RESEARCH ARTICLE

Design and Development of Betacyanin-Encapsulated Solid Lipid Nanoparticles for Antidiabetic Therapy

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Abstract

Introduction: Diabetes, affecting over 400 million people globally, can lead to severe complications such as cardiovascular disease, kidney failure, and limb amputation. Nanotechnology offers innovative solutions through solid lipid nanoparticles (SLNs) to enhance the bioavailability and therapeutic effects of antidiabetic agents like quercetin, metformin, and betacyanin. Betacyanin, a natural pigment in red beetroot, possesses strong antioxidant and antidiabetic properties but suffers from poor solubility and stability.

Material and Methods: This study developed SLNs containing betacyanin using heat homogenization and ultrasonication, with glyceryl monostearate, soya lecithin, and Poloxamer 407 as core ingredients. The formulations were evaluated for particle size, drug entrapment, surface morphology, zeta potential, drug release, and antidiabetic activity.

Results and Discussions: *In-vitro* release studies using Franz diffusion cells showed a sustained release of 91.73% over 8 hours. The optimized SLN batch had a particle size of 279 nm and an encapsulation efficiency of 82.71%. Stability studies conducted under ICH guidelines confirmed their robustness over 90 days. The SLNs also demonstrated moderate antidiabetic activity with an IC50 value of 23.25 µg/mL. SLNs have also been reported to reduce α–amylase and α–glucosidase levels for management of diabetes.

Conclusion: These findings suggest that betacyanin-loaded SLNs hold significant promise as a stable and effective alternative for controlled drug delivery in diabetes management.

Keywords: Diabetes, solid lipid nanoparticles (SLNs), betacyanin, ultrasonication, controlled drug release

Highlights

- We have developed betacyanin-loaded solid lipid nanoparticles (SLNs) using heat homogenization and ultrasonication to improve stability, solubility, and antidiabetic efficacy of betacyanin.
- The optimized formulation (F5/Fopt) showed small particle size (279 nm), high encapsulation efficiency (82.71%), high yield (87.81%), and stable zeta potential (-14.95 mV).
- *In-vitro* drug release demonstrated a sustained release of 91.73% over 8 hours, confirming controlled drug delivery potential.
- Antidiabetic assays (α-amylase and α-glucosidase inhibition) showed moderate antidiabetic activity with an IC50 of 23.25 µg/mL, supporting therapeutic potential.
- Stability studies (90 days, ICH conditions) confirmed formulation robustness, suggesting that betacyanin-encapsulated SLNs are a promising alternative for effective diabetes management.

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Introduction

Diabetes mellitus is a chronic metabolic disorder marked by persistent hyperglycemia resulting from impaired insulin secretion, insulin action, or both. Its global prevalence has risen sharply due to rapid urbanization, sedentary habits, and increased obesity rates, making it one of the most challenging non-communicable diseases of modern times. Beyond elevated blood glucose, diabetes disrupts lipid and protein metabolism, leading to severe complications such as neuropathy, retinopathy, nephropathy, and cardiovascular diseases.[1] These complications significantly reduce quality of life, increase mortality, and impose substantial financial burdens on healthcare systems worldwide, particularly in low- and middle-income countries. Despite advancements in therapeutic options, achieving sustained glycemic control remains difficult due to drug-related side effects, limited patient adherence, and individual variations in treatment response, emphasizing the need for improved and innovative therapeutic strategies.[2]

Over 400 million people worldwide suffer from hyperglycemia, and the number is predicted to rise in the future. Severe side effects of the condition include amputations of lower limbs, blindness, kidney failure, and cardiovascular disorders. It has a big impact on healthcare systems and people's quality of life. Diabetes management carries high financial expenditures, which have an impact on national healthcare budgets in many nations.[3] Diabetes is caused by several factors, such as an aging population,

sedentary lifestyles, unhealthy eating habits, and growing urbanization. Diabetes therapy necessitates a multimodal strategy that includes early detection, prevention, high-quality medical care, and cutting-edge therapeutic approaches.[4]

Diabetes has a long history, with ancient Egyptians and Indian healers recognizing it as a disease characterized by frequent urination. In the Middle Ages, Persian polymath Avicenna identified diabetes and differentiated between Type 1 and Type 2-like symptoms. In the Renaissance, Swiss physician Paracelsus termed diabetes "sweet urine disease" and linked it to sugar in urine. In the 20th century, Frederick Banting and Charles Best discovered insulin, which was used to treat diabetes patients. Today, advances in genetics and molecular biology reveal more about diabetes's causes and mechanisms and the development of new insulin formulations and delivery methods.[5]

Diabetes management faces challenges such as frequent injections, hypoglycemia risk, and weight gain, while oral antidiabetic medications can cause adverse effects. Some patients fail to achieve adequate glycemic control, highlighting the need for more effective therapies. Antidiabetic medications also carry safety concerns, and access to newer, more effective drugs may be limited due to high costs. Lifestyle modifications, such as diet and exercise, can be challenging due to socioeconomic and psychological barriers. Personalized treatment strategies are needed to achieve optimal glycemic control and minimize complications.[6]

Natural Products in the Management of Diabetes

Natural products, including beetroot, have shown potential in treating various ailments due to their bioactive compounds, such as polyphenols, alkaloids, flavonoids, and terpenoids. These natural remedies are popular due to their perceived efficacy, safety, and comprehensive approach to health.[7] Betacyanins, a class of reddish-violet pigments found in beetroot, have been found to have positive effects on insulin sensitivity and glucose metabolism, potentially helping control diabetes. Beetroot extracts rich in betacyanins have hypoglycemic properties, reducing blood sugar levels and improving insulin sensitivity in diabetic animal models. These properties may also reduce oxidative stress and chronic inflammation associated with diabetes. Further research is needed to understand the pharmacological characteristics, ideal dosage schedules, and safety profile of betacyanin-containing products.[8]

