WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.453
Volume 14, Issue 21, 925-945. Research Article ISSN 2277–7105

DESIGN AND DEVELOPMENT OF CHITOSAN COATED ALPHA LIPOIC ACID GRANULES

Manoj A. Sharon[1]*, Parthasarathi K. Kulkarni[2], Tanuja A. J.[3], Venkatesh K.[4], Hanumanthachar Joshi[5]

[1*,2,3,4]Department of Pharmaceutics, Sarada Vilas College of Pharmacy Mysuru, Karnataka, India.

[5]Department of Pharmacognosy, Sarada Vilas College of Pharmacy Mysuru, Karnataka, India.

Article Received on 04 October 2025,
Article Revised on 24 October 2025,
Article Published on 01 Nov. 2025,

https://doi.org/10.5281/zenodo.17479978

***Corresponding Author**

Manoj A. Sharon

Department of Pharmaceutics, Sarada Vilas College of Pharmacy Mysuru, Karnataka, India.

How to cite this Article: Manoj A. Sharon, Parthasarathi K. Kulkarni, Tanuja A. J., Venkatesh K., Hanumanthachar Joshi. (2025). Design And Development Of Chitosan Coated Alpha Lipoic Acid Granules. World Journal of Pharmaceutical Research, 14(21), 925–945.

ABSTRACT

The present study focused on the development and evaluation of chitosan-coated Alpha Lipoic Acid (ALA) formulations for gastric resistance and sustained release. Preformulation studies confirmed the physicochemical properties of ALA, consistent with pharmacopoeial standards, while FTIR and DSC compatibility assessments showed no significant drug–excipient interactions, supporting chitosan as the coating polymer. Micromeritic evaluation indicated good flow and compressibility. Coating efficiency increased with polymer concentration, with F-II achieving 10.7% and F-III/F-IV showing higher percentages, enhancing acid resistance and delaying release. Drug content and assay values remained within 98.5–99.0% of the label claim. *In vitro* dissolution revealed that higher polymer levels reduced release in acidic medium and promoted sustained release in phosphate buffer; F-IV showed good gastric resistance with most prolonged profile, and kinetic analysis with zero-order release (R^2 = 0.9585) and Korsmeyer–Peppas model fitting (R^2 = 0.9844), indicating non-Fickian diffusion. Overall, chitosan coating protected ALA from gastric degradation and modulated its release, indicating that further optimization of polymer concentration and coating thickness could achieve complete gastro-resistance and improve clinical applicability.

KEYWORDS: Alpha Lipoic Acid (ALA), Chitosan coating, Gastro-resistance, Gastric degradation.

INTRODUCTION

Alpha-lipoic acid (ALA), also known as thioctic acid, is a naturally occurring organosulfur compound synthesized in mitochondria, where it functions as a cofactor in various oxidative decarboxylation reactions.[1] Owing to its strong antioxidant potential, ALA neutralizes reactive oxygen and nitrogen species and regenerates endogenous antioxidants such as vit C, vit E, glutathione, and coenzyme Q10.[2] ALA improves insulin sensitivity, supports glucose and lipid metabolism, and exhibits neuroprotective and anti-inflammatory properties, making it beneficial in conditions such as diabetes, cardiovascular disorders, and neurodegenerative diseases.[3]

However, the clinical effectiveness of ALA is limited by its poor stability in acidic environments and low oral bioavailability (approximately 30%). In the gastric environment (pH < 4.7), ALA undergoes acid-catalyzed ring opening and oxidation, leading to degradation and reduced therapeutic efficacy. Consequently, protection of ALA from gastric acidity is critical for enhancing its intestinal absorption and bioavailability.[4,5]

Chitosan, a natural cationic polysaccharide derived from chitin, has gained significant attention in pharmaceutical applications due to its biocompatibility, biodegradability, mucoadhesiveness, and film-forming properties. The presence of protonated amino groups in chitosan facilitates strong electrostatic interactions with anionic drugs, enabling formation of stable complexes and protective coatings. Moreover, chitosan's pH-sensitive solubility allows it to form acid-resistant films that can minimize premature drug release in the stomach while promoting controlled release in the intestinal environment.[6,7]

