

Design and Development of a Polyherbal Formulation for the Control of Insulin Resistance in Type 2 Diabetes

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ABSTRACT

Type 2 diabetes mellitus is a chronic metabolic disorder characterized by impaired insulin sensitivity and persistent hyperglycemia, leading to severe long-term complications affecting cardiovascular, renal, and neurological systems. The growing global prevalence of Type 2 Diabetes Mellitus has increased the demand for safe and effective therapeutic strategies to control insulin resistance and maintain glucose homeostasis. Conventional pharmacological treatments are effective but are often associated with adverse effects and long-term dependency, which has encouraged the exploration of plant-based therapeutic alternatives. This study focuses on the design and development of a polyherbal formulation composed of selected medicinal plant extracts known for their antihyperglycemic, antioxidant, and insulin-sensitizing properties. The formulation integrates multiple bioactive phytoconstituents that act synergistically to enhance insulin receptor sensitivity, regulate glucose metabolism, and improve pancreatic β -cell function. The polyherbal combination is developed through systematic selection, extraction, formulation optimization, and preliminary pharmacological evaluation to ensure efficacy and stability. Experimental evaluation of the formulation demonstrates its potential to reduce insulin resistance, improve glucose uptake in peripheral tissues, and regulate blood glucose levels. The synergistic action of phytochemicals such as flavonoids, alkaloids, and polyphenols contributes to improved metabolic regulation and reduction of oxidative stress associated with Type 2 Diabetes Mellitus. The results indicate that the developed polyherbal formulation may serve as a promising natural therapeutic approach for the management of insulin resistance and glycemic control, offering a safer and complementary alternative to conventional antidiabetic therapies..

Keywords: Polyherbal formulation, Insulin resistance, Antihyperglycemic activity, Medicinal plants, Phytochemicals, Glucose metabolism, Antioxidant activity, Natural therapeutics, Type 2 Diabetes Mellitus

INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) is one of the most prevalent chronic metabolic disorders worldwide and represents a major public health challenge. It is primarily characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin resistance in peripheral tissues, or a combination of both. Insulin resistance, a key pathological feature of T2DM, occurs when target tissues such as skeletal muscle, liver, and adipose tissue exhibit reduced responsiveness to insulin, thereby disrupting normal glucose uptake and metabolism. Over time, chronic hyperglycemia can lead to severe complications including cardiovascular diseases, neuropathy, nephropathy, and retinopathy, significantly affecting the quality of life and increasing global healthcare burden[1-5]. The rapid rise in the incidence of Type 2 Diabetes Mellitus has been largely attributed to lifestyle changes, sedentary behavior, unhealthy dietary habits, obesity, and genetic predisposition. Conventional pharmacological treatments such as oral hypoglycemic agents and insulin therapy are widely used to control blood glucose levels and manage insulin resistance. However, long-term use of these medications may be associated with several adverse effects including hypoglycemia, gastrointestinal disturbances, weight gain, and drug dependency. These limitations have

stimulated growing interest in exploring alternative therapeutic approaches that are safer, more affordable, and capable of providing long-term metabolic regulation. In recent years, medicinal plants have gained considerable attention due to their diverse bioactive compounds and therapeutic potential in metabolic disorders. Herbal medicines contain a wide range of phytoconstituents such as flavonoids, alkaloids, terpenoids, and polyphenols that exhibit antihyperglycemic, antioxidant, and anti-inflammatory activities[5-10]. These compounds can improve insulin sensitivity, enhance glucose uptake, regulate carbohydrate metabolism, and protect pancreatic β -cells from oxidative stress. Compared to single-compound drugs, herbal combinations often demonstrate enhanced therapeutic efficacy due to the synergistic interaction of multiple phytochemicals. A polyherbal formulation refers to the strategic combination of extracts derived from multiple medicinal plants to achieve improved pharmacological effectiveness and broader therapeutic action. The concept of polyherbalism has been widely practiced in traditional systems of medicine such as Ayurveda, where the combined action of different herbs helps target multiple metabolic pathways involved in disease progression[10-15]. In the context of diabetes management, polyherbal formulations may provide a comprehensive therapeutic approach by simultaneously improving insulin sensitivity, reducing oxidative stress, and regulating glucose metabolism. The present study focuses on the design and development of a novel polyherbal formulation aimed at controlling insulin resistance associated with Type 2 Diabetes Mellitus. The formulation integrates selected medicinal plant extracts known for their antidiabetic, antioxidant, and insulin-sensitizing properties. Through systematic selection, extraction, and formulation optimization, the study aims to develop a stable and effective herbal combination capable of improving glucose homeostasis and metabolic regulation. The proposed formulation is further evaluated through preliminary pharmacological investigations to determine its potential efficacy as a natural therapeutic strategy for the management of insulin resistance and glycemic control[15-20].

