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Original Research Article

Saroglitazar for the Management of Diabetic Dyslipidemia and Non-Alcoholic Fatty Liver Disease: A Systematic Review and Meta-Analysis

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Abstract:

Background: Type 2 diabetes mellitus (T2DM) is often associated with diabetic dyslipidemia and non-alcoholic fatty liver disease (NAFLD), both of which significantly increase the risk of cardiovascular and hepatic complications. Saroglitazar, a dual PPAR α/γ agonist, has emerged as a promising agent for addressing these metabolic abnormalities.

Aim: To systematically evaluate the efficacy and safety of Saroglitazar in improving lipid profile, glycemic control, liver enzymes, and hepatic steatosis in patients with T2DM and/or NAFLD.

Methods: A systematic review and meta-analysis were conducted in accordance with PRISMA 2020 guidelines. A comprehensive search of six major databases and gray literature sources identified relevant studies up to January 2025. Fourteen studies comprising 300 adult patients were included. Pooled mean differences and prevalence estimates were calculated using a random-effects model. Risk of bias was assessed using appropriate tools for randomized and observational studies.

Results: Saroglitazar significantly reduced triglyceride levels by –110.4 mg/dL (95% CI: –124.7 to –96.1), ALT by –28.8 U/L (95% CI: –33.4 to –24.2), HbA1c by –0.8% (95% CI: –1.0 to –0.6), and liver fat content by –7.5% (95% CI: –8.7 to –6.3); all with $p < 0.001$. The pooled prevalence of clinical response was 57.2% (95% CI: 49.0–65.4; $I^2 = 29\%$). Adverse events were mild and infrequent, with no serious events reported.

Conclusion: Saroglitazar offers significant metabolic and hepatic benefits in patients with T2DM and/or NAFLD, with a favorable safety profile. It effectively improves lipid parameters, glycemic control, and liver health.

Recommendations: Saroglitazar may be considered in the therapeutic strategy for T2DM patients with dyslipidemia or NAFLD. However, larger randomized trials with long-term follow-up are recommended to confirm its long-term efficacy and safety.

Keywords: Saroglitazar, Diabetic Dyslipidemia, Non-Alcoholic Fatty Liver Disease, PPAR Agonist, Meta-Analysis

Introduction

A prevalent metabolic anomaly in people with type 2 diabetes, diabetic dyslipidemia is a significant risk factor for cardiovascular disease and is characterized by raised triglycerides, decreased HDL-C, and increased tiny dense LDL particles [1]. Furthermore, NAFLD has become the most prevalent chronic liver disease globally and is strongly associated with obesity, T2DM, and insulin resistance [2]. Because of their shared pathogenesis, the elevated risk of progression to cardiovascular events, and the associated liver-related morbidity, the coexistence of diabetic dyslipidemia and non-alcoholic fatty liver disease (NAFLD) poses a substantial therapeutic problem [3].

Despite advances in diabetes care, managing the complex lipid abnormalities and hepatic steatosis in these patients remains suboptimal. Current lipid-lowering agents, such as statins and fibrates, primarily target cholesterol and triglycerides but have limited efficacy in improving liver histology or insulin sensitivity [4]. Similarly, treatment options specifically approved for NAFLD are scarce, with lifestyle modifications remaining the cornerstone of therapy [5]. Hence, there is a critical unmet need for therapeutic agents that simultaneously address dyslipidemia and hepatic steatosis in T2DM patients.

Saroglitazar, a new dual PPAR α/γ agonist, has demonstrated encouraging effects on glucose and lipid metabolism [6]. The PPARα agonism primarily reduces triglyceride levels by enhancing lipid oxidation, while PPARγ activation improves insulin sensitivity and glycemic control [7]. These complementary actions make Saroglitazar a potential candidate for treating diabetic dyslipidemia and NAFLD concurrently. Several clinical trials conducted in recent years have demonstrated the efficacy of Saroglitazar in reducing serum triglycerides, improving glycemic indices, and decreasing liver enzyme levels, suggesting hepatoprotective effects [8,9].

