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(RESEARCH ARTICLE)

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Efficacy and Safety of Rasayanam Gluco-Care in Adults with Type 2 Diabetes Mellitus: A Randomized, Double-Blind, Placebo-Controlled Clinical Study

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Abstract

Background: Type 2 Diabetes Mellitus is a chronic metabolic condition marked by insulin resistance and β-cell impairment, resulting in hyperglycaemia and related consequences. While pharmaceutical interventions are standard, the increasing interest in nutraceuticals has driven research into herbal formulations.

Methods: This was a prospective, randomized, double-blind, placebo-controlled, two-arm, parallel-group, multi-center study conducted across two clinical sites in Pune, India. Forty adult patients (aged 18–70 years) with established T2DM on stable conventional therapy were grouped randomly in a 1:1 ratio to receive either Rasayanam Gluco-Care (30 ml twice daily) or a placebo juice for 30 days. An alteration in glycosylated haemoglobin (HbA1c) between baseline to Day 30 was the primary endpoint. Secondary endpoints encompassed alterations in Quality of Life (QoL) assessed with the QOLID22 questionnaire, safety assessments through adverse event (AE) monitoring, and changes in haematological parameters.

Results: All 40 randomized subjects completed the study, with no protocol deviations affecting analysis. Baseline demographics were balanced between groups with no statistically significant differences in age, gender, BMI, or clinical history. The Rasayanam group demonstrated significantly reduced HbA1c levels compared to the placebo group. The mean change in HbA1c from baseline to Day 30 was -1.04% in the Rasayanam group, compared to +0.08% in the placebo group ($p < 0.001$). The least squares mean difference in HbA1c between groups was -1.18% (95% CI: -1.44 to -0.92), demonstrating strong statistical and clinical relevance. No significant adverse events or treatment-emergent adverse events (TEAEs) were documented. The findings of this study can therefore act as a catalyst for incorporating proven Ayurvedic formulations into conventional diabetes management, in accordance with the WHO's global strategy on traditional medicine.

Keywords: Type 2 Diabetes Mellitus; Rasayanam Gluco-Care; Nutraceuticals; Hba1c; Herbal Medicine

1. Introduction

Diabetes mellitus (DM) is a non-infectious endocrine disorder marked by improper carbohydrate metabolism and hyperglycemia resulting from either deficiency or inadequacy of insulin. It results in problems including microvascular (e.g., nephropathy, retinopathy) and macrovascular diseases (e.g., coronary heart disease, peripheral vascular disease). The condition is categorized into two types: (a) Type 1 DM (T1DM) which is insulin-dependent due to the destruction of pancreatic β-cells and (b) Type 2 DM (T2DM) which is non-insulin-dependent and is associated with insulin resistance and obesity. Apart from this, Gestational DM which occurs during pregnancy, affects 2–4% of cases, usually in the second or third trimester [1].

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As per the International Diabetes Federation (2016), 415 million people globally are affected, which is expected to rise to 642 million by 2040. India, termed the "diabetes capital of the world", had 61.3 million diabetics, and is expected to double by 2030. Urbanization, lack of physical activity, stress, poor diet, malnutrition, alcohol consumption, and infections contribute to its rise. The condition is more prevalent among women and less educated individuals, particularly in developing countries [2].

Prediabetes is a crucial warning stage characterized by higher blood glucose levels that do not yet meet the criteria for T2DM. Without intervention, many individuals with prediabetes progress to full-blown diabetes within a few years. Diabetes is diagnosed using various blood sugar tests including finger-prick test, glucose tolerance test, fasting blood sugar test, and glycohemoglobin (HbA1c). Normally fasting glucose is around 80 mg/dL and postprandial up to 160 mg/dL [3]. There are several factors which affect diabetes, among them oxidative stress plays an important role in diabetes pathogenesis. It involves an imbalance between reactive oxygen species (ROS) and antioxidants. These ROS damage cells and tissues, contributing to atherosclerosis, β-cell dysfunction, and complications. Other key molecular pathways involved include the glucosamine pathway, sorbitol pathway, and protein kinase C stimulation [4].

The growing prevalence of T2DM and its antecedent, prediabetes, has intensified the global search for effective and safe preventive strategies. T1DM is managed with insulin, while Type 2 is treated with oral hypoglycemics like sulphonylureas, thiazolidinediones, and peptide analogs [5]. However, synthetic drugs often have adverse effects such as nausea, vomiting, dysentery, and anemia, thereby shifting the trend towards traditional and ayurvedic medications for curbing the cases of DM [6]. The WHO has identified 21,000 plants utilized for medical uses globally, of which 2,500 species are found in India. Approximately 800 plants have been documented to exhibit antidiabetic properties. A diverse array of plant-derived active molecules has demonstrated potential for application in diabetes treatment [7]. Widely used in Indian and Chinese traditional medicine for their minimal side effects, affordability, and accessibility, such herbal approaches include formulations like Rasayanam Gluco-Care (RGCare), an Ayurvedic polyherbal blend known for its rejuvenating, antidiabetic, antioxidant, and adaptogenic properties. It enhances metabolic health, supports pancreatic function, and mitigates oxidative stress and inflammation. The formulation contains key ingredients i.e. *Momordica charantia* (*Karela*) exhibits significant antidiabetic effects through various mechanisms such as insulin-mimetic activity, enhancement of glucose uptake, stimulation of insulin secretion, inhibition of gluconeogenesis, and modulation of key metabolic enzymes [8]. *Eugenia jambolana* (*Jamun*) contains malvidin and ferulic acid [9]. Its extract significantly restored antioxidant enzyme levels, including glutathione peroxidase**,** catalase**,** glutathione and superoxide dismutase (SOD) by free radical scavenging activity and bioactive phytochemicals in the seed kernel [10]. *Gymnema sylvestre* (*Gudmar*) promotes β-cell regeneration, suppresses of sweet taste receptors, which reduces sugar cravings and stimulates insulin secretion [11]. Gymnemic acids, gurmarin, and gymnemasaponins were highlighted for their potent biological activities related to glucose metabolism [12]. *Pterocarpus marsupium* (*Vijaysar*), a natural analog of resveratrol, known to enhance insulin sensitivity and reduce blood glucose levels [13-15]. Marsupsin and epicatechin demonstrated β-cell regenerative properties and improved insulin secretion. Liquiritigenin and berberine inhibit key enzymes like α-glucosidase and aldose reductase, reducing postprandial hyperglycemia. Other components of the RGCare have *Emblica officinalis (Amla)* which is rich in polyphenols and antioxidants [16]. It is rich in polyphenolics, particularly gallic acid**,** ellagic acid, and ascorbic acid**,** which reduces oxidative stress, a major contributor to insulin resistance and β-cell dysfunction, enhance insulin signalling pathways**,** thereby improving glucose uptake and improve lipid metabolism, reducing triglycerides and low-density lipoprotein levels. Research has also revealed decreased fasting blood glucose and HOMA-IR scores (Homeostatic Model Assessment for Insulin Resistance), improved serum insulin levels and reduced levels of malondialdehyde (MDA), a marker of lipid peroxidation - indicating reduced oxidative stress [17]. *Trigonella foenum-graecum* (Fenugreek) delays sugar absorption and enhances insulin release [18-20]. Diosgenin (a steroidal saponin), flavonoids, polyphenols, alkaloids (e.g., trigonelline), galactomannans (soluble fiber) are recognized for their hypoglycemic, insulin-sensitizing, and antioxidant properties [21]. *Azadirachta indica* (*Neem*) lowers blood glucose and improves circulation [22]. The silver particles exhibited strong inhibitory effects on α-glucosidase and α-amylase, enzymes critical for carbohydrate digestion. The inhibition of these digestive enzymes postpones the absorption of glucose in the intestine and helps in reducing postprandial hyperglycemia, a key therapeutic target in T2DM [23]. *Lagerstroemia speciosa* (Banaba) contains corosolic acid with insulin-like effects [24, 25]. The NiO nanoparticles developed using Banaba demonstrated inhibitory activity against α-glucosidase and α-amylase enzymes. The results were dose-dependent, with the NiO nanoparticles from *Lagerstroemia speciosa* showing the highest antidiabetic potential. As diabetes is a growing global concern, especially in developing countries, the use of traditional herbal medicine offers a safer, holistic alternative with minimal side effects, showing promise in long-term diabetes management and prevention.

