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Therapeutic effects of chiglitazar combined with *Rosa roxburghii Tratt.* in inpatients with antipsychotic-induced metabolic syndrome

Hui Jin[1], Jing Yi Zhang[2], Zi Yao Cai[3], Shun Yao Xu[1], Xiao Dong Lin[4], Jia En Ye[1], Yan Shan Zheng[5] and Jin Xuan Zheng[1]*

[1]Department of Psychiatry, Wenzhou Seventh People's Hospital, Wenzhou, China
[2]Department of Endocrinology, Wenzhou Seventh People's Hospital, Wenzhou, China
[3]Department of Outpatient, Wenzhou Seventh People's Hospital, Wenzhou, China
[4]Department of Traditional Chinese Medicine, Wenzhou Seventh People's Hospital, Wenzhou, China
[5]Department of Gastroenterology, Cangnan County People's Hospital, Wenzhou, China

Abstract: The objective of this study was to evaluate the therapeutic effects of Chiglitazar combined with *Rosa roxburghii Tratt* (RRT) in inpatients diagnosed with psychiatric disorders and antipsychotic-induced metabolic syndrome (MetS).100 cases were included and divided into the Siglitazar group (n=50) and the Siglitazar + RRT group (n=50) Anthropometric measurements, lipid and glucose metabolism indicators, inflammatory markers, and PANSS scores were assessed at baseline, 8 weeks and 12 weeks post-treatment. Both treatment groups exhibited significant reductions in waist circumference and improvements in lipid profiles and glucose metabolism indicators over the 12-week study period. The siglitazar + RRT group performed better in improving the lipid profile, with significant decreases in triglyceride (TG) and total cholesterol (TC) levels. Furthermore, levels of inflammatory markers (CRP, IL-6, TNF-α) decreased significantly in both groups, with consistently lower levels observed in the Chiglitazar + RRT group at 8 weeks and 12 weeks. Importantly, the Chiglitazar + RRT group exhibited a significantly lower PANSS score at 12 weeks compared to baseline, indicating improved psychiatric symptoms. Chiglitazar combined with RRT effectively improves metabolic parameters, reduces inflammation and ameliorates psychiatric symptoms in inpatients with antipsychotic-induced MetS.

Keywords: Metabolic syndrome, antipsychotic agents, chiglitazar; *Rosa roxburghii Tratt.*

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INTRODUCTION

Metabolic syndrome (MetS) represents a cluster of clinical and metabolic abnormalities closely linked to cardiovascular diseases (CVD), with the general population facing a four-fold increased risk of developing diabetes mellitus (DM) and a two-fold increased risk of coronary heart disease (CHD), stroke and premature mortality (Saarinen *et al.,* 2024). MetS induced by antipsychotic medications, also known as drug-induced MetS, is a significant concern in psychiatric patients undergoing treatment with antipsychotic drugs (Rostami. *et al*., 2023). This syndrome is characterized by a cluster of metabolic abnormalities, including central obesity, dyslipidemia (elevated triglycerides and reduced HDL cholesterol), elevated blood pressure and impaired glucose metabolism, which can increase the risk of cardiovascular disease and diabetes (Farzaneh *et al.*, 2024).

Chiglitazar is a dual peroxisome proliferator-activated receptor (PPAR) agonist with activity against both PPARα and PPARγ (Zhang *et al*., 2023). It exhibits potent effects on glucose and lipid metabolism, making it a promising therapeutic agent for metabolic disorders such as type 2 diabetes mellitus and dyslipidemia (Wang *et al*., 2024; Cheng *et al*., 2019). By targeting PPARα, Chiglitazar enhances fatty acid oxidation and reduces triglyceride (TG) levels, while its activation of PPARγ improves insulin sensitivity and adipogenesis (DeFronzo 2021; Deeks 2022). This dual mechanism of action contributes to its potential in managing insulin resistance, hyperglycemia and dyslipidemia associated with MetS. Chiglitazar's favorable pharmacological profile underscores its role as a therapeutic candidate for treating metabolic disorders.