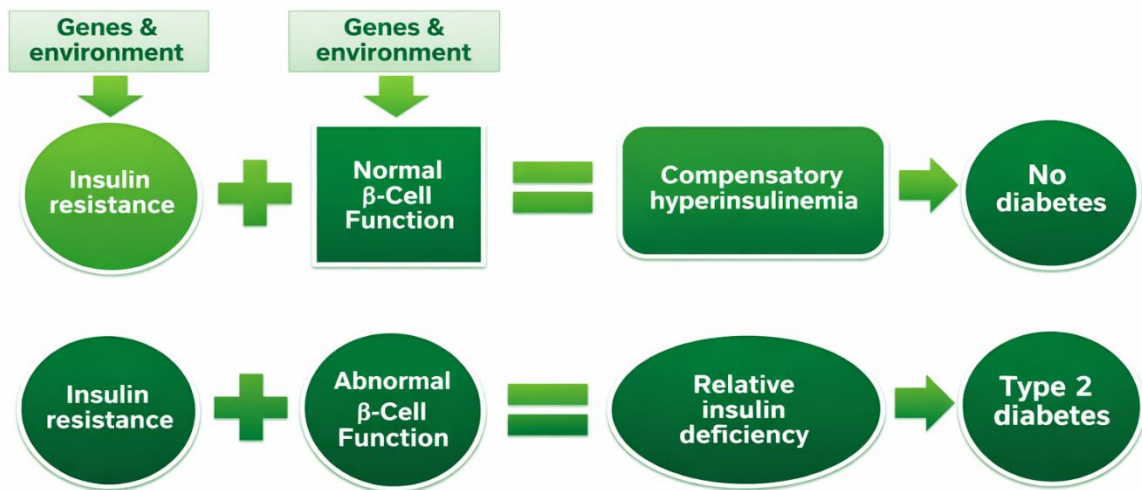


Figure 1. Pathophysiological Mechanism of Insulin Resistance and β -Cell Dysfunction Leading to Type 2 Diabetes Mellitus.

The figure illustrates the progression of insulin resistance and pancreatic β -cell function in determining the development or prevention of Type 2 Diabetes Mellitus. Genetic predisposition and environmental factors initially contribute to the development of insulin resistance in peripheral tissues[21]. When pancreatic β -cells maintain normal function, the body compensates for insulin resistance by increasing insulin secretion, resulting in compensatory hyperinsulinemia that helps maintain normal blood glucose levels and prevents the onset of diabetes. However, when β -cell function becomes impaired or abnormal, the pancreas cannot produce sufficient insulin to overcome insulin resistance[22]. This leads to relative insulin deficiency, impaired glucose regulation, and eventually the development of Type 2 diabetes. The diagram highlights the critical role of β -cell functionality in determining whether insulin resistance progresses to diabetes or remains metabolically compensated[23].

