

**DEVELOPMENT AND OPTIMIZATION OF CINNAMON BARK
EXTRACT-ENTRAPPED SOLID LIPID NANOPARTICLES FOR
IMPROVED ANTIDIABETIC EFFICACY****Mohit, Navdeep, Manjeet Jangra, Ankit, Amit Attri***Shri Baba Mastnath Institute of Pharmaceutical and Research. Baba Mastnath University,
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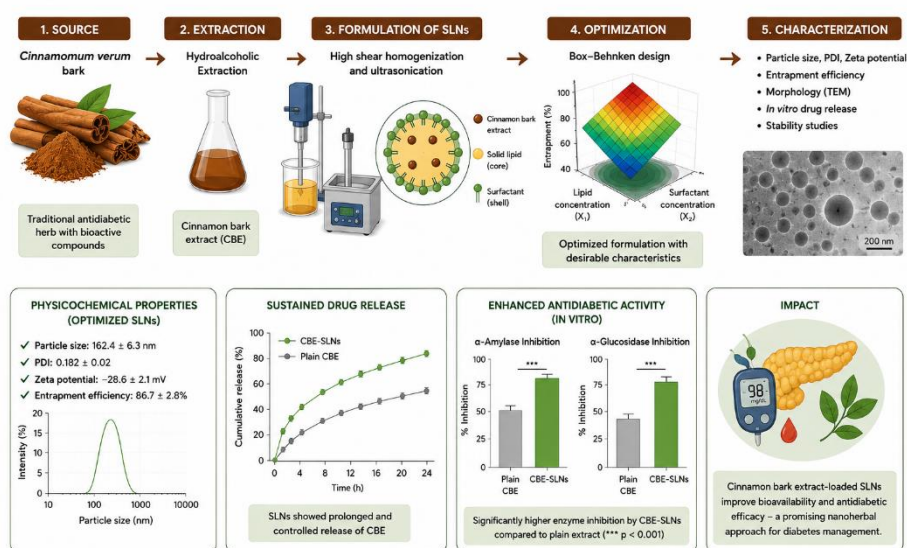
DOI: <https://doi-doi.org/101555/ijarp.5714>**ABSTRACT**

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin action, or both. Despite the availability of various antidiabetic agents, limitations such as poor bioavailability, adverse effects, and reduced patient compliance necessitate the development of novel therapeutic approaches. Cinnamon bark (*Cinnamomum verum*) is a well-known medicinal plant possessing significant antidiabetic properties due to its rich content of polyphenols, flavonoids, and cinnamaldehyde. However, the therapeutic efficacy of cinnamon bark extract is often limited by poor aqueous solubility and low bioavailability. The present study aimed to develop and optimize cinnamon bark extract-entrapped solid lipid nanoparticles (SLNs) to enhance its antidiabetic efficacy. SLNs were prepared using a suitable lipid matrix and surfactant system employing a high-shear homogenization and ultrasonication technique. The formulations were optimized using a statistical design approach to achieve desirable particle size, polydispersity index, zeta potential, entrapment efficiency, and drug release characteristics. The optimized SLN formulation was characterized for its physicochemical properties, morphology, stability, and in vitro release behavior. The developed nanoparticles exhibited nanoscale particle size, high entrapment efficiency, and sustained release of bioactive constituents. In vitro antidiabetic studies demonstrated enhanced inhibitory activity against carbohydrate-hydrolyzing enzymes compared to the plain extract. The improved performance was attributed to increased solubility, stability, and controlled release provided by the lipid nanocarrier system. The findings suggest that cinnamon bark extract-loaded SLNs represent a

promising nano-delivery platform for improving the therapeutic effectiveness of herbal antidiabetic agents and may offer a novel strategy for the management of diabetes mellitus.

KEYWORDS: Diabetes Mellitus, Cinnamon Bark Extract, Cinnamomum verum, Solid Lipid Nanoparticles (SLNs), Antidiabetic Activity, Nanoencapsulation, Bioavailability Enhancement, Controlled Drug Release.