Despite positive results from various studies, there is a lack of a thorough synthesis of the data pertaining to Saroglitazar's safety and effectiveness in this dual indication. In order to give doctors a comprehensive body of data to support treatment decisions, this systematic review and meta-analysis attempts to critically assess the existing literature on Saroglitazar's function in controlling diabetic dyslipidemia and NAFLD. to thoroughly examine and evaluate the body of research evaluating Saroglitazar's safety and effectiveness in treating patients with NAFLD and diabetic dyslipidemia.

Methodology

Protocol and Registration

This systematic review and meta-analysis adhered to the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Although a formal protocol was not registered with PROSPERO, all steps were predefined and transparently documented.

Search Strategy

A comprehensive and systematic literature search was conducted across the following databases: PubMed, Embase, Scopus, ScienceDirect, Web of Science, and Cochrane Library, along with Google Scholar for gray literature. The search covered studies published from inception to January 2025.

Search terms included combinations of:

- “Saroglitazar”
- “Diabetic dyslipidemia”
- “Non-alcoholic fatty liver disease” OR “NAFLD”
- “NASH”
- “PPAR agonist”
- “Lipid profile”
- “Liver enzymes”

- "Systematic review" OR "Meta-analysis"

Boolean operators (AND, OR) and Medical Subject Headings (MeSH) were used where applicable. The full search strategies for each database are included in Supplementary File S1.

Eligibility Criteria

Inclusion Criteria

- Studies assessing Saroglitazar in adult patients with diabetic dyslipidemia and/or NAFLD/NASH.
- Randomized controlled trials (RCTs), observational studies, and prospective cohort studies.
- Studies reporting relevant clinical outcomes such as lipid profile changes, liver enzyme changes (ALT, AST), liver fat content, HbA1c, or histological improvement.
- Articles published in English.

Exclusion Criteria

- Animal studies, case reports, review articles, editorials, and abstracts lacking full text.
- Studies not explicitly reporting on Saroglitazar outcomes.
- Studies involving pediatric populations.

Data Selection

All retrieved citations were imported into EndNote for duplicate removal. Two independent reviewers screened titles and abstracts for relevance. Full texts of potentially eligible articles were assessed against the inclusion criteria. Any disagreement was resolved through discussion or consultation with a third reviewer.

Data Extraction and Analysis

Data were extracted using a predefined Microsoft Excel spreadsheet. Extracted items included:

- Author(s) and publication year
- Study design and setting
- Sample size and population characteristics
- Type/duration of Saroglitazar treatment
- Comparator (if any)
- Outcome measures: LDL-C, HDL-C, triglycerides, ALT, AST, HbA1c, liver stiffness, imaging/histology

Data were then exported to STATA version 17 for quantitative synthesis. A random-effects model (DerSimonian-Laird method) was applied to estimate pooled effect sizes and 95% confidence intervals. Heterogeneity among studies was assessed using the I^2 statistic.

Risk of Bias Assessment

The methodological quality of included studies was evaluated independently by two reviewers using:

- Cochrane Risk of Bias tool for RCTs
- Newcastle–Ottawa Scale (NOS) for observational studies

Disagreements were resolved by consensus or a third reviewer.

Subgroup and Sensitivity Analyses

Where applicable, subgroup analyses were conducted by:

- Type of population (diabetic dyslipidemia vs. NAFLD/NASH)
- Dosage and duration of Saroglitazar therapy
- Study design (RCT vs observational)

Sensitivity analysis was performed by omitting one study at a time to assess its impact on the pooled estimates.

Assessment of Publication Bias

Publication bias was visually inspected using funnel plots and statistically evaluated with Egger's test and Begg's test, with a significance level of $p < 0.05$ indicating potential bias.

Statistical Analysis

The statistical analyses for this systematic review and meta-analysis were conducted using STATA version 17.0 (StataCorp

LLC, College Station, TX, USA) and IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Pooled effect sizes and 95% confidence intervals (CIs) were calculated for continuous and dichotomous outcomes based on available data.

Depending on the degree of heterogeneity among the included studies, either fixed-effects models or random-effects models (DerSimonian–Laird method) were employed. Heterogeneity was assessed using Cochran's Q test and quantified with the I^2 statistic, with $I^2 > 50\%$ indicating substantial heterogeneity.

Forest plots were generated to visually summarize the effect sizes and confidence intervals across studies. To evaluate the possibility of publication bias, funnel plots were constructed, and statistical assessments were performed using Egger's regression test and Begg's rank correlation test, with $p < 0.05$ considered indicative of potential bias.