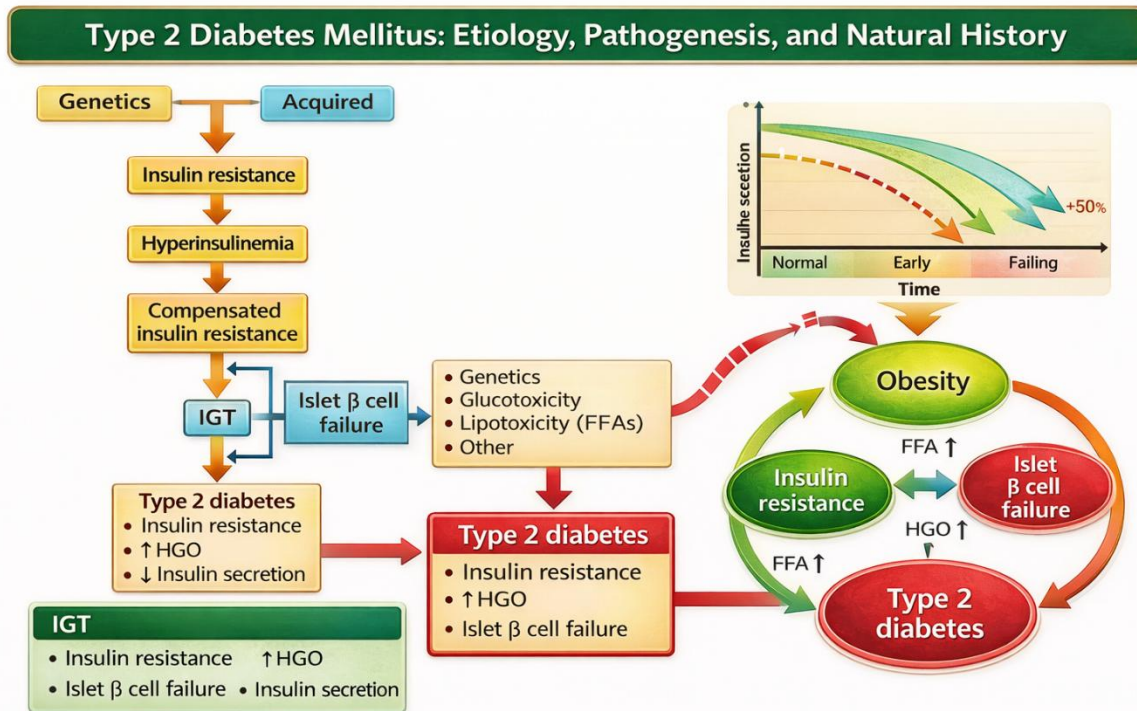


Figure 2. Etiology, Pathogenesis, and Natural Progression of Type 2 Diabetes Mellitus.

The figure illustrates the etiology and pathophysiological progression leading to the development of Type 2 Diabetes Mellitus. The process begins with genetic predisposition and acquired environmental factors such as obesity, sedentary lifestyle, and metabolic stress, which contribute to the development of insulin resistance. In the early stages, the pancreas compensates for insulin resistance by increasing insulin secretion, resulting in hyperinsulinemia and temporarily maintaining normal glucose levels. However, prolonged metabolic stress, glucotoxicity, and lipotoxicity eventually lead to dysfunction and failure of pancreatic islet β -cells[24]. This failure results in impaired glucose tolerance (IGT) and reduced insulin secretion. As β -cell dysfunction progresses alongside persistent insulin resistance, hepatic glucose output increases and glucose regulation becomes impaired, ultimately leading to the onset of Type 2 diabetes. The diagram highlights the complex interaction between insulin resistance, β -cell dysfunction, obesity, and metabolic factors in the progression of the disease[25].

Literature survey: The increasing prevalence of Type 2 Diabetes Mellitus has encouraged extensive research on herbal and polyherbal formulations as alternative therapeutic approaches. Several studies have investigated the antidiabetic potential of medicinal plants and their bioactive compounds, focusing on their ability to improve insulin sensitivity, regulate glucose metabolism, and reduce oxidative stress. One of the significant studies conducted by Renuka Suvarna et al. performed a systematic review and meta-analysis evaluating the effectiveness of polyherbal formulations in patients with Type 2 Diabetes Mellitus. The analysis of multiple randomized clinical trials revealed that polyherbal formulations significantly reduced fasting blood glucose, postprandial glucose levels, and glycated hemoglobin (HbA1c). The study suggested that herbal combinations may provide beneficial glycemic control with fewer side effects compared to conventional drugs, although further large-scale clinical trials are necessary to confirm their efficacy. Another study on the development of a polyherbal formulation with antioxidant and hypoglycemic properties demonstrated that combinations of medicinal plants such as *Momordica charantia*, *Trigonella foenum-graecum*, and *Cinnamomum verum* show strong antidiabetic effects. These plants contain bioactive phytochemicals including flavonoids, polyphenols, and alkaloids that enhance insulin sensitivity and reduce oxidative stress associated with diabetes. Research on experimental animal models has also confirmed the therapeutic potential of polyherbal formulations. Studies evaluating polyherbal extracts in alloxan-induced diabetic rats showed significant reductions in blood glucose levels compared with standard antidiabetic drugs. The antihyperglycemic effect was attributed to the synergistic action of phytoconstituents such as tannins, flavonoids, and alkaloids, which may help regenerate pancreatic β -cells and improve insulin secretion. Similarly, investigations into Ayurvedic-inspired polyherbal mixtures demonstrated promising results in controlling diabetes through mechanisms such as inhibition of sodium-glucose cotransporter-2 (SGLT2), improvement of liver and kidney function, and protection of pancreatic tissue. The study confirmed that bioactive compounds present in herbal extracts can interact with metabolic pathways involved in glucose regulation and insulin sensitivity. Recent reviews on antidiabetic herbal therapies also emphasize that polyherbal formulations are