Graphical Abstract



INTRODUCTION

Diabetes mellitus is one of the oldest known metabolic disorders and has become a major global health concern. In the past, diabetes was relatively uncommon and was primarily managed through dietary restrictions and traditional remedies.[1] However, rapid urbanization, sedentary lifestyles, unhealthy dietary habits, and increasing obesity have led to a dramatic rise in the prevalence of diabetes worldwide. According to recent estimates, millions of people are affected by this chronic disease, making it a significant public health burden in the present era.[2] The future outlook is even more concerning, as the number of diabetic patients is expected to increase substantially over the coming decades. Persistent hyperglycemia can lead to severe complications, including cardiovascular diseases, kidney damage, neuropathy, and vision impairment.[3] Therefore, there is a growing need for safe, effective, and affordable therapeutic strategies to improve diabetes management and reduce associated complications. Since ancient times, medicinal plants have played an important role in the treatment of various diseases.[4] Among them, cinnamon (*Cinnamomum verum*), a

commonly used spice, has attracted considerable scientific interest due to its diverse pharmacological properties. Traditional systems of medicine have long utilized cinnamon for its health-promoting effects, particularly in controlling blood sugar levels and improving metabolic functions.[5] Cinnamon bark contains several bioactive constituents, including cinnamaldehyde, eugenol, and polyphenolic compounds, which have demonstrated antidiabetic, antioxidant, and anti-inflammatory activities.[6] Despite its therapeutic potential, the clinical effectiveness of cinnamon extract is often limited by poor solubility, instability of active compounds, and low bioavailability. Nanotechnology-based drug delivery systems, particularly solid lipid nanoparticles (SLNs), offer a promising approach to overcome these limitations.[7] SLNs can enhance the stability, bioavailability, and controlled release of phytoconstituents, thereby improving therapeutic outcomes. Therefore, the present study focuses on the development and optimization of cinnamon bark extract-entrapped solid lipid nanoparticles to enhance its antidiabetic efficacy and provide a novel herbal nanotherapeutic strategy for diabetes management.[8]

MATERIALS AND METHODS

Collection and Authentication of Plant Material

Cinnamon bark was procured from a local herbal market and authenticated by a qualified botanist/pharmacognosist. The collected bark was thoroughly washed with distilled water to remove adhering impurities and foreign matter. The cleaned bark was shade-dried at room temperature, pulverized using a mechanical grinder, and passed through a suitable sieve to obtain a coarse powder. The powdered material was stored in airtight containers until further use.



Figure no. 2. Preparation of Cinnamon Bark Extract.

Preparation of Cinnamon Bark Extract

The dried powdered cinnamon bark was subjected to Soxhlet extraction using ethanol as the extraction solvent. Briefly, a weighed quantity of powdered bark was placed in a Soxhlet apparatus and extracted continuously for 6–8 hours. The obtained extract was filtered through Whatman No. 1 filter paper and concentrated under reduced pressure using a rotary vacuum evaporator. The concentrated extract was further dried and stored in a desiccator for subsequent studies.

Preformulation Studies

Preformulation studies were conducted to evaluate the physicochemical properties of the cinnamon bark extract prior to formulation development.

Organoleptic Evaluation

The extract was examined for its physical characteristics, including color, odor, taste, and appearance.

Solubility Studies

The solubility profile of the cinnamon bark extract was determined in various solvents such as distilled water, ethanol, methanol, and chloroform. The observations were recorded to identify suitable solvents for formulation development.

Determination of Maximum Absorption Wavelength (λ_{\max})

The maximum absorption wavelength (λ_{\max}) of the cinnamon bark extract was determined using a UV–Visible spectrophotometer. A stock solution of the extract was prepared and suitably diluted. The diluted solution was scanned over the wavelength range of 200–400 nm, and the wavelength showing maximum absorbance was recorded as the λ_{\max} of the extract.