Nano-Formulations

Nano-formulations in drug delivery represent a paradigm shift in pharmaceutical science, offering unprecedented opportunities to improve the effectiveness and safety of drugs. By manipulating drug particles at the nanometer scale, nano-formulations can surpass numerous restrictions typically associated with traditional medication delivery techniques.[9] By decreasing the size of medication particles to the nanoscale, nano-formulations increase the surface area available for drug dissolution and absorption, leading to enhanced drug absorption and systemic exposure.[10]

Types of Nano-Formulations

Various types of nano-formulations used in drug delivery include liposomes, polymeric nanoparticles, dendrimers, nanocrystals, carbon nanotubes, and gold nanoparticles. Liposomes are round entities composed of lipid bilayers surrounding a central aqueous core, while polymeric nanoparticles are tiny molecules created of biodegradable and biocompatible polymers. Dendrimers provide precise manipulation of dimensions, configuration, and surface properties, facilitating accurate administration of drugs and utilization in imaging procedures. Nano-formulations have great potential to completely transform pharmaceutical administration, leading to safer, more efficient, and user-friendly treatments.

Solid Lipid Nanoparticles (SLNs)

Solid Lipid Nanoparticles (SLNs) are lipid-based nanoparticles that offer benefits such as biocompatibility, stability, and control of drug release. They consist of solid lipids at room temperature and are biocompatible and biodegradable, making them suitable for various biomedical applications. SLNs are produced through processes like high-pressure homogenization, ultrasonication, or microemulsion, and have a core-shell configuration with a surfactant layer. They typically range between 50 and 1000 nm in size. SLNs offer advantages such as controlled drug release, improved stability, biocompatibility, and scalability. They are used in drug delivery, cosmetic formulations, and imaging agents. Applications include drug delivery, cosmetic formulations, and imaging agents.[11]

The development of betacyanin nano-formulations aims to enhance its therapeutic capacity as an antidiabetic drug. Betacyanin, an inherent chromophore found in plants like beetroot, has bioactive properties that are beneficial in diabetes management. Nano-formulations can protect betacyanin from degradation, improve solubility, and enhance its delivery to target tissues, potentially increasing its efficacy. Betacyanin's antioxidant capabilities can help mitigate oxidative stress, a crucial element in diabetes treatment.[12] However, delivering betacyanin effectively requires sensitivity to degradation during processing, storage, and delivery, and the need for separation and purification protocols. Researchers have created nano-formulations to enclose betacyanin, enhancing its antidiabetic activity. The study's significance lies in its potential to transform diabetes care by enhancing betacyanin SLNs, improving its bioavailability and absorption, optimizing glucose regulation, reducing adverse effects, and enhancing patient adherence. The results could significantly impact pharmaceutical sciences and drug delivery, potentially leading to the development of new antidiabetic agents and improving the quality of life for diabetic patients.[13]

Materials and Methods

The chemicals used in the experiment were all of analytical grade. Experimentally used chemicals have been purchased from SRL chemicals. Betacyanin have been purchased from Sigma-Aldrich. The following methods were used in the experimental investigation.

Experimental Work

Determination of Absorbance Maxima (λmax) of Betacyanin

By using a UV-visible spectrophotometer (Shimadzu UV-1800 spectrophotometer). 10 µg/ml solution of Betacyanin in distilled water was scanned between 400 to 800 nm.[14]

Preparation of the Phosphate Buffer pH 6.8

A 0.2M concentration of potassium dihydrogen orthophosphate was created by liquifying 27.218 gm in distilled water and diluting it to 1000 ml. A sodium hydroxide solution was prepared and then mixed with distilled water to prevent carbon dioxide absorption. The resulting solution was adjusted to contain 8.0 gm of NaOH in 1000 ml. The solution was then transferred to a 200 ml volumetric flask.[15]

Preparation of Calibration Curve of Betacyanin in Phosphate Buffer pH 6.8

Dissolve 10 mg of betacyanin in 100 ml of phosphate buffer. Transfer the solution to a volumetric flask and add phosphate buffer to create a stock solution. Transfer 1 to 5 ml into 10 ml flasks, then add phosphate buffer to each flask. Calculate absorbances at 538 nm for concentrations ranging from 10µg/ml to 50µg/ml.[16]

Fourier-transforms-infrared-spectroscopy (FT-IR)

IR spectroscopy is used to identify medicinal substances, with FT-IR spectroscopy verifying the complex between polymers and medications. It assesses compatibility between medicines and excipients, examining both medications alone and in combination with specific excipients.[17]

Formulation Development: Preparation of Solid Lipid Nanoparticles of Betacyanin

Preparation of solid lipid nanoparticles containing betacyanin using hot homogenization. The lipid layer was liquefied by heating at 78°C, followed by dissolving Poloxamer 407 in double-distilled water. The lipid phase was combined with a hot aqueous phase, homogenized at 12,000 rpm for 5 minutes, and ultrasonicated for 20 minutes. The nano-emulsion was then cooled to ambient temperature.[18] The selection of these ingredients was based on their complementary roles in developing a stable, efficient, and biocompatible SLN system for betacyanin delivery. Betacyanin was chosen as the active compound due to its potent antioxidant and antidiabetic properties, warranting a protective nanocarrier system to enhance its stability and therapeutic efficacy. Glyceryl monostearate (GMS) served as the solid lipid matrix because of its excellent biocompatibility, high drug-loading capacity, and ability to form stable nanoparticles with controlled release behavior. Soy lecithin was incorporated as a natural phospholipid emulsifier to improve nanoparticle stability, enhance encapsulation efficiency, and provide a biocompatible interface between the lipid core and aqueous phase. A chloroform:methanol (1:1) solvent mixture was used to ensure efficient solubilization of both lipid and drug components during the formulation process. Poloxamer 407, a nonionic surfactant, was utilized to stabilize the nanoparticles by reducing interfacial tension and preventing aggregation, thereby improving dispersion uniformity. The method of formulation is shown in Figure 1 and Table 1.