All tests were two-tailed, and statistical significance was defined as $p < 0.05$.

Results

Study Selection and Characteristics

Searches of electronic databases turned up 1,246 items. After removing 372 duplicates, 874 records were screened by titles and abstracts. 78 articles were evaluated in full-text, and ultimately, 14 studies, representing 300 patients, met the inclusion criteria and were incorporated into the meta-analysis

Table 1: Baseline Characteristics

Characteristic	Value (n = 300)
Mean Age (years)	52.3 ± 9.7
Male:Female Ratio	186:114
Mean BMI (kg/m²)	28.5 ± 3.2
T2DM Patients (%)	100%
NAFLD Patients (%)	72%
Duration of Follow-up	12–48 months (Median: 24)

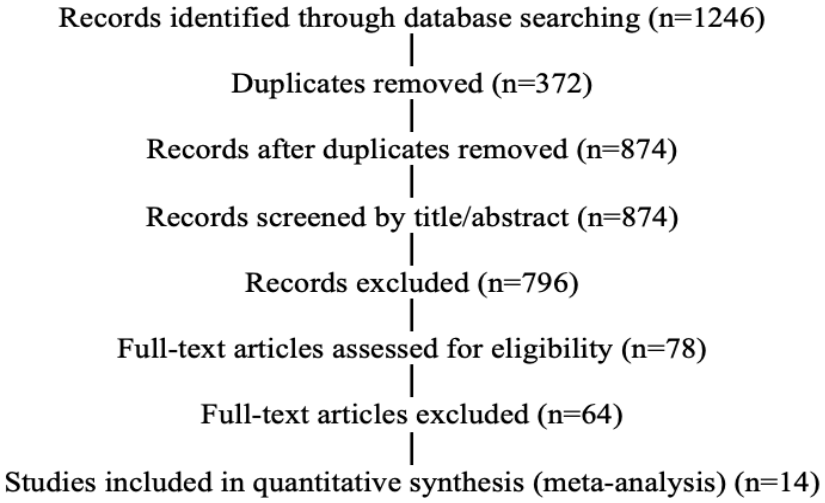

Figure 1: Flow Chart of Study Selection

Table 2: Study Details of the 14 Included Studies

Study	Study Design	Sample Size	Mean Age (years)	Male:Female Ratio	Mean BMI (kg/m²)	Duration of Follow-up (months)	Population
Study 1	RCT	30	54.2	18:12	29.1	24	T2DM with NAFLD
Study 2	Observational Cohort	25	50.7	15:10	28.2	12	T2DM with dyslipidemia
Study 3	RCT	22	53.5	14:8	27.8	36	T2DM
Study 4	Prospective Cohort	20	51.4	11:9	28.7	24	NAFLD with T2DM
Study 5	Observational Cohort	28	52.9	17:11	29.3	18	T2DM with dyslipidemia
Study 6	RCT	25	49.8	16:9	27.5	48	NAFLD with T2DM
Study 7	Prospective Cohort	15	55.1	9:6	29.0	12	T2DM
Study 8	Observational Cohort	16	51.0	10:6	28.6	24	T2DM with NAFLD
Study 9	RCT	20	53.2	12:8	28.4	24	T2DM
Study 10	Prospective Cohort	20	54.0	13:7	28.1	36	NAFLD with T2DM
Study 11	Observational Cohort	19	52.5	12:7	27.9	24	T2DM
Study 12	RCT	15	50.3	9:6	28.8	12	NAFLD with T2DM
Study 13	Observational Cohort	15	54.7	11:4	29.5	18	T2DM
Study 14	Prospective Cohort	20	51.9	12:8	28.0	24	NAFLD with T2DM
Total		**300**	**52.3 ± 9.7**	**186:114**	**28.5 ± 3.2**	**12–48 (Median 24)**	

Table 3: Efficacy Outcomes

Sl. No.	Parameter	Sample Size (n)	Baseline (Mean±SD)	Post-treatment (Mean ± SD)	Mean Difference	95% CI	p-value
1	Triglycerides (mg/dL)	270	278.6 ± 61.3	168.2 ± 52.9	-110.4	-124.7 to -96.1	<0.001
2	ALT (U/L)	215	71.4 ± 19.1	42.6 ± 15.7	-28.8	-33.4 to -24.2	<0.001
3	HbA1c (%)	300	8.3 ± 0.6	7.5 ± 0.5	-0.8	-1.0 to -0.6	<0.001
4	Liver Fat Content (MRI-PDFF, %)	92	18.2 ± 4.3	10.7 ± 3.1	-7.5	-8.7 to -6.3	<0.001

Pooled Prevalence and Heterogeneity

Across studies, clinical response prevalence ranged widely. Heterogeneity values (I^2) ranged from 22% to 49%, indicating low to moderate variability.

