

Original Article

Oral Mesoporous Silica Nanoparticles for Delaying Diabetes Progression in Adults With Prediabetes and Obesity

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ABSTRACT

Background: Prediabetes and obesity increase the risk of type 2 diabetes. Oral mesoporous silica nanoparticles (SiPore21) may influence gastrointestinal nutrient digestion and glycemic regulation. **Objective:** To evaluate the efficacy and short-term tolerability of oral SiPore21 gel in adults with prediabetes and obesity. **Methods:** A 12-week, double-blind, placebo-controlled randomized trial was conducted in urban Sindh, Pakistan, between June 2025 and January 2026. Eighty adults were randomized equally to SiPore21 gel (3 g three times daily) or matched placebo. Seventy-four participants completed follow-up and were included in complete-case analyses. Primary outcomes were changes in glycated hemoglobin (HbA1c) and fasting plasma glucose (FPG). Secondary outcomes included body composition, lipid parameters, and two-hour glucose. Between-group changes were compared using independent-samples t-tests. **Results:** HbA1c decreased by 0.31 ± 0.18 percentage points with SiPore21 versus 0.03 ± 0.19 with placebo. The between-group difference in change was -0.28 percentage points (95% CI: -0.37 to -0.19 ; $p < 0.001$). FPG changes differed by -9.00 mg/dL (95% CI: -11.55 to -6.45 ; $p < 0.001$). Secondary metabolic differences favored SiPore21. Mild gastrointestinal adverse events occurred in four intervention and three placebo participants; no severe events were reported. **Conclusion:** SiPore21 was associated with favorable short-term glycemic outcomes, but longer-term effectiveness, safety, and diabetes prevention remain unestablished. **Keywords:** Blood Glucose; Glycated Hemoglobin; Mesoporous Silica Nanoparticles; Obesity; Prediabetes; Randomized Controlled Trial; Silicon Dioxide.

INTRODUCTION

Prediabetes and obesity are major interconnected metabolic conditions associated with an increased risk of developing type 2 diabetes mellitus (T2DM) and cardiovascular complications. Prediabetes represents an

intermediate stage of dysglycemia characterized by elevated blood glucose concentrations that do not meet the diagnostic threshold for diabetes. It is commonly identified through impaired fasting glucose, impaired glucose tolerance, or elevated glycated hemoglobin (HbA1c). The coexistence of obesity further increases metabolic vulnerability through mechanisms involving insulin resistance, chronic low-grade inflammation, altered adipokine secretion, and pancreatic beta-cell dysfunction. Excess adiposity, particularly visceral fat accumulation, contributes to disturbances in glucose and lipid metabolism and may accelerate the transition from prediabetes to established T2DM. Consequently, individuals with both prediabetes and obesity constitute an important target population for interventions aimed at improving metabolic regulation and reducing future diabetes risk (1).

Current approaches to managing prediabetes and obesity primarily include dietary modification, increased physical activity, behavioral interventions, and selected pharmacological treatments. Lifestyle modification remains a fundamental component of diabetes prevention; however, achieving sustained behavioral changes may be challenging, particularly among individuals with long-standing obesity and multiple metabolic risk factors. Pharmacological interventions, including metformin and other glucose-lowering or weight-management agents, may improve metabolic parameters in appropriately selected patients, although treatment decisions require consideration of tolerability, cost, adherence, and individual clinical characteristics. Advances in pharmaceutical delivery systems have sought to improve the effectiveness and tolerability of metabolic treatments, reflecting continuing interest in therapeutic approaches that can complement conventional management strategies. Nevertheless, additional interventions that improve glycemic regulation without substantial systemic drug exposure warrant investigation, particularly for individuals at increased metabolic risk (2).

The gastrointestinal tract has become an important target for investigating alternative approaches to metabolic regulation because nutrient digestion and intestinal absorption substantially influence postprandial glucose concentrations, circulating lipid levels, and overall energy balance. Digestive enzymes, including pancreatic lipase and carbohydrate-hydrolyzing enzymes, facilitate the breakdown of dietary macronutrients into absorbable components. Modifying digestive enzyme activity or substrate accessibility may therefore influence the rate of nutrient digestion and subsequent metabolic responses. In particular, inhibition of pancreatic lipase has been investigated as a strategy for reducing intestinal fat digestion and absorption in obesity management. However, the effectiveness and tolerability of interventions targeting gastrointestinal digestive processes depend on their specific mechanisms, formulation properties, and effects on normal nutrient absorption (3).

Recent developments in nanotechnology have introduced mesoporous silica nanoparticles as potentially useful materials for biomedical and metabolic applications. These particles possess distinctive physicochemical characteristics, including high specific surface area, tunable pore size, porous architecture, and modifiable surface properties. Such characteristics enable interactions with biological molecules and have encouraged investigation of mesoporous silica nanoparticles as carriers for therapeutic compounds, including antidiabetic agents. Existing research has particularly emphasized their potential to improve drug loading, delivery, and release characteristics. However, evidence supporting nanoparticle-based drug delivery should be distinguished from evidence supporting the direct therapeutic effects of orally administered silica materials without an incorporated pharmacological agent. Although nanotechnological approaches have expanded opportunities for metabolic disease management, clinical translation requires careful evaluation of formulation-specific efficacy, gastrointestinal tolerability, and potential safety concerns (4,5).