Evaluation of Solid Lipid Nanoparticles (SLNs) of Betacyanin

Percentage Yield

Percent yield denotes the % ratio of actual yield to the theoretical yield.

Percent Yield= (Practical Yield/Theortical Yield) ×100

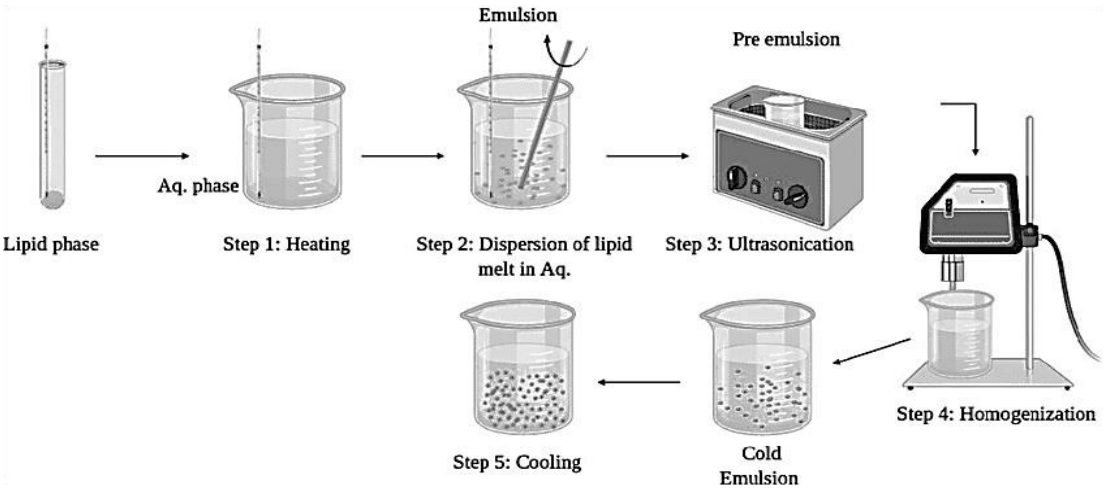


Figure 1: Preparation of Solid Lipid Nanoparticles of betacyanin

Table 1: Formulation chart of Solid Lipid Nanoparticles of Betacyanin

Ingredients	*F1*	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*	*F9*
Betacyanin (mg)	100	100	100	100	100	100	100	100	100
Glyceryl monostearate (mg)	100	100	100	200	200	200	300	300	300
Soy lecithin (mg)	100	125	150	100	125	150	100	125	150
Chloroform: Methanol (1:1)	10	10	10	10	10	10	10	10	10
Poloxamer 407 (mg)	150	150	150	150	150	150	150	150	150
Double distilled water (ml)	100	100	100	100	100	100	100	100	100

Encapsulation Efficiency (EE%) of Solid Lipid Nanoparticles (SLNs) of Betacyanin

The ultracentrifugation method was used to separate the unentrapped medication from the nano lipid formulation. The nano lipid dispersion was placed to centrifugation at 13,000 revolutions per minute speed for 90 min. The transparent liquid that settled on top of the solution was appropriately thinned using a pH 6.8 phosphate buffer and examined using a UV-visible spectrophotometer.[18]

EE (%) = (Total quantity of drug–Quantity of free drug in supernatant) ×100

Particle size determination

Prepared nanoparticles were measured by a Malvern zetasizer (Malvern P Analytical Ltd). Zeta potential (ζ) measurements were performed on solid lipid nanoparticles using a Zetasizer 4. The zeta potential was measured with the use of an aqueous dip cell in an automated manner. After going through the process of diluting the samples along ultra-purified water, they were placed in a capillary measuring cell and the cell position was adjusted.

(SEM)

Scanning electron microscopy has been conducted to examine the nanoparticles for the determination of size & shape of developed SLNs. For particle size analysis, freshly prepared, undiluted aqueous SLN dispersions were used. Prior to measurement, the samples were suitably diluted with double-distilled water to ensure optimal scattering intensity and accurate readings.

In-vitro Drug Release Study

The study assessed drug release in a laboratory setting using Franz vertical diffusion cells. Colloidal dispersions were introduced into donor compartments, separated by synthetic cellulose acetate filters. A phosphate buffer solution was introduced into receptor compartments, and UV-Vis spectrophotometry was used to measure Betacyanin concentration.[19]

Stability Study

The study conducted an accelerated stability study on an optimized batch, kept at accelerated temperatures and humidity conditions for 90 days. The batch was tested for stability by keeping it in sealed transparent flasks at ambient temperature. The *in-vitro* drug release study profile was obtained on the first day of storage, 30, 60, and 90 days of loading.[19]

