CLINICAL STUDY REPORT

Protocol Number: MHC/CT/25-26/007

(Version 2.00; dated, 31st July 2025)

A randomized, double-blind, parallel-arm clinical trial to assess the efficacy and safety of a Health supplement (Antox-D liquid) in participants with type 2 diabetes mellitus.

Nutrifeel Health Products Pvt. Ltd.

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Sponsor's Signatory **Nutrifeel Health Products Pvt. Ltd.**
Mr. Sadik Gous Shaikh Director

INVESTIGATOR DECLARATION

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We hereby certify the authenticity of the Clinical Study Report and declare that the results are an accurate interpretation of the data, to the best of our knowledge. We also hereby assure that this study was conducted in compliance with the protocol and as per applicable Good Clinical Practices and Ethical Guidelines laid down.

Site Address	Name of Investigator	Investigator role	Signature & Date
Omkar Multispeciality Hospital, Survey No.94, Plot No 81, opposite to Yashada Windosong, Ravet, Pune, Pimpri-Chinchwad, Maharashtra, 412101	Dr. Anuja Mukesh Phalak	Principal Investigator	

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Site Address	Name of Investigator	Investigator role	Signature & Date
Care Multispeciality Hospital, Kolte arcade, Nagar Rd, Wagholi, Pune, Maharashtra 412207	Dr. Dhyaneshwar Manwatkar	Principal Investigator	

3. STUDY SYNOPSIS

Table 1: Study synopsis

Study Title	A randomised, double-blind, parallel-arm clinical trial to assess the efficacy and safety of a Health supplement (Antox-D liquid) in participants with type 2 diabetes mellitus.
Type of Trial	Interventional
Study Design	A randomised, double-blind, parallel-arm, interventional, prospective, clinical trial.
Clinical Phase	Phase II
Treatment Arms with dosage	**Group A:** Health supplement + Oral hypoglycemic agents (OHA). [Take 10 ml twice daily, one hour before lunch and dinner, with water]. **Group B**: Placebo intervention + OHA. [Take 10 ml twice daily, one hour before lunch and dinner, with water].
Primary Objective	The primary objectives of the study were to assess the impact of a health supplement on blood glucose and insulin resistance in participants with type 2 diabetes mellitus compared to a placebo group.
Secondary Objective	The secondary objectives of the study were to determine the effect of a health supplement on lipid profile, metabolism, anthropometric parameters, inflammation, fatigue, and change in dose of oral hypoglycemic agents as compared to a placebo group.
Primary Endpoints	The primary endpoints of the study were to evaluate the changes in the following parameters – 1. Assessment of changes in ▪ HbA1c levels were done at screening and day 90. ▪ Fasting and post-meal plasma glucose were done at baseline, day 30, day 60, and day 90. 2. Assessment of changes in insulin resistance (HOMA-IR) were assessed at the baseline and day 90.
Secondary Endpoints	The secondary endpoints of the study were to evaluate changes in the following domain parameters – 1. Assessment of change in lipid profile was done at baseline and day 90. 2. Assessment of changes in metabolic syndrome severity Z score (MetS Z score) was done at baseline and day 90. 3. Assessment of change in anthropometric parameters was performed at screening, day 30, day 60, and day 90. 4. Assessment of changes in serum C-reactive protein (CRP) levels was assessed at the baseline and day 90.

	5. Assessment of change in fatigue severity scale score (FSS) was done at baseline, day 30, day 60, and day 90. 6. Assessment of change in diabetes related quality of life by DQOL was done at the baseline and day 90.
Safety Endpoints	The safety of the intervention was assessed by evaluating: 1. Change in major organ function on the basis of CBC, LFT, and RFT at the screening and day 90. 2. Changes in vital parameters at screening, baseline, day 30, day 60, and day 90. 3. Occurrence of adverse events assessed at day 30, day 60, & day 90. 4. Compliance and tolerability assessed at day 30, day 60, and day 90.
Sample Size	A total of 102 participants completed the study.
Inclusion criteria	Participants meeting all the following criteria were eligible for the study- 1. Male and female participants aged between 30 and 65 years (both inclusive); 2. Participants receiving oral hypoglycemic agents, biguanides, and sulfonylureas (Only combination); 3. Glycated hemoglobin (HbA1c) >7% and <9% (both inclusive); 4. Participants who were willing to comply with the study procedure and sign the written informed consent; 5. Participants with a BMI of less than 30 kg/m^2;
Exclusion criteria	Participants meeting any of the following criteria were not eligible for the study- 1. Participant with Type 1 diabetes mellitus; 2. Participant taking antidiabetic drugs except for those specified in the inclusion criteria, including Insulin treatment; 3. Participants with concurrent serious hepatic dysfunction (defined as AST and/or ALT >3 times the upper normal limit) or renal dysfunction (defined as S. creatinine >1.4 mg/dl), uncontrolled pulmonary dysfunction (asthmatic and COPD patients), or other concurrent severe disease; 4. Participants suffering from major systemic illness necessitating long-term drug treatment including but not limited to hematologic conditions (e.g., hemolytic anemias, sickle cell anemia), acute myocardial infarction, unstable angina, uncontrolled hypertension, congestive heart failure (class III or class IV NYHA), or cerebrovascular accident, psychiatric or neurological disorder, autoimmune condition, received chronic (>14 days) therapy with systemic glucocorticoids (excluding topical, intraocular, intranasal, intra-articular, or inhaled preparations) within six months prior to enrollment; 5. Participants who are smokers/alcoholics and/or known drug abusers; 6. Participants with evidence or history of malignancy;

	7. Participant enrolled in any other clinical trial requiring drug therapy; 8. Pregnant or lactating women or women of fertile age not using effective contraception; 9. Any condition that could, in the opinion of the investigator, preclude the participant's ability to complete the study or that may confound study outcomes.
Study Duration	Each participant participated in this study for 90 days.
Visit Schedule	The treatment period was 90 days. The study schedule was as follows; 1. Screening visit (-7 to day 0) 2. Baseline Visit 1: Day 1 3. Follow-up visit 2: Day 30 ± 5 4. Follow-up visit 3: Day 60 ± 5 5. Follow-up visit 4: Day 90 ± 5 (End of study)
Methodology	This was a parallel arm, double blind, randomized controlled clinical study designed to evaluate the efficacy of a health supplement (Antox-D liquid) in participants with type 2 diabetes mellitus. A total of 104 participants were randomly assigned to either one of the two arms to receive either a health supplement + Oral hypoglycemic agents (group A), or a Placebo + Oral hypoglycemic agents (group B), in a 1:1 ratio and 102 participants completed the study. With the dose of 10 ml twice daily, one hour before lunch and dinner, with water. The total study duration was 90 days. The efficacy of the interventional products was compared within & between groups. Concomitant diseases/medication assessment was performed on screening. Various efficacy parameters, such as change in fasting and post meal plasma glucose, anthropometric parameters, and fatigue severity scale score were evaluated at baseline, day 30, day 60, and day 90. HbA1c was assessed at Screening and Day 90, Change in fasting insulin, HOMA-IR, serum CRP levels, change in lipid profile, MetS Z-score, diabetes related quality of life was evaluated at baseline and day 90. Safety assessments of major organ function were evaluated on the basis of change in CBC, LFT, and RFT at screening and end of the study. Safety of the intervention was assessed on the basis of change in vital signs at each visit, and occurrence of ADR's at day 30, day 60, & day 90 day. Compliance and tolerability of the interventional product was assessed at day 30, day 60 and day 90 of the study.
Extension Phase	**Extension Phase: Evaluation of Antox-D in Responders** Responder: A responder is defined as a participant who demonstrates a significant improvement in HbA1c levels at Day 90 and, based on the investigator's discretion, is eligible to transition to a reduced dose of OHAs along with the health supplement

	for the follow-up phase (Day 91 to Day 180). Following the initial 90-day randomized treatment period with either Antox-D or placebo liquid administered alongside standard OHAs, participants from the Antox-D group who demonstrate adequate glycemic control were considered for an open-label extension phase. Based on the investigator's discretion, and after obtaining written informed consent, eligible and willing participants may participate in the extension phase with a reduced dose of OHAs. This extension is intended to evaluate the sustained glycemic effect of Antox-D with concurrent reduced dose OHAs in responders. Participants enrolled in the extension phase continued treatment with Antox-D along with the reduced dose of OHAs, and glycemic control was reassessed at Day 180 using HbA1c. The extension phase described in the protocol was not included in the present CSR analysis.
End of the Study	The end of the study was defined if a participant met the following criteria: 1. Completer of the study 2. Progression of disease, non-compliant participants, and as per the discretion of the investigator 3. Incidence of SAE (Termination from the study) 4. Participants withdrew consent. 5. Depended upon the Investigator's discretion
Statistics	All analyses were done using GraphPad Prism version 10.5.0. software. All data was summarized with descriptive statistics (number of participants, mean, standard deviation, minimum, median, and maximum) for continuous endpoints and frequency and percentage for categorical endpoints. Primary and secondary efficacy endpoints were analyzed using the PP (per protocol) population and Safety variables as per mITT (modified intention-to-treat). The modified intention-to-treat (mITT) population included participants who received at least one dose of investigational product and had at least one post-baseline safety assessment.
Participants Population for Analyses	All randomized participants were included in all participant populations and considered for statistical analyses. All data listings were based on this population. Where listings were separated by treatment arm, safety data listings were grouped by actual study treatment received and all other listings were grouped by treatment randomized. Given that, only randomized participants were entered into the study database. All efficacy analyses were based on the treatment arm to which the participants were randomized. Safety analysis was done for all randomized participants who had received at least one dose of IP.

	If any participant was randomized but had not received treatment, listings produced for all participants by treatment received included participants under the category "Treatment not given".
Efficacy Analyses	The primary and secondary endpoints were analyzed using Student's paired or unpaired t-test, Wilcoxon signed-rank test, as applicable. A significance level of $p<0.05$ was considered statistically significant.
Safety Analysis	AEs and SAEs were summarised by counting both the number of separate events and the number of participants experiencing events occurring during the study period. Tolerability score and vital signs were presented as mean ± SD, while compliance was expressed as a percentage.

4. TABLE OF CONTENTS

5. LIST OF ABBREVIATIONS

Table 2: List of abbreviations

Abbreviation	Full Form
ICH	International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use
GCP	Good Clinical Practice
WMA	World Medical Association
IRB	Institutional Review Board
CRO	Clinical Research Organization
OHA	Oral Hypoglycemic Agents
HOMA-IR	Homeostasis Model Assessment of Insulin Resistance
CRP	C-Reactive Protein
HbA1c	Hemoglobin A1c
BMI	Body Mass Index
AST	Aspartate Aminotransferase
ALT	Alanine Aminotransferase
COPD	Chronic Obstructive Pulmonary Disease
NYHA	New York Heart Association
CBC	Complete Blood Count
LFT	Liver Function Test
RFT	Renal Function Test
ADR	Adverse Drug Reaction
AE	Adverse Event
SAE	Serious Adverse Event
PP	Per Protocol
mITT	Modified Intention-To-Treat
SAP	Statistical Analysis Plan
IP	Investigational Product
T2DM	Type 2 Diabetes Mellitus
HDPE	High-Density Polyethylene
PI3K	Phosphoinositide 3-Kinase
Nrf2/NFκB	Nuclear Factor Erythroid 2–Related Factor 2 / Nuclear Factor Kappa B
GLUT4	Glucose Transporter Type 4
GLP-1	Glucagon-Like Peptide-1
AMPK	AMP-Activated Protein Kinase
PARP/PARG	Poly (ADP-ribose) Polymerase / Poly (ADP-ribose) Glycohydrolase
EOF	*Emblica officinalis*

Abbreviation	Full Form
SOD	Superoxide Dismutase
PPAR-γ	Peroxisome Proliferator-Activated Receptor Gamma
GAPDH	Glyceraldehyde-3-Phosphate Dehydrogenase
WS	*Withania Somnifera*
FPEt	Fenugreek Seed Polyphenolic Extract
SIRT1	Sirtuin 1
ROS	Reactive Oxygen Species
LDL	Low-Density Lipoprotein
HDL	High-Density Lipoprotein
FSSAI	Food Safety and Standards Authority of India
FSS	Fatigue Severity Scale Score
DQOL	Diabetes Quality of Life
CRF	Case Report Form
SE	Serious Event
ICF	Informed Consent Form
ADL	Activities of Daily Living
MedDRA	Medical Dictionary for Regulatory Activities
EC	Ethics Committee
CI	Confidence Interval
LAR	Legally Acceptable Representative
PIS	Participant Information Sheet
QA	Quality Assurance
QC	Quality Control
IPIB	Investigational Product Information Brochure
SOP	Standard Operating Procedure
CONSORT	Consolidated Standards of Reporting Trials
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
IPR	Intellectual Property Rights

6. STUDY MANAGEMENT TEAM AND CONTACT DETAILS

Sponsor	
Mr. Sadik Gous Shaikh Director Sadikshaikh7575@gmail.com	**Nutrifeel Health Products Pvt. Ltd.** 456-57 Vasant Park Sugar Mill Road, Kasaba Bavada, Kolhapur, Maharashtra-416006.
CRO (Medical Writing, Monitoring, Project Management, and Biostatistics)	
Dr. Gayatri Ganu Managing Director	**Mprex Healthcare Pvt. Ltd.** Office Number 813-816, Sai Millenium, Mumbai Pune Bypass Road Flyover, Punawale, Pune, Maharashtra – 411033
Dr. Avanti Todkar Medical Writer	
Dr. Vaishnavi Patil Head Clinical Operations	
Mr. Narendra Rasal Project Manager	
Ms. Swapnali Gavali Clinical Research Coordinator	
Ms. Anupama Nair QA/QC Executive	
Biostatistical Facility	

7. ETHICS

7.1 Ethics Committee

The study protocol and related documents were submitted to the ethics committee (EC) for review and approval. Participants were not recruited into the study until the EC approved the protocol. There were no changes made in the protocol after EC approval. Copies of the Ethics Committee approval letter have been included in the Appendix.

The study was conducted at two sites-: Omkar Multispeciality Hospital and Care Multispeciality Hospital. The study was initiated only after written approval was obtained from Institutional Ethics Commitee Sangvi Multispeciality Hospital for Omkar Multispeciality Hospital and Care.Multispeciality Hospital Institutional Ethics Committee for Care Multispeciality Hospital. The study utilized IEC oversight for participating study sites within the same regional operational framework. Additionally, the study was registered on the Clinical Trial Registry of India (CTRI) website. The study was conducted as per approved protocol and Good Clinical Practices guidelines.