Orally administered mesoporous silica materials have also been proposed as a non-systemic approach to influencing gastrointestinal nutrient digestion through physical interactions within the intestinal lumen. SiPore21 is a mesoporous silica formulation investigated for its potential to interact with digestive enzymes and modify the accessibility of dietary substrates. Its proposed mechanism involves the physical interaction or entrapment of digestive enzymes within a porous silica structure, potentially influencing carbohydrate and lipid digestion and subsequent postprandial metabolic responses. Unlike conventionally acting glucose-lowering medications, this approach is intended to act primarily within the gastrointestinal tract. Nevertheless, the extent to which these proposed interactions translate into meaningful improvements in glycemic control, body composition, and lipid metabolism requires direct clinical evaluation. Furthermore, improvements in metabolic biomarkers cannot independently establish long-term diabetes prevention, and the safety of repeated oral exposure must be assessed rather than assumed from the proposed mechanism of action (4–6).

Despite growing interest in nanotechnology-based metabolic interventions, important questions remain regarding the clinical effects and tolerability of orally administered mesoporous silica formulations in adults with concurrent prediabetes and obesity. Research concerning nanomaterials for diabetes management has frequently emphasized pharmaceutical delivery applications and broader therapeutic possibilities rather than direct assessment of gut-directed silica formulations using randomized, placebo-controlled clinical outcomes (4–6). Therefore, further clinical investigation is justified to evaluate whether SiPore21 produces measurable improvements in established indicators of glycemic regulation compared with placebo. Assessment of HbA1c and fasting plasma glucose provides information regarding glycemic control, while measurements of body composition, postprandial glucose, and lipid profiles may offer complementary information about metabolic responses. Monitoring gastrointestinal adverse events is also essential for evaluating short-term tolerability in this population.

The present study was designed as a double-blind, parallel-group randomized controlled trial to evaluate the efficacy and short-term safety of orally administered SiPore21 gel compared with a placebo gel in adults with prediabetes and obesity. The primary objective was to compare changes in HbA1c and fasting plasma glucose from baseline to 12 weeks between the intervention and control groups. Secondary objectives were to assess changes in body weight, body fat mass, postprandial glucose, and serum lipid parameters, together with gastrointestinal tolerability during the intervention period. It was hypothesized that participants receiving SiPore21 would demonstrate greater improvements in glycemic parameters than those receiving placebo. By evaluating these outcomes, the study aimed to provide clinical evidence regarding the potential of oral mesoporous silica formulations as a complementary strategy for short-term metabolic management in individuals at increased risk of developing T2DM.

MATERIAL AND METHODS

This study was conducted as a double-blind, parallel-group, placebo-controlled randomized controlled trial to evaluate the efficacy and short-term tolerability of orally administered mesoporous silica nanoparticles (SiPore21) in adults with prediabetes and obesity. The trial was carried out at a tertiary metabolic research facility in an urban region of Sindh, Pakistan, between June 2025 and January 2026. The overall study period included participant screening and recruitment, a 12-week intervention phase, and post-intervention outcome assessment. A randomized, placebo-controlled design was selected to compare changes in glycemic and metabolic parameters between participants receiving SiPore21 and those receiving a matched placebo while minimizing allocation-related bias and differences in outcome assessment.

The target population comprised adults aged 18–65 years with prediabetes and obesity. Individuals were eligible if they had a body mass index (BMI) between 27.0 and 38.0 kg/m² and met at least one of the specified biochemical criteria for prediabetes: glycated hemoglobin (HbA1c) between 5.7% and 6.4% or fasting plasma glucose (FPG) between 100 and 125 mg/dL. Participants with a previous diagnosis of type 2 diabetes mellitus, current use of glucose-lowering or weight-loss medications, chronic gastrointestinal disorders, or a history of major gastrointestinal surgery were excluded. Eligibility was determined through screening assessments that included relevant clinical history, anthropometric measurements, and biochemical evaluation. A total of 112 individuals were screened, of whom 80 met the eligibility criteria and were enrolled in the trial. The recruited participants were subsequently assigned to either the intervention or placebo group in a 1:1 allocation ratio.

The target sample size was established using estimates from previous early-phase clinical research involving mesoporous silica formulations in individuals with prediabetes. The calculation was based on an anticipated between-group difference of 0.30 percentage points in HbA1c, with an assumed standard deviation of 0.45 percentage points. A two-sided significance level of 0.05 and statistical power of 80% were specified, with an additional allowance for an anticipated 15% participant dropout rate. On this basis, a target sample of 80 participants was adopted, comprising 40 participants per treatment arm. HbA1c was the outcome used for the stated sample-size assumptions, while fasting plasma glucose was also designated as a primary outcome.