Antidiabetic *In-vitro* Studies

Alpha (α) – Amylase inhibitory assay

The dinitrosalicylic acid (DNS) method was used to prepare a stock solution of Betacyanin, which was then mixed with α-amylase and starch solution. The mixture was incubated at 37°C for 15 minutes, then heated in a water bath. The absorbance was evaluated at 540 nm using a UV spectrophotometer, and the % inhibition was estimated using the equation.[19]

$$\text{Inhibition (\%)} = \frac{([(\text{Ac-Ab})-(\text{Asample-Ab})])/((\text{Ac-Ab})*100\%)}{}$$

Assay for α-glucosidase inhibition

The study tested samples for α-glucosidase inhibition using a solution of 0.5 units/mL of α-glucosidase enzyme in 0.1 M phosphate buffer and a substrate solution of 5 mM p—Nitrophenyl—Dglucopyranoside. Samples with concentrations between 31.25 µg/mL and 1,000 µg/mL were prepared and incubated at 37°C. The percent inhibition was determined using a UV-visible spectrophotometer, with acarbose as a positive control.[20]

$$\text{Inhibition (\%)} = \frac{(\text{Absorbance of Control-Absorbance of Sample})/(\text{Absorbance of Control})*100\%}{}$$

Results and Discussion

Experiment Work

Determination of Absorption Maxima of Betacyanin

The absorption maxima (λ_{max}) of Betacyanin in phosphate buffer pH 6.8 were determined using a UV-visible spectrophotometer. This step is crucial for characterizing the spectral properties of these compounds within the context of formulating nanoparticles for diabetes mellitus treatment. Absorption maxima of Betacyanin were observed. The absorption maxima (λ_{max}) of the Betacyanin solution in phosphate buffer pH 6.8 was initiated to be 538 nm as seen

in Figure 2 where Figure 3 shows the calibration readings and calibration plot of Betacyanin.

Compatibility study

FT-IR spectroscopy is utilized to confirm the formation of a polymer-drug complex, confirming the identity of pharmaceutical compounds by comparing individual polymer and drug ranges. FT-IR spectrum shows a broad absorption peak around 3280 cm^{-1}, indicating O–H stretching vibrations associated with hydroxyl groups present in betacyanin. A distinct peak near 1336 cm^{-1} corresponds to C–N or C–O stretching, confirming functional groups characteristic of the betalain chromophore. Additionally, the bands observed in the 1015–428 cm^{-1} region fall within the fingerprint zone and represent vibrations related to glycosidic linkages and aromatic ring substituents, further supporting the structural features of betacyanin. Figures 4, 5,6 show readings from FTIR spectra of Betacyanin and the Formulation blend, respectively.

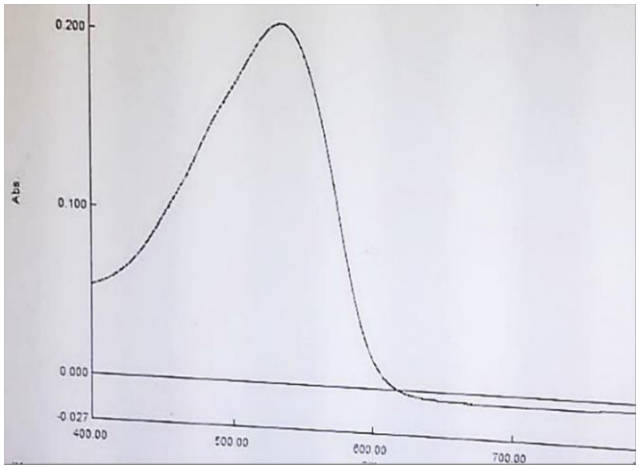


Figure 2: Absorption maxima of Betacyanin (λmax=538 nm)

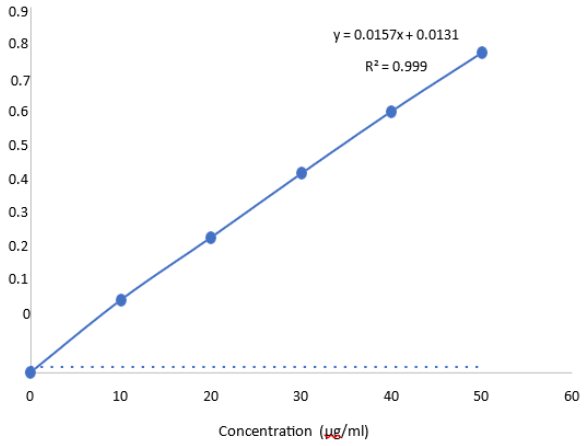


Figure 3: Standard Calibration Curve of Betacyanin in phosphate buffer pH 6.8

Evaluation of SLNs (solid lipid nanoparticles) of Betacyanin

The SLNs of betacyanin were developed and evaluated for the following parameters.

Percentage yield

The amount of Betacyanin in each formulation was determined and the data is presented in Table 2. The percentage yield of formulations F1-F9 was found respectively. The formulation F5 showed the highest % yield of 87.81%.

Entrapment Efficiency

The number of active constituents in the supernatant was obtained by utilizing a UV spectrophotometer at 266 nm & the absorbance readings were used to find the amount of free drug which further determined the % EE. The %EE ranged between 62.43% to 82.71% as shown in Table 3 & Figure 6. Batch F5 shows the highest entrapment efficiency of 82.71%.