The electrostatic interaction between chitosan ($–NH_3^+$) and the carboxylate groups ($–COO^-$) of ALA enhances formulation stability by reducing the drug's exposure to gastric acid and oxidative conditions. At higher intestinal pH, these interactions weaken, enabling the release of intact ALA at its optimal absorption site. Thus, chitosan presents a promising biopolymer for formulating enteric or gastro-resistant delivery systems of ALA.[8,9]

The present study aims to develop and evaluate chitosan-coated alpha-lipoic acid granules for enhanced gastric stability and intestinal drug release. Preformulation studies, compatibility

assessments (FTIR, DSC), *in vitro* dissolution profiling, and short-term stability studies were performed to assess the potential of chitosan as a protective coating polymer for ALA.

MATERIALS AND METHODS

Alpha-lipoic acid (ALA, USP grade) was obtained from Supreme Pharmaceutical Pvt. Ltd., Mysuru, India. Chitosan (75% deacetylated) was procured from Oxford Lab Fine Chem LLP, Maharashtra, India. Glacial acetic acid (analytical grade) was purchased from SD Fine-Chem **Ltd.**, Mumbai, India. All other reagents and solvents used were of analytical grade and used as received without further purification.

Formulation of Chitosan-Coated ALA Granules

Chitosan coating solution was prepared by dissolving the polymer (1–2.5% w/v) in 1% v/v glacial acetic acid under continuous stirring until a clear viscous solution was obtained. Five grams of ALA were placed in a stainless-steel bowl, and 1–2 mL of coating solution was added dropwise with gentle mixing. The coated mass was sieved (#10 mesh), partially dried at 35°C for 10 min, and recoated through multiple cycles (4–6 times) to ensure uniform layering. The final coated granules were dried at 35°C for 1 hour, sieved (#40 mesh), and stored in a desiccator. Four formulations (F-I to F-IV) were prepared, varying chitosan concentration (1–2.5% w/v) while keeping ALA and coating volume constant.

Table 1: Formulation Trial Batch.

Sl. No.	Ingredients	F- Ⅰ	F- Ⅱ	F-Ⅲ	F-Ⅳ
1.	Alpha Lipoic Acid-USP (g)	5.0	5.0	5.0	5.0
2.	Coating Solution Vol (mL)	40	40	40	40
4.	Chitosan (g)	0.40 (1.0%)	0.60 (1.5%)	0.80 (2.0%)	1.00 (2.5%)
5.	Glacial Acetic Acid (mL)	0.16 (0.4%)	0.24 (0.6%)	0.32 (0.8%)	0.40 (1.0%)

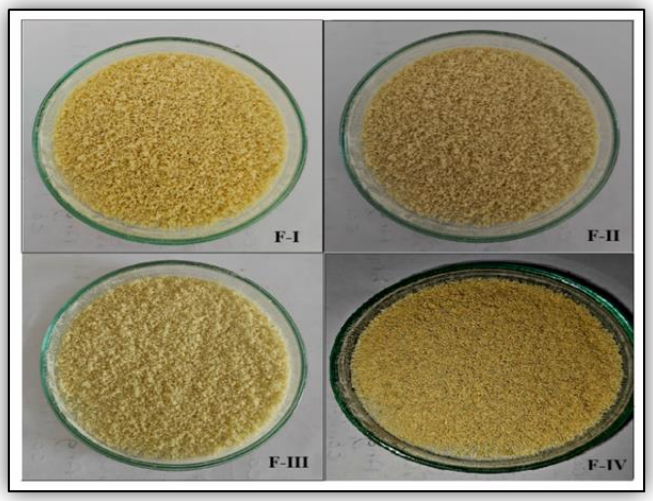

Fig. 1: Formulations of chitosan coated ALA granules.