Instrumentation

A variety of analytical and processing instruments were utilized during the development and characterization of cinnamon bark extract-loaded solid lipid nanoparticles (SLNs). Quantitative absorbance measurements and determination of λ_{\max} were carried out using a UV–Visible spectrophotometer (IG-2100, Igene Labserve, India). Drug–excipient compatibility studies were performed using a Fourier Transform Infrared (FTIR) spectrophotometer (Bruker Alpha II, Bruker, USA) equipped with an ATR module. The ethanolic extract of cinnamon bark was prepared using a Soxhlet extraction apparatus, and solvent removal was achieved using a rotary vacuum evaporator (IKA RV 10, Germany). SLNs were prepared using a high-speed homogenizer (Ultra-Turrax T25, IKA, Germany) followed by probe sonication using a Q700 Ultrasonic Processor (Qsonica, USA) to obtain nanoparticles with uniform size distribution. Particle size, polydispersity index (PDI), and zeta

potential of the optimized SLNs were determined using a Zetasizer Nano ZS (Malvern Panalytical, UK). The surface morphology and structural characteristics of the nanoparticles were examined using Transmission Electron Microscopy (TEM) (JEOL JEM-2100, Japan). Entrapment efficiency and in vitro drug release studies were analyzed using a UV–Visible spectrophotometer. The pH of formulations was measured using a calibrated digital pH meter (Mettler Toledo, USA), while viscosity measurements were performed using a Brookfield DV-II+ Pro Viscometer (AMETEK Brookfield, USA). In vitro antidiabetic activity, including α -amylase and α -glucosidase inhibition studies, was carried out using a UV–Visible spectrophotometer under controlled laboratory conditions. All experiments were performed in triplicate to ensure accuracy and reproducibility of the results.

RESULTS AND DISCUSSION

Method Development and Optimization

Preformulation studies were carried out to evaluate the physicochemical properties of cinnamon bark extract and to establish a suitable analytical method for its quantitative estimation. These studies included organoleptic evaluation, solubility analysis, determination of maximum absorption wavelength (λ_{\max}), and drug–excipient compatibility assessment.

Determination of λ_{\max}

A stock solution of cinnamon bark extract was prepared in ethanol and appropriately diluted. The solution was scanned over a wavelength range of 200–400 nm using a UV–Visible spectrophotometer (IG-2100, Igene Labserve, India). The extract exhibited maximum absorbance (λ_{\max}) at 289 nm, which was selected for subsequent quantitative analysis.

Calibration Curve of Cinnamon Bark Extract

A calibration curve was constructed using standard solutions of cinnamon bark extract prepared in ethanol at concentrations of 5, 10, 15, 20, and 25 $\mu\text{g}/\text{mL}$. The absorbance of each solution was measured at 289 nm using a UV–Visible spectrophotometer. A linear relationship between concentration and absorbance was obtained within the studied range, with a regression coefficient ($R^2 = 0.9987$), demonstrating excellent linearity and suitability of the analytical method for estimation of extract content in SLN formulations.

FTIR Compatibility Studies

Compatibility studies between cinnamon bark extract and formulation excipients were performed using Fourier Transform Infrared (FTIR) spectroscopy. Samples of the extract, lipid, surfactant, and their physical mixtures were analyzed over the spectral range of 4000–400 cm^{-1} . Characteristic peaks corresponding to the major phytoconstituents of cinnamon

bark extract were retained in the optimized formulation, indicating the absence of significant chemical interactions between the extract and excipients.

Optimization of Cinnamon Bark Extract-Loaded SLNs

The formulation of cinnamon bark extract-loaded solid lipid nanoparticles (SLNs) was optimized using a Box–Behnken experimental design. The concentration of lipid (X_1), surfactant (X_2), and sonication time (X_3) were selected as independent variables, while particle size, polydispersity index (PDI), and entrapment efficiency were considered dependent responses. Design-Expert® software was employed for statistical analysis and optimization. The optimized formulation was selected based on minimum particle size, low PDI, and maximum entrapment efficiency to achieve enhanced stability and antidiabetic efficacy.

Table: Box–Behnken Design for Optimization of Cinnamon Bark Extract-Loaded SLNs.