Following enrollment, participants were randomized into two equal groups using a computer-generated random allocation sequence. Allocation concealment was implemented through sequentially numbered, opaque, sealed envelopes managed by an independent data monitor who was not involved in trial execution. The intervention group comprised 40 participants allocated to SiPore21, while the control group comprised 40 participants allocated to placebo. Blinding was maintained by administering active and placebo preparations that were described as

identical in appearance, taste, texture, and packaging. Participants and outcome assessors remained unaware of treatment allocation during the intervention period. These procedures were intended to minimize selection, performance, and outcome-assessment biases.

Participants assigned to the intervention group received oral SiPore21 gel containing mesoporous silica nanoparticles at a prescribed dose of 3 g three times daily for 12 consecutive weeks. The assigned preparation was diluted in water and consumed immediately before the three main meals each day. The control group received a sensory-matched, cellulose-based placebo gel following the same dosing schedule and administration instructions. SiPore21 was investigated as a gastrointestinally acting formulation proposed to influence nutrient digestion through physical interactions between the porous silica material and digestive enzymes. The use of a matched placebo and identical administration schedules allowed comparison of the intervention under similar treatment conditions.

Treatment adherence was monitored throughout the intervention using participant-maintained daily compliance diaries and sachet counts conducted during biweekly clinic visits. Adherence was operationally defined as the proportion of prescribed doses consumed during the 12-week intervention. Participants consuming at least 80% of their assigned doses were classified as adherent, while those consuming less than 80% were classified as non-adherent. Follow-up visits also provided opportunities to evaluate tolerability, document gastrointestinal symptoms, and identify treatment discontinuations. Gastrointestinal adverse events were monitored using standardized visual analog scale symptom questionnaires. Reported symptoms and treatment discontinuations were considered in the assessment of short-term tolerability.

The primary outcomes were changes in HbA1c and fasting plasma glucose between baseline and week 12. HbA1c was expressed as a percentage and represented a measure of glycemic exposure over the preceding months, while fasting plasma glucose was recorded in mg/dL. These outcomes were selected to evaluate changes in glycemic regulation during the intervention period. Measurements were obtained at baseline before initiation of the assigned treatment and repeated at the completion of the 12-week intervention. The principal comparisons concerned changes in these outcomes within each treatment group and differences between the SiPore21 and placebo groups.

Secondary outcomes included body weight, BMI, body fat mass, two-hour glucose concentration following an oral glucose tolerance test, and serum lipid parameters. Anthropometric evaluation included measurement of body weight and calculation of BMI using body weight in kilograms divided by height in meters squared. Body composition was assessed using bioelectrical impedance analysis, with body fat mass expressed in kilograms. The lipid profile included total cholesterol, triglycerides, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol. Lipid concentrations and glucose measurements were expressed in mg/dL. The two-hour glucose measurement was used to evaluate the glycemic response following oral glucose administration. Secondary measurements were assessed at baseline and at the end of the 12-week intervention to examine changes in metabolic and body-composition parameters.

Clinical and biochemical measurements were organized according to treatment allocation and assessment time point. Baseline characteristics included age, sex, BMI, HbA1c, fasting plasma glucose, total cholesterol, and triglycerides. These variables were used to describe the randomized study population and examine the distribution of demographic and metabolic characteristics between the intervention and control groups. Outcome measures were compared across the two assessment periods using consistent units and variable definitions. Adherence records and gastrointestinal symptom assessments were maintained alongside metabolic outcome measurements to evaluate treatment exposure and reported tolerability.

Statistical analysis included descriptive and inferential procedures to evaluate baseline characteristics, treatment-related changes, and differences between the randomized groups. Continuous variables were summarized as means and standard deviations, while categorical variables were expressed as frequencies and percentages. The Shapiro-Wilk test was used to assess the normality of continuous variables. For normally distributed outcomes, paired-samples t-tests were applied to examine changes between baseline and week 12 within each treatment group, while independent-samples t-tests were used to compare continuous outcomes between groups. Repeated-measures analysis of variance (ANOVA) was applied to assess the effects of time, treatment group, and the interaction between time and treatment group. The time $\times$ group interaction was used to examine whether changes in glycemic outcomes differed between the SiPore21 and placebo groups. Pearson correlation analysis was

performed to evaluate the relationship between treatment adherence and glycemic parameters. Statistical tests were two-sided, and a p-value below 0.05 was considered statistically significant.

The randomized population comprised 80 participants, with 40 allocated to each treatment group. During the intervention period, six participants discontinued follow-up, including three in the SiPore21 group and three in the placebo group. Consequently, complete baseline and week-12 outcome data were reported for 74 participants, consisting of 37 participants in each group. The reported endpoint comparisons therefore represented a complete-case analysis of participants with available follow-up measurements, rather than a full intention-to-treat analysis of all randomized participants. The six participants without complete follow-up outcomes were not included in the reported primary endpoint comparisons. The analysis focused on the prespecified 12-week glycemic and metabolic measurements, without a longitudinal assessment of incident type 2 diabetes.

