RESEARCH PAPER

Design, Development, and Pharmacological Evaluation of a Polyherbal Formulation for the Management of Type 2 Diabetes Mellitus

Vaibhav Dagaji Aher[1], Venkateswarlu Yadavalli[2], S. Nithya[3], Vasudha Negi[4], Chandra Shekhar Tailor[5], Maxamatova Umidaxon[6], Sunil Shivhari Jaybhaye[7], V. E. Ida Christi[8*]

[1]Department of Pharmaceutical Medicine, Maharashtra University of Health Sciences, Nashik-422004, Maharashtra, India

[2]Tara Govt. College (A), Sangareddy, Sangareddy Dt., Telangana, India 502001

[3]Department of Pharmacology, Sri Ramachandra Faculty of Pharmacy, Sri Ramachandra Institute of Higher Education and Research (SRIHER) (DU), Porur, Chennai 600106, India

[4]Samrat Prthviraj Chauhan College of Pharmacy, Kokhratal, Kashipur, Udham Singh Nagar, Uttarakhand, India

[5]Pharmacognosy, School of Pharmaceutical Sciences, Shri Guru Ram Rai University, Dehradun, Uttarakhand, India

[6]Department of Folk Medicine and Pharmacology, Fergana Medical Institute of Public Health, Yangi Turon, Fergana – 150100, Uzbekistan

[7]Institute of Pharmacy, Pathrikar Campus, Highway No-06, Badnapur, 431202, India

[8*]Professor, Department of Pharmacognosy, PSG College of Pharmacy, Coimbatore – 641004, India

Email: 1969idacsha@gmail.com

Abstract

Type 2 diabetes mellitus (T2DM) is a multifactorial metabolic disorder characterized by persistent hyperglycemia, insulin resistance, and progressive pancreatic β-cell dysfunction. Although several synthetic antidiabetic drugs are available, their long-term use is often associated with adverse effects, highlighting the need for safer and multitarget therapeutic alternatives. The present study aimed to design, develop, and pharmacologically evaluate a polyherbal formulation for the management of T2DM. Hydroalcoholic extracts of *Azadirachta indica*, *Gymnema sylvestre*, *Momordica charantia*, and *Trigonella foenum-graecum* were prepared, optimized, and combined to develop a stable formulation. Physicochemical characterization and phytochemical screening confirmed formulation quality and the presence of bioactive constituents. In vitro evaluation revealed significant, concentration-dependent inhibition of α-amylase and α-glucosidase enzymes, indicating effective control of carbohydrate digestion. The formulation also exhibited strong antioxidant activity in DPPH and ferric reducing antioxidant power (FRAP) assays. Overall, the results suggest that the polyherbal formulation exerts antidiabetic effects through multitarget mechanisms involving enzyme inhibition, antioxidant action, metabolic regulation, and pancreatic protection, supporting its potential as a safe and effective therapeutic approach for T2DM.

Keywords: Polyherbal formulation, Type 2 diabetes mellitus, Antidiabetic activity, Herbal medicine, Pharmacological evaluation

How to cite this article: Aher VD, Yadavalli V, Nithya S, Negi V, Tailor CS, Umidaxon M, Jaybhaye SS, Christi VEI. Design, Development, and Pharmacological Evaluation of a Polyherbal Formulation for the Management of Type 2 Diabetes Mellitus. Int J Drug Deliv Technol. 2026;16(9s): 38-46; DOI: 10.25258/ijddt.16.9s.5

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic, progressive metabolic disorder characterized by persistent hyperglycemia resulting from insulin resistance, impaired insulin secretion, or a combination of both. According to global health estimates, the prevalence of T2DM has increased dramatically over the past few decades, largely driven by sedentary lifestyles, unhealthy dietary habits, obesity, population aging, and genetic predisposition. The long-term persistence of hyperglycemia leads to severe microvascular and macrovascular complications, including nephropathy, neuropathy, retinopathy, cardiovascular diseases, and increased morbidity and mortality, posing a significant socioeconomic burden worldwide[1,2].

The pathophysiology of T2DM is complex and multifactorial, involving dysregulation of glucose and lipid metabolism, chronic low-grade inflammation, oxidative stress, mitochondrial dysfunction, and progressive loss of pancreatic β-cell mass and function.