7.2 Ethical Conduct of the Study

The study was conducted, recorded, and reported strictly in accordance with approved protocol, applicable ethical principles, institutional ethics committee requirements and GCP guidelines. During the conduct of the clinical trial, the rights, safety, and well-being of the study participants were given prime importance. The study drug was prepared with compliance to Good Manufacturing Practices (GMP) as applicable in India.

7.3 Informed Consent

On the screening visit, voluntary written informed consent from participants for their participation in the study was obtained. Informed Consent Form (ICF) was printed in the language best understood by participants. During the informed consent process, participants were informed about the objectives of the study, the design of the study, and possible risks and benefits of participation in the study. They were given enough time to ask the questions to fully understand the study. If the participant was illiterate, an impartial witness read the ICF which was printed in the language best understood by the participant. After hearing from the ICF, if the participant agreed to participate in the study, his/her thumb impression was taken on the ICF and also the signature (with date) of the impartial witness was obtained on the same ICF. One copy of the ICF was handed over to the participant. The identity of the study participants was not to be provided to any party except study-related personnel, ethics committee, etc. Sufficient measures were taken not to disclose the identity of the participant. The data generated and recorded from the study was to be kept confidential and participant identity was in a coded form. The results of the study might be published by the sponsor with the investigator's consent in

peer-reviewed scientific journals without revealing the identity of any participant.

7.4 CTRI Registration

After getting approval from the ethics committee, the study was registered on the CTRI website with registration number CTRI/2025/10/095664 [Registered on: 06/10/2025] - Trial Registered Prospectively. Participants were enrolled in the study only after registration of the study on CTRI website.

8 BACKGROUND INFORMATION

8.1 Background

Diabetes mellitus is a condition where, human body becomes resistant to its insulin, which reduces glucose intake inside the cells, despite normal insulin secretion. This leads to retention of insulin in the blood, which causes hyperglycemia and other diabetes symptoms [1]. Diabetes is a larger health concern in India, where, according to 2019 estimates, there were 77 million diabetes cases in India, with projections indicating this number will exceed 134 million by 2045. Roughly 57% of these people do not yet have a diagnosis [2]. Several studies have indicated that a sedentary lifestyle and unhealthy diet are important risk factors for type 2 diabetes, and physical activity and dietary modifications may reduce the diabetes risk and reduce disease progression [3].

While pharmacologic agents such as metformin, sulfonylureas, and insulin remain central to Type 2 Diabetes Mellitus (T2DM) management, they are often limited by gastrointestinal side effects, risk of hypoglycemia, weight gain, and long-term compliance issues [4]. Consequently, there is growing interest in complementary and alternative therapies, particularly plant-based nutraceuticals, that offer glycemic control with a favourable safety and tolerability profile [5].

Antox-D is a multi-herbal liquid formulation comprising *Momordica charantia* (Karela), *Syzygium cuminii* (Jamun), *Trigonella foenum-graecum* (Methi), *Withania somnifera* (Ashwagandha), *Aegle marmelos* (Bael), *Azadirachta indica* (Neem), and *Triphala*, among others. Each of these ingredients has demonstrated individual anti-diabetic potential in preclinical and clinical studies [6-8].

Preliminary observational data from users in Maharashtra suggest that Antox-D may help blood glucose regulation in T2DM patients. However, these findings require validation through a rigorously designed clinical study to establish efficacy, safety, and dosage.

Therefore, the present investigation aims to evaluate the clinical efficacy and safety of Antox-D in T2DM individuals and to explore its effects on metabolic parameters and patient-reported outcomes. The study also intends to investigate potential mechanisms of action through in vitro pharmacological assays.

8.2 Rationale of the study

Type 2 Diabetes Mellitus is a chronic metabolic disorder characterized by insulin resistance, impaired insulin secretion, and elevated blood glucose levels. It presents a significant global health burden due to its associated complications, such as cardiovascular disease, nephropathy, neuropathy, and retinopathy. While

pharmacologic and lifestyle interventions are standard, limitations related to side effects, cost, and adherence have driven interest in safe, adjunctive nutraceutical options.

Antox-D is a liquid nutraceutical formulation comprising FSSAI-approved botanical extracts including *Momordica charantia* (Karela), *Syzygium cuminii* (Jamun), *Trigonella foenum-graecum* (Methi), *Withania somnifera* (Ashwagandha), *Aegle marmelos* (Bael), and others. These components are supported by traditional use and emerging evidence for their antidiabetic, lipid-lowering, antioxidant, and anti-inflammatory properties. Potential benefits of Antox-D include reductions in fasting and postprandial glucose, HbA1c, reduced reliance on allopathic medication, and improved quality of life. However, these observations require validation through a well-designed clinical trial.

Pharmacologically, Antox-D's ingredients exert complementary effects:

- Karela enhances insulin secretion and mimics insulin action.
- Jamun and Methi improve glycemic and lipid profiles.
- Bael offers nephroprotective and anti-glycation effects.
- Ashwagandha, Neem, and Triphala contribute neuroprotective, immunomodulatory, and detoxifying actions.

This study aims to evaluate the clinical efficacy and safety of Antox-D in T2DM individuals, assessing its impact on glycemic control, metabolic markers, and quality of life. Mechanistic insights from parallel in vitro studies will help rationalize observed outcomes and define its therapeutic potential.

Rationale for Dosing Interval – Investigational Product & OHA

Evidence suggests that certain phytoconstituent may modulate the pharmacokinetics and pharmacodynamics of oral hypoglycemic agents. Specifically, *Gymnema sylvestre* has been reported to reduce the bioavailability of metformin, whereas *Momordica charantia* (Karela) may potentiate its antihyperglycemic activity. Additionally, *Azadirachta indica* (Neem) and *Zingiber officinale* (Ginger) may antagonize the glucose-lowering effects of glibenclamide, while *Trigonella foenum-graecum* (Methi) and *Syzygium cumini* (Jamun) have been shown to prolong the action of gliclazide.

In light of these potential herb-drug interactions, the investigational product will be administered at least one hour prior to food intake to minimize the risk of altered glycemic control. As oral hypoglycemic agents (e.g., biguanides and sulfonylureas) are typically administered with or after meals, this dosing strategy ensures temporal separation, thereby reducing the likelihood of interaction-related hypoglycemic or hyperglycemic events [41,42].

9 STUDY OBJECTIVES AND PURPOSE

9.1 Primary Objective

The primary objective of this study was to assess the impact of a health supplement on blood glucose and insulin resistance in participants with type 2 diabetes mellitus compared to a placebo group.

9.2 Secondary Objective

Secondary objectives were to determine the effect of a health supplement on lipid profile, metabolism, anthropometric parameters, inflammation, fatigue, and change in dose of oral hypoglycemic agents as compared to a placebo group.

10 STUDY ENDPOINTS

10.1 Primary Endpoint

The primary endpoints of the study were

1. Assessment of changes in-
   - HbA1c levels at screening, and day 90.
   - Fasting and post-meal plasma glucose at baseline, day 30, day 60, and day 90.
2. Assessment of changes in insulin resistance (HOMA-IR) at baseline and day 90.

10.2 Secondary Endpoints

The secondary endpoints of the study were -

1. Assessment of change in lipid profile at baseline and day 90.
2. Assessment of changes in metabolic syndrome severity Z score (MetS Z score) at baseline and day 90.
3. Assessment of change in anthropometric parameters at screening, day 30, day 60, and day 90.
4. Assessment of changes in serum C-reactive protein (CRP) levels at the baseline and day 90.
5. Assessment of change in fatigue severity scale score (FSS) at baseline, day 30, day 60, and day 90.
6. Assessment of change in diabetes related quality of life by DQOL at the baseline and day 90.

10.3 Safety Outcomes

The safety endpoints of the study were -

1 Assessment of change in major organ function on the basis of CBC, LFT, and RFT at the screening and day 90.

2 Assessment of changes in vital parameters at screening, baseline, day 30, day 60, and day 90.

3 Occurrence of adverse events assessed on day 30, day 60, & day 90.

4 Compliance and tolerability assessed at day 30, day 60, and day 90.

11 INVESTIGATIONAL PLAN

11.1 Study design

A randomised, double-blind, parallel-arm, interventional, prospective, clinical trial.

11.2 Study groups

The study consisted of two treatment groups.
Group A (Test): Health supplement + Oral hypoglycemic agents (OHA).
Group B (Placebo): Placebo intervention + OHA.

11.3 Allocation of participants in study groups

A total of 104 participants were randomized and 102 participants completed in this study. Details are provided below:

Group A (Test): randomized n= 52 and completed n= 50.
Group B: Placebo: randomized n= 52 and completed n= 52.

11.4 Recruitment Plan

A total of 104 participants were screened and randomized. During the study, two participants discontinued, and 102 participants completed the study. Data was collected between October 2025 to March 2026.

The details are provided in CONSORT **Figure 1.** Participants providing written informed consent and who were ready to provide regular follow-ups till the completion of the study and meeting the inclusion and exclusion criteria were recruited in the study. Precautions were taken not to recruit the participants belonging to possible vulnerable groups like pregnant or lactating women.

11.5 Inclusion Criteria

Participants who met all of the following criteria were considered eligible for inclusion in the study: Participants eligible for the study were male and female participants aged between 30 and 65 years (both inclusive) and BMI of less than 30 kg/m^2. Participants receiving oral hypoglycemic agents, biguanides, and sulfonylureas (Only combination) were included. Eligible participants were required to have Glycated hemoglobin (HbA1c) >7% and <9%. In addition, participants were included only if they demonstrated clear willingness to participate, indicating their ability to comply with study protocol requirement and provide written informed consent.

11.6 Exclusion Criteria

Participants meeting any of the following criteria were excluded from the study: Participants with type 1 diabetes mellitus were excluded from the study. Participants were also excluded from the study if they were taking antidiabetic drugs except for those specified in the inclusion criteria, including Insulin treatment. Participants with concurrent serious hepatic dysfunction (defined as AST and/or ALT >3 times the upper normal limit) or renal dysfunction (defined as S. creatinine >1.4 mg/dl), uncontrolled pulmonary dysfunction (asthmatic and COPD patients), or other concurrent severe disease were also excluded. Participants suffering from major systemic illness necessitating long-term drug treatment including but not limited to hematologic conditions (e.g., hemolytic anemias, sickle cell anemia), acute myocardial infarction, unstable angina, uncontrolled hypertension, congestive heart failure (class III or class IV NYHA), or cerebrovascular accident, psychiatric or neurological disorder, autoimmune condition, received chronic (>14 days) therapy with systemic glucocorticoids (excluding topical, intraocular, intranasal, intra-articular, or inhaled preparations) within six months prior to enrollment were not included. Participants who were past or active smokers were not eligible. Participants were further excluded if they had history or evidence of malignancy. Participants enrolled in any other clinical trial requiring drug therapy were excluded. Pregnant or lactating women or women of fertile age not using effective contraception were excluded. Additionally, any condition that could, in the opinion of the investigator, preclude the participant's ability to complete the study or that may confound study outcomes.

11.7 Study Methodology

This study was designed as a parallel arm, double blind, randomized controlled clinical study conducted to evaluate the efficacy of a health supplement (Antox-D liquid) in participants with type 2 diabetes mellitus.

Participants in Group A received health supplement + Oral hypoglycemic agents. Participants in Group B received Placebo + Oral hypoglycemic agents. Concomitant diseases/medications were recorded at the screening.

Efficacy parameters, such as change in fasting and post meal plasma glucose, anthropometric parameters, and fatigue severity scale score were evaluated at baseline, day 30, day 60, and day 90. HbA1c was assessed at Screening and Day 90, Change in fasting insulin, HOMA-IR, serum CRP levels, change in lipid profile, MetS Z-score, diabetes related quality of life was evaluated at baseline and day 90. Safety assessments of major organ function were evaluated on the basis of change in CBC, LFT, and RFT at screening and end of the study.

Safety of the intervention was assessed on the basis of change in vital signs at each visit, and occurrence of ADR's at day 30, day 60, & day 90 day. Compliance and tolerability of the interventional product was assessed at day 30, day 60 and day 90 of the study.

12 SELECTION AND WITHDRAWAL PARTICIPANTS

12.1 Withdrawal Criteria

Two participants discontinued the study due to loss to follow-up

12.2. Participant Replacement Policy

Participants who were recruited for the study were not replaced.

12.3. Follow-up of Withdrawn Participants

No participants were withdrawn from the study due to adverse events; therefore, the follow-up of withdrawn participants was not applicable.

13 TREATMENT

13.1 Investigational Product Description

Composition, along with the content details, is expressed in the table below:

Table 3. Active ingredients of Antox-D liquid

Each 10 ml contains:

S.N.	Name of the Ingredient	Scientific Name	Each 10 ml contains (Composition)
1	Karela	*Momordica charantia* fruit extract	250 mg
2	Jamun	*Syzygium cuminii* seed extract	150 mg
3	Ashwagandha	*Withania somnifera* root extract	150 mg
4	Shatawar	*Asparagus racemosus* tuberous roots extract	150 mg
5	Methi	*Trigonella foenum-graceum* seeds	150 mg
6	Amla	*Emblica officinalis* fruit juice	2.5 ml
7	Harad	*Terminalia chebula* fruit pericarp extract	150 mg
8	Bahera	*Terminalia belerica* fruit pericarp extract	150 mg
9	Bael Pather	*Aegle marmelos* leaf extract	150 mg
10	Neem	*Azadirachta indica* leaves extract	50 mg
11	Kutaki	*Picorhiza kurroa* root extract	62.5 mg
12	Sonth	*Zingiber officinale*	25 mg
13	Gudmar	*Gymnema sylvestre* plant extract	250 mg

Inactive Ingredients: Water, Preservatives (sodium benzoate, potassium sorbate, methyl paraben, propyl paraben), stabiliser (xanthan gum), acidity regulator (citric acid).

- **Placebo**

  Ingredients of placebo: Composition of the placebo: Water, Preservatives (sodium benzoate, potassium sorbate, methyl paraben, propyl paraben), acidity regulator (citric acid).

13.2 Pharmacology of the ingredients

A. Karela (*Momordica charantia*) fruit extract:

M. charantia exerts its antidiabetic effects through multiple complementary mechanisms. It stimulates insulin secretion and preserves pancreatic β-cell function, thereby supporting endogenous insulin production. Additionally, it enhances peripheral glucose uptake in skeletal muscle via insulin-mimetic activity and activation of the PI3K signalling pathway. It also inhibits intestinal glucose absorption and suppresses key gluconeogenic enzymes in the liver, contributing to reduced hepatic glucose output.

Furthermore, *M. charantia* modulates lipid metabolism and regulates gene expression involved in glucose homeostasis reinforcing its role in improving glycemic control [6].