Rosa roxburghii Tratt. (RRT) is a perennial shrub native to southwestern China, known for its potent antioxidant properties (Jiang *et al*., 2024). The fermentation broth of *Rosa roxburghii Tratt*. fruit exhibits potent antioxidant and anti-photoaging effects, as demonstrated through cellular and molecular analyses, highlighting its potential as a protective agent against UVA-induced skin damage (Yuan *et al*., 2024). Additionally, wild *Rosa roxburghii Tratt.* juice from different altitudes demonstrates hypoglycemic effects in type 1 diabetic mice by improving glucose and lipid metabolism, reducing oxidative damage and activating the PI3K/Akt pathway, with the medium-altitude juice showing the highest overall efficacy (Zhu *et al*., 2023).

**Corresponding author:* e-mail: zjxnhb123@yeah.net

Given the therapeutic potential of Chiglitazar in modulating metabolic parameters and the antioxidant properties of *Rosa roxburghii Tratt.*, we hypothesize that combining Chiglitazar with RRT could offer synergistic benefits in mitigating antipsychotic-induced MetS. This study aims to assess the efficacy of Chiglitazar alone and in combination with RRT in improving metabolic profiles, inflammation markers and psychiatric symptoms in patients with antipsychotic-induced MetS. By investigating these outcomes, we aim to explore new avenues for managing metabolic abnormalities associated with antipsychotic medications and enhancing patient well-being.

MATERIALS AND METHODS

Ethical approvement

Ethical approvals were obtained from the Ethical Committees of Wenzhou Seventh People's Hospital vide No.20240212. The study protocol conforms to the guidelines of Declaration of Helsinki. All participants provided written informed consent.

Study participants

The study enrolled 100 inpatients diagnosed with psychiatric disorders who have developed MetS as a result of antipsychotic medication treatment at our hospital between December 2022 and November 2023. Inclusion criteria require participants to be aged between 18 and 60 years, diagnosed according to The 10th edition of the International Classification of Diseases (ICD-10) criteria (Gaebel *et al*., 2020) and meet the diagnostic criteria for MetS as per the International Diabetes Federation Criteria (Farzaneh. M, *et al,* 2024), which include a waist circumference of ≥90 cm in men and ≥ 80 cm in women, plus any two of the following: elevated triglycerides (TG>150mg/dL), reduced high-density lipoprotein cholesterol (HDL-C, <40mg/dL in men, <50 mg/dL in women), elevated blood pressure (systolic BP ≥130 mm Hg or diastolic BP ≥85 mm Hg) and elevated fasting plasma glucose (FBG ≥100mg/dL). Participants must not have used antipsychotic medications or medications for blood glucose or lipid regulation prior to enrollment, or must have discontinued these medications for at least one month before enrollment. Women of childbearing potential require a negative pregnancy test result. Exclusion criteria include comorbid personality disorders, affective disorders, mental retardation, or other mental disorders, as well as concurrent cardiovascular diseases, hematologic disorders, or treatment-resistant schizophrenia. Pregnant or lactating women and those at significant risk of suicide or self-harm are also excluded from the study to ensure the homogeneity and eligibility of the study population and minimize confounding factors in the evaluation of antipsychotic-induced MetS. All enrolled participants underwent scheduled physical examinations, electrocardiogram assessments and routine laboratory analyses, including complete blood count, liver function tests and kidney function tests.

Treatments

Two issues need to be paid attention to when confirming the sample size. One is the significance level of the study, and the other is statistical power. According to the research methods of many researchers, α=0.05 and statistical power of 80% are selected as the standard, taking into account the absence of response bias., determine the final sample size to be 100.A total of 100 patients were randomly assigned to two treatment groups: the Chiglitazar group (n = 50) and the Chiglitazar + RRT group (n = 50). In the Chiglitazar group, participants received oral Chiglitazar at a daily dose of 32 mg. For the Chiglitazar + RRT group, participants received the same dose of Chiglitazar (32 mg daily) along with *Rosa roxburghii Tratt* freeze-dried powder (5g/time, administered three times daily after meals). Assessments were conducted at three time points: baseline (0 weeks), 8 weeks and 12 weeks post-treatment. Dietary provisions were standardized and provided by the hospital cafeteria, with individualized meal plans tailored according to each patient' s medical condition.

Outcome measurements

Various parameters were monitored, including anthropometric measurements such as waist circumference and body mass index (BMI). Lipid metabolism indicators assessed were TG, total cholesterol (TC), HDL-C and low-density lipoprotein cholesterol (LDL-C). Glucose metabolism indicators included FBG and fasting insulin (FINS) levels.