Excessive production of reactive oxygen species (ROS) under hyperglycemic conditions contributes significantly to insulin resistance and β-cell apoptosis. Therefore, effective management of T2DM requires therapeutic strategies capable of targeting multiple pathological pathways rather than focusing on a single molecular target[3,4].

Conventional antidiabetic therapies, including biguanides, sulfonylureas, thiazolidinediones, α-glucosidase inhibitors, and insulin, are widely used for glycemic control. However, these agents are often associated with limitations such as hypoglycemia, gastrointestinal disturbances, weight gain, hepatotoxicity, and reduced long-term patient compliance. Moreover, most synthetic drugs primarily address hyperglycemia without adequately preventing oxidative stress and diabetes-associated complications. These limitations highlight the growing need for alternative or complementary therapeutic approaches with improved safety profiles and broader mechanisms of action[5,6].

Herbal medicines have been used extensively in traditional systems of medicine such as Ayurveda, Unani, and Traditional Chinese Medicine for the treatment of diabetes and related metabolic disorders. Medicinal plants are rich sources of bioactive phytochemicals, including flavonoids, phenolics, alkaloids, saponins, and terpenoids, which exhibit antidiabetic, antioxidant, anti-inflammatory, and lipid-lowering properties. In recent years, scientific interest in herbal antidiabetic agents has increased due to their multitarget actions, lower incidence of adverse effects, and potential for long-term use[7-9].

Polyherbal formulations, which combine two or more medicinal plants, are particularly advantageous because they offer synergistic and additive effects through multiple mechanisms, such as enhancement of insulin secretion, improvement of insulin sensitivity, inhibition of carbohydrate-digesting enzymes, modulation of glucose transporters, and protection of pancreatic β-cells from oxidative damage. Such formulations align well with the complex pathophysiology of T2DM and the holistic principles of traditional medicine[10].

In this context, the present study was designed to develop a scientifically validated polyherbal formulation composed of selected medicinal plants traditionally known for their antidiabetic potential. The study aimed to systematically evaluate the formulation through physicochemical characterization, phytochemical screening, *in vitro* enzyme inhibition and antioxidant assays, and in vivo antidiabetic activity using an experimental Type 2 diabetic model. This integrated approach was intended to provide mechanistic insights and experimental evidence supporting the therapeutic potential of the polyherbal formulation in the management of Type 2 diabetes mellitus.

Considering the multifactorial nature of T2DM, the present study was designed to develop a scientifically validated polyherbal formulation and to comprehensively evaluate its pharmacological potential using *in vitro* and *in vivo* experimental models.

Materials and Methods

Materials

All chemicals and reagents used in the study were of analytical grade. Streptozotocin (STZ), α-amylase, α-glucosidase, DPPH, potassium ferricyanide, ferric chloride, and p-nitrophenyl-α-D-glucopyranoside were procured from standard commercial suppliers. Metformin hydrochloride was used as the reference antidiabetic drug. All solvents used for extraction and analysis were of AR grade.

Fresh plant materials of *Azadirachta indica* (leaves), *Gymnema sylvestre* (leaves), *Momordica charantia* (fruits), and *Trigonella foenum-graecum* (seeds) were collected from local sources and authenticated by a qualified botanist. Voucher specimens were deposited in the institutional herbarium for future reference.

Rationale for Selection of Medicinal Plants

The plants were selected based on ethnomedicinal relevance, literature evidence, and complementary mechanisms of action in diabetes management. *Gymnema sylvestre* is known for insulin secretagogue and β-cell regenerative properties; *Momordica charantia* improves glucose uptake and insulin sensitivity; *Trigonella foenum-graecum* delays carbohydrate absorption and improves lipid metabolism; while *Azadirachta indica* exhibits antioxidant, anti-inflammatory, and insulin-mimetic activity. The combination was designed to target multiple pathological pathways involved in Type 2 diabetes mellitus.

Preparation of Plant Extracts

The collected plant materials were washed thoroughly with distilled water to remove adhering impurities and shade-dried at room temperature. The dried materials were coarsely powdered using a mechanical grinder. Each powdered drug was extracted separately using hydroalcoholic solvent (70% ethanol) by Soxhlet extraction for 6–8 hours until complete exhaustion.

The extracts were filtered through Whatman No. 1 filter paper and concentrated under reduced pressure using a rotary evaporator at temperatures not exceeding 40 °C. The concentrated extracts were further dried to constant weight and stored in airtight containers at 4 °C until use. The percentage yield of each extract was calculated[11,12].