B. Jamun (*Syzygium cuminii*) seed extract:

Syzygium cuminii seed extract exhibits potent antidiabetic activity through multiple mechanisms. It enhances insulin secretion and sensitivity, reduces fasting blood glucose levels, and improves glucose tolerance. The extract contains bioactive compounds like jamboline and ellagic acid, which inhibit α-glucosidase and modulate carbohydrate metabolism. Its antioxidant properties also protect pancreatic β-cells from oxidative stress-induced damage [9].

C. Ashwagandha (*Withania somnifera*) root extract

Withania somnifera shows promising antidiabetic potential in T2DM through enhancement of insulin sensitivity and reduction in blood glucose in preclinical studies. Withaferin A regulates oxidative stress and inflammation via Nrf2/NFκB pathways [10].

D. Shatawar (*Asparagus racemosus*) tuberous roots extract

Asparagus racemosus helps manage diabetes by enhancing insulin secretion, improving insulin sensitivity, and reducing oxidative stress. It also inhibits carbohydrate-digesting enzymes and may promote pancreatic β-cell regeneration [11].

E. Methi (*Trigonella foenum-graceum*) seeds

Fenugreek (*Trigonella foenum-graecum*) exerts antidiabetic effects by enhancing GLUT4 translocation and hexokinase activity, boosting insulin secretion, and preserving pancreatic β-cells. It also inhibits carbohydrate-digesting enzymes (α-amylase, maltase), downregulates gluconeogenic enzymes, and modulates pathways involving GLP-1, AMPK, thereby improving glycemic control and insulin sensitivity [12].

F. Amla (*Emblica officinalis*) fruit juice

Emblica officinalis exhibits antidiabetic activity through multiple mechanisms, including enhancement of antioxidant defence, inhibition of carbohydrate-metabolising enzymes, and regulation of glucose homeostasis. It also protects against diabetic complications by modulating PARP/PARG activity, reducing Age formation, and improving mitochondrial function. Additionally, EOF supports β-cell regeneration and inhibits the polyol pathway, contributing to long-term glycemic control [13].

G. Harad (*Terminalia chebula*) fruit pericarp extract

Terminalia chebula exhibits antidiabetic activity primarily due to its rich content of polyphenols such as chebulagic, chebulinic, gallic, and ellagic acids. These compounds exert antihyperglycemic effects by enhancing insulin secretion, improving insulin sensitivity, inhibiting α-glucosidase and aldose reductase, and protecting pancreatic β-cells from oxidative damage. Its antioxidant and anti-inflammatory properties also contribute to the mitigation of diabetic complications [14].

H. Bahera (*Terminalia belerica*) fruit pericarp extract

Terminalia belerica exhibits antidiabetic activity by significantly lowering blood glucose levels in alloxan-induced diabetic rats. It enhances antioxidant defense by increasing superoxide dismutase, catalase, and glutathione peroxidase activity. The extract reduces lipid peroxidation and oxidative stress, supporting pancreatic function. Its dual hypoglycemic and antioxidant actions contribute to its therapeutic potential in diabetes management [15].

I. Bael Pather (*Aegle marmelos*) leaf extract

Bael exhibits potent antidiabetic effects by lowering blood glucose, HbA1c, and improving lipid profiles in diabetic animal models. It enhances antioxidant defenses by increasing SOD, catalase, and glutathione activity. Aegeline and marmelosin, active constituents, modulate insulin secretion and PPAR-γ expression. Bael extracts also reduce oxidative stress and prevent diabetic complications including AGE formation [9].

J. Neem (*Azadirachta indica*) leaves extract

Neem exhibits antidiabetic properties through its hypoglycemic, hypolipidemic, and insulinotropic effects. Bioactive compounds in neem leaves regulate glucose metabolism and enhance pancreatic function. It also exerts antioxidant and hepatoprotective actions, reducing diabetes-related oxidative damage. Neem's traditional and pharmacological relevance supports its potential in herbal diabetes management [16].

K. Kutaki Picorhiza kurroa root extract

Picrorrhiza kurroa alcoholic extract significantly reduced blood glucose levels and improved metabolic parameters in alloxan-induced diabetic rats. It also attenuated oxidative stress, weight loss, and leukopenia associated with diabetes [17].

L. Sonth Zingiber officinale

Medicinal plants, including ginger, exert antidiabetic effects through mechanisms such as enhancing glucose uptake, increasing hepatic glycogen synthesis, inhibiting

carbohydrate-metabolising enzymes, and mimicking insulin activity. Ginger's bioactive compounds, like 6-gingerol and 6-shogaol, promote GLUT4 translocation and reduce oxidative stress, aiding in glucose regulation. Clinical trials consistently show that ginger supplementation reduces blood glucose, HbA1c, and insulin resistance [18].

M. Gudmar Gymnema sylvestre plant extract

Gymnemic acids lower blood glucose by stimulating insulin secretion, delaying glucose absorption, and blocking sugar receptors in the mouth and intestine. They mimic sugar at taste receptors, reducing sweet sensation and sugar uptake. Additionally, gymnemic acids modulate incretin activity, promote islet cell regeneration, and inhibit enzymes like GAPDH in the glycolysis pathway. These multi-targeted actions contribute to their potent antihyperglycemic effects [19].

13.3 Preclinical Pharmacology and Toxicity/Safety Data

In a preclinical study demonstrated the cardiometabolic benefits of momordicine I in isoproterenol-induced hypertrophic rat models. Beyond its cardio protective role, momordicine I modulated metabolic pathways by downregulating PLA2G6 and DGK-ζ, enzymes linked to glycerophospholipid metabolism, thereby reducing lipid accumulation and inflammation. These effects are relevant to antidiabetic therapy, as chronic inflammation and lipid dysregulation are key contributors to insulin resistance and diabetic cardiomyopathy [20].

A 60-day animal study was conducted to assess the antidiabetic potential of ethanolic extracts of *Syzygium cumini* (jamun) fruit and seeds. Male Sprague Dawley rats, both normal and high-sucrose diet-induced hyperglycemic, were administered these extracts to monitor changes in serum glucose and insulin levels. The seed extract produced a greater glucose-lowering effect (14.36%) and insulin enhancement (7.24%) compared to the fruit extract in hyperglycemic rats. These findings underscore the promising role of *S. cumini* extracts in dietary strategies for hyperglycemia management [21].

A study was conducted to establish the oral dose range and regimen of a standardised *Withania somnifera* root extract (WS) for managing diabetes-associated comorbidities. Normal and diabetic male mice received graded oral doses of WS for 10 days. While a single dose (up to 400 mg/kg) showed no significant effect, repeated daily administration resulted in dose- and duration-dependent improvements. WS mitigated stress-induced hyperthermia, prevented body weight loss, and reduced elevated plasma glucose, insulin, and cortisol levels. Additionally, it normalised adrenal and spleen weights in diabetic animals, supporting the adaptogenic and antidiabetic potential of WS [22].

A bioactivity-guided phytochemical investigation of *Asparagus racemosus* roots led to the isolation of six novel furostanol saponins (furoasparoside A–F) and five known compounds. Among them, furoasparoside E exhibited significant antidiabetic activity by enhancing GLUT4 translocation via the AMPK-dependent pathway in L6-GLUT4myc myotubes. In vivo studies in streptozotocin-induced diabetic rats and db/db mice revealed that furoasparoside E markedly reduced postprandial blood glucose levels. Pharmacokinetic profiling indicated its favourable bioavailability, suggesting its potential as a lead molecule for type 2 diabetes management [23].

Kannappan and Anuradha observed insulin-sensitizing actions of fenugreek seed-derived polyphenols and found it comparable to a well-known diabetic drug metformin in a rat model. In experimental rat's fructose-feeding caused increased levels of glucose, insulin, triglycerides and free fatty acid, altered insulin sensitivity indices, enzyme activities and reduced glycogen content. Further, fructose-rich diet leads to higher protein tyrosine phosphatase and lower protein tyrosine kinase activities, suggesting decreased tyrosine phosphorylation status in these rats. Administration of fenugreek seed polyphenolic extract (FPEt) improved insulin sensitivity and tyrosine phosphorylation status in fructose-fed animals compared to metformin-treated rats. This indicates that FPEt improved insulin signaling and sensitivity and thereby promoted the cellular actions of insulin [24].

Aqueous extract of *Terminalia chebula* fruits was evaluated for its antidiabetic effects in a type 2 diabetic rat model induced by a high-fat diet followed by low-dose streptozotocin (35 mg/kg). Treatment with the extract (500 and 1000 mg/kg) for six weeks significantly reduced plasma glucose levels, improved lipid profiles, and lowered liver enzymes (AST and ALT). The extract enhanced insulin sensitivity and decreased HOMA-IR, along with increased antioxidant enzyme levels. Histopathological and immunohistochemical analyses of pancreatic tissue revealed structural protection and upregulated SIRT1 expression, indicating the extract's potential in mitigating hyperglycemia-induced damage and managing type 2 diabetes [25].

The antidiabetic and antioxidant potential of 75% methanolic extract of *Terminalia belerica* fruits was evaluated in alloxan-induced hyperglycemic rats. Continuous oral administration of the extract significantly reduced blood glucose levels, with a 54% reduction observed by day 12. The extract also attenuated oxidative stress, as evidenced by decreased levels of thiobarbituric acid reactive substances, conjugated dienes, and hydroperoxides in blood and liver. Antioxidant defence was enhanced, marked by significant increases in superoxide dismutase, catalase, glutathione peroxidase, and

glutathione reductase activities. These findings suggest that the antidiabetic effects of *T. belerica* may be mediated, at least in part, through its antioxidant mechanisms [26].

Aegle marmelos leaf extract was evaluated for its antidiabetic, anti-inflammatory, and antioxidant activities. Phytochemical analysis revealed alkaloids, phenols, flavonoids, and saponins. The extract showed significant antioxidant activity, inhibited α-amylase (IC50=73.2 µg/mL) and α-glucosidase (IC50=43.9 µg/mL), and reduced egg albumin denaturation (IC50=102.8 µg/mL). It also decreased high glucose-induced ROS generation, inflammatory markers, and cell migration in rat kidney fibroblast cells. These findings highlight the therapeutic potential of *A. marmelos* leaf extract in managing diabetes and related complications [27].

The effects of *Azadirachta indica* aqueous leaf extract were evaluated in high-fat and fructose-induced type-2 diabetic rats. A daily dose of 400 mg/kg for 30 days normalized blood glucose, insulin levels, lipid profile, and insulin signaling molecules, including insulin receptor, IRS-1, Akt, and GLUT4 proteins. Additionally, glucose oxidation and glycogen concentration in the gastrocnemius muscle were improved. These findings suggest that *A. indica* may aid in managing type-2 diabetes by enhancing insulin signaling and glucose utilization [28].

The antidiabetic activity of *Picrorhiza kurroa* aqueous extract was evaluated in streptozotocin-induced diabetic rats. PkE (100 and 200 mg/kg/day) was administered for 14 days. Treatment significantly increased plasma insulin levels and GLUT-4 content in the soleus muscle. Histopathological analysis revealed regeneration of pancreatic β-cells. PkE enhanced insulin-mediated translocation of GLUT-4 to the plasma membrane, promoting glucose uptake by skeletal muscles in diabetic rats [29].

Preclinical evidence supports the antidiabetic potential of ginger. In this study, administration of ginger extract to streptozotocin-induced diabetic rats significantly reduced blood glucose levels, enhanced insulin sensitivity, and improved antioxidant enzyme activity. The extract also decreased lipid peroxidation, indicating a reduction in oxidative stress. These findings highlight ginger's potential in managing hyperglycemia and mitigating diabetes-associated complications [30].

Preclinical studies have demonstrated the significant hypoglycemic potential of *Gymnema sylvestre*. In diabetic rats, daily administration of an alcoholic extract (100 mg/kg) for one month led to a notable reduction in blood glucose levels. By the second week of treatment, the mean blood sugar level in the treated group dropped to 74 mg/dL compared to 106 mg/dL in the control group. These findings suggest that *Gymnema*

sylvestre may effectively support blood glucose regulation in diabetes management [31].

13.4 Clinical Study Data

A clinical study involving 32 volunteers, including 16 type 2 diabetic patients and 16 age- and gender-matched healthy controls, evaluated the effects of *Emblica officinalis* (Amla) fruit powder on blood glucose and lipid profiles. Diabetic patients, aged 30-60 years, were divided into groups receiving glibenclamide (control) or Amla powder (1, 2, or 3 g), while healthy controls received carboxymethyl cellulose or Amla powder. Measurements were taken at baseline, days 8, 15, and 21. Results indicated that Amla has significant antihyperglycemic and lipid-lowering effects, suggesting potential as a dietary supplement for managing diabetes and related conditions [32].

The single-center, randomized, double-blind, placebo-controlled study enrolled 96 Korean patients with type 2 diabetes. Participants were randomized in a 2:1 ratio to receive either bitter melon extract (2380 mg/day) or placebo capsules for 12 weeks. Inclusion criteria included a confirmed diagnosis of type 2 diabetes, stable treatment for 3 months, HbA1c ≤ 7.5%, and age 20-70 years. Exclusion criteria included treatment with α-glucosidase inhibitors, liver or renal dysfunction, and pregnancy. The primary outcome was the change in HbA1c, with secondary outcomes assessing fasting glucose, lipid profiles, and safety. Results suggest that bitter melon may be a beneficial adjunct in type 2 diabetes management [33].

In an open-label, randomized, parallel designed control trial, 15 newly diagnosed type 2 DM patients were administered with SC seed-based drug as Madhuhara Churna for period of 3 months. The study results suggested that the investigational drug showed significant effects in reduction of fasting blood glucose, insulin resistance and increased HDL level at the end three months' treatment but the drug did not have any impact on post prandial glucose and glycated hemoglobin contents at end of both 3 and 6 months of treatments. There was no change in triglycerides, LDL, total cholesterol in comparison to baseline [34].

A previous clinical study demonstrated that GS4, a *Gymnema sylvestre* leaf extract (400 mg/day, 18–20 months), significantly reduced fasting blood glucose, HbA1c, and glycosylated plasma proteins in 22 T2DM patients on oral anti-hyperglycemic agents, with five achieving glycemic control solely with GS4, suggesting enhanced beta-cell function. These findings support *Gymnema sylvestre's* potential as an adjunctive therapy in T2DM management [35].

A prior clinical study revealed that *Zingiber officinale* powder (2 g/day, 12 weeks) markedly lowered fasting blood glucose and HbA1c in 88 T2DM patients on oral anti-hyperglycemic agents, while also enhancing insulin sensitivity and lipid profiles. This randomised, double-blind, placebo-controlled trial further demonstrated reduced oxidative stress markers, such as malondialdehyde, highlighting ginger's multifaceted metabolic benefits. These compelling findings underscore *Zingiber officinale's* promise as an adjunctive therapy in T2DM management, with bioactive gingerols likely driving improved glucose metabolism [36].