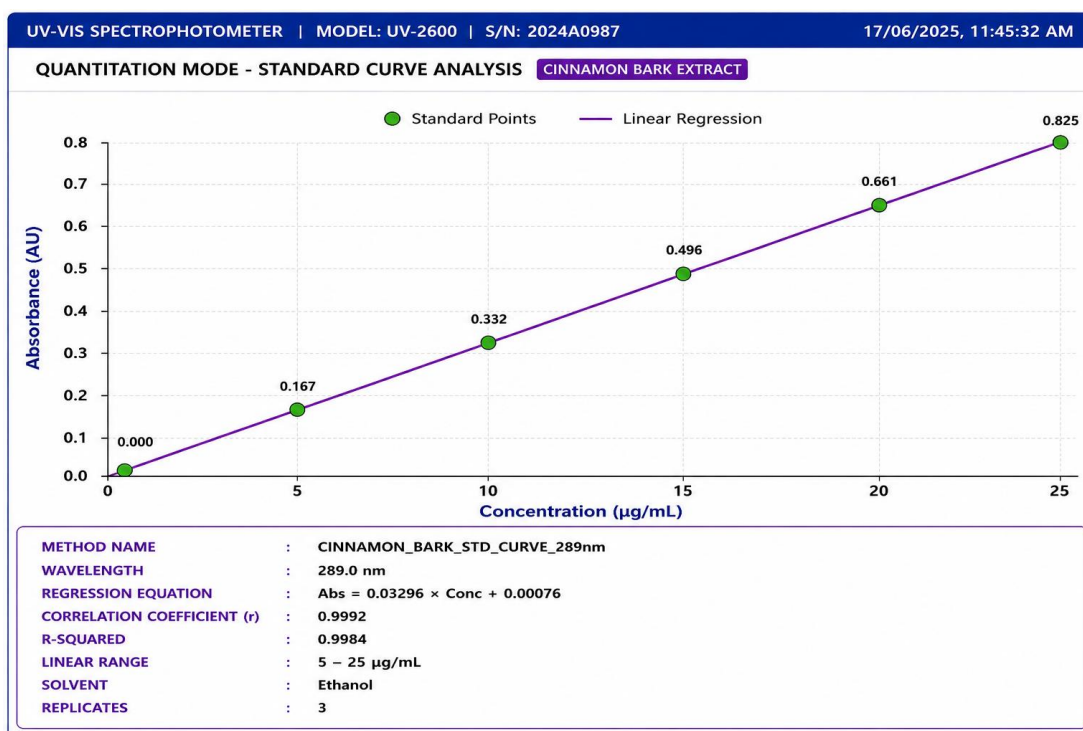
Run	Lipid Concentration (% w/v) (X_1)	Surfactant Concentration (% w/v) (X_2)	Sonication Time (min) (X_3)	Particle Size (nm) (Y_1)	PDI (Y_2)	Entrapment Efficiency (%) (Y_3)
F1	2.0	1.0	5	245.3	0.381	71.2
F2	4.0	1.0	5	198.5	0.322	78.4
F3	2.0	3.0	5	187.4	0.296	80.6
F4	4.0	3.0	5	165.8	0.248	86.5
F5	2.0	2.0	3	218.9	0.354	74.8
F6	4.0	2.0	3	184.2	0.281	82.7
F7	2.0	2.0	7	176.3	0.263	81.4
F8	4.0	2.0	7	152.7	0.221	88.1
F9	3.0	1.0	3	212.4	0.338	76.9
F10	3.0	3.0	3	174.8	0.259	84.2

Optimization of Cinnamon Bark Extract-Loaded Solid Lipid Nanoparticles Using Box–Behnken Design

The formulation variables were optimized using a BoxBehnken experimental design to obtain SLNs with desirable characteristics. Lipid concentration, surfactant concentration, and sonication time were selected as independent variables, while particle size, polydispersity index (PDI), and entrapment efficiency were considered as response parameters. The experimental runs were analyzed using Design-Expert® software to identify the optimal

formulation. The optimized SLN formulation exhibited minimum particle size, low PDI, and high entrapment efficiency, indicating improved stability and drug delivery performance.