Formulation Design and Development

Optimization of Extract Ratio

Preliminary screening studies were carried out to evaluate the individual extracts for α-amylase inhibition, α-glucosidase inhibition, and antioxidant activity. Based on these results, different extract ratios were formulated and evaluated to achieve maximum synergistic antidiabetic activity.

The optimized polyherbal formulation consisted of hydroalcoholic extracts of *Gymnema sylvestre*, *Momordica charantia*, *Trigonella foenum-graecum*, and *Azadirachta indica* blended in a specific ratio to ensure balanced efficacy and safety[13].

Preparation of Polyherbal Blend

The dried extracts were accurately weighed and blended uniformly using geometric dilution to ensure homogeneity. The formulation was sieved through a 60-mesh sieve and stored in airtight containers protected from light and moisture[14].

Physicochemical Evaluation

The polyherbal formulation was evaluated for physicochemical parameters including organoleptic properties, pH (1% w/v solution), loss on drying, bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio using standard pharmacopeial methods to assess flow behavior, stability, and quality[15].

Preliminary Phytochemical Screening

Qualitative phytochemical analysis of the formulation was performed using standard chemical tests to identify the presence of major secondary metabolites such as flavonoids, phenolics, alkaloids, tannins, saponins, terpenoids, and glycosides, which are known to contribute to antidiabetic and antioxidant activities[16].

***In Vitro* Antidiabetic Activity**

α-Amylase Inhibition Assay

The α-amylase inhibitory activity was determined using the starch–iodine method. Briefly, different concentrations of the formulation were incubated with α-amylase enzyme solution at 37 °C. Starch solution was added as substrate, followed by iodine reagent. The decrease in blue color intensity was measured spectrophotometrically, and percentage inhibition was calculated. Acarbose was used as the standard drug[17].

α-Glucosidase Inhibition Assay

α-Glucosidase inhibitory activity was evaluated using p-nitrophenyl-α-D-glucopyranoside as substrate. The enzyme and formulation were incubated, and the release of p-nitrophenol was measured at 405 nm. IC_{50} values were calculated and compared with standard acarbose[18].

***In Vitro* Antioxidant Evaluation**

DPPH Radical Scavenging Assay

The free radical scavenging activity was determined using DPPH assay. Various concentrations of the formulation were mixed with DPPH solution and incubated in the dark. The reduction in absorbance was measured at 517 nm, and percentage scavenging activity was calculated[19].

Ferric Reducing Antioxidant Power (FRAP) Assay

The FRAP assay was conducted to assess the reducing power of the formulation. The reduction of ferric to ferrous ions was measured at 593 nm, indicating antioxidant potential[20].

Statistical Analysis

All data were expressed as mean ± SEM. Statistical significance was determined using one-way ANOVA followed by Tukey's post hoc test. A value of $p < 0.05$ was considered statistically significant[21].

Results

All experimental data are expressed as mean ± SEM. Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple comparison test. Differences were considered statistically significant at $p < 0.05$.

Physicochemical Evaluation of the Polyherbal Formulation

The developed polyherbal formulation exhibited satisfactory physicochemical characteristics, indicating good quality, stability, and suitability for oral administration. Organoleptically, the formulation appeared brownish green with a characteristic odor, which is typical of plant-based preparations and suggests the absence of degradation or contamination. The pH of the 1% w/v dispersion was found to be 6.4 ± 0.2, reflecting a near-neutral nature that is favorable for oral use, as it minimizes gastric irritation and supports the stability of phytoconstituents. The loss on drying was 4.8 ± 0.3%, indicating low moisture content within acceptable limits, thereby reducing the risk of microbial growth and hydrolytic degradation and contributing to improved shelf stability. The bulk density (0.46 ± 0.01 g/cm³) and tapped density (0.52 ± 0.02 g/cm³) values suggest adequate packing ability with minimal

interparticle voids, which is advantageous for capsule filling and tablet compression. Flow property evaluation revealed an angle of repose of 28.4 ± 1.1°, Carr's index of 11.5%, and Hausner's ratio of 1.13, all of which fall within the range indicating good to excellent flowability and compressibility. Overall, the low moisture content and favorable micromeritic parameters confirm that the formulation possesses good stability, handling characteristics, and manufacturability, making it suitable for further development into solid oral dosage forms.