A prior randomized controlled trial revealed that a standardized *Azadirachta indica* leaf and twig extract (125–500 mg twice daily, 12 weeks) significantly lowered fasting blood glucose (by 8.4–19.4%), HbA1c (by 0.23–1.52%), and insulin resistance in 80 T2DM patients on metformin, while also enhancing endothelial function and suppressing systemic inflammation (IL-6, TNF-α) compared to placebo. These robust findings endorse *Azadirachta indica* as a promising adjunctive therapy for T2DM, with its bioactive constituents likely driving improved metabolic and vascular outcomes [37].

A randomized controlled trial, evaluated the effects of *Aegle marmelos* (L.) Correa leaf juice supplementation (20 g/100 ml for 60 days) in patients with type 2 diabetes mellitus and reported significant improvements across various metabolic parameters. The intervention led to marked reductions in fasting blood glucose, HbA1c, postprandial blood glucose, LDL-cholesterol, triglycerides, blood pressure, liver enzymes, and C-reactive protein, along with an increase in HDL-cholesterol and serum FRAP levels. These outcomes were observed without notable adverse effects, suggesting AMLC juice as a safe and effective adjunct to standard antidiabetic therapy [38].

A randomised, double-blind, placebo-controlled trial investigating the effects of *Terminalia chebula* (TC) aqueous extract (250 mg and 500 mg twice daily for 12 weeks) demonstrated significant improvements in endothelial function and oxidative stress biomarkers among T2DM patients. Notably, TC supplementation led to a dose-dependent reduction in reflection index, with the 500 mg group showing the most pronounced improvement (absolute change:5.21 ± 2.41%) compared to placebo. Additionally, favourable changes were observed in nitric oxide, malondialdehyde, glutathione, hs-CRP, HbA1c, and lipid profile parameters, indicating a decrease in cardiovascular risk. These findings support the use of TC, particularly at higher doses, as an effective adjunct in mitigating endothelial dysfunction and associated metabolic disturbances in T2DM, aligning with our study's outcomes [39].

A randomized, placebo-controlled trial evaluating Fenfuro® standardized fenugreek seed extract rich in furostanolic saponins, demonstrated significant glycemic benefits in type 2 diabetes patients on standard therapy. After 12 weeks, fasting and postprandial glucose levels decreased by 38% and 44%, respectively, while HbA1c was reduced by 34.7%, with no adverse effects or organ function abnormalities reported. These findings support the safety and efficacy of *Trigonella foenum-graecum* as an adjunctive antidiabetic agent, aligning with our study's outcomes on glycemic regulation through phytotherapeutic interventions [40].

13.5 Risk Benefit Assessment

In the present study, we aimed to recruit participants with diabetes mellitus type 2. The product is FSSAI certified and already available on the market. Trial participants received the clinical care. Various efficacy parameters such as change in fasting and post meal plasma glucose, anthropometric parameters, fatigue severity scale, fasting insulin, HbA1c, HOMA-IR score, serum CRP levels, change in lipid profile, MetS Z-score, diabetes related quality of life. Safety assessments of major organ function on the basis of change in CBC, LFT, and RFT was monitored.

Participant compliance and tolerability was critically assessed, ensuring that the benefits, such as glycaemic effect and quality of life, significantly outweigh any potential risks. Along with that adverse drug reactions were monitored throughout the study. The investigational product was provided free of cost, further enhancing participant benefit.

13.6 Indication

Type II diabetes

13.5 Dosage

Group A: Take 10 ml twice daily, one hour before lunch and dinner, with water.

Group B: Take 10 ml twice daily, one hour before lunch and dinner, with water.

13.6 Packaging for Clinical Trial Supply

For both test and placebo groups, the product was supplied in a round High-Density Polyethylene (HDPE) bottle containing 300 ml net.

13.7 Storage Condition

Store in a cool place, away from sunlight. Once opened close the lid tightly after every use, keep refrigerated and consume within 30 days.

13.8 Shelf Life

24 months from date of manufacturing.

Group A: Batch no. 39; Manufacturing Date: Feb 2025; Expiry Date: Jan 2027.

Group B: Batch no. 1; Manufacturing Date: Aug 2025; Expiry Date: July 2027.

13.9 Study Visits/Follow-Ups

The visit schedule for this study was as follows:

1. Screening visit (Day -7 to day 0)
2. Baseline Visit 1: Day 1
3. Follow-up visit 2: Day 30 ± 5
4. Follow-up visit 3: Day 60 ± 5
5. Follow-up visit 4: Day 90 ± 5 (End of study)

14 INVESTIGATIONAL PRODUCT HANDLING AND ACCOUNTABILITY

14.1 Storage Requirement & Handling Description of Investigational Product

Store in a cool place, away from sunlight. Once opened close the lid tightly after every use, keep refrigerated and consume within 30 days.

14.2 Labelling

Sponsor supplied investigational products to CRO. The study product was labelled with information such as study code, participant ID, manufacturing date, expiry date, storage conditions, dosage and usage instructions and a statement: 'For Clinical Study Use Only'. The labeled investigational products were dispatched to the study site as per the randomization schedule.

14.3 Investigational Product Accountability

There was a complete accounting for all the investigational products dispatched at the sponsor's end and received by the CRO, which was further supplied to the study investigator. The sponsor dispatched 684 bottles containing 300 ml each of investigational product and 475 Bottles Containing 300 ml in each of placebo. No supplies were damaged during transit from the sponsor to the CRO or from the CRO to the investigator site. Accurate records of investigational product receipt, storage, dispensing, and dates of dispensation were maintained in the drug accountability log.

The investigator or delegated site personnel dispensed the investigational products to enrolled participants according to the randomization schedule.

14.4 Return of Clinical Supplies

Below are the details of used and unused bottles of product:

Test
Used: 535 Bottles Containing 300 ml each.
Unused: 149 Bottles Containing 300 ml each.

Placebo
Used: 413 Bottles Containing 300 ml each.
Unused: 62 Bottles Containing 300 ml each.

15 METHOD OF ASSIGNING PARTICIPANTS TO TREATMENT GROUPS (MEASURES TAKEN TO AVOID BIAS)

15.1 Randomization

This was a randomized study wherein all the participants were randomly allocated (as per computer-generated randomization list) to either one of the study arms i.e. Test Group: Health supplement + Oral hypoglycemic agents (OHA) or Placebo Group: Placebo intervention + OHA.

15.2 Blinding

The present was a double-blind trial. All the investigators or their designated study staff, study participants, sponsors, and study monitors were blinded to the assigned treatment.

Each study site had a designated dispenser. The role of the dispenser was to dispense the study medication, maintain dispensing records, and ensure that the study medication logs were complete and accurate. The participants were requested not to discuss the appearance of the study medication with other study participants. To minimize potential bias, the randomization scheme was securely held by the packaging company until after the database was locked. The IPs were packaged and labeled in a manner that prevented the participants from identifying the treatment. Mprex Healthcare Pvt. Ltd., was responsible for blinding, packaging, and labeling of IPs.

15.3 Procedure for unblinding

Unblinding was intended to be performed only in the event of an SAE or other medically important event requiring knowledge of treatment allocation. In case emergency unblinding was considered medically necessary, the medical monitor (CRO) was to be contacted prior to breaking the blind, wherever feasible. In the event that blinding was broken for any reason, the sponsor and CRO were to be notified in writing as soon as possible with complete details of the occurrence. Any unblinding event was to be documented in the source records. However, no such event occurred during the conduct of the study. After study completion and database lock, each site was provided with a sealed envelope containing the full study randomization scheme, which was retained with the study documents.

15.4 Concealment of the investigational product:

The concealment of the investigational products was achieved by numbering the containers as per the participant ID and randomizing accordingly.

15.5 Permitted Concomitant and Rescue Therapy

Treatment for other concomitant diseases were continued at the investigator's discretion. Medication permitted as per the discretion of the investigator for the same was noted in CRF.

15.6 Prohibited Concomitant Therapy

The following medications were not permitted during the study: nutraceutical, herbal, ayurvedic or homoeopathic supplements, vitamin & mineral supplements, special or any natural/plant product for glycemic control, weight reduction as a preventive measure used.

16 STUDY ASSESSMENT

16.1 Primary efficacy assessment

The primary efficacy assessment involved evaluating the impact of a health supplement on blood glucose and insulin resistance in participants with type 2 diabetes mellitus compared to a placebo group.

16.2 Secondary efficacy assessment

The secondary efficacy assessments of the study were to determine the effect of a health supplement on lipid profile, metabolism, anthropometric parameters, inflammation, fatigue, and change in dose of oral hypoglycemic agents as compared to a placebo group.

16.3 Safety assessment

Safety of the Investigational Product was assessed throughout the study period by monitoring the adverse events profile, vital signs, tolerability and compliance.

17 STATISTICS

17.1 Sample size calculation

Primary Objectives for SS calculation: HbA1c mean between groups.
Reference Site: https://clincalc.com/stats/samplesize.aspx

Sample Size	
Group 1	50
Group 2	50
Total	**100**

Study Parameters	
Mean, group 1	6.99
Mean, group 2	6.52
Alpha	0.05
Beta	0.1
Power	0.9

$$k = \frac{n_2}{n_1} = 1$$

$$n_1 = \frac{(\sigma_1^2 + \sigma_2^2/K)(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2}$$

$$n_1 = \frac{(0.725^2 + 0.725^2/1)(1.96 + 1.28)^2}{0.4700000000000001^2}$$

$$n_1 = 50$$

$$n_2 = K * n_1 = 50$$

$\Delta = |\mu_2 - \mu_1|$ = absolute difference between two means
σ_1, σ_2 = variance of mean #1 and #2
n_1 = sample size for group #1
n_2 = sample size for group #2
α = probability of type I error (usually 0.05)
β = probability of type II error (usually 0.2)
z = critical Z value for a given α or β
k = ratio of sample size for group #2 to group #1

Based on assumptions of difference between the HbA1c mean of 6.99 ±0.725 and 6.52 in second group, a sample size of a total **100** completed cases needed to assess the study objective at 90% power and 5% level of significance.
The allocation of subjects in Group 1: Group 2 is 1:1 hence we require 50 subjects in the respective groups to attain the 90% power and 5% level of significance.

References:

1.Majeed, M., Majeed, A., Nagabhusahnam, K. et al. A randomized, double-blind clinical trial of an herbal formulation (GlycaCare-II) for the management of type 2 diabetes in comparison with metformin. Diabetol Metab Syndr 13, 132 (2021). https://doi.org/10.1186/s13098-021-00746-0

2. Rosner B. Fundamentals of Biostatistics. 7th ed. Boston, MA: Brooks/Cole; 2011.

17.2 Statistical analysis plan

General Principles

All statistical analyses were performed using GraphPad Prism version 10.5.0. software. All statistical tests were two-sided with a significance level (α) of 0.05.

Continuous variables were summarized using descriptive statistics: number of observations (n), mean, standard deviation (SD), median, minimum, and maximum. Categorical variables were summarized using frequency counts and percentages. Efficacy endpoints were analyzed using the PP (per protocol) population and safety variables as per mITT (modified intention-to-treat).

Statistical Methods

Continuous variables such as age and other demographical characteristics were summarized overall using summary statistics, i.e., the number of observations, mean and standard deviation with 95% CI (among normal distribution), or median with range (if non-normal distribution). Categorical values like gender and clinical examination were summarized using frequencies and percentages. For continuous data, a student t-test or Wilcoxon signed rank test was applied depending on normality.

18 ADVERSE EVENTS

An adverse event (AE) was defined as any untoward medical occurrence in a participant administered the investigational product, whether or not it was considered to have a causal relationship with the treatment. This included any unfavorable and unintended sign, symptom, disease, or abnormal laboratory finding temporally associated with the use of the investigational product. Adverse events were monitored throughout the study through participant self-reporting, clinical evaluation, and laboratory assessments. No adverse events or adverse drug reactions related to the investigational product were observed or reported during the entire duration of the study.

18.1 Procedures for Reporting and Recording Adverse Events

Procedures for the reporting and documentation of adverse events were in place throughout the study. All adverse events, were recorded appropriately in the adverse event log of the case record form (CRF). However, no adverse events related to IP were reported during the study.

18.2 Follow-up of Adverse Events ongoing at the End of the study

No adverse events were reported during the study period; therefore, no event-related follow-up was required beyond the scheduled study visits.

19 DATA RECORDING AND RETENTION OF STUDY DATA

The Investigator maintained adequate records for the study including CRFs, medical records, informed consent documents, drug disposition records, safety reports, and other pertinent data. All records are retained by the CRO for 3 years following the completion of a clinical study, and the digital version of all relevant data is transferred to the sponsor as well. The CRO will contact the sponsor for authorization before the destruction of any study records or in the event of accidental loss or destruction of any study records. The CRO shall also notify the sponsor regarding relocation etc. The sponsor master file would be transferred to the sponsor digitally. Completed original CRFs, dated and signed by the Investigator, and any data clarification forms shall be retained by the CRO/sponsor and on-site as well.

The following documents were archived:

- Protocols (all versions).
- Informed consent form (s) signed by participants.
- All correspondence with investigators, regulatory authorities, and between CRO and sponsor, etc., relating to the clinical study.
- All photocopies of the working papers are correctly dated and signed on each page.
- CRFs.
- All clinical and statistical reports and all necessary documentation required for re-creating/re-writing the final report.
- IEC approval, logs, communications, etc.

20 STUDY PARTICIPANTS

20.1 Participant disposition

The disposition of participants is presented in the CONSORT flow diagram.