RESULTS

A total of 112 individuals were screened for eligibility between June 2025 and January 2026, of whom 80 fulfilled the inclusion criteria and were randomly allocated to the SiPore21 intervention group ($n = 40$) or placebo group ($n = 40$). During the 12-week intervention period, six participants discontinued participation, including three from each group. Consequently, 74 participants completed follow-up, corresponding to an overall retention rate of 92.5%. The complete-case analysis included 37 participants in each treatment group. The reported reasons for discontinuation included relocation ($n = 2$), loss to follow-up ($n = 1$), abdominal bloating ($n = 2$), and voluntary withdrawal ($n = 1$). Participant disposition is presented in Table 2.

Baseline demographic and clinical characteristics of the randomized participants are summarized in Table 1. The mean age was 48.7 ± 7.2 years in the SiPore21 group and 47.9 ± 8.1 years in the placebo group ($p = 0.643$). Women accounted for 55.0% and 60.0% of the respective treatment groups. Baseline BMI was 32.6 ± 2.9 kg/m² in the SiPore21 group and 32.2 ± 2.7 kg/m² in the placebo group. The corresponding baseline HbA1c concentrations were $6.10 \pm 0.21\%$ and $6.06 \pm 0.23\%$, while fasting plasma glucose concentrations were 113.1 ± 6.5 mg/dL and 111.7 ± 7.1 mg/dL. No statistically significant baseline differences were reported for the demographic and metabolic characteristics examined.

Changes in the primary glycemic outcomes are presented in Tables 3 and 4. Among the 74 participants with complete follow-up data, mean HbA1c in the SiPore21 group decreased from $6.09 \pm 0.21\%$ at baseline to $5.78 \pm 0.24\%$ at week 12, representing a mean reduction of 0.31 ± 0.18 percentage points ($p < 0.001$). In contrast, the placebo group demonstrated a smaller change from $6.07 \pm 0.22\%$ to $6.04 \pm 0.25\%$, corresponding to a reduction of 0.03 ± 0.19 percentage points ($p = 0.342$). The between-group difference in HbA1c change was -0.28 percentage points (95% CI: -0.37 to -0.19 ; $p < 0.001$), with a standardized mean difference of -1.51 . At week 12, the unadjusted mean HbA1c difference between groups was -0.26 percentage points (95% CI: -0.37 to -0.15 ; $p < 0.001$).

Fasting plasma glucose demonstrated a similar pattern. In the SiPore21 group, mean fasting glucose decreased from 112.9 ± 6.4 mg/dL at baseline to 103.2 ± 6.1 mg/dL at week 12, corresponding to a reduction of 9.7 ± 5.2 mg/dL ($p < 0.001$). The placebo group demonstrated a smaller reduction of 0.7 ± 5.8 mg/dL, from 111.9 ± 7.0 mg/dL to 111.2 ± 6.9 mg/dL ($p = 0.468$). The difference in mean fasting glucose change between groups was -9.00 mg/dL (95% CI: -11.55 to -6.45 ; $p < 0.001$), with a standardized mean difference of -1.63 . The corresponding unadjusted week-12 between-group difference was -8.00 mg/dL (95% CI: -11.02 to -4.98 ; $p < 0.001$).

Secondary metabolic outcomes at week 12 are summarized in Table 5. Participants receiving SiPore21 had a lower mean body weight than placebo recipients (88.2 ± 8.1 kg versus 92.1 ± 8.5 kg), with an unadjusted between-group difference of -3.90 kg (95% CI: -7.75 to -0.05 ; $p = 0.047$). Body fat mass was also lower in the SiPore21 group, with a mean difference of -2.50 kg (95% CI: -4.54 to -0.46 ; $p = 0.017$). The between-group difference in two-hour glucose concentration was -19.30 mg/dL (95% CI: -25.43 to -13.17 ; $p < 0.001$). Similarly, triglycerides and LDL cholesterol were lower in the intervention group, with mean differences of -11.40 mg/dL (95% CI: -20.35 to -2.45 ; $p = 0.013$) and -7.30 mg/dL (95% CI: -14.07 to -0.53 ; $p = 0.035$), respectively.

Treatment adherence and adverse events are summarized in Table 6. The reported proportion of participants achieving at least 80% adherence was 92% in the SiPore21 group and 90% in the placebo group. Mild gastrointestinal adverse events were reported in four participants (10.0%) in the SiPore21 group and three participants (7.5%) in the

placebo group. Two participants in the placebo group discontinued treatment because of abdominal bloating. No severe adverse events were reported during the 12-week intervention period.

Table 1. Baseline Demographic and Clinical Characteristics of Randomized Participants (N = 80)

Characteristic	SiPore21 (n = 40)	Placebo (n = 40)	p-value
Age (years)	48.7 ± 7.2	47.9 ± 8.1	0.643
Female, n (%)	22 (55.0)	24 (60.0)	0.651
BMI (kg/m ²)	32.6 ± 2.9	32.2 ± 2.7	0.528
FPG (mg/dL)	113.1 ± 6.5	111.7 ± 7.1	0.358
HbA1c (%)	6.10 ± 0.21	6.06 ± 0.23	0.422
Total cholesterol (mg/dL)	209.2 ± 17.8	207.8 ± 19.2	0.738
Triglycerides (mg/dL)	177.5 ± 21.4	175.1 ± 23.0	0.632

Values are mean ± SD unless otherwise indicated. BMI = body mass index; FPG = fasting plasma glucose; HbA1c = glycated hemoglobin. P-values are retained from the original manuscript and are unadjusted descriptive comparisons.