Inflammatory markers measured were C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) in serum using ELISA (enzyme-linked immunosorbent assay) kits (Thermo Fisher Scientific Inc.). The CRP ELISA kit (catalog#: KHA0031) detects CRP levels with a sensitivity of <10 pg/mL and a range of 18.75-1200pg/mL, showing 9.7% inter-assay variability and 7% intra-assay variability. The IL-6 ELISA kit (catalog#: EH2IL6) measures IL-6 levels with <1pg/mL sensitivity and a range of 10.24-400pg/mL, exhibiting 10% inter-assay variability and 10% intra-assay variability. The TNF-α ELISA kit (catalog#: KAC1751) quantifies TNF-α levels with 3pg/mL sensitivity and a range of 15-1500pg/mL, showing 6% inter-assay variability and 3% intra-assay variability.

Psychopathological assessment using the Positive and Negative Syndrome Scale (PANSS) was conducted to evaluate psychiatric symptoms and treatment response. The PANSS comprises 30 items rated on a 7-point scale (1=absent, 7=extreme) to assess the presence and severity of symptoms, categorized into three subscales: Positive Symptoms, Negative Symptoms and General Psychopathology (Yuko *et al*., 2024).

STATISTICAL ANALYSIS

Statistical analysis was conducted using GraphPad Prism 10.1.2. Descriptive statistics such as mean and standard deviation were used for quantitative variables, while frequency and percentage were used for qualitative variables. Normality of the data was assessed with the Kolmogorov-Smirnov test. To assess differences between the placebo and intervention groups, a 2-way ANOVA followed by Sidak' s multiple comparisons test was employed for quantitative variables. Demographic variables between the two groups were compared using the chi-square test (or Fisher's exact test). The significance level for all tests was set at 0.05.

RESULTS

Baseline characteristics

As shown in table 1, Baseline characteristics of participants were comparable between the Chiglitazar group (n=50) and the Chiglitazar + RRT group (n=50). The mean ages were 39.3 years and 36.2 years, respectively, with no significant difference (P=0.138). Sex distribution (male/female) showed 26/24 in the Chiglitazar group and 21/29 in the Chiglitazar + RRT group, with no significant difference (P=0.423). Most participants were married in both groups (Chiglitazar: 36 married vs. 14 single/divorced/widowed; Chiglitazar + RRT: 38 married vs. 12 single/divorced/widowed), and the difference was not significant (P=0.820). Regarding antipsychotic regimen, most were on monotherapy (Chiglitazar: 34; Chiglitazar + RRT: 32), with a minority on combination therapy (Chiglitazar: 16; Chiglitazar + RRT: 18), showing no significant difference (P=0.997). Blood pressure measurements (systolic and diastolic) were similar between groups (systolic: Chiglitazar 118 mmHg, Chiglitazar + RRT 114 mmHg; diastolic: Chiglitazar 75.5 mmHg, Chiglitazar + RRT 72 mmHg), with no significant differences observed (P>0.05 for both).

Comparison of anthropometric measurements between Chiglitazar + RRT and Chiglitazar groups over 12 weeks waist circumference and BMI changes over a 12-week period were assessed in two groups using 2-way ANOVA followed by Sidak' s multiple comparisons test (fig. 1). Both the Chiglitazar + RRT group and the Chiglitazar group exhibited notable reductions in waist circumference from baseline (90cm) to 12 weeks (86 cm) (both P< 0.05). Additionally, the Chiglitazar + RRT group demonstrated significant decreases in BMI at 8 weeks (22.0±1.73kg/m²) and 12 weeks (22.0±1.74kg/m²) compared to baseline (23±1.72kg/m²) (P<0.05). However, within the Chiglitazar group, BMI at different time points did not show significant differences (all P>0.05). Furthermore, there were no significant differences in BMI or waist circumference across the three time points between the two groups (all P>0.05).