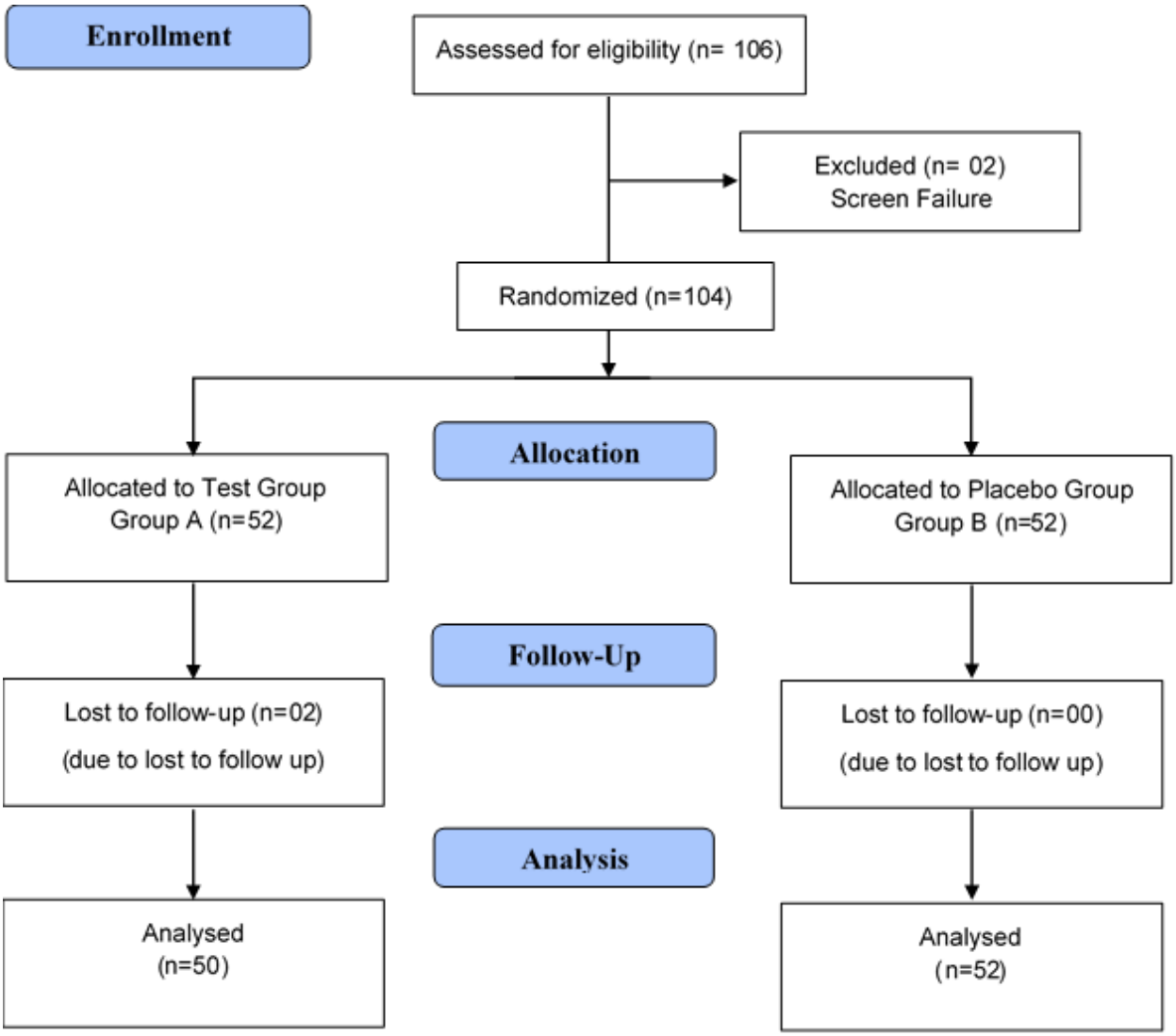

Figure 1: CONSORT diagram for the study.

A total of 104 participants were screened and randomized. All randomized participants received either of the intervention. During the study, 2 participants discontinued due to loss to follow up. As a result, 102 participants completed the study and were included in the final analysis.

20.2 Protocol Deviation

There was no protocol deviation in the said study.

21 OBSERVATIONS AND RESULTS

21.1 Assessment of demographic characteristics

Table 4 summarizes the demographic characteristics of the participants. The mean age was 49.88 ± 8.76 years in Group A and 50.29 ± 9.12 years in Group B.

Table 4: Demographic characteristics

Parameter	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)
Age (years)		
Male (n)	49.74 ± 8.72 (28)	50.43 ± 9.15 (32)
Female (n)	49.00 ± 8.47 (22)	50.32 ± 9.23 (20)
Mean Age	49.88 ± 8.76	50.29 ± 9.12

Values are expressed as mean ± SD

21.2 Assessment of HbA1c levels

Over the 90-day period, both groups demonstrated statistically significant reduction in HbA1c levels. Group A showed a reduction from 7.48 ± 0.32 to 6.85 ± 0.36 (8.34%), whereas Group B showed a decrease from 7.50 ± 0.33 to 7.30 ± 0.63 (2.72%). Both groups demonstrated reduction in HbA1c levels, indicating improved glycemic control. However, the magnitude of reduction observed in Group A is higher than Group B. Data represented in **Table 5 and Figure 2.**

Table 5: Assessment of change in HbA1c levels

Visits	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)	P value
Screening	7.48 ± 0.32	7.50 ± 0.33	0.696
Day 90	6.85 ± 0.36 (8.34%)	7.30 ± 0.63 (2.72%)	0.0002*
P value	<0.0001*	<0.0001*	-

*Values are expressed as mean ± SD with Percent change from screening. Data normality was evaluated using the Shapiro–Wilk test. Within group comparisons were conducted using Wilcoxon signed rank test and Between-group comparisons using Mann–Whitney U test. * indicates p < 0.05.*

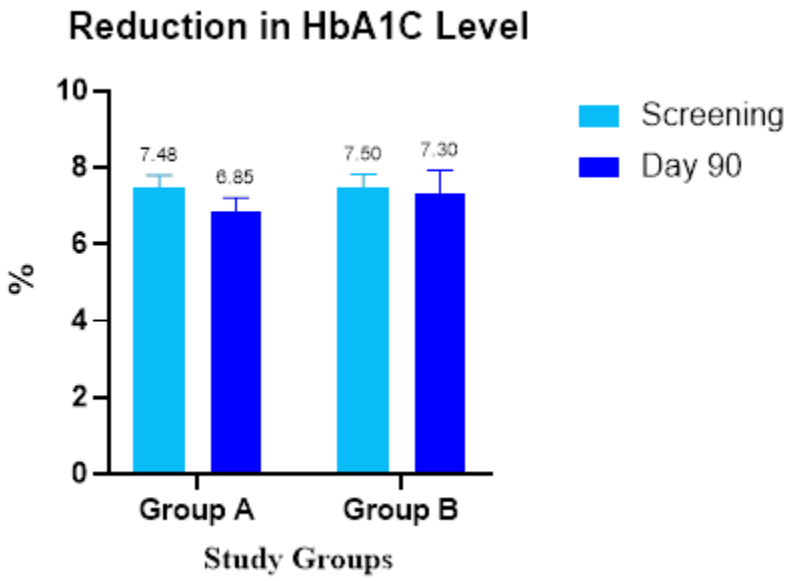

Figure 2: Change in HbA1C level

21.3Assessment of Fasting and post-meal plasma glucose

Table 6: Assessment of change in fasting and post-meal plasma glucose

Visits	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)	P value
Fasting Plasma glucose (mg/dL)			
Baseline	130.67 ± 27.33	133.02 ± 30.47	0.799
Day 30	131.24 ± 31.02 (0.44%)	128.79 ± 25.41 (3.17%)	0.581
P value	0.561	0.240	-
Day 60	120.04 ± 20.52 (8.13%)	130.50 ± 16.71 (1.89%)	0.028*
P value	0.004*	0.772	-
Day 90	119.32 ± 19.37 (8.68%)	139.15 ± 22.92 (4.61%)	0.002*
P value	0.007*	0.134	-
Post-meal plasma glucose (mg/dL)			

Baseline	196.43 ± 41.15	200.63 ± 35.08	0.346
Day 30	178.51 ± 30.92 (9.12%)	174.34 ± 32.95 (13.10%)	0.502
P value	0.0003*	<0.0001*	-
Day 60	164.70 ± 33.51 (16.15%)	174.25 ± 22.20 (13.15%)	0.353
P value	<0.0001*	<0.0001*	-
Day 90	166.80 ± 24.08 (15.09%)	184.58 ± 27.24 (8.00%)	0.097
P value	<0.0001*	0.009*	-

*Values are expressed as mean ± SD with Percent change from screening. Data normality was evaluated using the Shapiro–Wilk test. Within group comparisons were conducted using Wilcoxon signed rank test and Between-group comparisons using Mann–Whitney U test. * indicates $p < 0.05$.*

- **Fasting Plasma Glucose**

FPG levels demonstrated a sustained decline in Group A, reaching 120.04 ± 20.52 mg/dL at Day 60 and 119.32 ± 19.37 mg/dL at Day 90, whereas in Group B, the FPG values reduced to 130.50 ± 16.71 mg/dL and 139.15 ± 22.92 mg/dL at day 60 and day 90 respectively. Statistically significant differences between groups were observed at Day 60 ($p = 0.028$) and Day 90 ($p = 0.002$), indicating a consistent and clinically relevant improvement in fasting plasma glucose with the investigational product. Data represented in **Table 6 and Figure 3.**

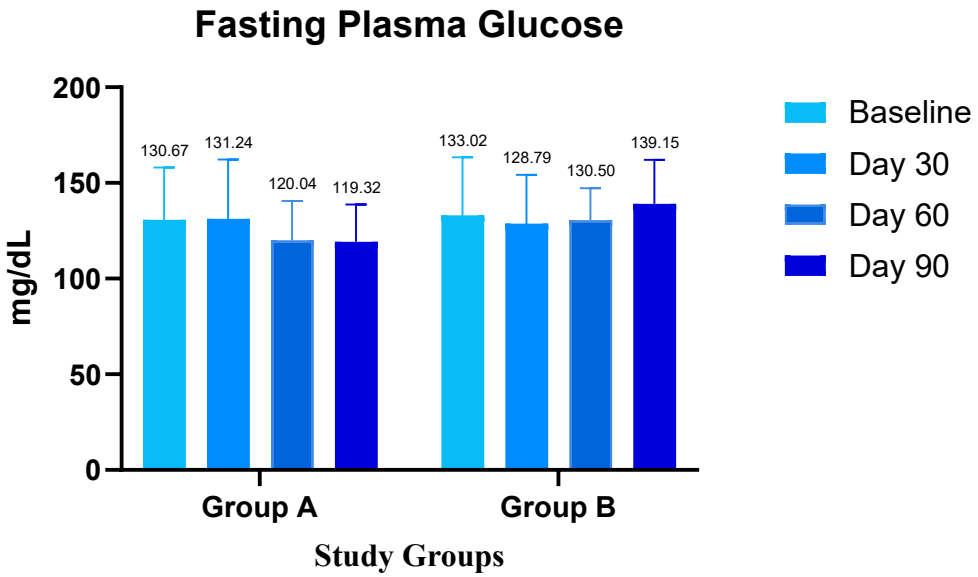

Figure 3: Change in Fasting Plasma Glucose

- **Post Meal Plasma Glucose**

Postprandial glucose levels decreased in both groups throughout the study period. In Group A, PPG reduced from 196.43 ± 41.15 mg/dL at baseline to 166.80 ± 24.08 mg/dL at Day 90 (15.09% reduction). In Group B, values decreased from 200.63 ± 35.08 mg/dL to 184.58 ± 27.24 mg/dL (8.00% reduction). Although reductions were observed in both groups, between group difference did not reach statistical significance, however, a numerical trend favoring the investigational product was observed. Data represented in **Table 6 and Figure 4.**

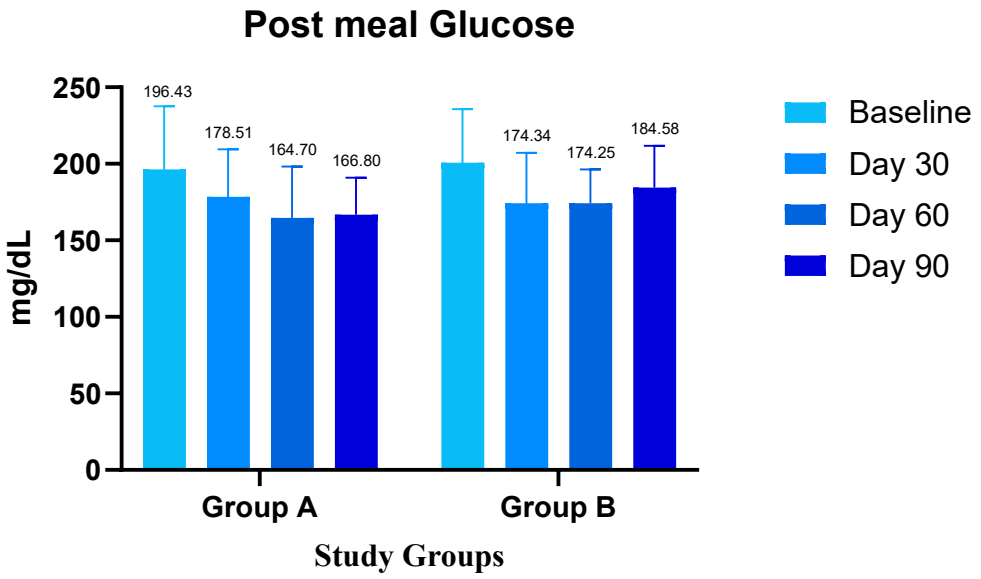

Figure 4: Change in Post Meal Plasma Glucose

21.4Assessment of Insulin Resistance

Table 7: Assessment of changes in Fasting insulin and HOMA-IR

Visits	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)	P value
Fasting insulin (mIU/L)			
Baseline	43.51± 7.66	44.00± 7.57	0.746
Day 90	39.36± 7.17 (9.53%)	42.81± 7.32 (2.70%)	0.009*
P value	<0.0001*	0.070	-
HOMA-IR			
Baseline	13.98± 4.00	14.35± 3.84	0.489
Day 90	11.67± 3.16 (16.49%)	14.75± 3.60 (2.77%)	0.0004*
P value	<0.0001*	0.412	-

Values are expressed as mean ± SD with Percent change from screening. Data normality was evaluated using the Shapiro–Wilk test. Within group comparisons were conducted using Paired t test and Wilcoxon signed rank test and Between-group comparisons using Unpaired t test and Mann–Whitney U test.