Table 2. Participant Screening, Allocation, Follow-up, and Treatment Discontinuation

Participant disposition	Total	SiPore21	Placebo
Screened, n	112	—	—
Excluded during screening, n	32	—	—
Randomized, n	80	40	40
Discontinued, n (%)	6 (7.5)	3 (7.5)	3 (7.5)
Relocation, n	2	2	0
Lost to follow-up, n	1	1	0
Abdominal bloating, n	2	0	2
Voluntary withdrawal, n	1	0	1
Completed intervention, n (%)	74 (92.5)	37 (92.5)	37 (92.5)
Included in complete-case analysis, n	74	37	37

Percentages are calculated using the total randomized sample or corresponding randomized group as the denominator. Screening exclusions are calculated from 112 screened minus 80 randomized. Em dashes indicate that group allocation was not applicable at screening.

Table 3. Changes in Primary Glycemic Outcomes From Baseline to Week 12 (n = 74)

Outcome and group	Baseline mean ± SD	Week 12 mean ± SD	Change mean ± SD	Within-group p-value
HbA1c (%)				
SiPore21 (n = 37)	6.09 ± 0.21	5.78 ± 0.24	−0.31 ± 0.18	<0.001
Placebo (n = 37)	6.07 ± 0.22	6.04 ± 0.25	−0.03 ± 0.19	0.342
FPG (mg/dL)				
SiPore21 (n = 37)	112.9 ± 6.4	103.2 ± 6.1	−9.7 ± 5.2	<0.001
Placebo (n = 37)	111.9 ± 7.0	111.2 ± 6.9	−0.7 ± 5.8	0.468

Change = week 12 minus baseline. Negative values denote reductions. Within-group p-values are from the reported paired-samples t-tests.

Table 4. Between-Group Treatment-Effect Estimates for Primary Outcomes (n = 74)

Outcome	Week-12 mean difference (95% CI)	p-value	Difference in change (95% CI)	p-value	Cohen's d for change
HbA1c (%)	−0.26 (−0.37 to −0.15)	<0.001	−0.28 (−0.37 to −0.19)	<0.001	−1.51
FPG (mg/dL)	−8.00 (−11.02 to −4.98)	<0.001	−9.00 (−11.55 to −6.45)	<0.001	−1.63

Mean differences are SiPore21 minus placebo. Week-12 differences are unadjusted comparisons of endpoint means. Differences in change compare group-specific baseline-to-week-12 changes. Confidence intervals and change-score p-values were calculated from the reported n = 37 per group, means, and SDs using independent-group Welch t methods. Cohen's d was calculated using the pooled SD of the reported change scores. Estimates are based on rounded summary data and are unadjusted for baseline covariates.

Table 5. Secondary Metabolic Outcomes at Week 12 (n = 74)

Outcome	SiPore21 (n = 37)	Placebo (n = 37)	Mean difference (95% CI)	p-value	Cohen's d
Body weight (kg)	88.2 ± 8.1	92.1 ± 8.5	−3.90 (−7.75 to −0.05)	0.047	−0.47
Body fat mass (kg)	31.4 ± 4.2	33.9 ± 4.6	−2.50 (−4.54 to −0.46)	0.017	−0.57
Two-hour glucose (mg/dL)	142.1 ± 12.3	161.4 ± 14.1	−19.30 (−25.43 to −13.17)	<0.001	−1.46
Triglycerides (mg/dL)	162.8 ± 18.5	174.2 ± 20.1	−11.40 (−20.35 to −2.45)	0.013	−0.59
LDL cholesterol (mg/dL)	124.5 ± 14.2	131.8 ± 15.0	−7.30 (−14.07 to −0.53)	0.035	−0.50

Continuous data are mean $\pm$ SD. Differences are SiPore21 minus placebo. Two-sided unadjusted p-values and 95% CIs were calculated using Welch independent-samples t-tests from rounded summary statistics. Cohen's d represents the standardized week-12 between-group mean difference. LDL = low-density lipoprotein.

Table 6. Treatment Adherence and Reported Gastrointestinal Adverse Events

Measure	SiPore21	Placebo
Randomized participants, n	40	40
Participants completing follow-up, n (%)	37 (92.5)	37 (92.5)
Reported adherence $\geq 80\%$ (%)	92	90
Participants with mild gastrointestinal adverse events, n (%)	4 (10.0)	3 (7.5)
Participants discontinuing due to bloating, n (%)	0 (0.0)	2 (5.0)
Severe adverse events, n	0	0

Event percentages use randomized group denominators of 40. Adherence percentages are retained as reported because their underlying numerators and denominators were not supplied. Adverse-event categories may overlap.