However, most of the herbal products are introduced in the market based on empirical knowledge rather than rigorous scientific trials. With India facing a growing diabetic population and rising concerns over the adverse effects of long-term use of synthetic drugs, such controlled trials are essential. This gap between traditional claims and clinical

validation is a significant barrier to integrating nutraceuticals into evidence-based healthcare. Therefore, the RGCare study, designed as a prospective, randomized, double-blind, placebo-controlled clinical trial addresses this gap by evaluating a well-established herbal formulation through robust scientific methodology. The effectiveness of RGCare was compared to an identical placebo in reducing HbA1c levels in adults diagnosed with T2DM. The study not only assesses the clinical efficacy in glycemic control but also evaluates the broader impact on quality of life of T2DM patients using the QOLID questionnaire after treatment with RGCare versus placebo and determines the safety and tolerability of RGCare based on adverse event reporting and changes in laboratory parameters. It also responds to the need for holistic, safer, and cost-effective options that can complement or substitute conventional antidiabetic therapies. These objectives are directly aligned with the research gap by aiming to generate concrete clinical evidence that either substantiates or challenges the therapeutic claims of herbal antidiabetic formulations through statistically valid, ethically sound research.

2. Materials and Methods

2.1. Drug details

2.1.1. Study drug (Rasayanam Gluco-Care Juice)

RGCare (https://rasayanam.in/products/glucocare-juice) is a polyherbal formulation made up of standardized extracts derived from eight medicinal plants traditionally used in Ayurvedic medicine for glycemic control and metabolic support. The approximate formulation (per 100 g) includes extracts derived from Jamun (*Syzygium cumini*) (15 %), Karela (*Momordica charantia*) (10 %), Gudmar (*Gymnema sylvestre*) (2.5 %), Vijaysar (*Pterocarpus marsupium*) (2 %), Methi (*Trigonella foenum-graecum*) (2 %), Neem (*Azadirachta indica*) (2 %), and Banaba (*Lagerstroemia speciosa* L.) (1.5 %) and Amla (*Emblica officinalis*) juice (33 mL).

2.1.2. Comparative drug - Placebo

The juice formulation consists of 1 liter of demineralized water as the base, complemented by 0.5 ml of caramel color to enhance visual appeal. Pectin (E440/INS 440) was used as a thickening agent (1 g) to improve texture and consistency. Kutki (200 mg), known for its distinct bitter profile and potential hepatoprotective benefits, was added to impart a characteristic bitter taste. Additionally, 1 g of salt was incorporated to balance the overall flavor profile.

2.2. Study design and plan

This study employed a prospective, randomized, double-blind, placebo-controlled, two-arm, parallel-group design to evaluate the effectiveness and safety of RGCare juice in people diagnosed with T2DM. The trial was conducted at two independent clinical sites. One was Sanjeevan Hospital F.P23, off Karve Road, Kashibai Khilare Path, Opposite Pune Central, Pune, Maharashtra-411004 and second was Dr. Kinholkar Speciality Clinic B104, Bhamini arcade, near PL Deshpanse Garden Sinhgad Pune, Opposite Roshan Kritika society Pune, Maharashtra- 411030, India, adhering strictly to the International Council for Harmonisation (ICH) Good Clinical Practice (GCP) norms and Indian regulatory frameworks, including the New Drugs and Clinical Trial Rules.

2.3. Study population

A total of 42 patients were screened, out of which 40 eligible participants were randomized in a 1:1 ratio into two groups: one receiving the investigational product (RGCare Juice) and the other an identical placebo juice. The randomization process was conducted using a pre-generated code held securely to maintain the blinding of both investigators and participants throughout the study. Each subject was instructed to consume 750 ml of the assigned juice twice daily, two hours before breakfast and dinner, for a treatment duration of 30 days.