- **Fasting Insulin**

At Day 90, fasting insulin levels decreased to 39.36 ± 7.17 mIU/L in Group A compared with 42.81 ± 7.32 mIU/L in Group B. This corresponded to a reduction of 9.53% in the Group A and 2.70% in the Group B. The difference between groups at Day 90 was statistically significant (p = 0.009). Data represented in **Table 7 and Figure 5.**

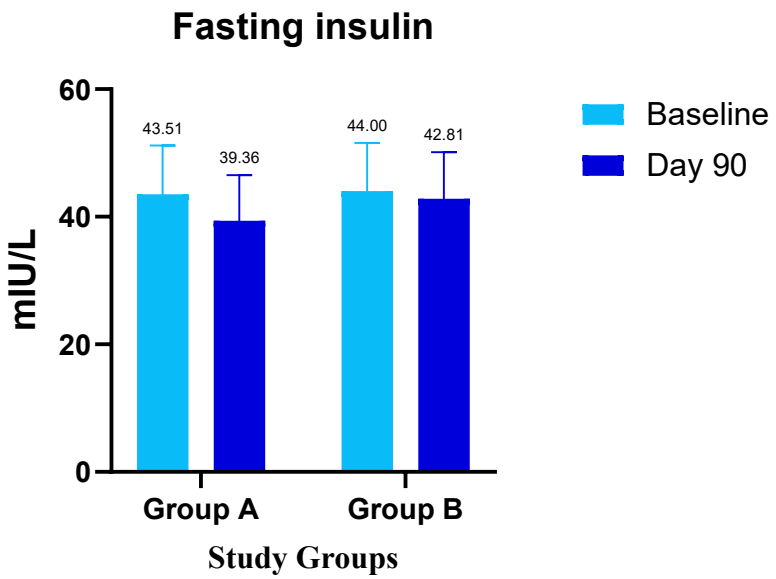

Figure 5: Change in Fasting Insulin

- **HOMA-IR**

At Day 90, HOMA-IR decreased to 11.67 ± 3.16 in Group A, whereas Group B showed a value of 14.75 ± 3.60. This represented a 16.49% reduction in Group A, while Group B showed a 2.77% increase from baseline. The difference between groups at Day 90 was statistically significant (p = 0.0004). Data represented in **Table 7 and Figure 6.**

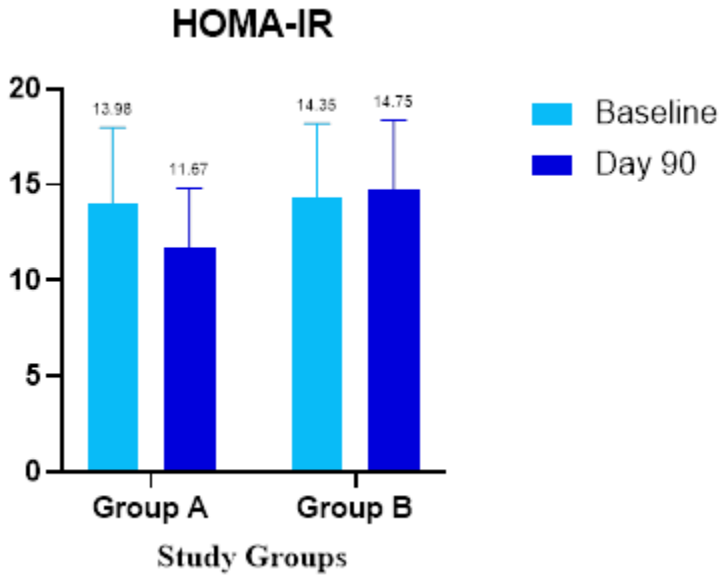

Figure 6: Change in HOMA-IR

21.5Assessment of Lipid Profile

Table 8 summarizes changes in lipid profile parameters over the 90-day treatment period. Both groups demonstrated reductions in total cholesterol by Day 90. In Group A, total cholesterol decreased from 184.31 ± 19.88 mg/dL to 173.73 ± 17.69 mg/dL, corresponding to a 5.74% reduction, while Group B showed a 3.58% reduction. Reductions from baseline were statistically significant in both groups ($p < 0.0001$), although the between-group difference was not statistically significant ($p = 0.143$).

LDL cholesterol decreased from 116.34 ± 13.24 mg/dL to 107.58 ± 12.06 mg/dL in Group A, representing a 7.53% reduction, compared with a 1.92% reduction in Group B. The between-group difference at Day 90 was statistically significant ($p = 0.0006$). HDL cholesterol remained generally stable in both groups, with no statistically significant changes observed. Triglycerides and VLDL cholesterol showed significant reductions from baseline in both groups, although between-group differences were not statistically significant at Day 90.

Reductions in Total Cholesterol/HDL and LDL/HDL ratios were greater in Group A compared with Group B; however, these differences did not reach statistical significance. Overall, the investigational product demonstrated favorable effects on lipid parameters, particularly LDL cholesterol reduction, over the 90-day treatment period.

Table 8: Assessment of change in lipid profile

Group / Visit	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)	P value
Total Cholesterol			
Screening	184.31±19.88	182.06±17.95	0.550
Day 90	173.73±17.69 (5.74%)	175.55±17.02 (3.58%)	0.143
P value	<0.0001	<0.0001	
LDL Cholesterol			
Screening	116.34±13.24	112.38±12.20	0.119
Day 90	107.58±12.06 (7.53%)	110.23±12.16 (1.92%)	0.0006*
P value	<0.0001	<0.0001	
HDL Cholesterol			
Screening	41.71±10.88	42.77±11.26	0.630
Day 90	41.90±8.30 (0.46%)	41.51±11.17 (-2.94%)	0.483
P value	0.919	0.159	
Triglycerides			
Screening	131.27±23.89	134.52±28.75	0.991
Day 90	121.22±34.85 (7.65%)	119.03±29.96 (11.51%)	0.745
P value	0.002*	0.0001*	
VLDL Cholesterol			
Screening	26.25±4.78	26.91±5.75	0.991
Day 90	24.24±6.97 (7.65%)	23.81±5.99 (11.52%)	0.745
P value	0.002*	0.0001*	
Total Chol /HDL Ratio			
Screening	4.66±1.07	4.52±1.14	0.479
Day 90	4.27±0.78	4.52±1.32	0.595

	(8.39%)	(0.00%)	
P value	0.180	0.297	
LDL/HDL Ratio			
Screening	2.98±0.86	2.84±0.90	0.369
Day 90	2.67±0.62 (10.55%)	2.89±1.05 (1.92%)	0.422
P value	0.205	0.435	

Values are expressed as mean ± SD with Percent change from screening. Data normality was evaluated using the Shapiro–Wilk test. Within group comparison were conducted using Paired t test and Wilcoxon signed rank test and Between-group comparisons using Unpaired t test and Mann–Whitney U test.

21.6 Assessment of Metabolic syndrome severity Z score (MetS Z score)

At Day 90, the MetS Z score decreased to 0.44 ± 0.40 in Group A, corresponding to a 35.47% reduction. In contrast, Group B increased to 0.79 ± 0.52, representing a 2.43% increase from baseline. The difference between groups at Day 90 was statistically significant (p = 0.027). Data represented in Table 9 and Figure 7.

Table 9: Assessment of change in MetS Z score

Visits	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)	P value
Baseline	0.69 ± 0.64	0.77 ± 0.53	0.273
Day 90	0.44 ± 0.40 (35.47%)	0.79 ± 0.52 (2.43%)	0.027*
	0.023*	0.800	

*Values are expressed as mean ± SD with Percent change from screening. Data normality was evaluated using the Shapiro–Wilk test. Within group comparison were conducted using Wilcoxon signed rank test and Between-group comparisons using Mann–Whitney U test. * indicates p < 0.05.*

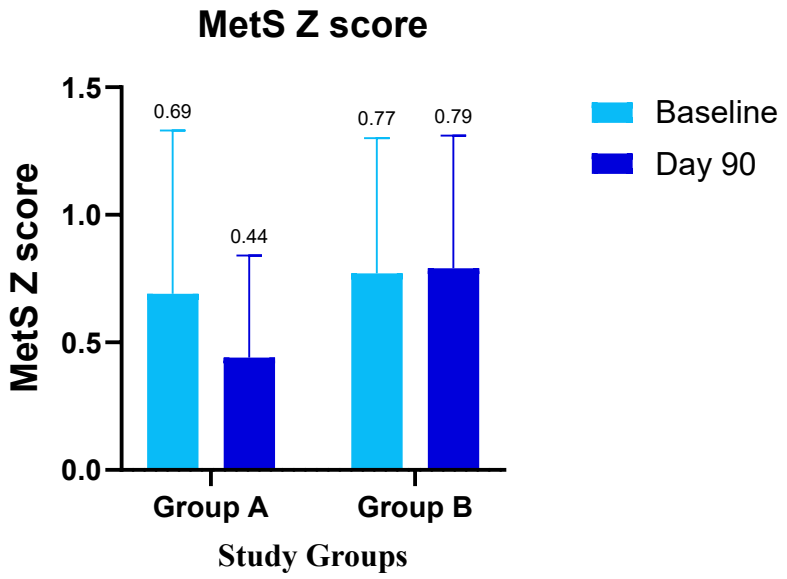

Figure 7: Change in Metabolic syndrome severity Z score

21.7Assessment of anthropometric parameters

The assessment of anthropometry refers to the systematic measurement and analysis of physical body parameters. **Table 10** presents anthropometric measurements, including weight, BMI, waist circumference, and height, for two groups over a 90-day period.

Over the course of the study, statistically significant reductions in body weight were observed. At Day 30, the mean weight decreased by 0.59 kg from screening; at Day 60, the reduction was 1.29 kg, and by Day 90, the reduction was maintained at 1.25 kg from screening. In contrast, Group B showed minimal changes, the mean body weight increased by 0.2 kg at Day 30, decreased by 0.08 kg at Day 60, and decreased by 0.1 kg by Day 90, compared to screening. Statistically significant differences between groups were observed at Day 30 ($p = 0.013$), Day 60 ($p = 0.0006$), and Day 90 ($p = 0.005$), indicating greater reduction in body weight in Group A.

BMI demonstrated a similar trend. In Group A, BMI reduced from 26.31 ± 2.14 kg/m² at screening to 25.85 ± 2.27 kg/m² on Day 90, representing a 1.77% statistically significant reduction. Group B showed a reduction from 26.65 ± 2.06 kg/m² to 26.59 ± 2.00 kg/m², corresponding to a 0.21% decrease. These findings indicate that the Group A was associated with improved body weight management and reduction in BMI compared with placebo.

Waist circumference values remained generally stable throughout the study period in both groups. At Day 90, waist circumference was 89.82 ± 11.63 cm in Group A and 92.10 ± 10.33 cm in Group B, corresponding to numerical increase of 0.17% in Group A and a minimal decrease of 0.15% in Group B. No statistically significant difference between groups was observed at Day 90 (p = 0.906).

Table 10: Assessment of change in anthropometric parameters

Visits	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)	P value
Height (cm)			
Screening	162.59 ± 5.73	161.69 ± 5.28	0.601
Weight (Kg)			
Screening	69.67± 7.63	69.79 ± 6.03	0.933
Day 30	69.08 ± 7.65 (0.85%)	69.81 ± 5.94 (0.03%)	0.013*
P value	0.016*	0.724	-
Day 60	68.38 ± 7.26 (1.85%)	69.71 ± 5.80 (0.11%)	0.0006*
P value	0.0002*	0.560	-
Day 90	68.42 ± 7.70 (1.80%)	69.69 ± 5.67 (0.14%)	0.005*
P value	0.002*	0.478	-
BMI (kg/m²)			
Screening	26.31 ± 2.14	26.65 ± 2.06	0.425
Day 30	26.09 ± 2.13 (0.86%)	26.71 ± 2.01 (0.23%)	0.009*
P value	0.019*	0.289	-
Day 60	25.84 ± 2.10 (1.81%)	26.67 ± 1.96 (-0.08%)	0.0004*
P value	0.0002*	0.774	-
Day 90	25.85 ± 2.27 (1.77%)	26.59 ± 2.00 (0.21%)	0.013*
P value	0.001*	0.520	-
Waist Circumference (cm)			

Screening	89.67 ± 11.18	92.24 ± 10.05	0.264
Day 90	89.82 ± 11.63 (0.17%)	92.10 ± 10.33 (0.15%)	0.906
P value	0.092	0.076	-

*Values are expressed as mean ± SD with Percent change from screening. Data normality was evaluated using the Shapiro–Wilk test. Within group comparisons were conducted using Paired t test and Wilcoxon signed rank test and Between-group comparisons using Unpaired t test and Mann–Whitney U test. * indicates $p < 0.05$.*

21.8 Assessment of serum C-reactive protein (CRP) levels

Table 11 presents the changes in serum C-reactive protein (CRP) levels over the 90-day treatment period in both study groups. At Day 90, serum CRP levels were 5.38 ± 1.59 mg/L in Group A and 5.71 ± 1.81 mg/L in Group B, corresponding to numerical increases of approximately 3.42% and 4.14%, respectively, compared with baseline values. The difference between groups at Day 90 was not statistically significant ($p = 0.904$).

Table 11: Assessment of changes in serum CRP levels

Visits	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)	P value
Baseline	5.20 ± 1.77	5.48 ± 1.64	0.398
Day 90	5.38 ± 1.59 (3.42%)	5.71 ± 1.81 (4.14%)	0.904
P value	0.284	0.427	-

Values are expressed as mean ± SD with Percent change from screening. Data normality was evaluated using the Shapiro–Wilk test. Within group comparisons were conducted using Paired t test and Wilcoxon signed rank test and Between-group comparisons using Unpaired t test and Mann–Whitney U test.

21.9 Assessment of fatigue Severity Scale score (FSS)

Table 12 and Figure 8 presents the changes in Fatigue Severity Scale (FSS) scores over the 90-day treatment period in both study groups. Baseline FSS scores were comparable between the groups, with mean values of 33.34 ± 11.11 in Group A and 33.54 ± 8.49 in Group B ($p = 0.752$), indicating similar fatigue status.

A progressive reduction in FSS scores was observed in both groups during the study period, with greater improvement noted in Group A. At Day 60, FSS scores decreased to 30.46 ± 9.33 in Group A and 32.65 ± 7.96 in Group B, representing reductions of 8.64% and 2.64%, respectively. The difference between groups was statistically

significant (p = 0.0003). By Day 90, Group A demonstrated a reduction in FSS score to 29.30 ± 8.71, corresponding to a 12.12% decrease from baseline, whereas Group B showed a reduction to 31.98 ± 7.73, corresponding to a 4.64% decrease. The between-group difference at Day 90 was statistically significant (p = 0.012).

Overall, Group A demonstrated greater improvement in fatigue severity compared with Group B over the 90-day treatment period, with statistically significant differences between groups observed at Day 60 and Day 90.