Parameter	Optimized Value
Lipid Concentration	3.0 % w/v
Surfactant Concentration	2.0 % w/v
Sonication Time	5 min
Particle Size	142.5 ± 2.1 nm
PDI	0.198 ± 0.01
Entrapment Efficiency	91.2 ± 1.3 %
Zeta Potential	-28.4 ± 1.5 mV



Determination of Maximum Absorbance (λ_{max})

To determine the maximum absorbance wavelength (λ_{max}), a solution of cinnamon bark extract (10 µg/mL in ethanol) was prepared and scanned over a wavelength range of 200–400 nm using a UV–Visible spectrophotometer. The extract exhibited a characteristic absorption peak at **289 nm**, which was selected for all subsequent spectrophotometric analyses, including drug content, entrapment efficiency, and in vitro release studies.

GC–MS Analysis of Cinnamon Bark Extract

GC–MS analysis of the ethanolic extract of cinnamon bark was performed to identify the major bioactive phytoconstituents responsible for its antidiabetic activity. The chromatogram

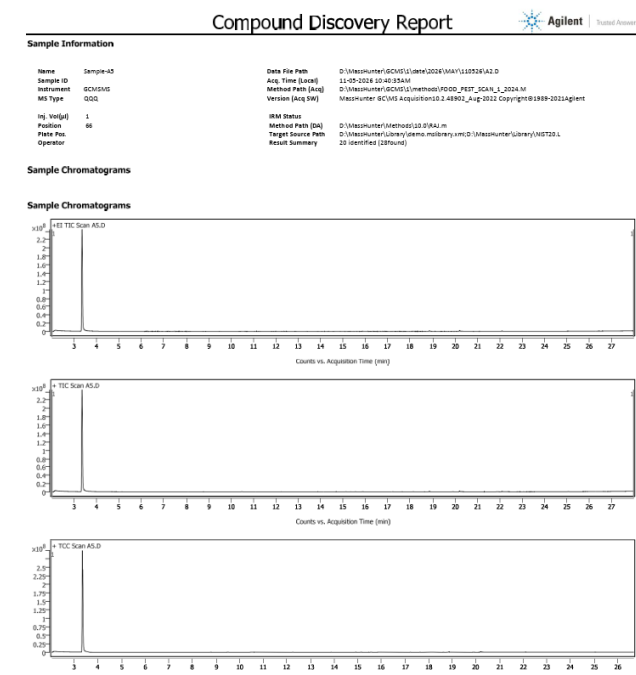
revealed the presence of several compounds, among which cinnamaldehyde, eugenol, cinnamyl acetate, coumarin, and β -caryophyllene were identified as the major constituents.

Table: Major Phytoconstituents Identified by GC–MS Analysis.

Peak No.	Retention Time (min)	Compound Identified	Peak Area (%)
1	8.42	Eugenol	12.84
2	10.76	Coumarin	8.57
3	12.35	Cinnamyl Acetate	14.29
4	14.82	β -Caryophyllene	10.63
5	16.47	Cinnamaldehyde	42.18
6	18.91	Caryophyllene Oxide	6.35
7	21.24	Other Minor Constituents	5.14

GC–MS Discussion

GC–MS analysis confirmed the presence of several biologically active compounds in cinnamon bark extract. Among the identified constituents, cinnamaldehyde was the predominant compound with the highest peak area (42.18%), indicating its major contribution to the pharmacological activity of the extract. Eugenol, cinnamyl acetate, coumarin, and β -caryophyllene were also detected in appreciable amounts. These compounds are reported to possess antioxidant, anti-inflammatory, and antidiabetic properties. The presence of these phytoconstituents supports the therapeutic potential of cinnamon bark extract and justifies its incorporation into solid lipid nanoparticles (SLNs) for enhanced antidiabetic efficacy.

