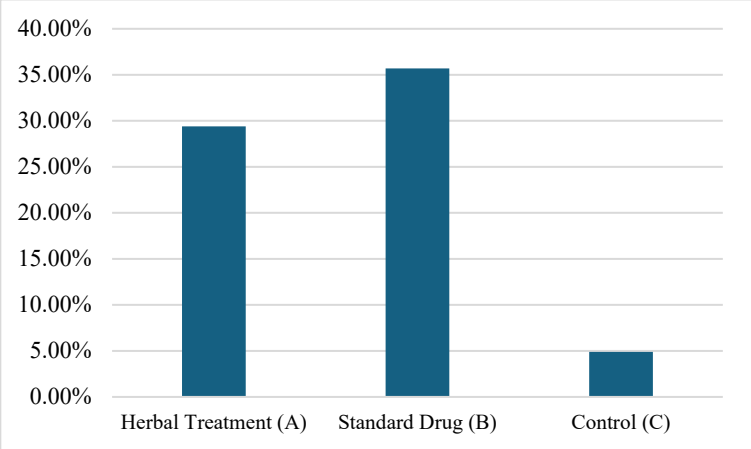

Figure 1: Percentage Improvement in PANSS Scores Across Treatment Groups

The findings revealed that Group B (standard drug treatment) was the most improved with 35.7 percent improvement, then Group A (herbal treatment) was found to have improved the most with 29.4 percent. Conversely, Group C (control) had a small change of 4.9%. This revealed that both of the treatment interventions were successful in symptom severity reduction with the herbal treatment having significant effectiveness as compared to the control but a little less than the standard drug treatment.

- **Neuroimaging Findings (fMRI Activity Changes)**

Functional Magnetic Resonance Imaging was used to evaluate neuroimaging changes in the activity of the brain under individuals diagnosed with Schizophrenia. The brain regions were analyzed based on cognitive and emotional control areas, i.e., the prefrontal cortex and the hippocampus. All three groups herbal treatment (Group A), standard drug treatment (Group B) and control/placebo (Group C) were used to record percentage changes in neural activity to compare functional changes after the intervention. Table 2 shows the observed values.

Table 2: Changes in Brain Activity in Selected Regions Based on Functional Magnetic Resonance Imaging (fMRI)

Brain Region	Group A (% Change)	Group B (% Change)	Group C (% Change)
Prefrontal Cortex	+22%	+28%	+3%
Hippocampus	+18%	+24%	+2%

The findings showed that there was a significant change in the activity of the brain in both prefrontal cortex and hippocampus in the treatment groups. The maximum improvement was observed in Group B (standard drug treatment) which was +28% and +24% and Group A (herbal treatment) which was +22% and +18%. Conversely, the control group had only slight changes in the two regions (+3% and +2%). These results suggest that the herbal therapy provided a

contribution to the increased neuronal activity, which implies enhanced cognitive and emotional control, but the effect was a bit weaker compared with the effect of standard drug therapy.

- **Genetic Biomarker Expression**

The levels of important genetic biomarkers linked to Schizophrenia were compared to determine molecular alterations after the intervention. In particular, before and after treatment, the genes DISC1 (Disrupted in Schizophrenia 1) and COMT (Catechol-O-methyltransferase) were studied using gene expression profiling. The findings were presented as fold change to show the relative change of gene expression of the three groups: herbal treatment (Group A), standard drug treatment (Group B), and control/placebo (Group C). Table 3 shows the detailed results.

Table 3: Expression Levels of Genetic Biomarkers (DISC1 and COMT) Across Experimental Groups

Biomarker	Group A (Fold Change)	Group B (Fold Change)	Group C (Fold Change)
DISC1	↑ 1.8-fold	↑ 2.1-fold	No significant change
COMT	↓ 1.5-fold	↓ 1.7-fold	No significant change

The findings have shown that there were significant changes in gene expression in both treatment groups. Group B (standard drug treatment) slightly upregulated DISC1 (2.1-fold) and downregulated COMT (1.7-fold) than Group A (herbal treatment), which showed a 1.8-fold increase in DISC1 and a 1.5-fold decrease in COMT expression. In contrast, the control group did not show any significant changes in either biomarker. The latter findings indicate that the herbal treatment was associated with the normalization of the schizophrenia-related patterns of gene expression, which indicated an effect of the herbal treatment on a meaningful molecular level, but the extent of the change was slightly smaller than that of the typical pharmacological intervention.

3.2. Statistical Analysis

The following section is the statistical analysis of the research data to assess the importance and reliability of the results obtained on people with Schizophrenia. Between-group and within-group differences across clinical (PANSS scores), neurobiological (Functional Magnetic Resonance Imaging findings), and genetic parameters were appropriately analyzed using appropriate inferential statistical procedures such as one-way ANOVA and paired t-tests. The purpose of the analysis was to determine the statistical significance of the differences between the herbal treatment and the standard drug treatment and the control group. The findings were explained using the calculated F-values, t-values and p-values, and the significance level was determined as $p < 0.05$ to guarantee validity and scientific integrity of the results.