Comparison of lipid and glucose metabolism between Chiglitazar + RRT and Chiglitazar groups over 12 weeks as shown in table 2, there were no significant differences between the Chiglitazar + RRT group and the Chiglitazar group in baseline lipid and glucose metabolism indicators, including TG, TC, HDL-C, LDL-C, FBG, and FINS (all P >0.05). Both treatment groups showed significant improvements compared to baseline. Specifically, TG, TC, LDL-C, FBG and FINS levels decreased, while HDL-C levels increased significantly at 8 and 12 weeks (all P<0.05). Notably, the Chiglitazar + RRT group exhibited more significant improvements in lipid profiles compared to the Chiglitazar group at 8 and 12 weeks of treatment. Specifically, TG levels decreased to 89.24±36.62mg/dL at 8 weeks and further to 43.55±20.86mg/dL at 12 weeks in the Chiglitazar + RRT group, compared to 114±42.92 mg/dL and 73.94±34.57mg/dL in the Chiglitazar group, respectively (P=0.010 at 8 weeks, P=0.001 at 12 weeks). Similarly, TC levels decreased to 158.4±23.83mg/dL at 8 weeks and 137.8±12.33mg/dL at 12 weeks in the Chiglitazar + RRT group, compared to 172.9±22.32 mg/dL and 153.9±16.18mg/dL in the Chiglitazar group (P=0.003 at 8 weeks, P=0.001 at 12 weeks). Additionally, LDL-C and HDL-C levels showed similar trends with more substantial improvements in the Chiglitazar + RRT group compared to the Chiglitazar group. For instance, at 8 weeks, LDL-C levels were 100.3±26.95mg/dL in the Chiglitazar + RRT group versus 114.9±23.16mg/dL in the Chiglitazar group (P=0.007), and at 12 weeks, they were 75.27±14.21mg/dL in the Chiglitazar + RRT group versus 92.57±15.88mg/dL in the Chiglitazar group (P=0.001). Similarly, HDL-C levels at 8 weeks were 44.34±7.397 mg/dL in the Chiglitazar + RRT group compared to 39.16 ±5.534mg/dL in the Chiglitazar group (P<0.001) and at 12 weeks, they were 51.16±5.911mg/dL in the Chiglitazar + RRT group versus 43.64±4.913mg/dL in the Chiglitazar group (P<0.001).

Comparison of inflammatory marker levels between Chiglitazar + RRT and Chiglitazar groups over 12 weeks as illustrated in fig. 2, levels of CRP, IL-6, and TNF-α were assessed at baseline, 8 weeks, and 12 weeks in the Chiglitazar + RRT group and the Chiglitazar group. At baseline, there were no significant differences between the groups for CRP (P=0.554), IL-6 (P=0.554) and TNF-α (P=0.736) levels. However, both the Chiglitazar + RRT group and the Chiglitazar group exhibited significant reductions in CRP, IL-6, and TNF-α levels at 8 weeks and 12 weeks compared to baseline (all P<0.05). Importantly, the Chiglitazar + RRT group consistently showed lower levels of CRP, IL-6 and TNF-α than the Chiglitazar group at both 8 weeks and 12 weeks. At 8 weeks, the Chiglitazar + RRT group demonstrated significantly reduced CRP (88.82±28.05 *vs.* 108.8±31.41, P=0.001), IL-6 (139.3±80.73 *vs.* 188.5±74.77, P=0.007) and TNF-α (369.3±166.2 *vs.* 461.3±192.2, P=0.043) levels compared

Table 1: Baseline characteristics

Variables	Chiglitazar group (n = 50)	Chiglitazar + RRT (n = 50)	P value
Age (year)	39.3 ± 11.3	36.2 ± 10.8	0.138
Sex			
Male	26	21	
Female	24	29	0.423
Marital status			
Single/divorced/widowed	14	12	
Married	36	38	0.820
Antipsychotic regimen	0.997		
Monotherapy	34	32	
Combination therapy	16	18	0.833
Systolic blood pressure, mmHg	118 (103.5~131)	114 (105~126.5)	0.740
Diastolic blood pressure, mmHg	75.5 (67~82)	72 (64~82.5)	0.506

Table 2: Improvement of Lipid and Glucose Metabolism Over 12 Weeks with Chiglitazar + RRT Therapy