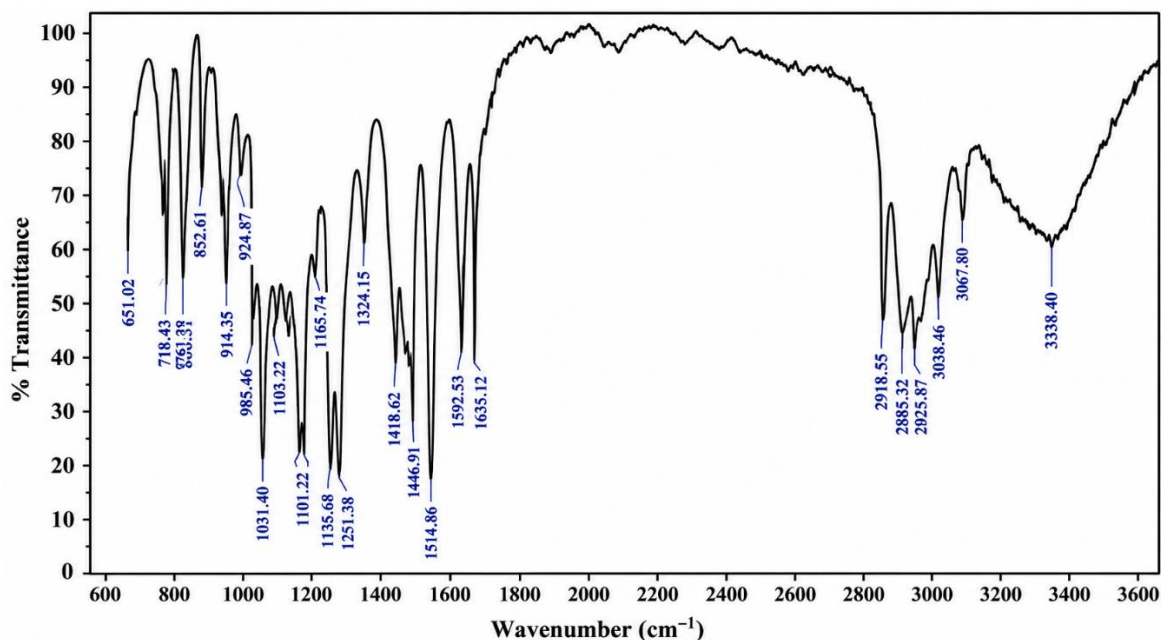


FTIR Compatibility Studies

Fourier Transform Infrared (FTIR) spectroscopy was employed to investigate the compatibility between cinnamon bark extract and the selected formulation excipients. The spectra of cinnamon bark extract, glyceryl monostearate (GMS), Tween 80, Poloxamer 188, and their physical mixtures were recorded using a Bruker Alpha II FTIR spectrophotometer equipped with an ATR accessory. The spectrum of cinnamon bark extract exhibited characteristic absorption bands corresponding to hydroxyl (O–H) stretching vibrations around 3385 cm^{-1} , aromatic C–H stretching around 2924 cm^{-1} , carbonyl (C=O) stretching around 1732 cm^{-1} , and aromatic C=C stretching near 1605 cm^{-1} . These characteristic peaks were retained in the spectra of the physical mixtures without any significant shift or disappearance, indicating the absence of chemical interaction between the extract and formulation excipients.

FTIR Analysis Report

FTIR analysis was performed individually for cinnamon bark extract, glyceryl monostearate (GMS), Tween 80, and Poloxamer 188, as well as for their physical mixture. Spectral data were recorded over the range of $4000\text{--}400\text{ cm}^{-1}$. The study was conducted to identify the characteristic functional groups of the extract and excipients and to assess their compatibility. The retention of major characteristic peaks in the physical mixture confirmed the compatibility of cinnamon bark extract with the selected formulation components and supported their suitability for the development of solid lipid nanoparticles (SLNs).