Table 12: Assessment of change in fatigue severity scale score (FSS)

Visits	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)	P value
Baseline	33.34 ± 11.11	33.54 ± 8.49	0.752
Day 30	32.54 ± 10.78 (2.40%)	33.13 ± 8.29 (1.20%)	0.174
P value	0.0005*	0.016*	-
Day 60	30.46 ± 9.33 (8.64%)	32.65 ± 7.96 (2.64%)	0.0003*
P value	<0.0001*	0.002*	-
Day 90	29.30 ± 8.71 (12.12%)	31.98 ± 7.73 (4.64%)	0.012*
P value	<0.0001*	<0.0001*	-

*Values are expressed as mean ± SD with Percent change from screening. Data normality was evaluated using the Shapiro–Wilk test. Within group comparisons were conducted using Wilcoxon signed rank test and Between-group comparisons using Mann–Whitney U test. * indicates p < 0.05.*

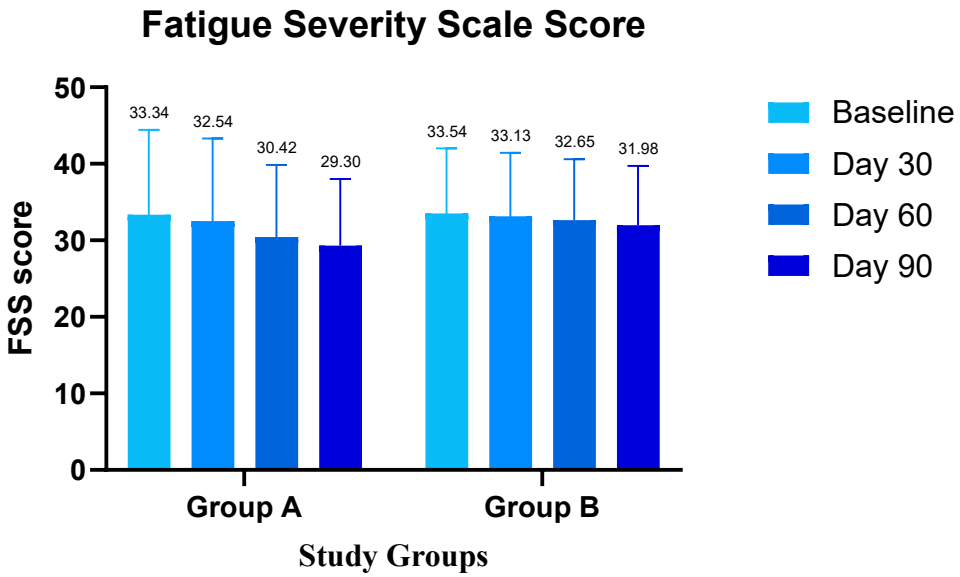

Figure 8: Change in fatigue Severity Scale score (FSS)

21.10 Assessment of Diabetes related quality of life by DQOL

Table 13 summarizes changes in diabetes-related quality of life over the 90-day treatment period. By Day 90, improvements in treatment satisfaction and diabetes management were more pronounced in Group A compared with Group B. Satisfaction with current diabetes treatment improved significantly in Group A, with the proportion of subjects reporting "Moderately Dissatisfied" decreasing from 40% to 8%, while "Moderately Satisfied" responses increased from 38% to 80%. The between-group difference at Day 90 was statistically significant ($p = 0.0001$).

Significant improvements favoring Group A were also observed for satisfaction with the time required to manage diabetes ($p = 0.015$), time spent on exercise ($p = 0.014$), time spent obtaining diabetes check-ups ($p = 0.0009$), and knowledge about diabetes ($p = 0.028$). Although numerical improvements were observed in satisfaction related to determination of blood glucose levels, sex life, and family burden, these differences did not reach statistical significance between groups at Day 90. Overall, Group A demonstrated favorable effects on multiple domains of diabetes-related quality of life compared with placebo over the 90-day study period.

Table 13: Assessment of change in diabetes related quality of life

Visits	GROUP A (Test)	GROUP B (Placebo)	P value Screening	P value Day 90

How satisfied are you with your current diabetes treatment?						
	Baseline	**Day 90**	**Baseline**	**Day 90**		
Moderately Dissatisfied	20 (40%)	4 (8%)	18 (34%)	17 (32%)	0.693	0.0001*
Moderately Satisfied	19 (38%)	40 (80%)	23 (44%)	26 (50%)		
Neither	9 (18%)	3 (6%)	10 (19%)	8 (15%)		
Very Dissatisfied	1 (2%)	0 (0%)	1 (1.9%)	1 (1.9%)		
Very Satisfied	1 (2%)	3 (6%)	0 (0%)	0 (0%)		
How satisfied are you with the amount of time it takes to manage your diabetes?						
Moderately Dissatisfied	19 (38%)	6 (12%)	20 (38%)	14 (26%)	0.684	0.015*
Moderately Satisfied	16 (32%)	34 (68%)	20 (38%)	26 (50%)		
Neither	14 (28%)	7 (14%)	12 (23%)	12 (23%)		
Very Dissatisfied	0 (0%)	0 (0%)	0 (0%)	0 (0%)		
Very Satisfied	1 (1.9%)	3 (5.7%)	0 (0%)	0 (0%)		
How satisfied are you with the time it takes to determine your sugar level?						
Moderately Dissatisfied	19(38%)	6(12%)	22(42%)	15(28%)	0.393	0.321
Moderately Satisfied	12(24%)	24(48%)	18(34%)	21(40%)		
Neither	17(34%)	18(36%)	12(23%)	16(30.7%)		
Very Dissatisfied	1(2%)	0(0%)	0(0%)	0(0%)		
Very Satisfied	1(2%)	2(4%)	0(0%)	0(0%)		
How satisfied are you with the time you spent on exercise						
Moderately Dissatisfied	29(58%)	12(24%)	30(57%)	23(44%)	0.794	0.014*
Moderately Satisfied	6(12%)	20(40%)	8(15%)	13(25%)		
Neither	11(22%)	13(26%)	14(26%)	16(30%)		
Very Dissatisfied	1(2%)	0(0%)	0(0%)	0(0%)		
Very Satisfied	3(6%)	5(10%)	0(0%)	0(0%)		
How satisfied are you with your sex life?						
Moderately Dissatisfied	13(26%)	2(4%)	12(23%)	9(17%)	0.437	0.138
Moderately Satisfied	2(4%)	11(22%)	5(9%)	7(13%)		
Neither	34(68%)	35(70%)	35(67%)	36(69%)		
Very Dissatisfied	1(2%)	0(0%)	0(0%)	0(0%)		

Very Satisfied	0(0%)	2(4%)	0(0%)	0(0%)		
How satisfied are you with the burden your diabetes is placing on your family?						
Moderately Dissatisfied	15(30%)	7(14%)	17(32.6%)	14(26%)	0.826	0.298
Moderately Satisfied	13(26%)	19(38%)	15(28%)	15(28%)		
Neither	21(42%)	23(46%)	20(38%)	23(44%)		
Very Dissatisfied	1(2%)	0(0%)	0(0%)	0(0%)		
Very Satisfied	0(0%)	1(2%)	0(0%)	0(0%)		
How satisfied are with the time spent getting check-ups for your diabetes?						
Moderately Dissatisfied	13(26%)	3(6%)	17(32%)	10(19%)	0.533	0.0009*
Moderately Satisfied	17(34%)	31(62%)	16(30%)	18(34%)		
Neither	18(36%)	13(26%)	19(36%)	24(46%)		
Very Dissatisfied	0(0%)	0(0%)	0(0%)	0(0%)		
Very Satisfied	2(4%)	3(6%)	0(0%)	0(0%)		
How satisfied are you with your knowledge about your diabetes?						
Moderately Dissatisfied	13(26%)	2(4%)	9(17%)	5(9%)	0.548	0.028*
Moderately Satisfied	20(40%)	27(54%)	19(36%)	24(46%)		
Neither	11(22%)	13(26%)	21(40%)	22(42%)		
Very Dissatisfied	3(6%)	0(0%)	2(3.8%)	1(1.9%)		
Very Satisfied	3(6%)	8(16%)	1(1.9%)	0(0%)		

Data are presented as n (%). Between-group comparisons for each questionnaire item were performed between Group A (Test) and Group B (Placebo) at Baseline and Day 90. For statistical analysis, responses were dichotomized into two categories: ***Satisfied*** *(Very Satisfied + Moderately Satisfied) and* ***Not Satisfied/Neutral*** *(Neither + Moderately Dissatisfied + Very Dissatisfied). Comparisons between treatment groups were analyzed using the Fisher's exact test. A p-value <0.05 was considered statistically significant. Statistically significant improvements in the Test group compared with the Placebo group at Day 90 are indicated by an asterisk (*).*

21.11 Safety Assessment

- **Assessment of laboratory investigations**

Hematological and biochemical investigations were performed at screening and end of the study for all participants, including complete blood count and routine biochemical parameters. Although some parameters exhibited statistically significant changes but all values remained within clinically acceptable ranges. Observed eosinophil changes were not associated with any clinically significant hypersensitivity events or related adverse events during the study period. A statistically significant baseline difference in monocyte count was observed between groups; however, all values remained within

normal clinical range. These variations were not clinically significant indicating that the investigational product was well tolerated and safe. **(Table 14 and 15).**

Table 14: Assessment of CBC

Group / Visit	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)	P value
Total Leukocyte Count			
Screening	8101.88 ± 2105.12	8100.44 ± 1736.20	0.997
Day 90	7070.83 ± 1622.44 (12.73%)	7124.62 ± 1678.55 (12.05%)	0.905
P value	0.008*	0.001*	-
Neutrophils			
Screening	60.01 ± 10.38	61.44 ± 8.33	0.698
Day 90	56.24 ± 8.90 (6.27%)	56.99 ± 8.56 (7.23%)	0.773
P value	0.011*	0.004*	-
Lymphocytes			
Screening	32.56 ± 5.86	32.08 ± 5.11	0.292
Day 90	32.12 ± 5.68 (1.36%)	32.01 ± 5.54 (0.24%)	0.051
P value	0.524	0.933	-
Monocytes			
Screening	3.14 ± 1.40	2.48 ± 0.54	0.019*
Day 90	2.80 ± 1.65 (10.83%)	2.79 ± 1.67 (12.40%)	0.051
P value	0.001*	0.522	-
Eosinophil			
Screening	2.30 ± 0.71	2.17 ± 0.43	0.757
Day 90	2.66 ± 0.75 (15.65%)	2.60 ± 1.05 (19.47%)	0.725
P value	0.001*	0.001*	-
Basophils			

Screening	0.00 ± 0.00	0.00 ± 0.00	NA
Day 90	0.00 ± 0.00	0.00 ± 0.00	NA
Total RBC Count			
Screening	5.30 ± 0.63	5.39 ± 0.57	0.368
Day 90	5.28 ± 0.46 (0.44%)	5.32 ± 0.62 (1.33%)	0.730
P value	0.820	0.468	-
Platelets			
Screening	308.46 ± 97.19	305.69 ± 90.17	0.830
Day 90	304.18 ± 72.24 (1.39%)	279.71 ± 68.30 (8.50%)	0.182
P value	0.761	0.121	-
Hemoglobin			
Screening	14.09 ± 1.45	14.64 ± 1.25	0.041*
Day 90	13.90 ± 1.36 (1.29%)	14.20 ± 1.67 (3.00%)	0.464
P value	0.427	0.102	-
Hematocrit			
Screening	46.04 ± 5.23	48.04 ± 3.87	0.022*
Day 90	46.71 ± 3.69 (1.45%)	47.58 ± 4.14 (0.97%)	0.201
P value	0.416	0.438	-

Values are expressed as mean ± SD with Percent change from screening. Data normality was evaluated using the Shapiro–Wilk test. Within group comparisons were conducted using Paired t test and Wilcoxon signed rank test and Between-group comparisons using Unpaired t test and Mann–Whitney U test.

Table 15: Assessment of Liver function test & Renal function test

Group / Visit	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)	P value
Bilirubin Total			
Screening	0.82 ± 0.23	0.76 ± 0.31	0.495

Day 90	0.62 ± 0.28 (24.41%)	0.61 ± 0.24 (19.58%)	0.740
P value	0.0001*	0.021*	-
Bilirubin Direct			
Screening	0.27 ± 0.10	0.31 ± 0.18	0.273
Day 90	0.25 ± 0.11 (4%)	0.25 ± 0.07 (18.56%)	0.339
P value	0.613	0.086	-
Bilirubin Indirect			
Screening	0.62 ± 0.26	0.79 ± 0.24	0.0006*
Day 90	0.71 ± 0.27 (14.84%)	0.68 ± 0.28 (13.10%)	0.003*
P value	0.110	0.013*	-
SGOT			
Screening	27.53 ± 6.84	27.09 ± 7.17	0.755
Day 90	28.30 ± 5.55 (2.81%)	26.72 ± 5.92 (1.38%)	0.541
P value	0.549	0.784	-
SGPT			
Screening	31.72 ± 8.72	33.09 ± 8.10	0.411
Day 90	33.00 ± 7.67 (4.04%)	32.58 ± 7.76 (1.55%)	0.170
P value	0.301	0.355	-
Alkaline Phosphatase			
Screening	100.15 ± 25.50	104.61 ± 24.27	0.331
Day 90	103.87 ± 22.83 (3.72%)	103.07 ± 24.23 (1.47%)	0.434
P value	0.373	0.782	-
Total Proteins			
Screening	7.10 ± 0.59	6.93 ± 0.65	0.215
Day 90	7.01 ± 0.58 (1.27%)	7.08 ± 0.56 (2.19%)	0.138
P value	0.414	0.202	-

Albumin			
Screening	4.32 ± 0.52	4.38 ± 0.60	0.592
Day 90	4.21 ± 0.48 (2.45%)	4.31 ± 0.56 (1.60%)	0.823
P value	0.345	0.543	-
Globulin			
Screening	2.79 ± 0.58	2.55 ± 0.93	0.131
Day 90	2.80 ± 0.75 (0.43%)	2.77 ± 0.68 (8.60%)	0.327
P value	0.927	0.187	-
A/G Ratio			
Screening	1.64 ± 0.50	2.17 ± 1.53	0.231
Day 90	1.67 ± 0.69 (1.46%)	1.71 ± 0.71 (21.24%)	0.561
P value	0.566	0.276	-
Blood Urea Nitrogen			
Screening	16.44 ± 4.15	14.15 ± 3.38	0.003*
Day 90	14.02 ± 3.33 (14.73 %)	14.23 ± 3.90 (0.59 %)	0.019*
P value	0.006*	0.926	-
Blood Urea			
Screening	35.19 ± 8.89	30.29 ± 7.24	0.003*
Day 90	30.01 ± 7.13 (14.73%)	30.46 ± 8.34 (0.58%)	0.019*
P value	0.006*	0.926	-
Serum Creatinine			
Screening	0.97 ± 0.28	0.87 ± 0.30	0.0495*
Day 90	0.85 ± 0.25 (12.39%)	0.96 ± 0.32 (10.07%)	0.007*
P value	0.027*	0.106	-
Uric Acid			
Screening	5.43 ± 1.48	4.91 ± 1.35	0.065
Day 90	4.97 ± 1.20	4.95 ± 1.44	0.206

	(8.58%)	(0.77%)	
P value	0.115	0.918	-
Glomerular Filtration Rate (GFR)			
Screening	114.07 ± 17.54	122.67 ± 34.52	0.452
Day 90	149.60 ± 50.38 (31.15%)	135.57 ± 33.90 (10.51%)	0.118
P value	<0.0001*	0.018*	-

Values are expressed as mean ± SD with Percent change from screening. Data normality was evaluated using the Shapiro–Wilk test. Within group comparisons were conducted using Paired t test and Wilcoxon signed rank test and Between-group comparisons using Unpaired t test and Mann–Whitney U test.