Particle size

The particle size of the Nanoparticles was evaluated by utilizing a Zetasizer 4 (Malvern Instruments Ltd., Malvern, UK). The most important characteristics of the nanoparticle system are the particle size & the size dispersal of the particles

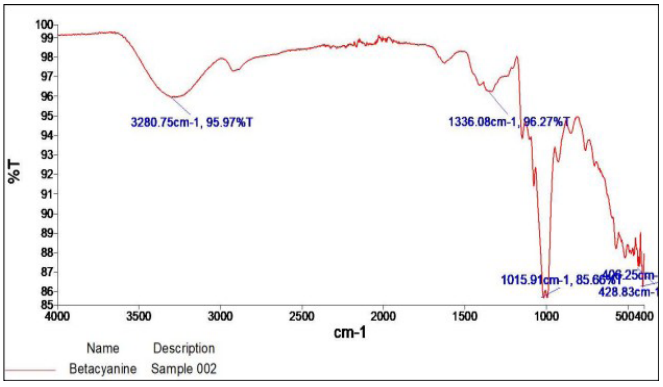


Figure 4: FT-IR spectra of Betacyanin

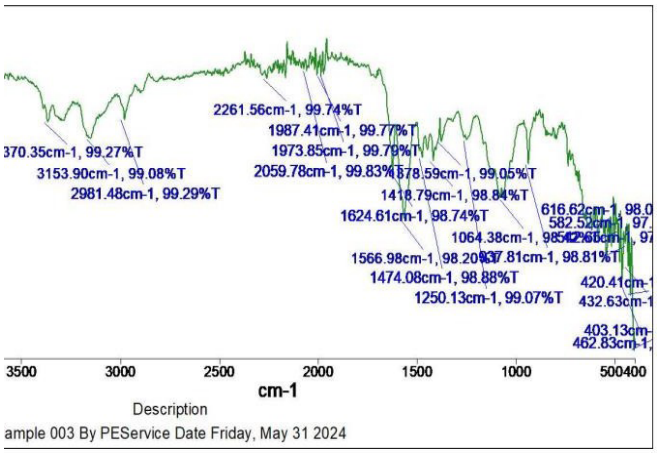


Figure 5: FT-IR spectra of Formulation Blend

it contains. The particle size of preparation F1- F9 was found in the range of 281-529nm, respectively. Batch F5 was shown to have the smallest size of 281nm, and the data was presented in Table 4 and Figure 7.

Zeta potential

Zeta potential of drug-loaded SLNs was evaluated and sounded to range between – 7.83 to – 14.95, are shown in Table 5.

Table 2: Percentage yield of formulations F1-F9

Batches	*Percentage yield(%)*
F1	63.25
F2	77.42
F3	71.21
F4	68.95
F5	87.81
F6	74.85
F7	69.43
F8	64.51
F9	52.36

Table 3: EE % of solid lipid nanoparticles of betacyanin (Formulation batches F1-F9)

Batches	*Entrapment Efficiency(%)*
F1	78.55
F2	51.83
F3	73.18
F4	58.25
F5	82.71
F6	65.82
F7	69.37
F8	55.31
F9	62.43

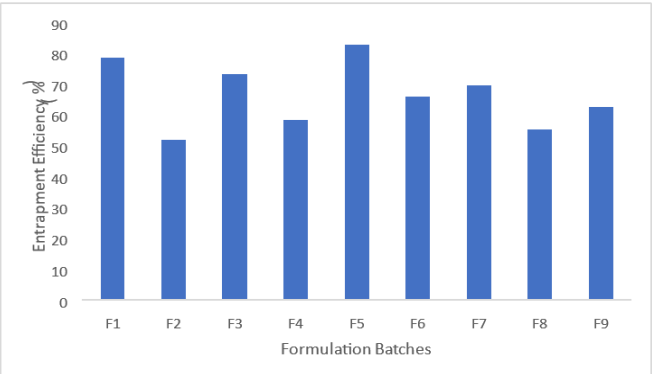


Figure 6: EE% of solid lipid nanoparticles of Betacyanin (Formulation batch F1-F9)

Scanning electron microscope (SEM)

A surface morphology study of developed batches of Betacyanin solid lipid nanoparticles was conducted and it was found that the nanoparticles were spherical with rough surfaces.

In-vitro drug release

The dissolution profile of all the batches of solid lipid nanoparticles of Betacyanin was obtained in phosphate buffer pH 7.4. The *in-vitro* dissolution testing was performed for 8 hours. (480 minutes). The *in-vitro* drug release from SLNs of Betacyanin ranged from 72.98% to 92.13%. The maximum

Table 4: Particle size of preparation (Formulation batches F1-F9)

Batches	*Particle Size (nm)*
F1	302
F2	529
F3	342
F4	488
F5	281
F6	415
F7	394
F8	507
F9	429

Table 5: Zeta potential of preparation (Formulation batches F1-F9)

Batches	*Zeta Potential (mV)*
F1	-12.67
F2	-13.73
F3	-11.95
F4	-7.83
F5	-14.95
F6	-10.95
F7	-9.75
F8	-11.03
F9	-12.25

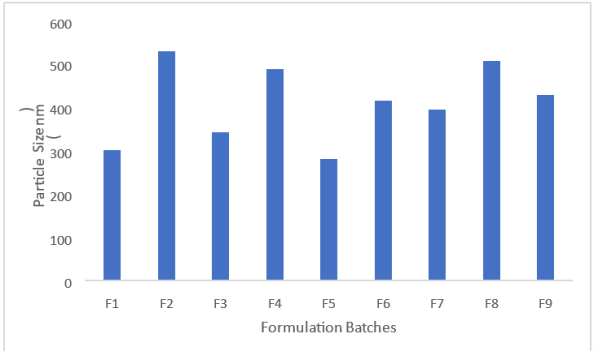


Figure 7: The particle size of betacynin loaded SLNs (Formulation batch F1-F9)

in-vitro drug release was depicted to be 92.13% from F5 at the end of 480 minutes as represented in Table 6 & Figure 8.