Preformulation Studies[10]

Physical Characterization

Organoleptic properties such as color, odor, and appearance were evaluated visually. The melting point of ALA was determined by the open capillary method using a calibrated melting point apparatus.[11] Solubility studies were carried out by dissolving 100 mg of ALA in various solvents (water, methanol, ethanol, phosphate buffer, and 0.1N HCl), and absorbance was measured at 330 nm using a UV–Vis spectrophotometer.[12]

Analytical Method Development

The λmax of Alpha Lipoic Acid (ALA) was determined by scanning a 10 µg/mL methanolic solution in the range of 200–400 nm. Calibration curves were constructed for concentrations ranging from 20–100 µg/mL, and the absorbance of each solution was measured at the wavelength corresponding to the maximum absorption using methanol as the blank.[13]

Drug–Excipient Compatibility

Physical mixtures of ALA and chitosan (1:1 ratio) were prepared and stored at room temperature for 30 days. Compatibility was assessed using Fourier Transform Infrared (FTIR) spectroscopy (4000–400 cm^{-1}) and Differential Scanning Calorimetry (DSC) (30–100°C at 3°C/min under nitrogen atmosphere).[14,15]

FT- IR Spectral Analysis[14]

The infrared (IR) spectral matching method was employed to investigate potential chemical interactions between the drug and excipients. A physical mixture of the drug and excipients in

a 1:1 ratio was prepared and blended with an appropriate amount of potassium bromide. Approximately 100 mg of this mixture was compressed into a transparent pellet using a hydraulic press at 10 tons of pressure and scanned in the range of 4000–400 cm^{-1} with a Perkin Elmer FT-IR spectrophotometer. The resulting spectrum of the mixture was then compared with those of the pure drug and individual excipients to identify any shifts, disappearance, or appearance of characteristic peaks.

Differential Scanning Calorimetry (DSC) Analysis[15]

Differential Scanning Calorimetry (DSC) analyzes the heat flow associated with a sample as it undergoes controlled heating, cooling, or isothermal conditions, providing insight into its thermal properties such as melting point. The thermal characteristics of the pure drug and its physical mixtures with the polymer were examined using a Shimadzu Differential Scanning Calorimeter (Japan). Accurately weighed samples were sealed in aluminum pans and subjected to heating from 30°C to 100°C at a rate of 3°C/min. During the analysis, a continuous flow of nitrogen gas was maintained to ensure an inert atmosphere.

Micromeritic Properties[16]

Flow behavior of the coated granules was evaluated by **angle of repose**, **bulk density**, **tapped density**, **Carr's compressibility index**, and **Hausner's ratio** using standard USP methods.

Angle of Repose[16]

Angle of repose is defined as the maximum angle possible between the surface of the pile of powder and the horizontal plane. The angle of repose is designated by θ. It was determined by funnel method. The powder blend was passed through funnel so that it forms a pile. The height (h) of the pile and the radius of the pile (r) were measured and angle of repose was calculated using following formula.

$$\mathbf{Tan\ \theta = h/r}$$

$$\mathbf{\theta = Tan^{-1}\ (h/r)}$$

Where,

θ = Angle of repose.

h = Height of the pile.

r = Radius of the pile.

Bulk density and Tapped density[10]

An accurately weighed quantity of the powder (W), was carefully poured into the graduated cylinder and the volume (V_0) was measured. Then the graduated cylinder was closed with lid, mounted onto the density determination apparatus (bulk density apparatus). The density apparatus was set for 100 taps and after that, the volume (V_f) was measured and the operation was continued till the two consecutive readings are same. The bulk density and tapped density were calculated using the following formulae.

$$\textbf{Bulk density} = W/V_0$$

$$\textbf{Tapped density} = W/V_f$$

Where, W= Weight of powder, (gm)

V_0= Initial volume of powder, (ml)

V_f = Final volume of powder, (ml)

Measurement of Powder Compressibility[17]

A) Compressibility Index

The term compressibility is the ability of powder to reduce its volume under pressure. The compressibility index of the powder was determined by the Carr's compressibility index. It is used as an indication of the flowability of a powder. A compressibility index greater than 25 is an indication of poor flowability and below 15 indicates good flowability.

$$\text{Compressibility index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

B) Determination of Hausner's Ratio

The hausner's ratio is a number that is correlated to the flowability of a powder or granular material. The ideal range should be 1.2 - 1.5. Hausner's ratio was determined by the ratio of tapped density and bulk density.