The inclusion criteria required subjects to be adults (aged 18–70 years) with confirmed T2DM diagnosis, who are on standard medication, capable of providing informed consent in writing, complying with the investigation's visit schedule, agree to take investigational product till 30th day, willing to follow the procedures as per the study protocol and treatment. Additionally, women of childbearing potential were required to employ double-barrier contraception throughout the study and must present a negative pregnancy test prior to enrollment. Subjects were excluded from the study if they had a history of insulin use for more than two weeks within two months prior to the screening visit, underwent bariatric surgery or any gastric bypass, or planned to undergo such a procedure during the study. Additional exclusion criteria included a history of unstable angina, congestive heart failure (CHF), peripheral arterial event, cerebrovascular accident, transient ischemic attack, myocardial infarction, or any revascularization procedure within the six months preceding the screening visit, as well as planned vascular procedures or surgeries during the

study period. Furthermore, individuals with a history of cancer or malignancy, pregnancy or breastfeeding, intent to become pregnant during the study, known or suspected infection with human immunodeficiency virus, or any condition, laboratory abnormality, or concomitant therapy that, in the Investigator's opinion, could pose a risk to the subject or render participation contrary to the subject's best interest were also excluded. The history or presence of any medical conditions which impacts the quality of life, hypersensitivity to product or placebo, use of prescription medications and/or non-prescription medications for weight loss, current diagnosis or medical history of alcoholism and drug dependence, use of medications that are prohibited with the herbal products as per investigator discretion, any other condition which the principal investigator thinks may jeopardize the safety of subjects - patients with uncontrolled, unstable comorbidities and subjects currently enrolled in or who have not completed at least 30 days since concluding another investigational study or who are receiving other investigational agents are also pertinent considerations. The flow chart of the study is represented in Figure 1.

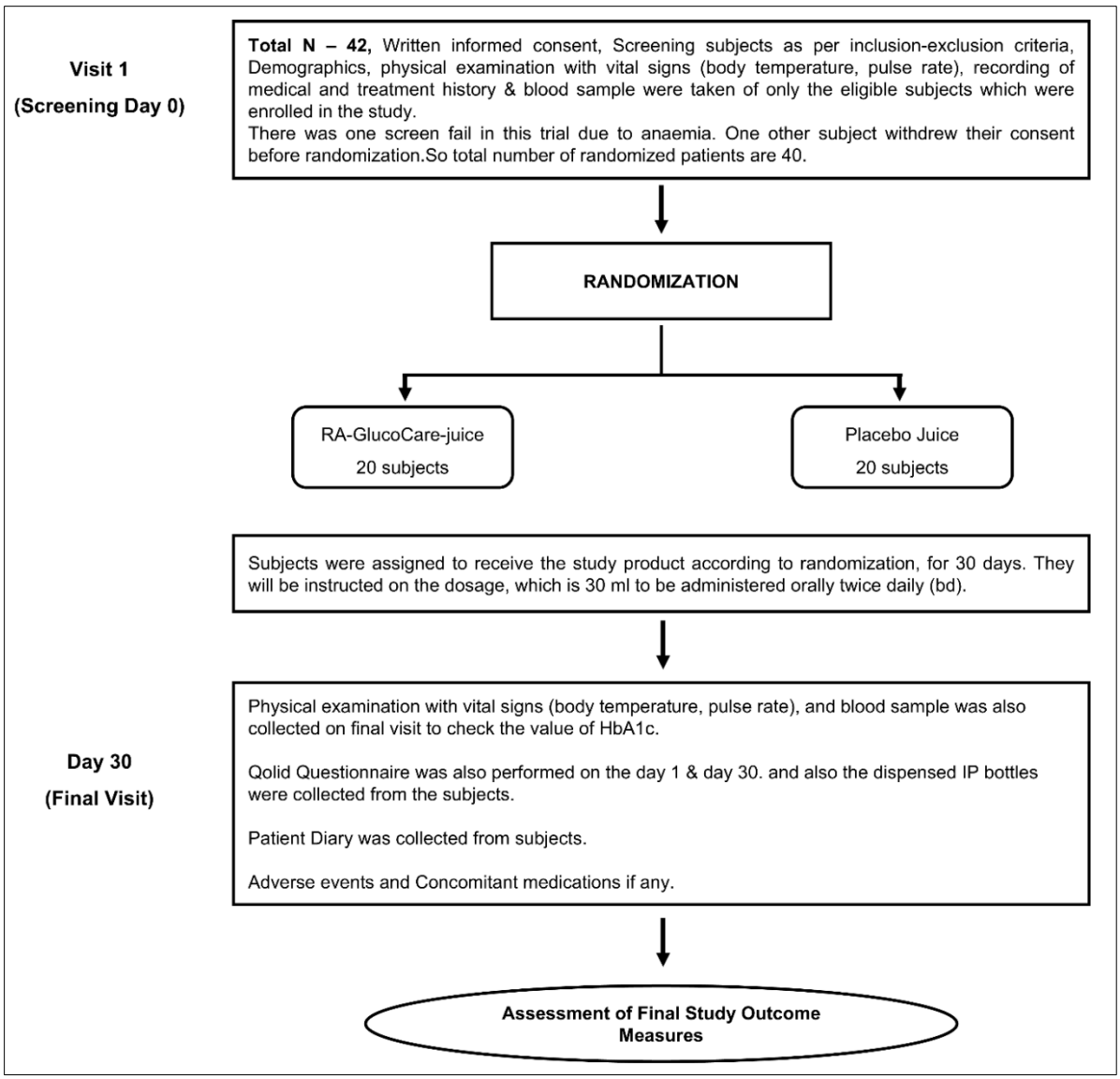

Figure 1 Study flow chart

2.4. Clinical endpoints and statistical approach

Clinical assessments were performed at baseline (Day 0) and at the end of the study (Day 30). The primary endpoint was the change in HbA1c levels, while secondary endpoints included changes in quality of life assessed by the QOLID-22 questionnaire, monitoring of TEAEs, and changes in basic haematological parameters. Compliance was monitored by tracking the return of used investigational product bottles and patient diaries. All safety and efficacy data were analyzed statistically using Analysis of Covariance (ANCOVA), and significance was defined at $p < 0.05$. The study

ensured 100% treatment compliance and reported no major protocol deviations, withdrawals, or adverse safety concerns.

This rigorous and ethically structured methodology aimed to provide robust clinical evidence for the efficacy and safety of RGCare, addressing the urgent need for validated herbal interventions in diabetes care.