	Chiglitazar + RRT group	Chiglitazar group	*P*
TG (mg/dL)			
Baseline	152.2 ± 54.5	167.8 ± 51.75	0.177
8 weeks	89.24 ± 36.62 *	114 ± 42.92 *	0.010
12 weeks	43.55 ± 20.86 *#	73.94 ± 34.57 *#	0.001
TC (mg/dL)			
Baseline	184.7 ± 26.33	190.7 ± 24.35	0.415
8 weeks	158.4 ± 23.83 *	172.9 ± 22.32 *	0.003
12 weeks	137.8 ± 12.33 *#	153.9 ± 16.18 *#	0.001
HDL-C (mg/dL)			
Baseline	36.42 ± 7.822	34.08 ± 6.119	0.188
8 weeks	44.34 ± 7.397 *	39.16 ± 5.534 *	<0.001
12 weeks	51.16 ± 5.911 *#	43.64 ± 4.913 *#	<0.001
LDL-C (mg/dL)			
Baseline	132.1 ± 29.78	134.6 ± 27.61	0.935
8 weeks	100.3 ± 26.95 *	114.9 ± 23.16 *	0.007
12 weeks	75.27 ± 14.21 *#	92.57 ± 15.88 *#	0.001
FBG (mg/dL)			
Baseline	109.4 ± 8.942	108.4 ± 9.201	0.953
8 weeks	97.58 ± 10.49 *	100.4 ± 10.68 *	0.464
12 weeks	87.27 ± 12.33 *#	91.8 ± 11.96 *#	0.101
FINS (uIU/mL)			
Baseline	22.06 ± 6.611	21.16 ± 6.172	0.849
8 weeks	16.56 ± 6.952 *	15.98 ± 5.176 *	0.953
12 weeks	11.44 ± 6.973 *#	12.19 ± 4.913 *#	0.906

Note: Triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG) and fasting insulin (FINS); * denotes significance compared to baseline, and # denotes significance compared to the 8-week time point.

to the Chiglitazar group. Similarly, at 12 weeks, the Chiglitazar + RRT group showed significantly lower CRP (52.2±20.85 *vs.* 83.94± 30.55, $P<0.001$), IL-6 (69.08±42.38 *vs.* 114.5±64.72, $P=0.015$) and TNF-α (212.2±129 *vs.* 326.2±181, $P=0.008$) levels compared to the Chiglitazar group.

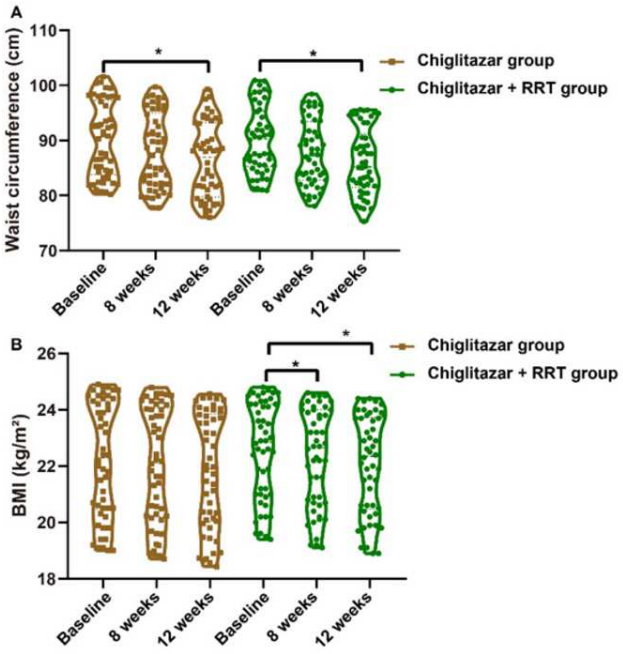
Comparison of PANSS score Between Chiglitazar + RRT and Chiglitazar Groups over 12 weeks

The PANSS scores were compared between the Chiglitazar + RRT group and the Chiglitazar group over 12 weeks (fig. 3). At baseline, there were no significant differences between the groups in PANSS scores (Chiglitazar +RRT group: 89.94±18.22, Chiglitazar group: 91.2±17.46, $P=0.980$). Over the 12-week period, although both groups showed a decreasing trend in PANSS scores, only the Chiglitazar +RRT group exhibited a significantly lower PANSS score at 12 weeks compared to baseline (75.88±18.43 vs. 89.94±18.22, $P<0.001$).

DISCUSSION

The results of this study highlight the potential therapeutic benefits of combining Chiglitazar, a dual PPAR agonist,

with RRT for managing antipsychotic-induced MetS. Our findings across anthropometric measurements, lipid and glucose metabolism, inflammatory markers and psychiatric symptoms shed light on the synergistic effects of Chiglitazar and RRT in addressing the multifaceted nature of MetS.