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

Determination of percentage coating[18]

The efficiency of the coating process is evaluated by determining the percentage weight gain on the drug-loaded core particles. The coating thickness directly affects drug protection, release profile, and mechanical stability of the formulation. In the present study, gravimetric

analysis was employed as the primary method due to its simplicity, reproducibility, and suitability for polymeric coatings.

The uncoated Alpha Lipoic Acid (ALA) cores were pre-dried at 40 °C until constant weight was achieved. The initial mass of the dried cores was denoted as W_1(dry). After application of the chitosan-based coating solution and subsequent drying, the final dried mass was denoted as W_2(dry). Moisture content was determined by loss on drying (LOD) and correction was applied to both uncoated and coated samples to avoid overestimation of coating weight due to residual water. The percentage coating (weight gain) was calculated according to the following equation:

$$\% \text{ Coating} = \frac{W_{coated} - W_{core}}{W_{coated}} \times 100$$

Determination of percentage drug content[19]

The drug content of the coated granules was determined to verify that the actual amount of ALA corresponded to the theoretical label claim. Approximately 100 mg of the coated sample was accurately weighed, transferred to a volumetric flask, and extracted with a methanol–water mixture containing a small amount of acid under sonication to ensure complete release of ALA from the chitosan coat. The extract was filtered and analyzed using HPLC with UV detection at 330 nm, while UV–visible spectrophotometry was employed for preliminary screening. A calibration curve prepared with pure ALA standards was used for quantification. The drug content was expressed as a percentage of the label claim according to the equation:

$$\% \text{ Drug content} = \frac{\text{Assayed ALA (mg/g)}}{\text{Label claim (mg/g)}} \times 100$$

***In-Vitro* Dissolution Studies**[20]

Dissolution testing was conducted using a USP Type II (paddle) apparatus at 50 rpm and 37 ± 0.5 °C. Each formulation equivalent to 100 mg of ALA was subjected to a two-stage release study:

- **Stage I:** 0.1 N HCl (pH 1.2) for 2 h,
- **Stage II:** phosphate buffer (pH 7.4) for 4 h.

5 mL were withdrawn at specified intervals, filtered, and analyzed spectrophotometrically at 330 nm, replacing each with fresh medium to maintain sink conditions.

Stability Studies

Accelerated stability testing was performed as per ICH guidelines. Optimized formulations were stored in ALU–ALU packs at 40 ± 2°C / 75 ± 5% RH for 3 months. Samples were evaluated at 0, 1, 2, and 3 months for physical appearance, drug content, and *in vitro* release profile.

RESULTS AND DISCUSSION

Preformulation Studies

Organoleptic Properties

The organoleptic characteristics of alpha-lipoic acid (ALA) such as color, odor, and taste were evaluated visually and organoleptically. ALA appeared as a pale yellow to yellow crystalline powder with a faint, characteristic nutty or caramel-like odor and a distinctly bitter taste. These observations were consistent with the specifications reported in the Indian Pharmacopoeia (I.P.), confirming the authenticity and quality of the sample.

Melting Point

The melting point of ALA was determined by the capillary method and found to be 61.5 °C, which lies within the official USP range of 60–62 °C. This indicates good purity and the absence of significant impurities or degradation products.

Solubility Studies

The solubility of ALA was determined in various solvents including water, methanol, ethanol, propylene glycol, and dimethyl sulfoxide (DMSO). The drug was found to be sparingly soluble in water and propylene glycol, while freely soluble in methanol, ethanol, and DMSO, indicating its amphiphilic nature suitable for both aqueous and organic formulations.