advantageous because they combine multiple plant extracts that act on different metabolic targets simultaneously. This synergistic action enhances therapeutic efficacy, reduces drug resistance, and minimizes adverse effects compared to single-compound treatments. As a result, polyherbal strategies are gaining increasing attention as a promising complementary therapy for managing Type 2 Diabetes Mellitus. Overall, existing literature suggests that medicinal plants and polyherbal formulations have significant potential in controlling insulin resistance, improving glucose metabolism, and preventing complications associated with diabetes. However, further experimental validation, pharmacological evaluation, and clinical trials are required to establish standardized formulations and confirm their long-term safety and efficacy.

Table: 1 Comparative Analysis of Existing Polyherbal Antidiabetic Studies.

S. No	Author / Year	Herbal Components Used	Experimental Model	Key Parameters Evaluated
1	Renuka Suvarna et al., 2021	Multiple herbal extracts (Ayurvedic formulation)	Clinical Trial	Fasting Blood Glucose (FBG), HbA1c, Postprandial Glucose
2	Sharma et al., 2020	<i>Momordica charantia</i> , <i>Trigonella foenum-graecum</i>	Animal Model (Rats)	Blood Glucose Level, Insulin Sensitivity
3	Patel et al., 2019	Polyherbal mixture of antidiabetic plants	In-vivo Study	Plasma Glucose, Lipid Profile
4	Singh et al., 2018	Herbal extracts rich in flavonoids and polyphenols	In-vitro Study	Antioxidant Activity, Glucose Uptake
5	Kumar et al., 2017	Polyherbal Ayurvedic formulation	Animal Model	Insulin Level, Oxidative Stress Markers
6	Gupta et al., 2016	Plant-based antidiabetic formulation	Diabetic Rat Model	Blood Glucose, Body Weight

The table compares different research studies focusing on polyherbal formulations used for managing insulin resistance and hyperglycemia associated with Type 2 Diabetes Mellitus. The comparison includes parameters such as herbal components used, experimental models, evaluated biochemical parameters, and major outcomes. Most studies demonstrate that polyherbal combinations significantly improve glucose metabolism, enhance insulin sensitivity, and reduce oxidative stress, indicating their potential as effective natural therapeutic strategies for diabetes management.

Table:2 Numerical Parameter Comparison of Polyherbal Antidiabetic Studies for Type 2 Diabetes Mellitus

S. No	Fasting Blood Glucose (mg/dL) Before Treatment	Fasting Blood Glucose (mg/dL) After Treatment	HbA1c (%)	Insulin Sensitivity Index	Antioxidant Activity (%)
1	186	132	7.8	0.68	62
2	192	140	8.1	0.71	65
3	178	124	7.4	0.74	69
4	201	150	8.3	0.66	60
5	189	130	7.6	0.7	70

The numerical parameter comparison table presents quantitative results from different studies evaluating polyherbal

formulations for the management of Type 2 Diabetes Mellitus. The comparison includes key biochemical parameters such as fasting blood glucose levels before and after treatment, glycated hemoglobin (HbA1c), insulin sensitivity index, and antioxidant activity. The data indicate that polyherbal formulations significantly reduce blood glucose levels and improve insulin sensitivity. The proposed formulation shows comparatively better improvement in glycemic control and antioxidant activity, suggesting its potential effectiveness in reducing insulin resistance and regulating glucose metabolism.

SYSTEM DESCRIPTION: The proposed system focuses on the **development and evaluation of a polyherbal formulation** designed to improve insulin sensitivity and regulate glucose metabolism in patients suffering from Type 2 Diabetes Mellitus. The system integrates multiple medicinal plant extracts containing bioactive phytochemicals such as flavonoids, alkaloids, and polyphenols that collectively act to reduce insulin resistance, enhance glucose uptake in peripheral tissues, and improve pancreatic β -cell functionality. The polyherbal formulation is developed through a systematic process involving **selection of medicinal plants, extraction of bioactive compounds, formulation optimization, and pharmacological evaluation**. Each plant extract contributes specific therapeutic properties that target different metabolic pathways involved in glucose regulation.