- **Assessment of Vitals**

Table 16 presents the evaluation of vital parameters in the Test and Placebo groups over a 90-day period. All vital parameters remained within the clinically normal range, demonstrating the safety of the intervention throughout the study duration.

Table 16: Assessment of vital Signs

Visits	GROUP A (TEST) (n=50)	GROUP B (Placebo) (n=52)
Body Temperature (^{0}F)		
Screening	96.91 ± 1.16	96.61 ± 1.17
Baseline	96.94 ± 1.09 (0.02%)	96.73 ± 1.13 (0.12%)
Day 30	96.91 ± 0.83 (0.002%)	96.53 ± 0.88 (0.09%)
Day 60	96.52 ± 0.82 (0.40%)	97.05 ± 1.14 (0.45%)
Day 90	96.65 ± 0.86 (0.27%)	96.32 ± 1.10 (0.31%)
Respiratory Rate (BPM)		
Screening	18.60 ± 1.25	18.19 ± 1.51
Baseline	18.50 ± 1.36 (0.54%)	18.00 ± 1.56 (1.06%)
Day 30	18.46 ± 1.63 (0.75%)	18.12 ± 1.62 (0.42%)

Day 60	18.50 ± 1.53 (0.54%)	18.73 ± 1.42 (-2.94%))
Day 90	19.02 ± 1.48 (2.26%)	18.67 ± 1.63 (-2.64%)
Pulse Rate (Per minute)		
Screening	74.16 ± 6.36	74.83 ± 4.63
Baseline	75.98 ± 7.19 (2.45%)	76.58 ± 5.98 (2.34%)
Day 30	74.92 ± 5.97 (1.02%)	73.52 ± 4.13 (1.75%)
Day 60	75.28 ± 5.45 (0.92%)	75.64 ± 7.12 (1.08%)
Day 90	78.48 ± 5.92 (5.83%)	75.19 ± 5.77 (0.49%)
Blood Pressure (Systolic) (mmHg)		
Screening	122.10 ± 7.81	122.06 ± 6.55
Baseline	122.06 ± 7.68 (0.03%)	121.58 ± 5.91 (0.39%)
Day 30	121.12 ± 5.11 (0.80%)	121.42 ± 4.51 (0.52%)
Day 60	120.18 ± 6.65 (1.57%)	121.91 ± 4.66 (0.12%)
Day 90	122.56 ± 5.23 (-0.38%)	119.85 ± 5.39 (1.81%)
Blood Pressure (Diastolic) (mmHg)		
Screening	77.08 ± 6.50	77.56 ± 4.64
Baseline	77.32 ± 6.48 (0.31%)	77.88 ± 5.18 (0.42%)
Day 30	75.94 ± 4.00 (1.48%)	75.87 ± 4.03 (2.18%)
Day 60	76.32 ± 5.70 (0.99%)	76.18 ± 4.07 (1.77%)
Day 90	78.12 ± 5.92 (1.35%)	75.79 ± 4.95 (2.28%)

Values are expressed as mean ± SD with Percent change.

- **Assessment of Tolerability**

  Tolerability was evaluated based on the incidence and severity of AEs related to the investigational products using the following scoring criteria: 0 (Poor Tolerability): The occurrence of severe or SAEs related to the IP, necessitating study discontinuation; 1 (Fair Tolerability): The occurrence of moderate to severe AEs related to the IP, which resolved with or without medication and did not require discontinuation of the study intervention; 2 (Good Tolerability): The occurrence of mild AEs related to the IP, which resolved with or without medication and 3 (Excellent Tolerability). In this study, all participants demonstrated excellent- tolerability **(Table 17).**

- **Assessment of Compliance**

  The compliance rates for IP consumption were consistently high across all study groups throughout the study duration indicating excellent participant adherence

Table 17: Assessment of Tolerability

Tolerability Score		
Visits	**GROUP A (TEST) (n=50)**	**GROUP B (Placebo) (n=52)**
Day 30	03 ± 00	03 ± 00
Day 60	03 ± 00	03 ± 00
Day 90	03 ± 00	03 ± 00
Compliance		
Day 30	99.73	99.87
Day 60	99.87	99.87
Day 90	100	99.62

Values are expressed as mean ± SD and percentage.

22. DISCUSSION

The present randomized, double-blind, parallel-arm clinical trial evaluated the efficacy and safety of Antox-D liquid, a multi-herbal nutraceutical formulation, as an adjunct to standard oral hypoglycemic therapy in participants with type 2 diabetes mellitus (T2DM). Over the 90-day intervention period, the investigational product demonstrated statistically significant improvements in multiple glycemic and metabolic parameters compared with placebo, while maintaining a favorable safety and tolerability profile.

At baseline, demographic and disease-related characteristics were comparable between the study groups, minimizing the likelihood of confounding due to imbalance in participant characteristics. Both groups continued background oral hypoglycemic agents, thereby enabling evaluation of the adjunctive effect of Antox-D under conditions reflective of real-world clinical practice.

The primary efficacy findings of the study demonstrated that supplementation with Antox-D resulted in significant improvements in glycemic control. HbA1c levels demonstrated statistically significant decrease from screening to Day 90, with reduction of 8.34% in Antox-D group and 2.72% in placebo. The between-group difference at Day 90 was statistically significant ($p = 0.0002$). Reduction in HbA1c is clinically relevant because even modest decreases are associated with reduced risk of microvascular and macrovascular complications in T2DM (43).

Fasting plasma glucose (FPG) and postprandial plasma glucose (PPG) levels also improved over the treatment period, further supporting the glycemic efficacy of the investigational product. Group A demonstrated a sustained reduction in FPG beginning at Day 60 and maintained through Day 90, with statistically significant differences compared with placebo at both time points. In contrast, the placebo group exhibited minor changes without sustained improvement. The observed reduction in fasting glucose may potentially be associated with pharmacological activities previously reported in published literature for certain botanical constituents contained in the formulation, including bitter melon, fenugreek, neem, and ginger extracts. (6,12,16,18).

PPG levels showed progressive improvement in both groups; however, numerically greater reductions were observed in the Antox-D group. Although the between-group difference did not reach statistical significance at Day 90, the trend favoring the investigational product may potentially be clinically meaningful, particularly considering the association of postprandial hyperglycemia and cardiovascular risk. The reduction in PPG may potentially be associated with pharmacological effects previously

described for certain constituent herbs in preclinical and clinical literature, including possible effects on carbohydrate digestion and glucose metabolism (9,12,14).

The findings observed in the present study are consistent with published evidence on several constituent ingredients of Antox-D. Clinical studies involving *Momordica charantia* have reported reductions in fasting blood glucose in patients with T2DM (33). Similarly, fenugreek (*Trigonella foenum-graecum*) supplementation has demonstrated improvement in glycemic indices and insulin sensitivity in randomized controlled trials (40). *Gymnema sylvestre* and *Syzygium cumini* have also shown beneficial effects on glycemic regulation and pancreatic β-cell function in both preclinical and clinical settings (21,35). Collectively, the polyherbal composition of Antox-D may provide complementary effects on glycemic and metabolic parameters.

A notable finding of the study was the improvement in markers of insulin resistance. Fasting insulin levels and HOMA-IR values demonstrated significant reductions in the Antox-D group compared with placebo. HOMA-IR decreased by 16.49% in the treatment group, whereas a slight increase was observed in the placebo group. Insulin resistance is a core pathophysiological abnormality in T2DM and is strongly associated with obesity, dyslipidemia, and chronic inflammation. Therefore, improvement in insulin sensitivity represents an important therapeutic target. Several ingredients contained in Antox-D, including *Withania somnifera*, fenugreek, ginger, and *Gymnema sylvestre* have previously demonstrated potential insulin-sensitizing and metabolic regulatory effects in preclinical and clinical studies (10,12,18,19).

The study also demonstrated favorable effects on metabolic syndrome severity, as evidenced by a significant reduction in the MetS Z score in the treatment group, whereas the placebo group showed a slight increase from baseline. Anthropometric assessments further supported the metabolic benefits of Antox-D. Participants receiving the investigational product experienced statistically significant reductions in body weight and BMI over the 90-day study period compared with placebo. Although the magnitude of weight reduction was modest, weight reduction is clinically desirable in T2DM management, especially when compared with certain antidiabetic therapies associated with weight gain. Improvement in body weight may potentially be associated with metabolic effects reported for some constituent ingredients in published literature. Notably, waist circumference did not change significantly between groups, possibly due to the relatively short duration of intervention.

The study also demonstrated favorable effects on lipid parameters over the 90-day treatment period. Participants receiving Antox-D showed greater improvement in lipid

profile markers compared with placebo, particularly with respect to LDL cholesterol reduction. LDL cholesterol decreased by 7.53% in the treatment group compared with 1.92% in the placebo group, with a statistically significant between-group difference at Day 90. Total cholesterol, triglycerides, and VLDL cholesterol also demonstrated reductions from baseline in both groups, while HDL cholesterol remained stable throughout the study period. Improvement in lipid parameters may potentially be associated with the combined effects of phytoconstituents such as fenugreek, jamun, bitter melon, neem, and amla, which have previously demonstrated hypolipidemic, antioxidant, and metabolic regulatory properties in published preclinical and clinical studies (5,21,24,32,37).

The beneficial effects observed on fatigue severity and diabetes-related quality of life are clinically important findings of this study. Chronic fatigue is a commonly reported symptom among patients with T2DM and may result from persistent hyperglycemia, insulin resistance, psychological stress, and reduced physical activity. Participants receiving Antox-D demonstrated greater improvement in Fatigue Severity Scale scores compared with placebo beginning at Day 60 and continuing through Day 90.

Similarly, improvements observed in several domains of diabetes-related quality of life suggest that participants perceived better disease management and treatment satisfaction while receiving the investigational product. Statistically significant improvements were observed in satisfaction related to diabetes treatment, time required for disease management, exercise, diabetes check-ups, and knowledge regarding diabetes. These findings are particularly relevant because treatment satisfaction and quality of life strongly influence long-term adherence to therapeutic interventions in chronic metabolic diseases.

The present study did not demonstrate statistically significant reductions in serum CRP levels in both groups. Chronic low-grade inflammation is recognized as an important contributor to insulin resistance and diabetes progression. Although several ingredients of Antox-D possess documented anti-inflammatory activity, the 90-day duration of the study may have been insufficient to demonstrate measurable reductions in CRP, particularly in participants with relatively modest baseline inflammatory burden. Additionally, CRP is influenced by multiple physiological and environmental variables, which may have contributed to variability in results.

No major safety concerns related to the investigational product were identified during the 90-day study period. No serious adverse events, clinically significant laboratory abnormalities, or discontinuations related to the investigational product were reported.

Hematological, hepatic, renal, and vital sign assessments remained within clinically acceptable limits in both groups.

The strengths of the present study include its randomized, double-blind, placebo-controlled design, use of clinically relevant glycemic and metabolic endpoints, and evaluation of both objective biochemical parameters and patient-reported outcomes. The inclusion of participants receiving stable oral hypoglycemic therapy also reflects routine clinical practice and enhances the practical applicability of the findings.

Nevertheless, certain limitations should be acknowledged. The duration of the study was limited to 90 days, which may not fully capture long-term efficacy, sustainability of glycemic benefits, or delayed adverse effects. The sample size, although adequate to detect differences in primary outcomes, may not have been sufficiently powered for certain secondary endpoints such as CRP and quality-of-life subdomains. In addition, the study evaluated a polyherbal formulation; therefore, the relative contribution of individual ingredients to the observed effects cannot be determined. Dietary intake, physical activity, and adherence to lifestyle modifications were not quantitatively standardized, which may also have influenced outcomes.

Overall, the findings of the present clinical study suggest that Antox-D liquid may serve as a beneficial adjunctive nutraceutical intervention in individuals with T2DM receiving conventional oral hypoglycemic therapy. The formulation demonstrated improvements in glycemic control, insulin resistance, metabolic parameters, fatigue, and quality of life while maintaining an acceptable safety and tolerability profile These findings suggest that Antox-D may have potential as an adjunctive nutraceutical intervention in individuals with T2DM receiving conventional oral hypoglycemic therapy.

23. CONCLUSION

- HbA1c levels decreased significantly in the Antox-D group from 7.48 ± 0.32% at screening to 6.85 ± 0.36% at Day 90, corresponding to an 8.34% reduction, compared with a 2.72% reduction in the placebo group ($p = 0.0002$).
- Fasting plasma glucose demonstrated significant improvement in the Antox-D group, with statistically significant between-group differences observed at Day 60 ($p = 0.028$) and Day 90 ($p = 0.002$).
- Postprandial plasma glucose levels showed greater numerical reduction in the Antox-D group (15.09%) compared with placebo (8.00%) at Day 90.
- Antox-D was associated with statistically significant improvements in insulin resistance parameters compared with placebo. Fasting insulin levels decreased by 9.53% in the treatment group compared with 2.70% in the placebo group ($p = 0.009$).
- HOMA-IR decreased by 16.49% in the Antox-D group, whereas the placebo group showed a 2.77% increase from baseline. The between-group difference at Day 90 was statistically significant ($p = 0.0004$).
- Metabolic syndrome severity improved significantly in the Antox-D group, with a 35.47% reduction in MetS Z score, whereas the placebo group showed a 2.43% increase in MetS Z score over the study period ($p = 0.027$).
- Antox-D demonstrated favorable effects on lipid profile parameters over the 90-day treatment period, with significant reduction in LDL cholesterol compared with placebo ($p = 0.0006$). Total cholesterol, triglycerides, and VLDL cholesterol also demonstrated numerical improvements from baseline.
- Statistically significant reductions in body weight and BMI were observed in the Antox-D group compared with placebo over the 90-day treatment period.
- Fatigue Severity Scale scores improved significantly in the Antox-D group at Day 60 and Day 90 compared with placebo, indicating improvement in participant-reported fatigue.
- Diabetes-related quality of life demonstrated significant improvement in the Antox-D group across multiple domains, including satisfaction with diabetes treatment, diabetes management, exercise, diabetes check-ups, and knowledge regarding diabetes.
- No statistically significant changes were observed in serum CRP levels between the study groups during the 90-day study period.
- No serious adverse events, clinically significant safety concerns, or treatment discontinuations related to the investigational product were reported.
- Overall tolerability scores remained within the ‘excellent tolerability’ category throughout the study period in both groups.

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