Determination of λ max

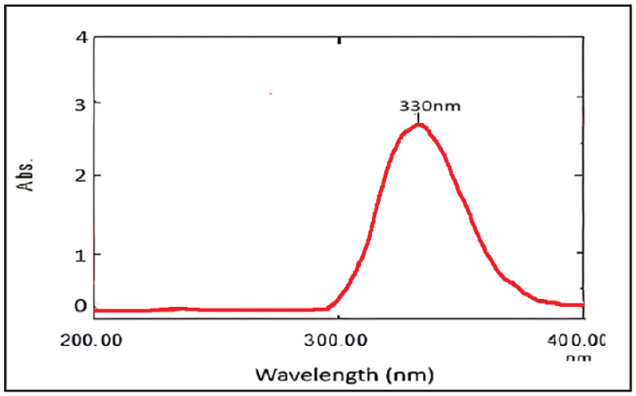

Fig. 2: Peak representing absorption maximum (λ max) of Alpha Lipoic Acid at 330nm

Standard calibration plot.

Standard calibration curve of Alpha lipoic acid was drawn by plotting absorbance v/s concentration. The λmax of Alpha lipoic acid in Methanol was determined to be 330 nm as shown in Figure 3. The absorbance values are tabulated in Table 2.

Table 2: Standard plot of Alpha lipoic acid.

Concentration (µg/ml)	Absorbance (mean ± SD)
0	0
2	0.162 ± 0.011
4	0.295 ± 0.012
6	0.421 ± 0.005
8	0.547 ± 0.001
10	0.672 ± 0.009

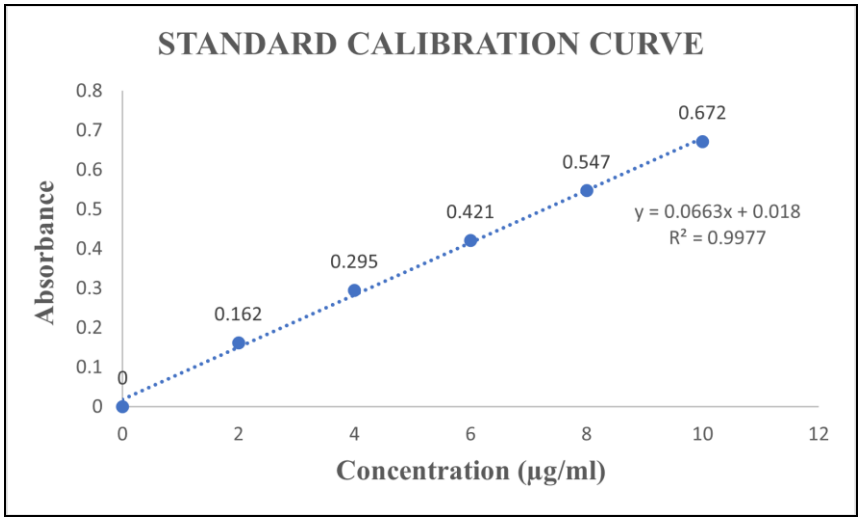

Fig. 3: Standard calibration curve of Alpha lipoic acid.

Drug–Excipient Compatibility

From the drug excipients compatibility study, it was observed that there was no characteristic change found between drug and excipients. Thus, it was concluded that the excipients selected for the formulation were compatible with Alpha Lipoic Acid and suitable for formulation development.

FT- IR Spectral Analysis

FT-IR analysis of pure Alpha Lipoic Acid and its physical mixtures with excipients was performed to check for any possible interactions. The spectra were recorded using a Perkin Elmer FT-IR spectrophotometer and obtained spectra are shown in Fig. 4.