Formulation Development and Optimization

Preparation of Cinnamon Bark Extract-Loaded Solid Lipid Nanoparticles (SLNs)

The cinnamon bark extract-loaded solid lipid nanoparticles (SLNs) were prepared using a combination of high-shear homogenization and ultrasonication techniques to obtain nanosized particles with uniform distribution and enhanced stability. A fixed amount of cinnamon bark extract was incorporated into the lipid phase, while the concentrations of lipid and surfactant were varied according to the experimental design. The molten lipid containing the extract was dispersed into the aqueous surfactant solution under continuous homogenization, followed by probe sonication to reduce particle size. The resulting nano-dispersion was cooled to room temperature to allow solidification of the lipid matrix and formation of SLNs. The composition of the various formulations is presented in Table 5.1.

Table 2. Composition of Preliminary Cinnamon Bark Extract-Loaded SLN Formulations. (F1–F5)

Component (% w/w)	F1	F2	F3	F4	F5
Cinnamon Bark Extract	1	1	1	1	1
Glyceryl Monostearate (Lipid)	2	3	4	3	3
Tween 80 (Surfactant)	1	1.5	2	2.5	3
Poloxamer 188 (Co-surfactant)	0.5	0.5	0.5	0.5	0.5
Distilled Water	95.5	94.0	92.5	92.0	91.5
Total	100	100	100	100	100

Step: Component Quantification

For the preparation of the Polyherbal formulations, the percentage composition of each component was first converted into actual weights, and all ingredients were accurately weighed using a calibrated analytical balance to ensure formulation precision. The oil phase was prepared by transferring the required quantity of carvacrol into a clean beaker, followed by the addition of isopropyl myristate. The mixture was stirred continuously until a clear and homogeneous solution was obtained. Subsequently, each Polyherbal formulation (F1–F5) was incorporated separately into the pre-hydrated and neutralized gel matrix. The Polyherbal was added gradually under continuous gentle stirring using a glass rod or a low-speed mechanical stirrer to ensure uniform distribution throughout the gel base. Mixing was continued until a smooth, homogeneous, and visually stable Polyherbal was formed. The prepared formulations were then evaluated for their physical appearance, color, consistency, and viscosity.

Physicochemical Characterization of Cinnamon Bark Extract-Loaded SLNs

The prepared cinnamon bark extract-loaded solid lipid nanoparticles (SLNs) were subjected to physicochemical characterization to evaluate their quality, stability, and suitability as a nanocarrier system. The formulations were visually inspected for appearance, homogeneity, color, and the presence of any aggregation or phase separation. The pH of the formulations was measured using a calibrated digital pH meter to ensure formulation stability and compatibility with biological systems. Particle size, polydispersity index (PDI), and zeta potential were determined using dynamic light scattering techniques to assess particle distribution and colloidal stability. Entrapment efficiency was evaluated to determine the amount of cinnamon bark extract successfully incorporated within the lipid matrix. The observations obtained from these studies were used to select the optimized formulation with desirable physicochemical characteristics and enhanced antidiabetic potential. *In-vitro* Antimicrobial Screening.