2.5. Assessment Criteria

The assessment criteria included a comprehensive evaluation of demographic parameters such as age, date of birth, gender, race, weight, height, and Body Mass Index (BMI). A detailed physical examination was conducted, encompassing vital signs and systemic evaluations, including general appearance, head and neck, cardiovascular, respiratory, gastrointestinal, and nervous systems, along with blood pressure (B.P.), body temperature, and pulse rate measurements. Clinical laboratory investigations comprised hematological tests, including red blood cell (RBC) count, white blood cell (WBC) count, platelet count, hemoglobin concentration, and hematocrit levels. For women of childbearing age, a urinary pregnancy test (UPT) was performed to rule out pregnancy. Glycemic control was assessed using HbA1c levels. Quality of life was evaluated using the QOLID questionnaire. Additionally, any adverse events and prior medications, if applicable, were recorded throughout the study duration.

3. Results and discussion

The evaluation of RGCare for the management T2DM provides compelling clinical evidence regarding its efficacy and safety profile. The study recruited 40 patients, randomized into two equal groups receiving either RGCare Juice or a placebo. The primary efficacy endpoint was the change in HbA1c, while secondary endpoints included changes in quality of life (QOLID scores) and safety outcomes.

3.1. Change in Glycated Haemoglobin (HbA1c) and QOLID assessment

At baseline, the mean HbA1c levels were 7.68 ± 1.55 % in the RGCare group and 8.20 ± 1.89 % in the placebo (Figure 2). After 30 days of intervention, the mean HbA1c level in the treatment group significantly decreased to 6.64 ± 1.53 %, while it slightly increased to 8.28 ± 1.61 % in the placebo group. The adjusted least squares mean difference between the groups was -1.18 (SE = 0.126), with a p-value of <0.001, indicating significant difference (Table 1). This reflects a 13.6 % reduction in the treatment group compared to a marginal 1.0 % increase in the placebo group. This outcome is significant as even a 1% drop in HbA1c is associated with a 21% decrease in diabetes-related mortality and a 14% decline in myocardial infarctions, as reported by the United Kingdom Prospective Diabetes Study (UKPDS) [26].

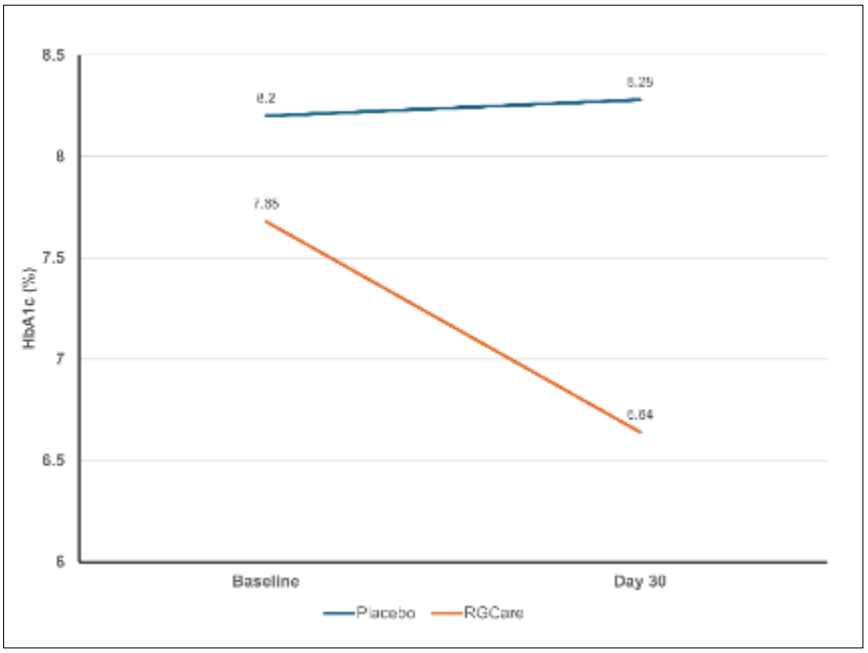

Figure 2 Mean HbA1c at baseline and Day 30 between RGCare and Placebo

The findings align with earlier studies examining the effects of herbal interventions on glycemic control. A study by Baskaran et al. [27] evaluating *Gymnema sylvestre*, one of the key ingredients in RGCare, reported a significant HbA1c reduction over 10 months in diabetic patients. Similarly, *Momordica charantia* (bitter melon) and *Pterocarpus marsupium* (*Vijaysar*) have been shown to lower blood glucose and improve insulin sensitivity in previous trials [14, 27]. Comparable polyherbal formulations often report reductions between 0.5% and 1.0% over longer periods, and a recent randomized controlled trial on a standardized multi-herb formula showed a significant but smaller HbA1c reduction over 90 days [28]. However, what sets the current study apart is the polyherbal approach, which integrates the synergistic effects of multiple adaptogenic herbs, thereby offering a broader therapeutic mechanism through antioxidant, anti-inflammatory, and beta-cell regenerative pathways. The rapid decline observed here suggests a synergistic action among the herbal components. Intensive glycemic control, with reductions of this magnitude, is well-established as a means to reduce microvascular complications in T2DM patients according to large-scale studies. Mechanistically, the efficacy may be attributed to the complementary actions of ingredients such as *Momordica charantia* (acting via insulin-mimetic effects), *Syzygium cumini* (enhancing insulin sensitivity and providing antioxidant activity), *Gymnema sylvestre* (stimulating β-cell regeneration), and others substantiated in both experimental and clinical research [29].

Table 1 Effect of Rasayanam Gluco-Care versus placebo on glycated hemoglobin (HbA1c) over 30 days in adults

	RG Care (N = 20)		**Placebo (N = 20)**	
	Observed	**Change from baseline**	**Observed**	**Change from baseline**
Baseline				
N	20		20	
Mean	7.68		8.20	
SD	1.522		1.889	
Median	7.35		7.80	
Min	5.30		5.90	
Max	12.20		13.80	
Day 30				
N	20	20	20	20
Mean	6.64	-1.04	8.28	0.08
SD	1.527	0.448	1.607	0.425
Median	6.50	-1.10	8.00	0.05
Min	4.50	-2.10	6.00	-0.80
Max	11.50	-0.40	13.00	0.90
LS Mean (SE)		6.87 (0.089)		8.05 (0.089)
95% CI (LS Mean)		(6.69, 7.05)		(7.87, 8.23)
LS Mean Difference (SE)		-1.18 (0.126)		
p-value		<0.001*		
95% CI (LS Mean Diff)		(-1.44, -0.92)		