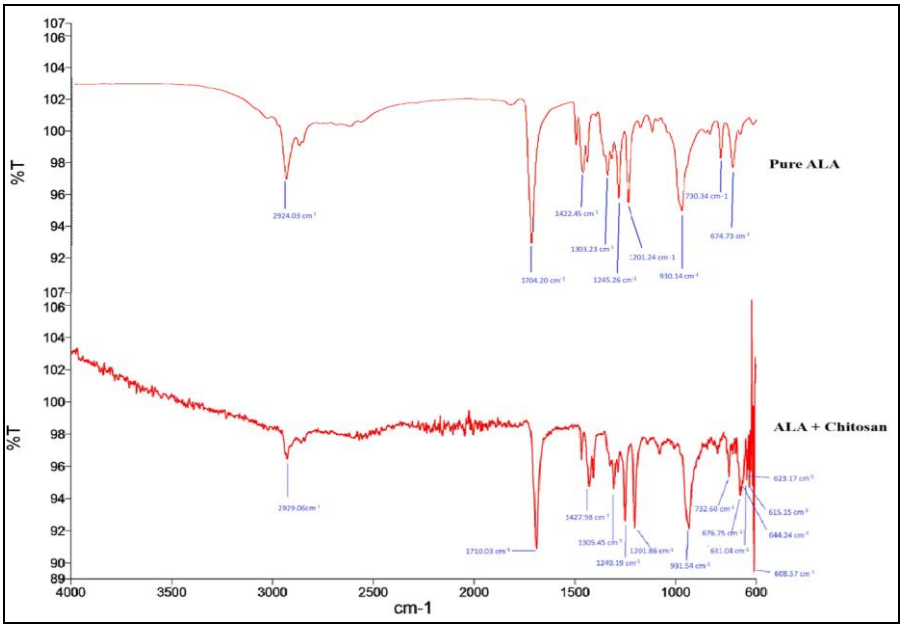

Fig. 4: FT-IR spectra of pure Alpha Lipoic Acid and ALA + Chitosan.

Table 3: Comparison of the peak of functional groups of Alpha lipoic acid observed in FTIR spectra of compatibility studies.

SI. No.	Types of Vibrations	Characteristics Peaks (cm^{-1})	Alpha lipoic acid (cm^{-1})	ALA + Chitosan (cm^{-1})
1	C-H stretching	2950-2850	2924.03	2929.06
2	C=O stretching	1725-1700	1704.20	1710.03
3	C-H bending	1470-1380	1422.45	1427.98
4	C–O stretching	1320-1240	1303.23	1305.45
5	C–O stretching	1260-1200	1245.26	1249.19

6	C–S stretching	1210-1150	1201.24	1201.86
7	C–H out-of-plane bending	950-900	930.14	931.54
8	C–H rocking	750 – 720	730.34	732.60
9	S–S stretching	700 – 500	674.73	676.75

Differential Scanning Calorimetry (DSC)

The DSC thermogram (Fig. 5) displayed a characteristic endothermic peak at 61°C corresponding to the melting point of pure ALA, while chitosan exhibited its typical broad endothermic transition. In the physical mixture of ALA and chitosan, the endothermic peak of ALA appeared with no significant shift or alteration in intensity, indicating the absence of chemical interaction between the drug and the polymer. These findings confirm that chitosan is thermally and physically compatible with Alpha Lipoic Acid.