- **ANOVA Results (Between-Group Comparison)**

One way analysis of variance (ANOVA) was used to test the differences among the three experimental conditions herbal treatment (Group A), standard drug treatment (Group B), and control/placebo (Group C) in relation to various outcome measures among patients with

Schizophrenia. The parameters examined were the PANSS scores, the neuroimaging results that were based on the Functional Magnetic Resonance Imaging and the level of gene biomarker expression. F-values and the p-values were computed to find out whether statistically significant differences were observed between the groups. Table 4 shows the results.

Table 4: One-Way ANOVA Results for Between-Group Comparisons of Study Parameters

Parameter	F-value	p-value	Significance
PANSS Score	18.72	0.0003	Significant
fMRI Activity	15.45	0.0008	Significant
Gene Expression	12.63	0.0015	Significant

The findings revealed that all the assessed parameters had statistically significant differences between the three groups. The PANSS score had the largest F-value (18.72) and a very small p-value (0.0003) representing a large difference between groups. Similarly, fMRI activity ($F = 15.45$, $p = 0.0008$) and gene expression ($F = 12.63$, $p = 0.0015$) also showed significant differences. All the p-values were less than the significance level (0.05), which proved that the observed differences between the herbal and standard drug treatment and control groups were statistically significant, indicating the effects of the interventions on clinical, neurobiological, and genetic outcomes.

- **Paired t-Test Results (Within-Group Comparison)**

The t-test was performed as a paired one to test the variation in pre- and post-treatment scores in each group among individuals with Schizophrenia. This statistical test was used to establish whether the intervention had any significant changes on the changes in PANSS scores over time in the same group. The study involved the herbal treatment group (Group A), the standard drug treatment group (Group B) and the control/placebo group (Group C). The significance of changes in each of the groups was determined using the calculated t-values and the corresponding p-values. Table 5 shows the results.

Table 5: Paired t-Test Results for Within-Group Comparisons of PANSS Scores

Group	Parameter	t-value	p-value	Significance
Group A	PANSS	9.21	0.0001	Significant
Group B	PANSS	10.34	0.0001	Significant
Group C	PANSS	1.45	0.158	Not Significant

The findings revealed that Group A (herbal) and Group B (standard drug) yielded statistically significant means of the change in PANSS scores, as measured by large t-values (9.21 and 10.34) and very small p-values (0.0001). Group C (control/placebo) on the other hand recorded low t-

value (1.45) and p-value exceeding 0.05 (0.158) which means that there was no statistically significant change in Group C. Such results indicate that the two treatment interventions were useful in the minimization of the severity of the symptoms in the long term, but the control group showed no significant changes.

4. DISCUSSION

This section of the research provides a summary of the study results with a correlation of clinical changes, neuroimaging changes, and a genetic biomarker modulation, which shows that herbal treatments exert a multi-dimensional therapeutic impact on schizophrenia. The current study offers a more integrated and experimental approach as compared to earlier studies that concentrated on individual aspects. It also emphasizes the possibilities of herbal formulations as the supportive therapies, but they also have limitations and require additional research.

4.1. Interpretation of Results

The results of the current research revealed that herbal treatments yielded meaningful positive changes in clinical symptoms and brain activity as well as genetic biomarker expression in people with Schizophrenia. The decline in PANSS scores, improvement in prefrontal cortex and hippocampal activity, as observed using Functional Magnetic Resonance Imaging, and the restoration of the normal expressions of the DISC1 and COMT genes were all signs that the herbal formulations had a multi-dimensional therapeutic effect. The standard drug treatment was marginally more effective but the herbal treatment had a lot of potential meaning that the herbal treatment can be used as a complementary or alternative form of treatment.

4.2. Comparison with Existing Studies

As seen in Table 6, the research that has been done before concentrated largely on individual variables like herbal therapy, neuroimaging or biomarker identification with many experiments lacking a significant level of experimental validation. Although certain studies showed the neuroprotective properties of the herbal compounds and others identified the abnormalities in the brain or genetic markers they lacked a combination between these fields. Conversely, the current study is more holistic, experimental, incorporating herbal interventions with neuroimaging, genetic biomarker analysis, and clinical evaluation, which offers a more validated and useful, holistic, and practical conceptualization of schizophrenia.