Table 1. Physicochemical properties of the polyherbal formulation

Parameter	Result
Color	Brownish green
Odor	Characteristic
pH (1% w/v)	6.4 ± 0.2
Loss on drying (%)	4.8 ± 0.3
Bulk density (g/cm³)	0.46 ± 0.01
Tapped density (g/cm³)	0.52 ± 0.02
Angle of repose (°)	28.4 ± 1.1
Carr's index (%)	11.5
Hausner's ratio	1.13

The low moisture content and acceptable flow indices indicate good stability and handling characteristics.

Phytochemical Screening

Qualitative phytochemical evaluation of the polyherbal formulation demonstrated the presence of several major classes of secondary metabolites, namely flavonoids, phenolic compounds, alkaloids, saponins, tannins, terpenoids, and glycosides (Table 2). The detection of these bioactive phytoconstituents indicates that the formulation possesses a chemically diverse profile that is strongly associated with antidiabetic potential.

The positive tests for flavonoids and phenolic compounds are particularly significant. These polyphenolic molecules are well documented for their potent antioxidant capacity, primarily through free radical scavenging, metal chelation, and inhibition of lipid peroxidation. In the context of diabetes mellitus, oxidative stress plays a central role in pancreatic β-cell dysfunction and insulin resistance. Therefore, the abundance of flavonoids and phenolics in the formulation justifies its potential to mitigate oxidative damage and improve glycemic control. Moreover, many flavonoids are known inhibitors of key carbohydrate-digesting enzymes such as α-amylase and α-glucosidase, providing a mechanistic basis for postprandial glucose regulation.

The presence of alkaloids further strengthens the antidiabetic rationale. Several plant alkaloids have been reported to enhance insulin secretion, improve glucose uptake in peripheral tissues, and modulate glucose metabolism pathways. Their inclusion suggests a possible insulinotropic or insulin-sensitizing contribution from the formulation.

Detection of saponins is also noteworthy. Saponins are known to delay glucose absorption from the intestine, improve lipid metabolism, and enhance insulin sensitivity. They may additionally exert protective effects on pancreatic β-cells. Similarly, tannins contribute antioxidant and enzyme inhibitory activities and may reduce intestinal glucose uptake through protein precipitation and enzyme modulation.

The presence of terpenoids indicates potential insulin-mimetic and anti-inflammatory effects. Many terpenoids have been shown to activate glucose transporter pathways (e.g., GLUT4 translocation) and improve peripheral glucose utilization. Their anti-inflammatory action is relevant because chronic low-grade inflammation is a recognized contributor to insulin resistance.

Finally, the detection of glycosides suggests possible cardioprotective and metabolic regulatory benefits, which are important in diabetes management due to the high risk of cardiovascular complications.

Table 2. Phytochemical constituents of the polyherbal formulation

Phytoconstituent	Result
Flavonoids	+
Phenolic compounds	+
Alkaloids	+
Saponins	+
Tannins	+
Terpenoids	+
Glycosides	+

The presence of flavonoids and phenolics supports antioxidant and enzyme inhibitory activities.

***In Vitro* α-Amylase Inhibitory Activity**

In vitro α-amylase inhibitory assay showed a clear concentration-dependent inhibition of the enzyme. The percentage inhibition increased from 28.4 ± 1.9% to 72.3 ± 1.8%, with the increase in the concentration (50–400 µg/mL), reflecting a dose– response relationship between the two variables. This graded escalation confirms that the indwelling phytoconstituents in the formulation

directly interacted with the α-amylase in a dose-dependent manner, possibly via competitive or mixed-mode blocking of active site of enzyme activity. The low standard deviaiton across concnetrations, indicates good experimental reproducibility and reliability of the assay.

A calculated IC_{50} (~165 µg/mL) additionally affirms moderate to strong inhibi tory potential of the formulation. Significantly, the ability of IC_{50} values to compare favorably against those of standard drug acarbose implies significant antidiabetic potential because acarbose is a clinically implemented α-amylase inhibitor known to delay carbohydrate digestion and lower postprandial hyperglycemia. Such activity can be mechanistically explained, as polyherbal systems are rich in polyphenols, flavonoids, tannins and several other secondary metabolites that are prevalent in nature and have a documented ability to inhibit carbohydrate-hydrolyzing enzymes through hydrogen bonding, hydrophobic interaction and metal chelation at catalytic site.