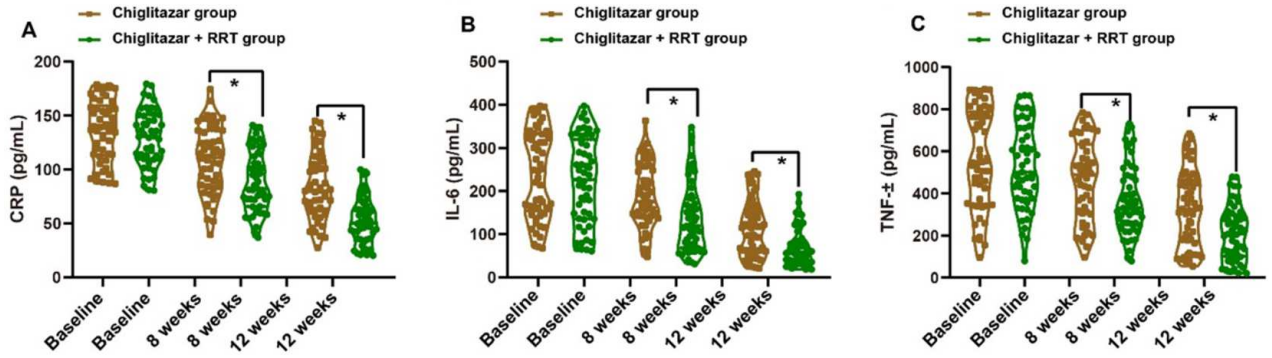
Note: A: Waist Circumference; B: Body Mass Index (BMI); *P<0.05

Fig. 1: Changes in anthropometric measurements over a 8 and 12-week period in two treatment groups.

Both the Chiglitazar + RRT group and the Chiglitazar group demonstrated significant reductions in waist circumference over the 12-week study period. This reduction in central adiposity is indicative of improved metabolic health and may contribute to reducing cardiovascular risk. The observed decrease in BMI in the Chiglitazar + RRT group further supports the potential of this combination therapy in promoting weight loss and improving body composition. Mechanistically, Chiglitazar's activation of PPARγ promotes adipocyte differentiation and reduces visceral fat accumulation (Chu *et al*., 2023 and Han *et al*., 2021), while RRT's antioxidant properties may support adipose tissue remodeling (Jiang *et al*., 2024 and Ma *et al*., 2023).

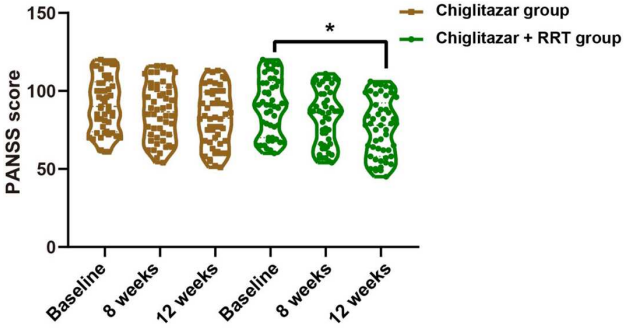
Previous studies have elucidated diverse bioactive properties of RRT, including its role in disrupting intracellular ATP levels, inducing ROS generation, and improving gut microbiota diversity, which may contribute to its beneficial effects in metabolic disorders. For instance, RRT pomace crude extract (RRPCE) effectively inactivates Cronobacter sakazakii and eliminates biofilms (Fei *et al*., 2024). Additionally, RRT fruit vinegar (RFV) intervention improves obesity, dyslipidemia and gut micro biota diversity (Li *et al*., 2022). The seed oil of RRT shows promise in improving mitochondrial function and reducing lipid accumulation through the PPARalpha/PGC-1alpha signaling pathway, with potential implications for managing metabolic disorders such as non-alcoholic fatty liver disease (NAFLD) (Hong *et al*., 2024). Moreover, fermented *Rosa roxburghii Tratt* juice (FRRT) demonstrates significant hypolipidemic effects by modulating gut microbiota composition and associated metabolites, highlighting its potential as a dietary intervention strategy for dyslipidemia management (Ji *et al*., 2022). Metabolic outcomes are also related to exercise, sleep, stress management, water intake, mitigating factors, etc. Chiglitazar is a dual agonist of PPARγ and PPARα, which exerts its pharmacological effects by activating these two receptors. PPARγ and PPARα are members of the nuclear receptor superfamily and they play an important role in regulating physiological processes such as lipid metabolism, glucose metabolism and inflammatory response. Chiglitazar binds to PPARγ and PPARα receptors, causing the two receptors to form heterodimers and bind to the PPAR response element (PPRE). In this way, Chiglitazar can regulate the expression of multiple genes, thereby affecting physiological processes such as lipid metabolism, glucose metabolism and inflammatory response. Specifically, activation of PPARγ can promote adipocyte differentiation and lipid storage, thereby improving insulin sensitivity and preventing atherosclerosis. Activation of PPARα can promote fat oxidation and reduce triglyceride synthesis, which helps to lower blood lipids and improve atherosclerosis. The main effects of RRT are anti-oxidation and anti-inflammatory. It combines with Chiglitazar to aggravate metabolism and further reduce inflammatory response. In our study, significant improvements in lipid profiles, including reductions in TG, TC and LDL-C, as well as increases in HDL-C, were observed in both treatment groups. The combination of Chiglitazar and RRT resulted in more pronounced improvements in lipid parameters compared to Chiglitazar monotherapy. Chiglitazar's dual activation of PPARα and PPARγ contributes to lipid modulation (Hempel *et al*., 2023), whereas RRT's antioxidant effects may protect against lipid oxidation and enhance lipid profile improvements. Furthermore, reductions in FBG and FINS levels reflect improved glycemic control in both groups. The study demonstrated that a polysaccharide from *Rosa roxburghii Tratt* fruit effectively mitigated hyperglycemia, hyperlipidemia and gut dysbiosis in type-2 diabetic db/db mice (Hempel *et al*., 2020).