DISCUSSION

The findings of this double-blind, placebo-controlled randomized trial suggest that oral administration of mesoporous silica nanoparticles (SiPore21) was associated with favorable short-term changes in glycemic parameters among adults with prediabetes and obesity. Over the 12-week intervention period, participants receiving SiPore21 demonstrated greater reductions in glycated hemoglobin (HbA1c) and fasting plasma glucose (FPG) than those receiving placebo. Additional differences in body weight, body fat mass, two-hour glucose concentrations, and selected lipid parameters were observed in the intervention group. These findings suggest that orally administered mesoporous silica formulations may have potential as a gastrointestinally targeted approach to metabolic management. However, the clinical interpretation should remain limited to short-term changes in measured metabolic outcomes rather than established prevention or delayed onset of type 2 diabetes mellitus (T2DM).

The observed glycemic differences are relevant to the metabolic disturbances associated with prediabetes and obesity. Obesity contributes to insulin resistance through several interconnected processes, including excess visceral adiposity, chronic low-grade inflammation, altered adipokine signaling, and disturbances in glucose and lipid metabolism. Ruze et al. described the complex relationship between obesity and T2DM, emphasizing the importance of metabolic dysfunction in disease development and progression (1). In the present study, the greater reduction in HbA1c observed in the SiPore21 group may indicate improved glycemic regulation during the treatment period. The between-group difference in HbA1c change was approximately -0.28 percentage points, while the corresponding difference in fasting glucose change was approximately -9.0 mg/dL. Although these estimates suggest a measurable metabolic response, their long-term clinical importance remains uncertain because the study did not assess sustained glycemic control after treatment discontinuation or actual progression to diabetes. Furthermore, statistical significance should not be interpreted as sufficient evidence of a clinically established preventive effect.

Conventional management of prediabetes and obesity primarily involves lifestyle modification and, where clinically indicated, pharmacological treatment. Metformin and other metabolic therapies influence glucose regulation through mechanisms that differ from the proposed gastrointestinal action of mesoporous silica materials. Abbasi et al. reviewed advances in metformin-delivery systems for diabetes and obesity management, highlighting continuing efforts to optimize therapeutic delivery and treatment performance (2). Unlike pharmacological delivery strategies intended to improve the administration or availability of active compounds, SiPore21 has been investigated as a material-based intervention with a proposed local gastrointestinal mechanism. The present findings therefore address a different therapeutic approach rather than establishing equivalence or superiority to existing glucose-lowering medications. Because no active pharmacological comparator was included, direct conclusions regarding the relative effectiveness of SiPore21 and metformin or other established treatments cannot be drawn.

One possible explanation for the observed glycemic differences involves interactions between the porous silica material and digestive processes within the gastrointestinal lumen. The rate of carbohydrate and lipid digestion influences nutrient availability and subsequent metabolic responses. Inhibition of digestive enzymes, particularly pancreatic lipase, has been investigated as an approach to limiting intestinal lipid digestion in obesity management.

Subramaniyan and Hanim discussed the biological rationale and practical challenges of pancreatic lipase inhibition, including its potential implications for obesity treatment (3). SiPore21 has been proposed to influence nutrient digestion through physical interactions between mesoporous silica structures and digestive enzymes. Such interactions could theoretically modify macronutrient hydrolysis and contribute to changes in postprandial glucose concentrations. Nevertheless, the present study did not directly measure digestive enzyme activity, intestinal nutrient absorption, or gastrointestinal transit. Consequently, the reported glycemic changes cannot be attributed definitively to a particular luminal mechanism.

The physicochemical characteristics of mesoporous silica materials provide further context for understanding their possible biological applications. These materials possess porous architectures, relatively large surface areas, and modifiable surface properties that may facilitate interactions with biological molecules. Sarkar et al. reviewed mesoporous silica nanoparticles as carriers for antidiabetic molecules, describing their potential in pharmaceutical delivery applications (4). Similarly, Stoleru et al. examined nanotechnological approaches involving natural compounds for diabetes management, emphasizing the expanding interest in nanomaterials for metabolic treatment (5). However, evidence from drug-delivery systems does not necessarily establish the biological effectiveness of orally administered silica particles acting without an incorporated therapeutic drug. The present findings provide preliminary clinical observations relevant to this distinction, although direct mechanistic investigations are required to determine whether the observed changes were mediated by physical enzyme interactions, altered nutrient absorption, changes in body composition, or a combination of pathways.

The differences observed in body weight and body fat mass may also have contributed to the glycemic findings. Excess adiposity is closely associated with insulin resistance, and changes in body composition may influence glucose regulation through alterations in metabolic and inflammatory pathways (1). At week 12, participants receiving SiPore21 had a lower mean body weight and body fat mass than placebo recipients, with unadjusted between-group differences of -3.90 kg and -2.50 kg, respectively. These observations are compatible with a potential relationship between body composition and glycemic regulation. However, baseline-to-follow-up changes in these secondary outcomes were not fully available for comparative evaluation, and the study did not perform mediation analyses to determine whether changes in adiposity explained any proportion of the glycemic response. Therefore, the contribution of weight-related mechanisms remains uncertain. Similarly, although lower triglyceride and low-density lipoprotein cholesterol concentrations were observed at week 12, these differences should be interpreted as exploratory secondary findings rather than evidence of established cardiovascular risk reduction.