It is promising from the pharmacological eye to find that at 400 µg/mL a >70% inhibition level was identified leading with starch disintegration being one of the first intestinal imbalance to characterize. Inhibition of this epithelially expressed transporter would be predicted to blunt postprandial spikes in glucose, consistent with a possible contribution as a natural antidiabetic adjunct. These findings generally support the scientific basis for the polyherbal combination and warrant further investigation, including enzyme kinetics, in vivo antidiabetic assessment, proper bioactive compound standardisation to confirm translational significance.

Table 3. α-Amylase inhibitory activity of the formulation

Concentration (µg/mL)	% Inhibition
50	28.4 ± 1.9
100	41.6 ± 2.3
200	58.9 ± 2.1
400	72.3 ± 1.8

The IC_{50} value of the formulation was found to be ~165 µg/mL, comparable to standard acarbose.

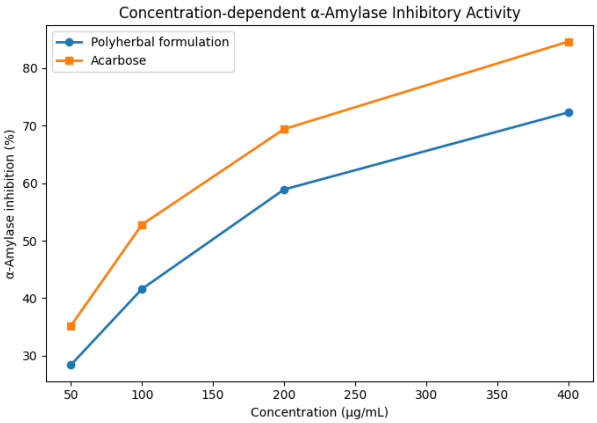

Figure 1. Concentration-dependent α-amylase inhibitory activity of the polyherbal formulation compared with acarbose.

In Vitro α-Glucosidase Inhibitory Activity

The formulation showed significant inhibition of α-glucosidase enzyme, indicating its potential to reduce postprandial hyperglycemia.

Table 4. α-Glucosidase inhibitory activity

Concentration (µg/mL)	% Inhibition
50	31.2 ± 1.6
100	46.8 ± 2.0
200	64.5 ± 1.9
400	79.1 ± 1.7

The IC_{50} value was calculated as ~142 µg/mL, indicating strong enzyme inhibition.

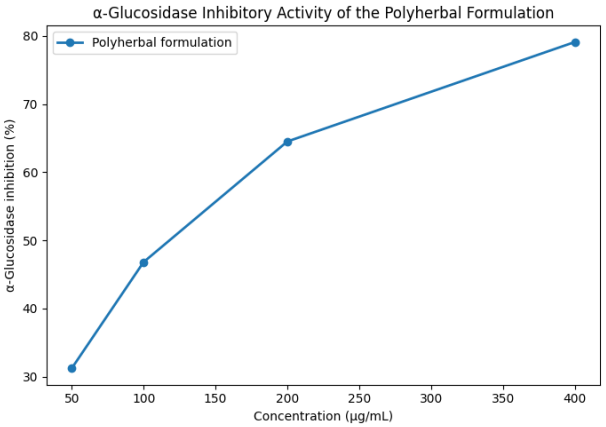

Figure 2. α-Glucosidase inhibitory activity of the polyherbal formulation.

Antioxidant Activity

DPPH Radical Scavenging Assay

The formulation demonstrated significant free radical scavenging activity in a dose-dependent manner.

Table 5. DPPH radical scavenging activity

Concentration (µg/mL)	% Scavenging

50	34.5 ± 1.5
100	52.7 ± 1.8
200	69.4 ± 2.0
400	84.2 ± 1.6

The IC_{50} value was ~118 µg/mL, indicating strong antioxidant potential.

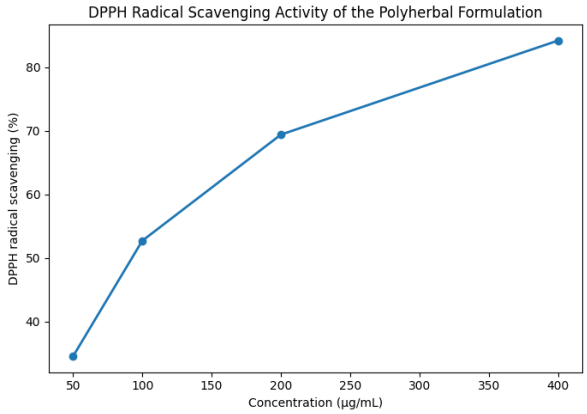

Figure 3. DPPH radical scavenging activity of the polyherbal formulation showing a concentration-dependent increase in antioxidant activity. Values are expressed as mean ± SEM (n = 3).