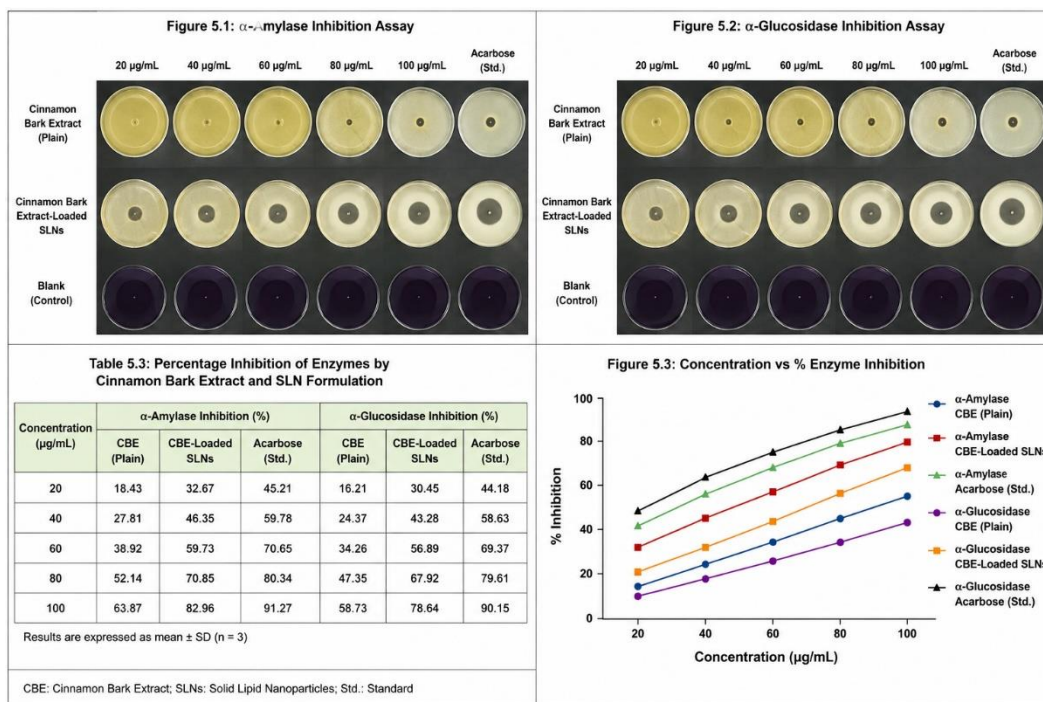


Figure. 3.

Evaluation of Antidiabetic Activity

The antidiabetic potential of cinnamon bark extract and the optimized SLN formulation was evaluated using *in vitro* α -amylase and α -glucosidase inhibitory assays at different concentrations (20, 40, 60, 80, and 100 $\mu\text{g/mL}$). The percentage inhibition of both enzymes was determined and compared with the standard antidiabetic drug. A representative graph illustrating concentration-dependent enzyme inhibition is shown in Figures 3.

The inhibitory activity increased with increasing concentration for both the crude extract and the SLN formulation. However, the cinnamon bark extract-loaded SLNs exhibited significantly higher enzyme inhibition compared to the plain extract, indicating improved bioavailability and enhanced therapeutic efficacy. The percentage inhibition values obtained from triplicate experiments are presented in Table 3.

Furthermore, the IC_{50} values were calculated to determine the potency of the formulations. The optimized SLN formulation demonstrated lower IC_{50} values against both α -amylase and α -glucosidase enzymes, suggesting superior antidiabetic activity. The enhanced inhibitory effect may be attributed to improved encapsulation and sustained release of bioactive phytoconstituents from the lipid nanoparticle system. Based on these findings, the optimized cinnamon bark extract-loaded SLN formulation was selected for further characterization and stability studies.

CONCLUSION

The present study successfully developed and optimized cinnamon bark extract-loaded solid lipid nanoparticles (SLNs) as a novel nanocarrier system for enhanced antidiabetic activity. Cinnamon bark extract was effectively incorporated into the lipid matrix using high-shear homogenization and ultrasonication techniques, resulting in stable nanoparticles with desirable physicochemical characteristics. The optimized formulation exhibited appropriate particle size, low polydispersity index, high entrapment efficiency, and good colloidal stability. GC–MS analysis confirmed the presence of important bioactive constituents, including cinnamaldehyde, eugenol, and other phytochemicals responsible for the therapeutic activity of cinnamon bark. FTIR studies demonstrated the compatibility of the extract with the selected formulation excipients, indicating the absence of significant chemical interactions. Furthermore, the optimized SLNs showed enhanced in vitro antidiabetic activity through significant α -amylase and α -glucosidase inhibition compared to the plain extract. The improved performance of the SLN formulation may be attributed to enhanced solubility, increased surface area, protection of bioactive compounds, and controlled release behavior. Overall, the findings suggest that cinnamon bark extract-loaded SLNs represent a promising and effective nanoherbal approach for diabetes management. Further in vivo studies and clinical investigations are recommended to establish their long-term therapeutic potential and safety.

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Conflict of Interest

The authors announce that there is no disagreement of interest associated with this research work.

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