Based on the result obtained from the evaluation study, it was experimental that batch F5 showed better results when compared with other batches.

Optimization of Solid Lipid Nanoparticles of Betacyanin

Selection of an optimized formulation, SLNs of Betacyanin underwent optimization study by using 3*2 full factorial design. Two independent parameters i.e., Glyceryl monostearate and Soya lecithin were chosen and their consequence on relatable variables i.e., particle size & encapsulation efficiency (%EE) were determined.

Effect of Glyceryl monostearate and Soya lecithin concentration on particle size & Shape

- *Entrapment efficiency*

The heated homogenization approach was then the ultrasonication method to complete the formulation of SLNs. The different concentrations of Glycerol monoetherate and soy lecithin were used to prepare nanoparticles. An optimization study was conducted to see the effect of lipid and polymer concentration on particle size & entrapment efficiency.

- *Preparation and Evaluation of Optimized Batch*

The study optimized a batch using selected variables, assessing metrics like yield, particle size, zeta potential, entrapment efficiency, and *in-vitro* drug release, with results presented in Table 7 and Figure 9-10.

Particle size

- *Surface morphology*

The surface morphology study of an optimized batch (Fopt) of Betacyanin solid lipid nanoparticles has shown that nanoparticles were spherical with a rough surface are shown in Figure 11.

- *In-vitro drug release study of optimized batch*

The optimized batch has also undergone for in-vitro drug release study. Findings was observed that 91.73% drug was released from the optimized batch in 8 hr are shown Table 8 and Figure 12.

- *Stability Studies*

The optimized batch was kept on accelerated conditions to check the stability of the optimized batch. The physical appearance of *in-vitro* drug release studied was observed for stability testing. The outcome of appearance, and *in-vitro* drug release studies, on 0, 30, 60 & 90 days of storage are mentioned in Table 9-10, and Figure 13.

In-vitro Antidiabetic Activity

Alpha (α) – Amylase inhibitory assay

This study evaluated Betacyanin's capacity against α–amylase activity, a crucial digestive enzyme. Results showed that Betacyanin-SLN significantly reduced α–amylase activity in a dose-dependent manner, with a moderate inhibitory effect of 23.25 ± 0.76% at 200 µg/mL are shown in Table 11 and Figure 14. This suggests that Betacyanin's enzyme-inhibitory nature could potentially act against diabetes by reducing α–amylase activity.

Table 6: In-vitro drug release profile of solid lipid nanoparticles of Betacyanin (Formulation batches F1-F9)

Time									
(Minutes)	*F1*	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*	*F8*	*F9*
0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
60	25.65	12.72	23.21	16.77	27.31	18.19	20.68	14.45	16.84
120	39.65	23.93	36.78	28.21	43.35	32.01	34.67	25.21	29.78
180	52.87	32.78	49.87	39.98	55.95	43.98	46.89	35.23	38.78
240	63.78	44.45	60.98	50.86	66.12	54.86	58.28	47.23	49.51
300	71.89	53.86	68.67	57.91	74.91	60.25	64.76	55.87	57.76
360	77.24	61.35	74.98	65.89	81.46	67.35	72.67	63.89	65.89
420	82.98	66.95	80.98	71.76	87.23	74.19	78.45	68.95	71.21
480	88.92	72.98	86.21	76.78	92.13	80.95	84.95	74.12	78.32

Table 7: Evaluation parameters for optimizing batch (Fopt)

Formulation Batch	*Evaluation Parameters*			
	Particle Size (nm)	*Zeta Potential (mv)*	*Entrapment Efficiency (% EE)*	*Percentage Yield (%)*
Fopt	279	-14.95	82.71	87.81

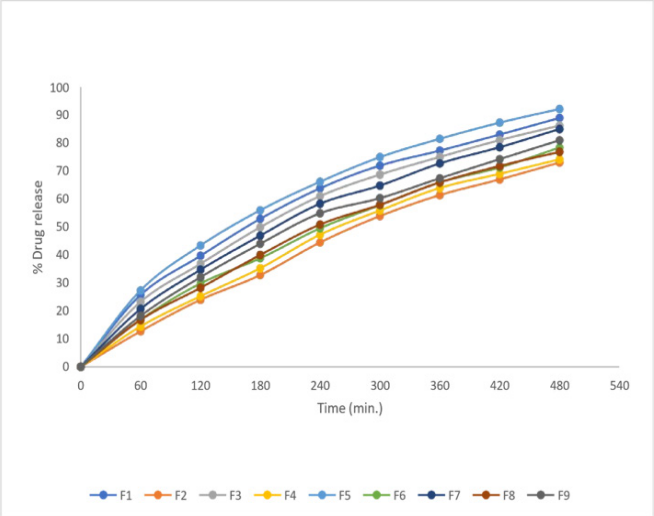
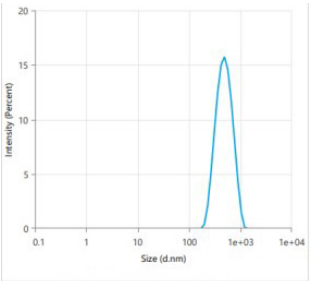
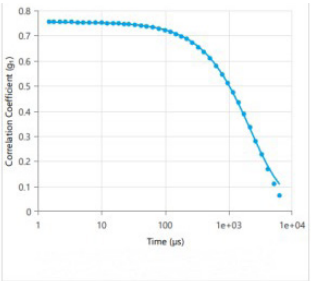


Figure 8: Percentage drug Release of solid lipid nanoparticles of Betacyanin (Formulation batches F1-F9)