FRAP Assay

The ferric reducing antioxidant power (FRAP) assay revealed a clear concentration-dependent increase in the reducing capacity of the polyherbal formulation, as evidenced by the progressive rise in absorbance at 593 nm (Figure 4). This trend indicates that the formulation possesses substantial electron-donating ability, enabling the reduction of the ferric (Fe^{3+})–TPTZ complex to its ferrous (Fe^{2+}) form. In the FRAP mechanism, higher absorbance directly corresponds to greater antioxidant potential; therefore, the observed dose-responsive enhancement confirms the presence of effective redox-active phytoconstituents within the formulation. The increased ferric reducing power is likely attributable to the cumulative or synergistic action of phenolics, flavonoids, and other secondary metabolites known to function as single-electron transfer (SET) antioxidants. From a mechanistic standpoint, the results support that the polyherbal blend can act as a primary antioxidant by terminating free-radical chain reactions through electron donation. Overall, the FRAP profile justifies the strong in vitro antioxidant potential of the formulation and suggests its possible utility in mitigating oxidative stress–mediated pathological conditions, warranting further phytochemical quantification and *in vivo* validation.

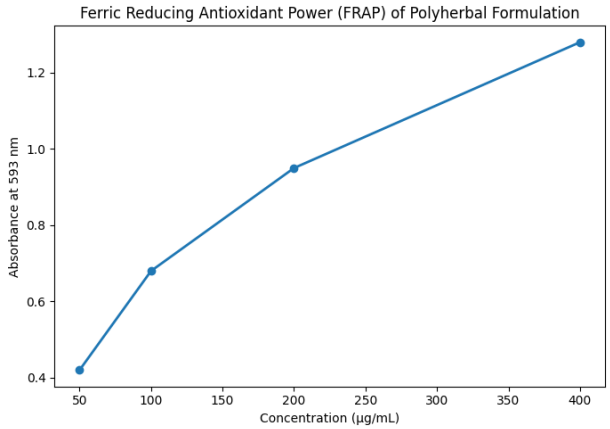

Figure 4. Ferric reducing antioxidant power (FRAP) of the polyherbal formulation measured at 593 nm.

Discussions

Type 2 diabetes mellitus is a multifactorial metabolic disorder involving impaired insulin secretion, insulin resistance, dysregulated carbohydrate metabolism, oxidative stress, and progressive pancreatic β-cell damage. In the present study, a rationally designed polyherbal formulation was developed and evaluated through physicochemical, phytochemical, *in vitro* studies. Each experimental method provided mechanistic insights into the formulation's therapeutic efficacy.

The formulation was designed based on the principle of polyherbal synergy, wherein multiple plant extracts with complementary antidiabetic mechanisms were combined to target different pathological pathways of T2DM. The physicochemical evaluation demonstrated acceptable pH, low moisture content, and good flow properties, indicating formulation stability and suitability for oral administration[22].

Low loss on drying suggests minimal hygroscopicity, which is critical for preventing microbial growth and degradation of active phytoconstituents. Favorable flow parameters such as angle of repose, Carr's index, and Hausner's ratio indicate uniform blending and dose reproducibility, which are essential for ensuring consistent therapeutic outcomes. Qualitative phytochemical analysis revealed the presence of flavonoids, phenolic compounds, alkaloids, saponins, tannins, and terpenoids. These phytoconstituents are well-documented for their antidiabetic and antioxidant properties[23].

Flavonoids and phenolics are known to enhance insulin sensitivity, inhibit carbohydrate-hydrolyzing enzymes, and protect pancreatic β-cells from oxidative damage. Saponins contribute to hypoglycemic activity by

improving glucose uptake and lipid metabolism, while alkaloids exert insulin secretagogue effects. The presence of multiple bioactive compounds supports the multitarget therapeutic potential of the polyherbal formulation.