Least squares mean, standard errors, and confidence intervals come from analysis using an analysis of covariance (ANCOVA) model with change in HbA1c as the dependent variable, treatment as fixed effect and baseline score as a covariate.
*indicates significant result

The secondary outcome - quality of life, was measured using the validated QOLID questionnaire, and it improved significantly in both groups; however, the RGCare exhibited a larger gain than placebo (Figure 3). At baseline, the mean QOLID score in the Rasayanam group was 82.65, which rose to 93.70 at Day 30, representing a significant improvement of 11.05 points (13.4%). In contrast, the placebo group showed an increase from 83.65 to 92.20, or 8.55 points (10.2%). Although both groups exhibited improvement, likely due to general trial engagement and supportive care, the treatment

group's superior outcome was statistically significant (p = 0.036) (Table 2). This supports the hypothesis that RGCare not only aids in physiological glucose control but also enhances patients perceived health and well-being. Improvements likely reflect not only better metabolic status but also mitigation of symptomatic burden and improved overall wellbeing, trends observed in prior trials involving integrative or herbal diabetes interventions. Literature increasingly recognizes that even modest glycemic improvements can translate to meaningful QOL gains in people with chronic diabetes [29].

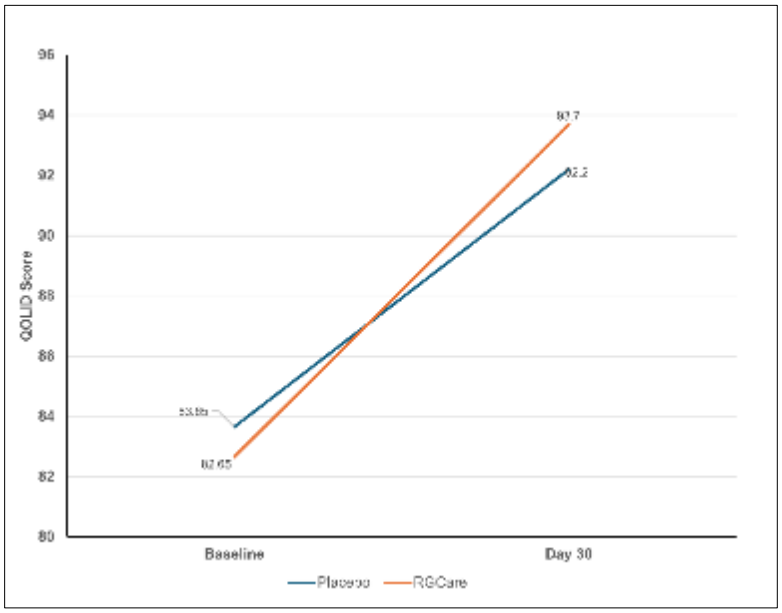

Figure 3 Mean QOLID Assessment Score change from baseline between RGCare and Placebo

Table 2 Change in Quality of Life in Diabetes (QOLID-22) scores over 30 days in the Rasayanam Gluco-Care and placebo groups

	RG Care (N = 20)		**Placebo (N = 20)**	
	Observed	**Change from baseline**	**Observed**	**Change from baseline**
Baseline				
N	20		20	
Mean	82.65		83.65	
SD	5.860		5.779	
Median	83.00		84.00	
Min	70.00		73.00	
Max	95.00		95.00	
Day 30				
N	20	20	20	20
Mean	93.70	11.05	92.20	8.55
SD	3.080	5.586	3.334	3.663
Median	93.50	11.50	93.50	9.00
Min	86.00	-1.00	86.00	2.00
Max	99.00	22.00	97.00	15.00
LS Mean (SE)		93.86 (0.591)		92.04 (0.591)

95% CI (LS Mean)		(92.66, 95.06)		(90.84, 93.24)
LS Mean Difference (SE)		1.82 (0.837)		
p-value		0.036*		
95% CI (LS Mean Diff)		(0.13, 3.52)		

Least squares mean, standard errors, and confidence intervals come from analysis using an analysis of covariance (ANCOVA) model with change in QOLID Assessment Score as the dependent variable, treatment as fixed effect and baseline score as a covariate.
*indicates significant result

From a pharmacological standpoint, RGCare exhibits multidirectional antidiabetic mechanisms including inhibition of carbohydrate-metabolizing enzymes, regulation of glucose homeostasis, improvement of mitochondrial function, regeneration of pancreatic beta-cells, inhibition of glucose absorption in the intestine and enhancement of glucose uptake in peripheral tissues [30]. These mechanisms are not speculative; rather, they are supported by both *in vivo* and *in vitro* studies for individual components, such as *Gymnema sylvestre* [12, 29]**,** *Azadirachta indica* [31] and *Emblica officinalis* [32].

In this context, a recent randomized, placebo-controlled, proof-of-concept clinical study offers valuable insights into how traditional Ayurvedic medicine can play a role in curbing this progression. The research evaluated the efficacy and safety of *Nisha-Amalaki* capsules, a standardized Ayurvedic formulation combining *Curcuma longa* (turmeric) and *Emblica officinalis* (*amla*), to prevent the transition from prediabetes to diabetes over a six-month period. Conducted on 62 prediabetic participants, the study was designed to compare *Nisha-Amalaki* capsules with a placebo, while all participants also received dietary and lifestyle counseling. The primary goal was to assess changes in the Indian Diabetes Risk Score, a validated screening tool that includes both modifiable and non-modifiable risk factors. Secondary outcomes encompassed variations in fasting and post-glucose blood sugar levels, HbA1c, insulin levels, insulin resistance (assessed using HOMA-IR), and indicators of inflammation and oxidative stress. Additionally, the study evaluated traditional Ayurvedic symptom scores and health-related quality of life using the SF-36 questionnaire. Participants who received *Nisha-Amalaki* showed marked improvements in glycemic parameters: fasting glucose, post-OGTT glucose, HbA1c, and insulin levels all declined meaningfully compared to baseline and to the placebo group. Insulin sensitivity improved, as indicated by a reduction in HOMA-IR. Moreover, there was a favorable modulation of oxidative stress markers (decreased MDA and increased SOD levels) and inflammation (reduced C-reactive protein levels). These biochemical changes suggest that the formulation not only aided in glucose regulation but also addressed underlying metabolic dysfunctions associated with the progression of diabetes. Importantly, participants reported improvement in Ayurvedic symptoms associated with prediabetes, such as excessive thirst, urination, fatigue, and burning sensations. Moreover, for the treatment group, quality of life improved significantly, particularly in aspects related to energy levels, emotional well-being, and general health, especially in regions where Ayurveda is culturally rooted and healthcare resources are limited, such formulations could be instrumental in reducing the burden of diabetes [33].