The lower two-hour glucose concentrations observed in the SiPore21 group represent another potentially relevant finding. Post-challenge glucose measurements provide information about glucose handling that may not be fully reflected by fasting glucose concentrations alone. In the present study, the unadjusted between-group difference in two-hour glucose at week 12 was -19.30 mg/dL, suggesting a favorable difference in the measured glycemic response. This observation is compatible with the proposed gastrointestinal action of SiPore21, but it cannot independently establish delayed carbohydrate absorption or digestive enzyme inhibition. In particular, the physiological processes governing glucose concentrations following an oral glucose load are influenced by insulin secretion, insulin sensitivity, hepatic glucose metabolism, and gastrointestinal factors. Because these individual mechanisms were not directly assessed, further investigation would be required to determine which pathways account for the observed between-group difference.

The findings may also be considered within the broader development of nanomedicine for metabolic disorders. Kamran discussed emerging nanomedicine applications for metabolic diseases, illustrating the range of approaches being investigated to improve therapeutic delivery and metabolic management (6). Although these developments provide a scientific basis for further exploration, the successful application of nanotechnology in one therapeutic context does not necessarily establish effectiveness or safety in another. The potential clinical value of a gut-directed silica formulation depends on demonstrating reproducible metabolic benefits, acceptable tolerability, appropriate product quality, and a favorable long-term benefit-risk profile. Accordingly, the present trial should be viewed as an assessment of short-term glycemic and metabolic responses rather than definitive evidence supporting routine clinical implementation.

With respect to tolerability, the reported adverse-event profile was broadly similar between the intervention and placebo groups during the 12-week observation period. Mild gastrointestinal adverse events occurred in four

participants receiving SiPore21 and three receiving placebo, and no severe adverse events were reported. These findings provide limited reassurance regarding short-term tolerability under the study conditions. Nevertheless, the relatively small sample and short follow-up period restrict the ability to detect uncommon adverse reactions, delayed gastrointestinal complications, or potential effects on nutrient absorption. The proposed gastrointestinal localization of SiPore21 should not be interpreted as proof of absent systemic exposure or toxicity because such outcomes were not directly evaluated. Future safety assessments should therefore include longer follow-up and appropriate evaluation of gastrointestinal function and nutritional consequences (9,10).

Several methodological features strengthen the interpretation of the study. The randomized, placebo-controlled design was intended to reduce systematic differences between treatment groups, while sensory matching of the active and placebo preparations supported participant blinding. The use of both HbA1c and fasting plasma glucose provided complementary measures of glycemic regulation, and the inclusion of anthropometric, lipid, and two-hour glucose measurements allowed a broader description of metabolic outcomes. The reported retention rate of 92.5% and regular adherence assessments were additional favorable features. Nevertheless, these strengths depend on adequate implementation of the reported procedures, and the original allocation, outcome-assessment, and statistical records remain important for confirming the reliability of the findings (11,12).

Several limitations should be considered when interpreting the results. First, the 12-week intervention was insufficient to establish whether SiPore21 delays progression from prediabetes to T2DM, as incident diabetes and long-term disease trajectories were not assessed. Second, the relatively small sample size and recruitment from a single urban setting in Sindh limit the precision of some findings and their generalizability to populations with different demographic, dietary, and metabolic characteristics. Third, although 80 participants were randomized, the reported primary analysis included only 74 participants with complete follow-up data. Exclusion of participants with missing outcome measurements may introduce attrition-related bias, particularly if missingness is associated with tolerability or treatment response. Fourth, the available treatment estimates were not adjusted for baseline covariates, and the analysis of multiple secondary outcomes increases the possibility of chance findings. Fifth, detailed information concerning concurrent dietary intake, physical activity, and changes in other metabolic risk factors was not reported, limiting assessment of alternative explanations for the observed outcomes. Finally, the study did not directly evaluate digestive enzyme inhibition, intestinal absorption, insulin sensitivity, gut microbiome changes, or systemic exposure to silica, preventing confirmation of the proposed biological mechanism (13,15).

The clinical implications of these findings should therefore be considered preliminary. The observed reductions in HbA1c and fasting plasma glucose suggest that SiPore21 warrants further investigation as a potential adjunctive intervention for adults with prediabetes and obesity. However, the available evidence does not justify replacing established lifestyle-based or pharmacological approaches, nor does it establish a reduction in incident diabetes or cardiovascular events. Larger randomized trials with complete intention-to-treat analyses, prespecified primary estimands, standardized monitoring of dietary and physical activity factors, and longer observation periods would be valuable for determining the reproducibility and durability of the findings. Incorporating direct mechanistic measurements and comprehensive safety assessments would also help clarify the biological effects and clinical suitability of orally administered mesoporous silica formulations. Overall, the present findings suggest a potentially useful direction for metabolic intervention research while underscoring the need for more rigorous evidence before conclusions regarding long-term effectiveness and diabetes prevention can be established (16).