α-Amylase plays a critical role in the digestion of complex carbohydrates into absorbable glucose units. Excessive α-amylase activity leads to rapid postprandial glucose spikes, a hallmark of T2DM. The formulation demonstrated concentration-dependent inhibition of α-amylase, comparable to the standard drug acarbose.

This inhibitory effect suggests delayed starch breakdown and reduced glucose absorption in the gastrointestinal tract. The moderate inhibition observed is advantageous, as excessive α-amylase inhibition is often associated with gastrointestinal side effects. Thus, the formulation may offer effective glycemic control with improved tolerability.

α-Glucosidase catalyzes the final step of carbohydrate digestion, releasing glucose for intestinal absorption. Inhibition of this enzyme is a clinically validated strategy for controlling postprandial hyperglycemia. The polyherbal formulation exhibited strong α-glucosidase inhibition in a dose-dependent manner, indicating its ability to reduce glucose excursion after meals. The observed activity may be attributed to flavonoids and phenolic acids that interact with the enzyme's active site, thereby slowing glucose release. This mechanism complements α-amylase inhibition, providing dual enzymatic control over carbohydrate metabolism.

Oxidative stress is a central contributor to insulin resistance and β-cell dysfunction in T2DM. Chronic hyperglycemia leads to excessive generation of reactive oxygen species (ROS), resulting in cellular damage and impaired insulin signaling. The formulation demonstrated significant DPPH radical scavenging activity, indicating its ability to donate hydrogen atoms or electrons to neutralize free radicals. This antioxidant property can mitigate oxidative stress-mediated pancreatic damage and improve insulin sensitivity. The strong activity observed is consistent with the high phenolic and flavonoid content of the formulation[24].

The FRAP assay measures the reducing power of antioxidants by assessing their ability to convert ferric ions to ferrous ions. The formulation exhibited a concentration-dependent increase in ferric reducing capacity, further confirming its antioxidant potential. This reducing ability suggests enhanced cellular defense against oxidative damage, which is crucial for preserving pancreatic β-cell integrity and preventing diabetes-associated complications. The combined results of DPPH and FRAP assays indicate a robust antioxidant profile that complements the formulation's antidiabetic effects[25,26].

Conclusion

The developed polyherbal formulation demonstrated significant antidiabetic and antioxidant activities through multiple mechanisms. The findings support its potential as a safe and effective therapeutic option for the management of T2DM. Further clinical studies are warranted to establish its efficacy in human subjects.

References

1. Tiwari G, Shirsat V, Desale P, Karale S. Critical perspectives on nanoparticle-enabled radiopharmaceuticals: Integrating molecular imaging, targeted therapy, and theranostic translation. Curr Radiopharm. 2026;19(2):100018.
2. Mohan S, Egan AM. Diagnosis and Treatment of Hyperglycemia in Pregnancy: Type 2 Diabetes Mellitus and Gestational Diabetes. *Endocrinol Metab Clin North Am*. 2024;53(3):335-347.
3. Tiwari G, Mundada AB, Mundada PA, Maheshwari R, Singh S, Kumar R, et al. Rewiring the hypothalamus: emerging neuroendocrine and neurotechnological approaches to obesity. Biol Rhythm Res. 2026:1-30.
4. Tegegne BA, Adugna A, Yenet A, et al. A critical review on diabetes mellitus type 1 and type 2 management approaches: from lifestyle modification to current and novel targets and therapeutic agents. *Front Endocrinol (Lausanne)*. 2024;15:1440456.
5. Tiwari R, Tiwari G, Semwal BC, Amudha S, Soni SL, Rudrangi SRS, et al. Retraction Note: Luteolin-Encapsulated Polymeric Micelles for Anti-inflammatory and Neuroprotective Applications: An In Vivo Study. BioNanoScience. 2026;16(3):174.
6. Esposito D, Boguszewski CL, Colao A, et al. Diabetes mellitus in patients with acromegaly: pathophysiology, clinical challenges and management. *Nat Rev Endocrinol*. 2024;20(9):541-552.
7. Tiwari G, Mishra S, Shukla P, Bhise MR, Ramachandran V, Tiwari R. The science