A recent placebo-controlled clinical study evaluated the impact of daily supplementation with 500 mg of a standardized *amla* formulation on various health biomarkers in healthy adults. The study demonstrated that *amla* intake led to significant improvements in blood fluidity, a primary marker of endothelial function, and reductions in oxidative stress biomarkers such as von Willebrand Factor (vWF) and 8-hydroxy-2-deoxyguanosine (8-OHdG), both of which are associated with endothelial dysfunction and diabetic vasculopathy. Furthermore, fasting glucose levels showed a statistically significant reduction after four weeks of supplementation, suggesting a potential glycemic benefit even in non-diabetic individuals. This supports earlier preclinical and clinical evidence that *amla* and its polyphenolic constituents, particularly ellagitannins and their gut-derived metabolites such as urolithins, can improve glucose metabolism, modulate insulin secretion, and reduce systemic oxidative damage, which are key mechanisms implicated in diabetes pathogenesis. The clinical translation of these findings, especially when extended to at-risk populations with prediabetes could inform integrative healthcare models that blend traditional nutraceuticals with contemporary lifestyle interventions. Nevertheless, the results provided compelling preliminary evidence that *amla* supplementation can modulate key risk factors and pathophysiological processes involved in diabetes, making it a valuable adjunct in the global effort to halt the diabetes epidemic [34].

This study also provides an exploration of *Gymnema sylvestre*, a medicinal plant traditionally used in Ayurvedic medicine for managing DM. This study bridges ethnopharmacological knowledge with contemporary biomedical research, demonstrating that *G. sylvestre* exerts a broad spectrum of antidiabetic effects. Central to its activity are gymnemic acids, a group of bioactive saponins that not only suppress the perception of sweetness, thereby helping reduce sugar cravings, but also modulate multiple metabolic pathways involved in glucose and lipid homeostasis.

Mechanistically, gymnemic acids inhibit intestinal glucose absorption, stimulate insulin secretion, promote the regeneration of pancreatic β-cells, and improve insulin sensitivity through interaction with PPARγ receptors. These actions collectively contribute to lowering fasting blood glucose, enhancing glucose uptake in peripheral tissues, and reducing postprandial glucose spikes. Notably, extracts of *G. sylvestre* have also been associated with β-cell repair in diabetic models, supporting its role not just in symptom control but in addressing disease pathogenesis. Furthermore, its influence on lipid metabolism indicates a potential role in mitigating diabetes-associated cardiovascular risks. Overall, *G. sylvestre* is a promising candidate for adjunct therapy in diabetes management, with potential to inspire the development of novel plant-derived antidiabetic agents [35].

The antidiabetic potential of the methanolic heartwood extract of *Pterocarpus marsupium* (MPME) through its dual action on oxidative stress and glucose uptake in liver-derived HepG2 cells was reported by Dar et al. [36]. Using advanced analytical techniques such as GC–MS, UPLC–MS, and HPTLC, they identified a rich profile of bioactive phenols, flavonoids, and terpenoids, notably quercetin and epicatechin. At concentrations ranging from 23.43 to 93.75 µg/mL, MPME demonstrated no cytotoxicity while significantly reducing oxyradical levels and attenuating apoptosis induced by high-glucose and H_2O_2-mediated oxidative stress. Importantly, treatment with 93.75 µg/mL of MPME enhanced glucose uptake in HepG2 cells, suggesting improved insulin sensitivity and glucose metabolism. By mitigating reactive oxygen species (ROS)-induced cellular damage and promoting hepatic glucose clearance, MPME tackles critical pathophysiological features of type 2 diabetes. These *in-vitro* studies provide a compelling mechanistic basis for traditionally using *P. marsupium* in diabetes management and support further investigation into its bioactive constituents as natural therapeutic agents [36].

A study on *Momordica charantia* highlighted strong evidence for its supportive and therapeutic effects in diabetes management. Numerous *in vitro* and animal studies show reduced fasting glucose levels, improved insulin sensitivity, and better glycemic control with bitter melon extracts. It contains cucurbitane-type triterpenoids (like charantin and momordicosides), flavonoids, and polypeptide-p (an insulin-like peptide). These compounds are believed to exert antidiabetic effects. Human trials have reported modest reductions in blood glucose, though results are inconsistent [8].

Another study characterized the antidiabetic potential of *Syzygium cumini* bark decoction and a ready-to-serve drink through phytochemical profiling. Employing activity-guided fractionation, Thin Layer Chromatography, and HPLC, the researchers validated the existence of key bioactive compounds, namely umbelliferone, ellagic acid, and gallic acid, known for their antidiabetic effects. These phenolic compounds have been shown to improve insulin sensitivity, regulate glucose metabolism, and inhibit carbohydrate-digesting enzymes. The study supports the effective use of *S. cumini* based preparations in managing hyperglycemia and provides a scientific rationale for their incorporation into diabetes prevention and control strategies [37].