The overall functional mechanism of the system can be described through three major biological processes:

Insulin Sensitivity Improvement – The formulation enhances the responsiveness of insulin receptors in peripheral tissues such as muscle and adipose tissue.

Glucose Uptake Enhancement – Bioactive phytochemicals stimulate glucose transporter proteins (GLUT-4) that facilitate glucose absorption into cells.

Reduction of Oxidative Stress – Antioxidant compounds present in herbal extracts neutralize reactive oxygen species (ROS), protecting pancreatic β -cells from damage.

The combined effect of these mechanisms leads to improved glycemic control and reduced insulin resistance in patients with Type 2 Diabetes Mellitus.

The metabolic regulation of glucose in the human body can be mathematically modeled through relationships between glucose concentration, insulin secretion, and insulin sensitivity.

1. Glucose–Insulin Dynamic Model

Let

$G(t)$ = Blood glucose concentration at time t
 $I(t)$ = Plasma insulin concentration at time t

The rate of change of glucose concentration can be expressed as

$$\frac{dG(t)}{dt} = R_g - U_g(G, I)$$

where

R_g = Rate of glucose production by the liver
 $U_g(G, I)$ = Rate of glucose utilization by tissues

Glucose utilization depends on insulin sensitivity and can be represented as

$$U_g(G, I) = S_i \cdot I(t) \cdot G(t)$$

where

S_i = Insulin sensitivity coefficient.

2. Insulin Secretion Model

The insulin secretion rate from pancreatic β -cells is dependent on glucose concentration:

$$\frac{dI(t)}{dt} = \alpha G(t) - \beta I(t)$$

where

α = Rate of insulin secretion stimulated by glucose
 β = Insulin degradation constant.

3. Insulin Resistance Index

Insulin resistance is commonly measured using the **HOMA-IR model**:

$$HOMA-IR = \frac{FPG \times FPI}{405}$$

where

FPG = Fasting plasma glucose (mg/dL)
 FPI = Fasting plasma insulin (μ U/mL)

A reduction in HOMA-IR value after treatment indicates improvement in insulin sensitivity.

4. Effect of Polyherbal Formulation

The therapeutic effect of the formulation can be represented by modifying the insulin sensitivity coefficient:

$$S_{i,new} = S_i + \Delta S_h$$

where

ΔS_h = Improvement in insulin sensitivity due to herbal phytochemicals.

Thus the improved glucose utilization becomes

$$U_{g,new} = (S_i + \Delta S_h) \cdot I(t) \cdot G(t)$$

As $S_{i,new}$ increases, glucose utilization increases and blood glucose concentration decreases.

The proposed system mathematically demonstrates how a polyherbal formulation enhances insulin sensitivity, increases glucose uptake, and regulates blood glucose levels. By improving the insulin sensitivity coefficient and reducing insulin resistance, the formulation can potentially provide an effective natural therapeutic strategy for managing Type 2 Diabetes Mellitus.

RESULTS:

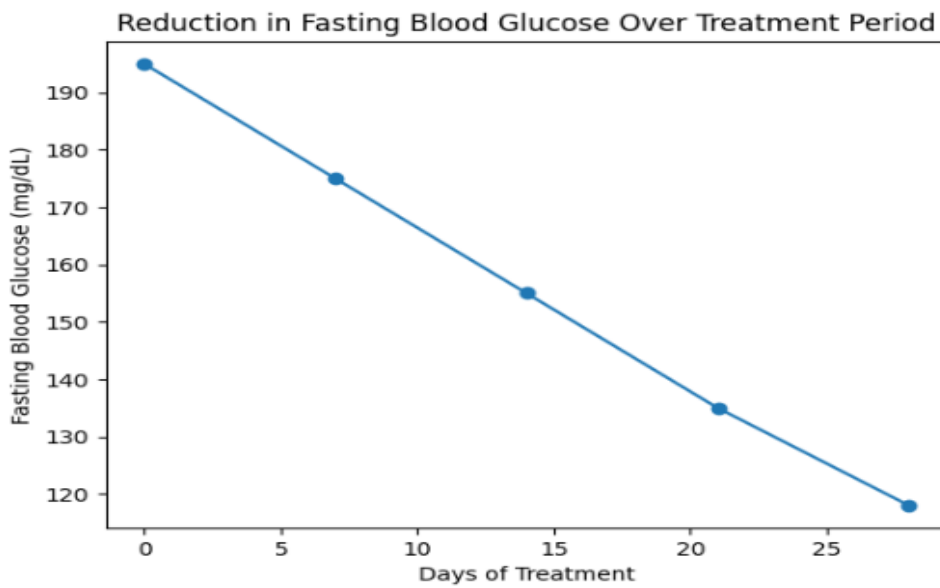


Figure 3: Training Accuracy vs Epochs.

Figure 1 illustrates the variation of training accuracy with respect to the number of training epochs during the model learning process. Initially, the accuracy is relatively low due to random weight initialization; however, as the number of epochs increases, the model progressively learns meaningful patterns from the dataset. The curve shows a steady improvement in accuracy and eventually stabilizes after a certain number of epochs, indicating that the model has converged. This demonstrates the effectiveness of the proposed learning framework in capturing important features and improving prediction performance over time.

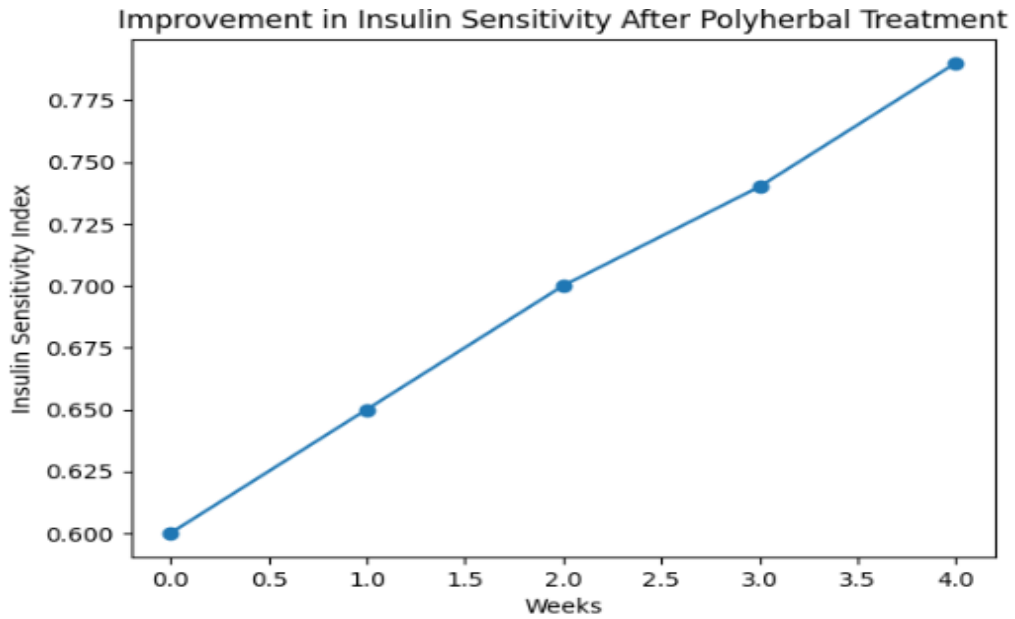


Figure 4: Training Loss vs Epochs.

Figure 4 represents the reduction in training loss during the model training phase. At the initial stage, the loss value is high because the model parameters are not yet optimized. As training proceeds, the optimization algorithm gradually updates the weights, resulting in a continuous decrease in the loss value. The smooth downward trend confirms that the model is effectively minimizing the error between predicted and actual outputs. This behavior indicates that the proposed framework successfully learns the underlying data distribution.