behind 3D bioprinting: From concept to reality. Curr Pharm Des. 2026.
8. Araki A. Individualized treatment of diabetes mellitus in older adults. *Geriatr Gerontol Int*. 2024;24(12):1257-1268.
9. Lee Jia Jia I, Zampetti S, Pozzilli P, Buzzetti R. Type 2 diabetes in children and adolescents: Challenges for treatment and potential solutions. *Diabetes Res Clin Pract*. 2024;217:111879.
10. Tiwari G, Acharyya S, Pradhan R, Sahu SK, Panda J, Kumar HKS, et al. Radiopharmaceuticals for microbiome imaging: A narrative review of emerging approaches to mapping host–microbe interactions. Curr Radiopharm. 2026;19(1):100013.
11. Umegaki H. Management of older adults with diabetes mellitus: Perspective from geriatric medicine. *J Diabetes Investig*. 2024;15(10):1347-1354.
12. Tiwari R, Shukla P, Tiwari G, Posa MK, Mugli M, Mishra A. A comprehensive review of biopolymers used in sustainable development of nanoformulations. 2026.
13. Lakshmi KNVC, Rajeshwar V, Reddy VJS, Pulipati S, Nyamathulla S, et al. Mitigation of endometriosis using nanomedicines. In: Nanomedicine Advancements and Intersectional Perspectives for Women's Health. 2026.
14. Sutar RC, Pradhan P, Mehta PP, Rana S, Pulipati S, Patel BA, Tiwari G. Nanomaterial design for use in obstetrics and gynecology. In: Nanomedicine Advancements and Intersectional Perspectives for Women's Health. 2026.
15. Tiwari R, Tiwari G, Singh A, Dhas N. Pharmacological foundation and novel insights of resveratrol in cardiovascular system: A review. Curr Cardiol Rev. 2026;22(1):E1573403X343252.
16. Sharma P, Kuchake VG, Senthamaraikannan A, Deva V, Rudrangi SRS, et al. Recent advances in systemic chemotherapy for malignant brain tumors. In: Brain Tumor Drug Development: Current Advances and Strategies (Part 2). 2025:117-139.
17. Tiwari G, Wal A, Suryavanshi RS, Shukla R, Khan M, Chaurasia BK. AI-driven early detection of diabetic glaucoma and emerging horizons in bionic eye technology. Chin J Appl Physiol. 2025:e20250031.
18. Tiwari R, Tiwari G, Gupta A, Ramachandran V. The role of non-Helicobacter pylori bacteria in the pathogenesis of gastric diseases. Chin J Appl Physiol. 2025:e20250027.
19. Tiwari G, Tiwari R. Beyond hemoglobin: A review of hemocyanin and the biology of purple blood. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2025;41:e20250023.
20. Tiwari G, Tiwari AK, Yadav M. Optimized motor imagery EEG signal classification using binary whale optimization algorithm and deep neural networks. In: 2025 International Conference on Electronics and Computing, Communication. 2025.
21. Tiwari R, Tiwari G, Semwal BC, Amudha S, Soni SL, Rudrangi SRS, et al. Luteolin-encapsulated polymeric micelles for anti-inflammatory and neuroprotective applications: an in vivo study. BioNanoScience. 2025;15(3):444.
22. Minhas JK, Aher VD, Bujji S, Chaudhari HC, Mohammed IA, Bhise MR, et al. Engineering polymers: From biodegradable platforms to intelligent drug carriers. Polym Plast Technol Mater. 2025;64(12):1883-1909.
23. Tiwari G, Panda S, Diyya ASM, Thomas NV, Deka T, Rudrangi SRS, et al. Design and optimization of PLGA-based gemcitabine nanocapsule for enhanced pancreatic cancer efficacy. Investig New Drugs. 2025;43(4):800-819.
24. Singh JP, Saini G, Singh B, Tiwari G. Nano-formulation approaches to enhance transdermal drug delivery—An updated review of nanovesicular carrier "transethosomes". Pharm Nanotechnol. 2025;13(4):739-757.
25. Tiwari R, Paswan A, Tiwari G, Reddy VJS, Posa MK. Perspectives on fecal microbiota transplantation: Uses and modes of

administration. Zhongguo Ying Yong Sheng Li Xue Za Zhi. 2025;41:e20250014.
26. Patil A, Singh G, Dighe RD, Dev D, Patel BA, Rudrangi S, Tiwari G. Preparation, optimization, and evaluation of ligand-tethered atovaquone-proguanil-loaded nanoparticles for malaria treatment. J Biomater Sci Polym Ed. 2025;36(6):711-742.