Patil et al. [38] presented a comprehensive evaluation of *Azadirachta indica* as a promising botanical agent in the management of DM. Drawing on various *in vitro* and *in vivo* studies, the article outlined *neem's* multifaceted mechanisms which contribute to its antidiabetic effects. A major finding was *neem's* ability to enhance glucose tolerance and reduce fasting blood glucose levels in diabetic animal models, suggesting its role in improving insulin sensitivity. *Neem* leaf and seed extracts also stimulate peripheral glucose uptake and regulate essential enzymes implicated in carbohydrate metabolism, including α-glucosidase and α-amylase. Inhibiting these enzymes helps to slow carbohydrate digestion and glucose absorption, thereby preventing postprandial blood glucose spikes. Furthermore, neem is rich in polyphenols, flavonoids, and limonoids that exert strong antioxidant activity. These compounds help scavenge free radicals, protect oxidative stress-induced damage in pancreatic β-cells, and improve overall vascular health, which are critical factors in preventing diabetes complications. The review also suggested *neem's* anti-inflammatory and hepatoprotective effects, which may support metabolic homeostasis in diabetic individuals. Overall, *Azadirachta indica* emerges as a potent candidate for adjunct therapy in diabetes management, acting through diverse pathways including glucose regulation, enzyme inhibition and oxidative stress reduction. Similarly, another study by Rivera et al. [39] employs an integrative network pharmacology and molecular docking approach to uncover the basis of the antihyperglycemic effects of *Momordica charantia* (bitter melon) and *Lagerstroemia speciosa* (banaba) in T2DM. Using advanced computational techniques, the researchers identified key protein targets implicated in T2DM, such as TNF-α, HSP90AA1, MAPK3, ALDH2, glucokinase (GCK), AKR1B1, transthyretin (TTR), and retinol-binding protein 4 (RBP4), and assessed the binding affinity of specific phytochemicals from bitter melon (e.g., cucurbitane terpenoids) and banaba (e.g., decanoic acid). The favorable docking results suggest that these bioactive compounds can engage multiple diabetes-relevant targets, potentially exerting synergistic effects on pathways related to inflammation, insulin resistance, metabolic regulation, and protein stability. In particular, terpenoids from bitter melons demonstrate promising interactions with TNF-α and HSP90AA1, while banaba components bind effectively to enzymes like GCK, which plays a central role in hepatic glucose metabolism. This multi-target engagement aligns with the therapeutic need in T2DM to modulate complex and interrelated pathophysiological processes. Although the study is computational, it provides a strong

mechanistic rationale for the traditional use of these botanicals and underscores the potential of combining bitter melon and banaba in complementary herbal formulations for diabetes management.

Equally important is the formulation's safety profile. Across the study population, no adverse effects, serious or otherwise, were reported in either the treatment or placebo group. The hematological and biochemical parameters remained within normal clinical limits, reaffirming the safety of RGCare even with daily administration over 30 days. This absence of side effects is particularly critical in the context of diabetes, where long-term use of conventional drugs like sulfonylureas [40], metformin [41] and insulin can lead to complications such as hypoglycemia, gastrointestinal discomfort, and renal impairment. Another notable observation is the study's exceptionally high compliance rate, achieved through structured patient education and close follow-up. This highlights the acceptability and palatability of the herbal juice formulation, which is a known barrier in phytotherapy but was well addressed here.

3.2. Hematological and laboratory safety

A comprehensive analysis of hematological indices was also conducted at baseline and at the end of the 30-day intervention to assess the safety profile of RGCare in comparison to placebo. The parameters evaluated included hemoglobin (Hb), platelet count, RBC and WBC count (Figure 4).

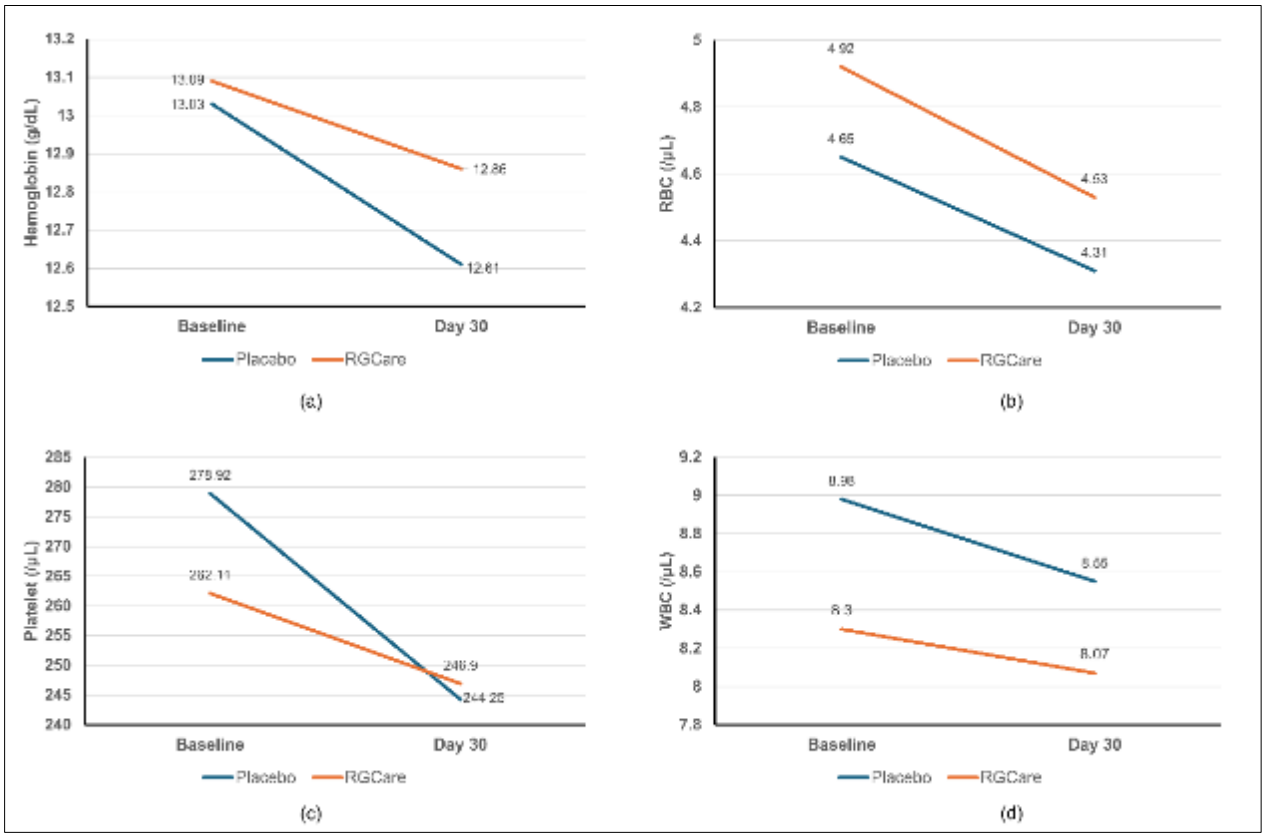

Figure 4 Mean (a) Haemoglobin, (b) RBC, (c) Platelet and (d) WBC change from baseline between RGCare and Placebo