CONCLUSION

In this 12-week, double-blind, placebo-controlled randomized trial, oral SiPore21 administration was associated with greater reductions in HbA1c and fasting plasma glucose than placebo among adults with prediabetes and obesity who completed follow-up. Favorable differences in two-hour glucose, body weight, body fat mass, and selected lipid parameters were also observed, with no severe adverse events reported during the intervention period. These findings suggest that oral mesoporous silica formulations may have potential for short-term improvement of glycemic and metabolic parameters. However, the small sample size, complete-case analysis, and limited follow-up prevent conclusions regarding sustained clinical effectiveness, long-term safety, or delayed progression to type 2 diabetes.

REFERENCES

1. Roy R, Chakraborty A, Jana K, Sarkar B, Biswas P, Madhu NR. The broader aspects of treating diabetes with the application of nanobiotechnology. In *Advances in Diabetes Research and Management* 2023 Mar 10 (pp. 137–162). Singapore: Springer Nature Singapore.
2. Castellano JM, Ramos-Romero S, Perona JS. Oleanolic acid: extraction, characterization and biological activity. *Nutrients*. 2022 Jan 31;14(3):623.
3. Tan H, Yue T, Chen Z, Wu W, Xu S, Weng J. Targeting FGF21 in cardiovascular and metabolic diseases: from mechanism to medicine. *International Journal of Biological Sciences*. 2023 Jan 1;19(1):66.
4. Abbasi M, Heath B, McGinness L. Advances in metformin-delivery systems for diabetes and obesity management. *Diabetes, Obesity and Metabolism*. 2024 Sep;26(9):3513–29.
5. Kamran SH. Nanomedicine in the Treatment of Metabolic Diseases. In *Nanomedicine in Treatment of Diseases* 2024 Jan 28 (pp. 213–255). Singapore: Springer Nature Singapore.
6. Stoleru OA, Burlec AF, Mircea C, Felea MG, Macovei I, Hăncianu M, Corciovă A. Multiple nanotechnological approaches using natural compounds for diabetes management. *Journal of Diabetes & Metabolic Disorders*. 2024 Jun;23(1):267–87.
7. Sarkar S, Ekbal Kabir M, Kalita J, Manna P. Mesoporous silica nanoparticles: drug delivery vehicles for antidiabetic molecules. *ChemBioChem*. 2023 Apr 3;24(7):e202200672.
8. Yang X, Lin R, Feng C, Kang Q, Yu P, Deng Y, Jin Y. Research progress on peptide drugs for type 2 diabetes and the possibility of oral administration. *Pharmaceutics*. 2024 Oct 23;16(11):1353.
9. Tuccinardi D, Masi D, Watanabe M, Zanghi Buffi V, De Domenico F, Berti S, Cipriani V, Manco M, Manfrini S, Pagotto U. Precision obesity medicine: A phenotype-guided framework for pharmacologic therapy across the lifespan. *Journal of Endocrinological Investigation*. 2025 Dec;48(12):2761–98.
10. Ayub H, Islam M, Saeed M, Ahmad H, Al-Asmari F, Ramadan MF, Alissa M, Arif MA, Rana MU, Subtain M, Rahim MA. On the health effects of curcumin and its derivatives. *Food Science & Nutrition*. 2024 Nov;12(11):8623–50.
11. Ruze R, Liu T, Zou X, Song J, Chen Y, Xu R, Yin X, Xu Q. Obesity and type 2 diabetes mellitus: connections in epidemiology, pathogenesis, and treatments. *Frontiers in endocrinology*. 2023 Apr 21;14:1161521.
12. Islam MS, Sharif A, Kwan N, Tam KC. Bile acid sequestrants for hypercholesterolemia treatment using sustainable biopolymers: Recent advances and future perspectives. *Molecular Pharmaceutics*. 2022 Mar 25;19(5):1248–72.
13. Zahkhouk SA, Eid FA, Abdelhafez HM, El-Wahsh AM. Effect of Aphanizomenon flos-aquae (AFA) or Orlistat on hyperlipidemic adult male Albino rats. *Journal of Medical and Life Science*. 2019 Dec 1;1(4):83–103.
14. Guan HP, Xiong Y. Learn from failures and stay hopeful to GPR40, a GPCR target with robust efficacy, for therapy of metabolic disorders. *Frontiers in pharmacology*. 2022 Oct 25;13:1043828.
15. Subramaniyan V, Hanim YU. Role of pancreatic lipase inhibition in obesity treatment: mechanisms and challenges towards current insights and future directions. *International Journal of Obesity* (2005). 2025 Feb 27;49(3):492.
16. Guyton JR. Lipoproteins in Diabetes: Risk and Opportunity. In *Type 2 Diabetes Mellitus: An Evidence-Based Approach to Practical Management* 2008 (pp. 265–288). Totowa, NJ: Humana Press.