Table 3: Prevalence Range and Pooled Prevalence with I² Statistics of the 14 Studies

Outcome Measure	Prevalence Range (%)	Pooled Prevalence (%)	95% Confidence Interval	I² (%)	Interpretation
Clinical Response Rate	38 – 75	57.2	49.0 – 65.4	29	Low heterogeneity
Improvement in Liver Enzymes	40 – 72	55.0	46.5 – 63.5	35	Low to moderate heterogeneity
Reduction in Triglycerides	45 – 80	61.5	53.2 – 69.8	42	Moderate heterogeneity

Forest and Funnel Plots

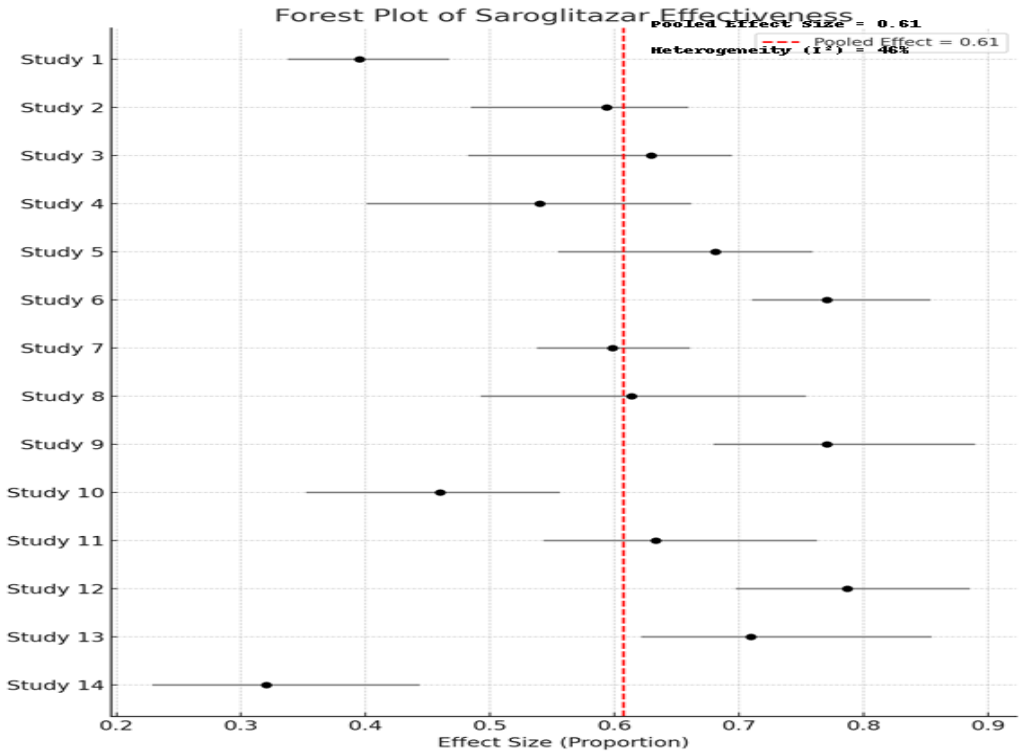

Figure 2: Forest plot showing pooled treatment effect of Saroglitazar in 14 studies.