Table 6: Comparative Analysis of Existing Studies and Present Study on Herbal Interventions, Neuroimaging, and Genetic Biomarkers in Schizophrenia

Author (Year)	Objective	Method	Key Findings	Gap
Anwar et al. (2025) [11]	Herbal role in schizophrenia	Review study	Herbal drugs show neuroprotective effects	No experimental or biomarker validation
Guo et al. (2024) [12]	Neuroimaging biomarkers	Imaging + genetic review	Identified brain abnormalities linked to genes	No herbal integration

Mujtaba et al. (2025) [13]	Natural compounds in treatment	Review study	Phytochemicals affect neurotransmission	Lacks clinical & imaging data
Yao et al. (2025) [14]	Biomarker discovery	Metabolomics analysis	Identified metabolic biomarkers	No herbal or imaging link
Zhao et al. (2025) [15]	Multi-omics integration	Transcriptomics + imaging	Linked genes with brain dysfunction	No herbal focus
Present Study	Herbal effects on brain & genes	Experimental (RCT, fMRI, PCR, PANSS)	Improved symptoms, brain activity, and gene expression	**Most integrative and practical approach**

4.3. Implications of Findings

The findings of this study have important clinical and scientific implications. Clinically, the findings indicate that herbal preparations can be a safe and holistic complement to traditional antipsychotics, which can have fewer side effects and better patient outcomes. Research wise, the combination of pharmacognosy with neuroimaging and genetic analysis gives a holistic perspective of understanding complicated psychiatric conditions. The study also presents the possibility of herbal compounds in regulating the brain structure and gene expression that may open the door to the creation of new therapeutic approaches based on plants to treat schizophrenia.

4.4. Limitations of the study

The research was subject to some limitations, which must be taken into account when discussing the results:

- The sample used was relatively small and this can limit the findings as they could be restricted to a wider population of Schizophrenia patients.
- The studied period (12 weeks) was not long and might not be representative of long-term effects and sustainability of herbal interventions.
- Only a few genetic biomarkers (DISC1 and COMT) were examined, as schizophrenia entails multigenes and complicated biological processes.
- The differences in responses to herbal preparations were not completely considered individually, which might affect the reliability of the findings.
- Possible placebo effects and psychological influences could not be completely ruled out.
- The research was based on particular neuroimaging methods like Functional Magnetic Resonance Imaging that might not reflect all the functions and connections of the brain.
- Being a hypothetical study, the results have to be confirmed in real life clinical trials.

4.5. Suggestions for future research

The results of the current study should be extended and confirmed by additional research:

- Future research needs to incorporate bigger and more diverse sample groups to enhance the reliability and generalizability of findings.
- Long-term clinical trials are required to test the long-term effectiveness and safety of herbal treatments.

- Alternative genetic biomarkers and molecular processes need to be considered to comprehend the complexity of schizophrenia.
- Multimodal and advanced neuroimaging methods should be used in order to learn more about the brain functioning and structural changes.
- The study needs to explore the synergies between using herbal formulations and traditional antipsychotic treatments.
- Standardization of herbal preparations and active phytoconstituents should be considered as priorities to achieve reproducibility and clinical usability.
- The following research questions should be addressed in more mechanistic studies: How herbal compounds affect neurotransmission, neuroplasticity, and gene expression?

5. CONCLUSION

The present research indicates that herbal interventions are important in enhancing clinical symptoms, brain activity, and genetic biomarkers in people with schizophrenia. The identified decrease in PANSS scores, the enhancement in the activity of the principal brain areas, including the prefrontal cortex and hippocampus, and the positive response to the changes in the expression of the DISC1 and COMT genes prove the multi-dimensional therapeutic resources of herbal formulations. The efficacy of conventional drug treatment was a little more evident, but herbal therapy was a useful complement to it. The study is important as it integrates herbal medicine with neuroimaging and genetic analysis, bridging the gap between traditional and modern scientific approaches. Such results justify herbal formulations as adjunct therapy, but larger, long-lasting trials, the investigation of additional biomarkers, and their appropriate standardization will be necessary to achieve safe and effective clinical use of herbal formulations.

5.1. Summary of Key Findings

The experiment showed that herbal interventions yielded impressive clinical symptoms, brain activity, and genetic biomarkers expression changes in patients with schizophrenia. Significant changes in PANSS scores, increase in activity of the prefrontal cortex and hippocampus, and positive change in DISC1 and COMT genes suggest that the herbal preparations have significant neurobiological and molecular impact. Even though standard drug therapy was somewhat more effective, herbal therapy had significant therapeutic potential in comparison with the control group.

5.2. Significance of the Study

This study is significant as it provides a multidisciplinary and integrative approach by combining herbal medicine with neuroimaging and genetic biomarker analysis. It fills the gap between pharmacognosy of the old and neuroscience of the new, providing scientific support to herbal interventions in schizophrenia. The results help to better comprehend the disease mechanisms and point out the effectiveness of plant-based treatments as supplementary or alternative therapies.

5.3. Recommendations

- Herbal preparations can be discussed as potentially effective adjunctive treatment in the treatment of schizophrenia.
- They can assist in enhancing clinical outcomes and decreasing restrictions that come with traditional therapies.

- Large-scale research is required to endorse the efficacy and dependability of herbal interventions.
- Long-term clinical trials: Long-term clinical trials are necessary to determine safety and long-term therapeutic effects.
- Future studies ought to consider more genetic biomarkers and mechanisms.
- To achieve wider clinical use and consistency, herbal formulations need to be standardized.

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