A modest decline in hemoglobin levels (Fig. 4 (a)) was observed in both groups over the study period (RGCare: mean change –0.24 g/dL; placebo: –0.42 g/dL). Importantly, all post-treatment hemoglobin values remained within the laboratory-defined reference range. The greater decrease in the placebo was not statistically significant when compared with the RGCare group, nor was it associated with symptoms of anemia or any clinical manifestations (Table 3). Such minor variations are frequently observed in short-duration nutritional intervention trials and are considered to reflect normal physiological variability, possibly influenced by dietary habits, hydration status, or minor intercurrent illnesses during the study period [42]. The platelet count (Fig. 4 (c)) also decreased by the end of the intervention, yet all values stayed well within normal limits. There were no instances of clinically significant thrombocytopenia or related bleeding complications in any participant (Table 4). Subtle fluctuations in platelet count over time are common in outpatient settings and are rarely of clinical concern in the absence of other symptoms or abnormal laboratory findings.

Table 3 Haemoglobin levels (g/dL) at baseline and Day 30 in Rasayanam Gluco-Care and placebo groups

	RG Care (N = 20)		**Placebo (N = 20)**	
	Observed	**Change from baseline**	**Observed**	**Change from baseline**
Baseline				
N	20		20	
Mean	13.09		13.03	
SD	2.287		1.806	
Median	13.00		13.45	
Min	8.10		8.30	
Max	16.60		16.00	
Day 30				
N	20	20	20	20
Mean	12.86	-0.24	12.61	-0.42
SD	1.645	0.862	1.883	0.665
Median	12.85	-0.15	12.85	-0.45
Min	10.00	-1.40	9.00	-1.90
Max	15.50	1.90	15.60	0.70
Paired t-test Result				
Mean Diff (SE)		-0.24 (0.193)		-0.42 (0.149)
95% CI (Mean Diff)		(-0.64, 0.17)		(-0.73, -0.11)
p-value		0.237		0.011*
ANCOVA Result				
LS Mean (SE)		12.83 (0.147)		12.63 (0.147)
95% CI (LS Mean)		(12.53, 13.13)		(12.34, 12.93)
LS Mean Diff (SE)		0.20 (0.208)		
p-value		0.349		
95% CI (LS Mean Diff)		(-0.22, 0.62)		

*indicates significant result

Minor changes were seen in RBC and WBC count in both groups (Fig. 4 (b, d)), with no value dropping below reference minimums. All measured values remained inside reference ranges, and no trend indicated immune suppression, infection, or allergic responses attributable to the RGCare or placebo group. Crucially, none of the participants in either arm developed laboratory abnormalities of clinical consequence, nor were any interventions or discontinuations required due to changes in hematological parameters. No TEAEs relating to blood or immune function were observed. The overall pattern of hematological safety is strongly consistent with previously reported polyherbal and Ayurvedic antidiabetic formulations, which are generally well-tolerated and not associated with hematological toxicity in controlled studies [43, 44]. These findings reinforce the hematological safety of RGCare when used as an adjunct to conventional oral anti-diabetic therapy for at least 30 days.

Table 4 Platelet count (/μL) changes from baseline to Day 30 in Rasayanam Gluco-Care and placebo groups

	RG Care (N = 20)		**Placebo (N = 20)**	
	Observed	**Change from baseline**	**Observed**	**Change from baseline**
Baseline				
N	20		20	
Mean	262.11		278.92	
SD	73.672		67.071	
Median	242.00		271.50	
Min	120.00		152.00	
Max	420.20		409.00	
Day 30				
N	20	20	20	20
Mean	246.90	-15.21	244.25	-34.67
SD	68.951	20.829	79.280	36.820
Median	230.00	-12.50	240.50	-22.50
Min	110.00	-51.00	16.00	-164.00
Max	390.00	25.00	350.00	18.00
Paired t-test Result				
Mean Diff (SE)		-15.21 (4.658)		-34.67 (8.233)
95% CI (Mean Diff)		(-24.96, -5.46)		(-51.90, -17.44)
p-value		0.004*		<0.001*
ANCOVA Result				
LS Mean (SE)		255.02 (6.782)		236.13 (6.782)
95% CI (LS Mean)		(241.28, 268.76)		(222.39, 249.87)
LS Mean Diff (SE)		18.89 (9.627)		
p-value		0.057		
95% CI (LS Mean Diff)		(-0.62, 38.39)		

*indicates significant result

4. Conclusion and future directions

When comparing this study's outcomes with other herbal-based clinical trials, it stands out in its methodological robustness. Many earlier studies lacked placebo control or were open-label, thereby exposing outcomes to bias. The present study, by being randomized, double-blind, and placebo-controlled, eliminates much of this subjectivity and strengthens the reliability of the results. Furthermore, the current study is unique in its incorporation of both biomedical markers (HbA1c) and patient-reported outcomes (QOLID), which provides a comprehensive assessment of therapeutic efficacy. Too often, clinical trials focus solely on physiological endpoints, neglecting how patients feel and function, a limitation which is effectively overcome in this study.

Another aspect worth highlighting is the broader implication of this study on public health and integrative medicine. India faces a dual burden wherein on one hand, a rapidly increasing diabetic population and on the other, economic constraints limiting access to lifelong medication. Herbal formulations like RGCare, if clinically validated, offer an affordable, safer, and culturally acceptable alternative or adjunct to conventional therapy. The outcomes of this study

can thus serve as a catalyst for integrating validated Ayurvedic formulations into mainstream diabetes care, in alignment with WHO's global strategy on traditional medicine.

Overall, the clinical trial of RGCare yielded highly favorable results in reducing HbA1c and improving quality of life among Type 2 diabetic patients. These outcomes were achieved without adverse effects and with excellent patient compliance. The statistical significance of results, the rigorous study design, and the consistency with mechanistic understanding of the constituent herbs collectively establish this formulation as a promising candidate for integrative diabetes management.

Future studies with longer durations and larger, more diverse populations to confirm the long-term benefits and safety, might be carried out. Moreover, exploring its use as an adjunct therapy in patients already on allopathic medications could expand its clinical utility. Given the growing interest in evidence-based traditional medicine, this study contributes significantly to the evolving landscape of herbal therapeutics in chronic disease management.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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