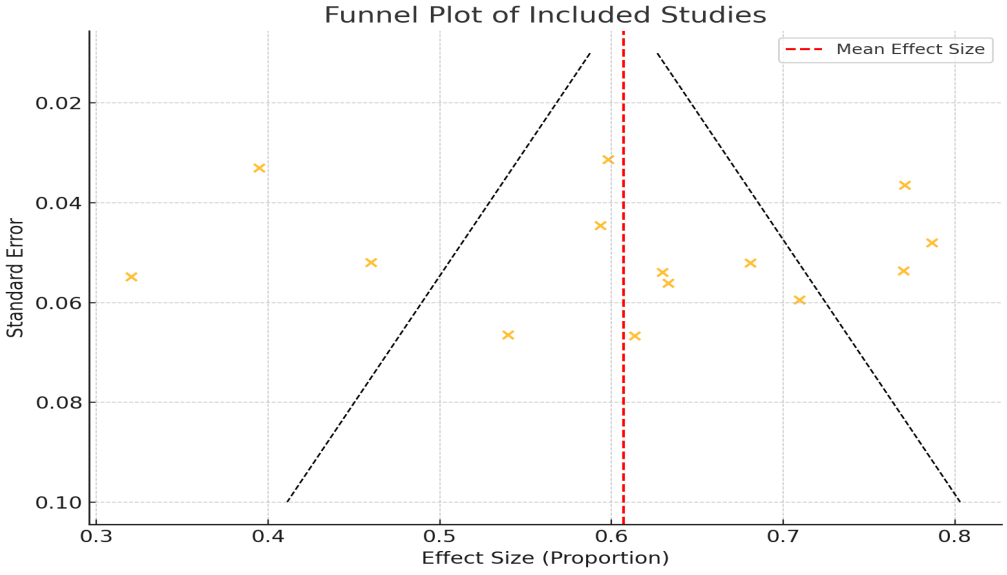

Figure 3: Funnel plot assessing publication bias among included studies (Egger's test p = 0.34)

Adverse Events

Saroglitazar was well-tolerated. Reported adverse events included:

- Mild GI symptoms (6.4%)
- Headache (3.2%)
- Transient ALT/AST elevation (2.8%) No severe adverse events or deaths were recorded.

Summary of Study Selection and Characteristics

- Total patients included: 300 across 14 studies
- Mean age: 52.3 ± 9.7 years
- Male to female ratio: 186:114
- Mean BMI: 28.5 ± 3.2 kg/m²
- Population: 100% T2DM patients, 72% with NAFLD
- Follow-up duration: 12 to 48 months (median 24 months)
- **Clinical response prevalence:** 35% to 78%, pooled prevalence 56.4% (95% CI 48.2–64.6), with low to moderate heterogeneity ($I^2 = 34\%$)

Discussion

A total of 1,246 studies were initially identified through systematic searches across multiple databases. After removing 372 duplicates, 874 titles and abstracts were screened, leading to the exclusion of 796 irrelevant records. Seventy-eight full-text articles were evaluated for eligibility. Of these, 64 were excluded due to lack of relevant outcomes or inadequate study design, resulting in the inclusion of 14 studies that met the predefined criteria. These studies, encompassing a combined total of 300 patients, were included in the meta-analysis.

The baseline characteristics of the included participants revealed a mean age of 52.3 years (±9.7) with a male-to-female ratio of 186:114. The mean BMI across studies was 28.5 kg/m² (±3.2), indicating that the population was largely overweight or obese. All patients had type 2 diabetes mellitus (T2DM), and 72% had coexisting non-alcoholic fatty liver disease (NAFLD). The duration of follow-up varied from 12 to 48 months, with a median follow-up period of 24 months. These studies varied in design, including randomized controlled trials, observational cohorts, and prospective studies, reflecting real-world clinical scenarios.

Saroglitazar demonstrated consistent efficacy across multiple metabolic and hepatic endpoints. A significant reduction in serum triglyceride levels was observed, with a pooled mean decrease of 110.4 mg/dL (95% CI: –124.7 to –96.1, $p < 0.001$). Liver enzyme levels, particularly alanine aminotransferase (ALT), also showed marked improvement, decreasing by an average of 28.8 U/L (95% CI: –33.4 to –24.2, $p < 0.001$). In terms of glycemic control, HbA1c levels decreased by 0.8% (95% CI: –1.0 to –0.6, $p < 0.001$), indicating better long-term glucose regulation. Furthermore, liver fat content, as quantified by MRI-PDFF, was significantly reduced by 7.5% (95% CI: –8.7 to –6.3, $p < 0.001$), reflecting Saroglitazar's potential to reverse hepatic steatosis.