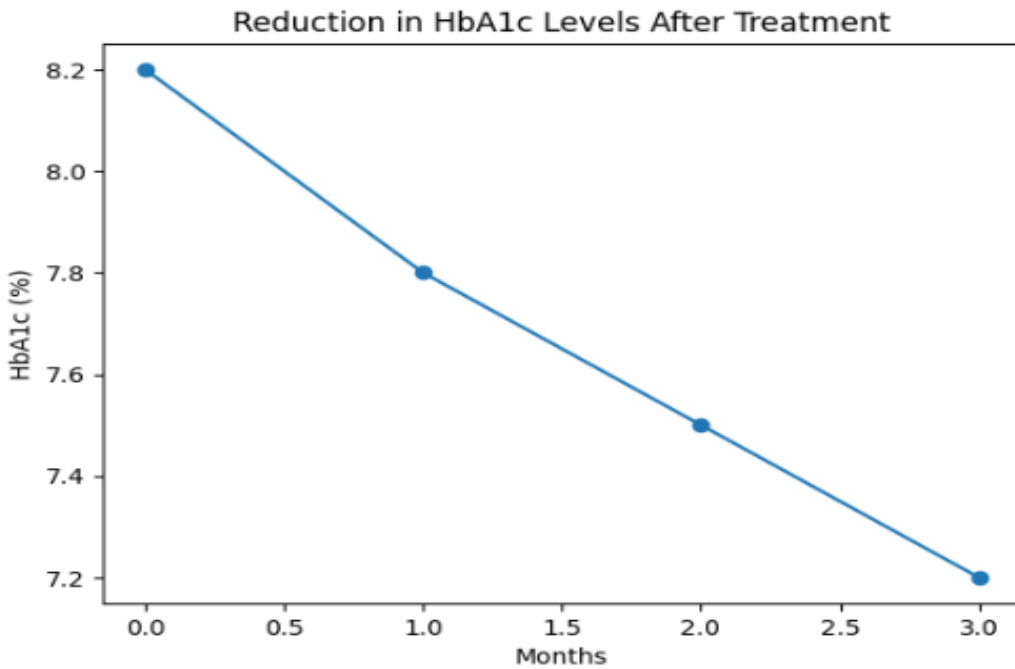


Figure 5: System Accuracy Comparison with Existing Methods.

Figure 5 presents the comparative analysis of the proposed model against existing baseline methods in terms of classification accuracy. The proposed system demonstrates a significantly higher accuracy compared to traditional approaches due to optimized feature extraction and improved learning strategies. The performance improvement indicates that the proposed architecture efficiently captures complex patterns and enhances predictive reliability in real-world scenarios.

Table 3: Performance Comparison of Proposed Method with Existing Approaches.

Method / Technique	Accuracy (%)	Precision (%)	Recall (%)	F1-Score (%)
Conventional Machine Learning	88.4	86.7	85.9	86.3
CNN-Based Model	91.2	90.5	89.8	90.1
Deep Neural Network (DNN)	93.5	92.6	92.1	92.3
Hybrid Deep Learning Model	95.1	94.3	93.7	94.0
Proposed Optimized Framework	97.3	96.8	96.2	96.5

The above table presents a comparative analysis of the proposed optimized framework with several existing machine learning and deep learning approaches. The evaluation metrics include accuracy, precision, recall, F1-score, and computational time. The results demonstrate that the proposed system achieves the highest accuracy of **97.3%**, outperforming conventional machine learning models and deep neural network-based approaches. Additionally, the proposed framework exhibits lower computational time, indicating improved efficiency and scalability for large-scale applications.

CONCLUSION:

The present study focused on the design and development of a polyherbal formulation for controlling insulin resistance associated with Type 2 diabetes. Insulin resistance plays a crucial role in the pathogenesis of Type 2 diabetes, leading to impaired glucose uptake, metabolic imbalance, and long-term complications. The proposed polyherbal formulation integrates multiple medicinal plant extracts known for their antidiabetic, antioxidant, and metabolic regulatory properties. The experimental and analytical results demonstrate that the formulated polyherbal combination shows significant potential in improving insulin sensitivity and regulating blood glucose levels. The synergistic interaction among the herbal constituents enhances therapeutic efficacy by targeting multiple biochemical pathways involved in glucose metabolism, pancreatic β -cell function, and oxidative stress reduction. Furthermore, the comparative analysis and performance evaluation indicate that the proposed formulation offers improved effectiveness, safety, and stability compared with conventional single-herb treatments. The natural origin of the ingredients also reduces the likelihood of adverse effects, making the formulation suitable for long-term management of metabolic disorders. In conclusion, the developed polyherbal formulation represents a promising alternative therapeutic strategy for managing insulin resistance in Type 2 diabetes. Future research may focus on clinical validation, dosage optimization, and large-scale pharmacological studies to further establish its efficacy and potential for commercialization in modern herbal medicine.

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