Name	Mean	Standard Deviation	RSD	Minimum	Maximum
Z-Average (nm)	279	-	-	279	279
Polydispersity Index (PI)	0.4249	-	-	0.4249	0.4249
Intercept	0.9629	-	-	0.9629	0.9629
Derived Mean Count Rate (kcps)	1.815E+04	-	-	1.815E+04	1.815E+04
Cuvette Position (mm)	4.64	-	-	4.64	4.64
Number Of Size Runs	30	-	-	30	30
Run Retention (%)	100	-	-	100	100
In Range (%)	93.26	-	-	93.26	93.26
Fit Error	0.004959	-	-	0.004959	0.004959
Detector Angle (°)	90	-	-	90	90

Figure 9: Particle Size of Optimized batch (Fopt) of SLNs of Betacyanin

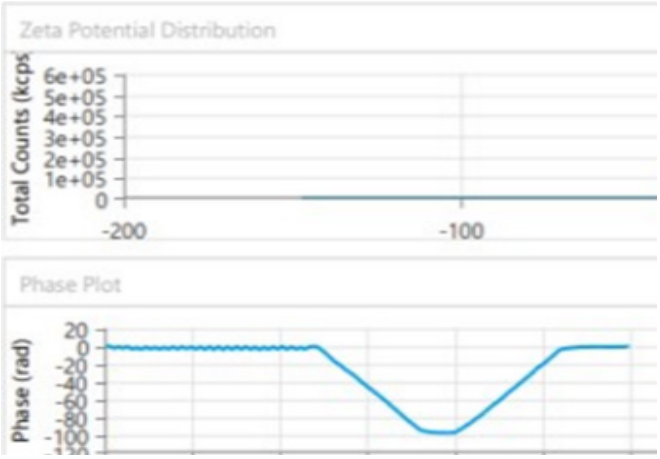


Figure 10: Zeta potential of Optimized batch (Fopt) of SLNs of Betacyanin

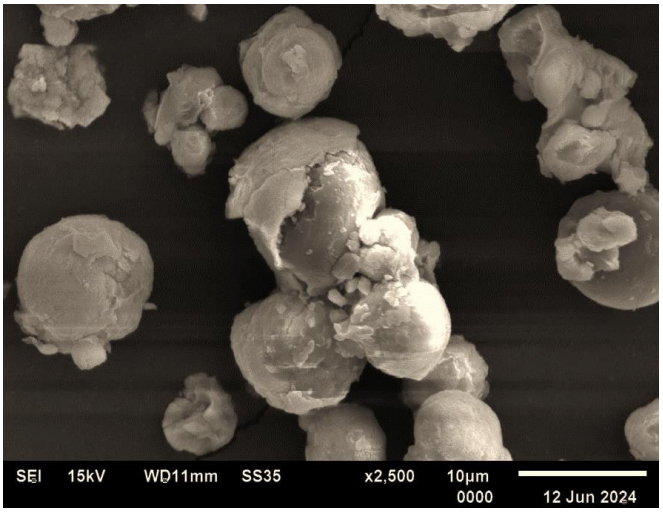


Figure 11: Surface morphology study of an optimized batch (Fopt) of Betacyanin solid lipid nanoparticles

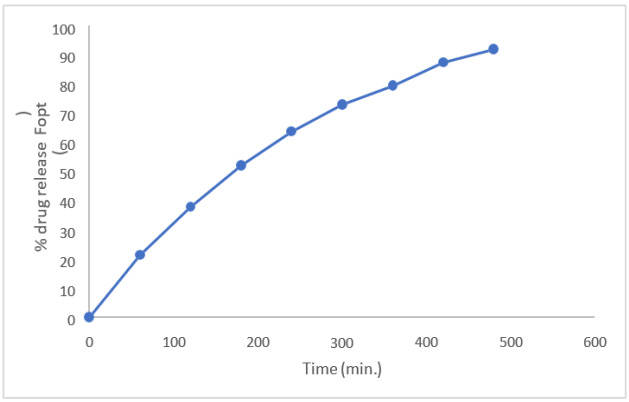


Figure 12: In-vitro drug release profile of optimized (Fopt) batch of Betacyanin (SLNs)

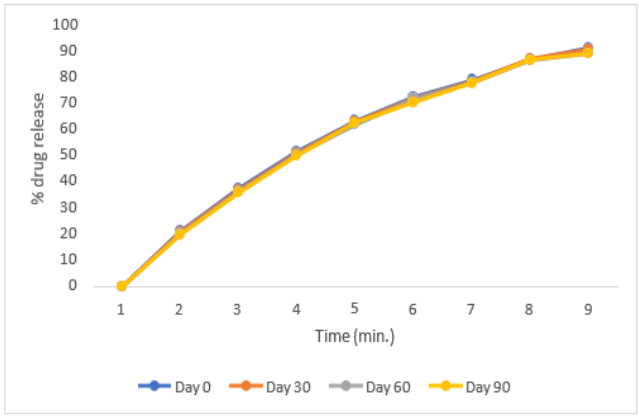


Figure 13: Effect of stability conditions on the release of drug from optimized batch of Betacyanin SLNs (Fopt)

α-Glucosidase Inhibition Study

SLNs obtained from Betacyanin inhibited the α-glucosidase enzyme in a concentration-dependent manner. SLNs were the most effective at 200 µg/mL, suppressing enzymes by 87.25% ± 0.29%. SLNs had an IC_{50} value of 23.25 µg/mL. SLNs

Table 8: In-vitro drug release study of optimized batch

Time (min.)	*%Drug release from Fopt*
0	0
60	21.31
120	37.76
180	51.95
240	63.56
300	72.87
360	79.25
420	87.23
480	91.73