Rosa roxburghii Tratt fruit extract (RRTE) demonstrates preventive effects against ulcerative colitis (UC) by modulating gut microbiota composition, enhancing intestinal barrier function, reducing inflammation and oxidative damage and regulating the IL-17 signaling pathway, suggesting its potential as a natural therapeutic approach for UC management (Yasiukaits N and Pavlova O 2021).



Note: Inflammatory markers including C-reactive protein (CRP, A), interleukin-6 (IL-6, B) and tumor necrosis factor-alpha (TNF-α, C) were measured in serum using enzyme-linked immunosorbent assay (ELISA). * denotes significance at $P<0.05$.

Fig. 2: Comparison of inflammatory marker levels in serum between Chiglitazar + RRT and Chiglitazar groups over 8 and 12 weeks.



Note: *denotes significance at $P<0.05$.

Fig. 3: Comparison of positive and negative syndrome scale (PANSS) scores between Chiglitazar + RRT and Chiglitazar groups over 8 and 12 weeks.

Rosa roxburghii Tratt fruit polyphenols exhibit protective effects against lung injury by attenuating inflammatory cytokine levels and affecting key metabolic pathways, highlighting their potential therapeutic role in mitigating inflammation-related complications (Tang *et al*., 2022). *Rosa roxburghii Tratt* juice exhibits anti-inflammatory effects by inhibiting NF-κB and increasing IL-2 levels, contributing to the alleviation of Foxp3-mediated regulatory T cell (Tregs) imbalance in arseniasis patients, highlighting its potential as a therapeutic intervention for immune inflammation associated with arsenic exposure (Wang *et al*., 2024). Both treatment groups also exhibited significant reductions in inflammatory markers (CRP, IL-6, TNF-α), with greater reductions seen in the Chiglitazar + RRT group. Chiglitazar's anti-inflammatory effects, mediated through PPARγ activation, likely contribute to suppressing pro-inflammatory pathways. RRT's antioxidant properties may further mitigate oxidative stress and inflammatory cytokine production, enhancing the anti-inflammatory effects of Chiglitazar. The combination therapy shows promise in attenuating chronic low-grade inflammation, a hallmark of MetS and cardiovascular risk.

Improvements in psychiatric symptoms, as measured by the PANSS, were observed specifically in the Chiglitazar + RRT group. This finding suggests a potential role of RRT in improving neurocognitive function and psychiatric symptoms in patients receiving antipsychotic medications. RRT' s neuroprotective effects observed in improving psychiatric symptoms among patients receiving antipsychotic medications could potentially be linked to its ability to mitigate inflammation and other related factors. Future research should focus on elucidating the specific molecular mechanisms underlying the synergistic effects of Chiglitazar and RRT.

CONCLUSION

In conclusion, the combination of Chiglitazar, a dual PPAR agonist, with RRT holds significant promise in the management of antipsychotic-induced MetS. Our study provides evidence of synergistic effects across multiple metabolic and psychiatric parameters. Future research should focus on elucidating the specific molecular mechanisms underlying the synergistic effects of this combination therapy and conducting long-term randomized controlled trials to assess its efficacy and safety across diverse patient populations.

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