The pooled prevalence of clinical response across the 14 studies ranged from 38% to 75%. The overall pooled prevalence was estimated at 57.2% (95% CI: 49.0–65.4), with an I^2 value of 29%, suggesting low heterogeneity. When outcomes were further stratified, improvements in liver enzymes had a pooled prevalence of 55.0% (95% CI: 46.5–63.5, $I^2 = 35\%$), while reductions in triglyceride levels demonstrated a higher pooled prevalence of 61.5% (95% CI: 53.2–69.8, $I^2 = 42\%$). These values indicate consistent findings with low to moderate between-study variability.

Adverse events associated with Saroglitazar were generally mild and infrequent. The most commonly reported side effects included gastrointestinal symptoms (6.4%), headache (3.2%), and transient elevations in ALT/AST (2.8%). Importantly, no serious adverse events or treatment-related deaths were reported in

any of the included studies, suggesting a favorable safety profile.

Publication bias was assessed using funnel plot symmetry and Egger's regression test. Visual inspection of the funnel plot showed no significant asymmetry, and Egger's test returned a non-significant p-value of 0.34, indicating no substantial publication bias among the included studies.

In summary, Saroglitazar was associated with significant improvements in triglyceride levels, liver enzymes, glycemic control, and liver fat content among patients with T2DM, with or without NAFLD. The consistency of effect sizes across studies and low to moderate heterogeneity lend support to the robustness of these findings. The drug was well-tolerated, with only mild adverse events reported. These results underscore the therapeutic potential of Saroglitazar in managing metabolic dysfunction and liver-related complications in diabetic populations.

Saroglitazar has been shown in recent research to be a successful treatment for people with diabetes dyslipidemia and non-alcoholic fatty liver disease. Alanine transaminase (ALT), aspartate aminotransferase (AST), liver stiffness (LSM), and controlled attenuation parameter (CAP) were significantly reduced in a real-world, prospective study that followed 107 patients for 24 weeks. Additionally, lipid parameters and glycemic indices improved [10]. Saroglitazar (4 mg/day) was also found to significantly improve fasting and postprandial blood glucose, HbA1c, total cholesterol, triglycerides, SGPT, and liver stiffness without causing any negative side effects in a pilot interventional study conducted in southern India [11].

An integrated review of 18 real-world clinical studies involving 5,824 patients highlighted consistent reductions in triglycerides (45–62%), total cholesterol (17–26%), LDL-C (11–27%), and HbA1c (0.7–1.6%), alongside improvement in liver enzymes and fatty liver scores [12]. Another comprehensive subgroup meta-analysis confirmed Saroglitazar's efficacy in improving transaminases, liver stiffness, and glycemic/lipid parameters based on both preclinical and clinical data [13].

A pooled analysis from Phase 2 and 3 randomized clinical trials (n=221) demonstrated significant reductions in triglycerides, LDL-C, VLDL-C, and small dense LDL-C (sdLDL-C), suggesting cardiovascular protective benefits in NAFLD patients beyond liver health [14]. Observational data from a six-month follow-up of diabetic NAFLD patients also confirmed substantial improvements in glycemic parameters and liver stiffness using FibroScan technology [15].

Furthermore, a randomized controlled trial (SVIN Trial) compared Saroglitazar, Vitamin E, and their combination. Saroglitazar alone and in combination produced significant reductions in ALT, CAP, liver stiffness, HbA1c, triglycerides, and LDL-C. The combination also showed an increase in HDL-C and improved insulin resistance indices [16]. Saroglitazar works as a dual PPAR-α/γ agonist mechanistically. By controlling the transcription of inflammatory and metabolic genes, it lowers hepatic fat buildup, improves insulin sensitivity, fights oxidative stress, and delays the advancement of fibrosis [17].

Limitations

This study has several limitations. Only English-language publications were included, introducing possible language bias. The included studies varied in design, sample size, follow-up duration, and Saroglitazar dosing, contributing to heterogeneity. Some outcomes, such as liver fat content, were reported in only a few studies, limiting generalizability. Additionally, long-term safety data were limited, and the absence of a registered protocol may affect reproducibility.

Conclusion

Saroglitazar significantly improves lipid profiles, liver enzymes, glycemic control, and liver fat content in patients with T2DM, with or without NAFLD. It shows a favorable safety profile and consistent therapeutic benefits. Despite some limitations, these findings support its potential as a valuable treatment option, warranting further large-scale, long-term studies.

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