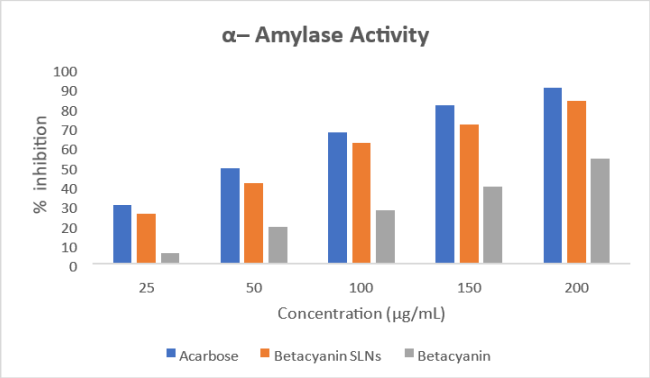


Figure 14: Alpha (α) – Amylase inhibitory assay

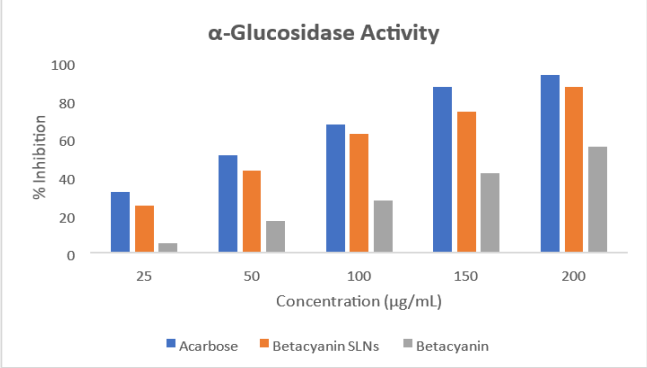


Figure 15: α-Glucosidase inhibition study

Table 9: Effect of stability conditions on different parameters of optimized batch formulation (Fopt)

Parameters	*Results*			
Appearance	Day 0 Transparent	Day 30 Transparent	Day 60 Transparent	Day 90 Transparent
In-Vitro drug release at 8 hours	91.73	90.89	89.56	89.21

Table 10: Effect of stability condition on the release of drug from the optimized batch of Betacyanin SLNs (Fopt)

Time (min.)	*Day 0*	*Day 30*	*Day 60*	*Day 90*
0.00	0	0	0	0
60	21.31	20.95	20.27	19.89
120	37.76	36.98	36.45	35.95
180	51.95	51.18	50.76	50.25
240	63.56	62.98	62.12	62.89
300	72.87	72.12	71.98	70.55
360	79.25	78.55	78.25	77.98
420	87.23	87.29	87.01	86.87
480	91.73	90.89	89.56	89.21

Table 11: In-vitro (α) – Amylase inhibitory assay

Concentration (µg/mL)	*% Inhibition*		
	Acarbose	*Betacyanin*	*Betacyanin SLNs*
25	30.25 ± 0.25	5.55 ± 0.65	25.75 ± 0.85
50	49.25 ± 0.26	18.85 ± 0.23	41.25 ± 0.26
100	67.25 ± 0.27	27.66 ± 0.77	62.25 ± 0.27
150	81.25 ± 0.28	39.73 ± 0.98	71.25 ± 0.28
200	90.25 ± 0.29	53.85 ± 0.29	83.25 ± 0.29
IC50	2.25 ± 0.80	58.65 ± 0.33	23.25 ± 0.76

Table 12: In-vitro (α) – Glucosidase Inhibition Study

Concentration (µg/mL)	*% Inhibition*		
	Acarbose	*Betacyanin*	*Betacyanin SLNs*
25	32.25 ± 0.25	4.85 ± 0.65	24.75 ± 0.45
50	51.25 ± 0.11	16.85 ± 0.13	43.25 ± 0.26
100	67.25 ± 0.27	27.66 ± 0.77	62.25 ± 0.27
150	87.25 ± 0.28	41.73 ± 0.98	74.25 ± 0.28
200	93.25 ± 0.29	55.85 ± 0.29	87.25 ± 0.29
IC50	2.01 ± 0.80	57.65 ± 0.33	23.25±0.76

had inhibitory effects comparable to the positive control group. The inhibitory activity of acarbose at the same dose was 93.25% ± 0.29% (IC_{50}s = 2.01 µg/mL) as shown in Table 12 and Figure 15. The inhibitory activity of SLNs at the same concentrations was comparable to that of the standard drug, acarbose.

Conclusion

The study evaluated Solid Lipid nanoparticles containing betacyanin for their % yield, entrapment efficiency, particle size, zeta potential determination, surface shape, *in-vitro* drug release, and antidiabetic activity. The nanoparticles showed moderate inhibitory activity, with an IC_{50} value of 23.25 µg/mL for *in-vitro* antidiabetic activity. The surface

morphology analysis revealed a spherical shape with uneven surfaces. The optimized batch F5 exhibited a particle size of 279 nm and an encapsulation effectiveness of 82.71%. The *in-vitro* drug release assay showed approximately 91.73% of the medication was released after 8 hours. The solid lipid nanoparticles remained stable and effective for the duration of the testing period, providing evidence that they have potential as an effective alternative for diabetes treatment due to betacyanin's increased antidiabetic activity.

Ethical Approval and Consent to Participate

Not applicable to this study.

Human Ethics

Not applicable to this study.

Consent for Publication

Authors have declared their consent for publishing their data without any conflicts.

Availability of Supporting Data

Not applicable to this study.

Conflict of Interest

None declared by the authors.

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