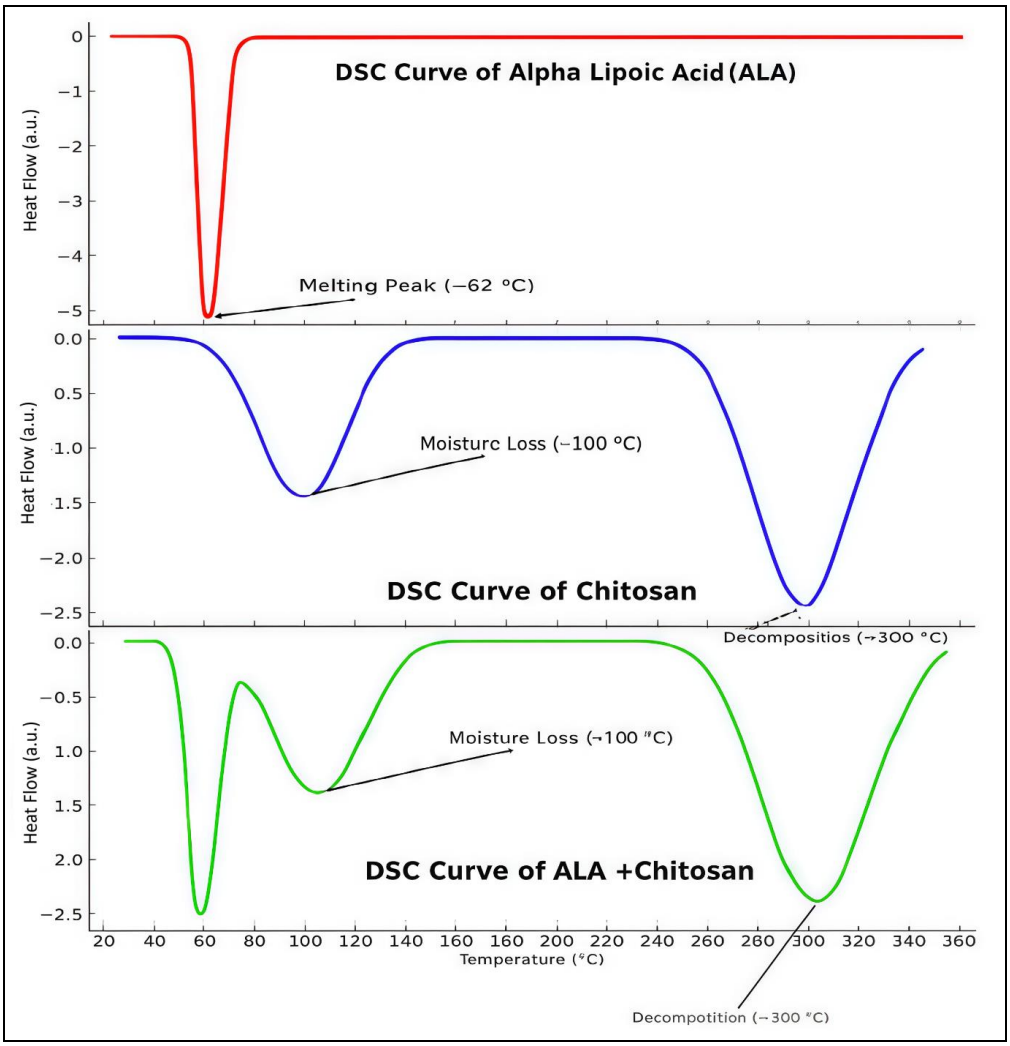

Fig. 5: DSC thermogram of Alpha lipoic acid, Chitosan, Alpha lipoic acid + Chitosan.

Micromeritic Properties

Alpha Lipoic Acid powder blends were evaluated for different precompression parameters and the results are mentioned in table 4.

Table 4: Micromeritic properties of formulations.

Formulation Code	Angle of Repose (θ)	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Compressibility Index (%)	Hausner's Ratio
F-I	30.09±0.7	0.640±0.1	0.745±0.3	14.09±0.2	1.16±0.6
F-II	28.56±0.3	0.467±0.2	0.543±0.5	13.99±0.7	1.16±0.7
F-III	25.46±0.2	0.305±0.3	0.351±0.5	13.11±0.1	1.15±0.2
F-IV	25.23±0.6	0.317±0.7	0.367±0.1	13.63±0.6	1.15±0.5

***All the values are expressed as mean ± SD, n=3**

Angle of repose of Alpha Lipoic Acid powder blend was found in the of 24º.23' to 30°.09'. These values are well within the limit of 25º – 30° which indicates the flow of Alpha Lipoic Acid was excellent. The above results revealed that the all the formulations (F-I to F-IV) possess excellent flow. Bulk density of Alpha Lipoic Acid was found between 0.305 ± 0.3 to 0.640 ± 0.1 g/cm^3. Tapped density ranges between 0.351 ± 0.5 to 0.745 ± 0.3 g/cm^3. Compressibility index values were found to be in the range of 13.11 ± 0.1 to 14.09 ± 0.2 % and the hausner's ratio lies between 1.15 ± 0.2 to 1.16 ± 0.7. Compressibility index and hausner's ratio of formulations indicates that the blend belongs to good flow property.

Determination of Percentage Coating

The coating efficiency of chitosan on Alpha Lipoic Acid granules was evaluated by determining the percentage weight gain using a gravimetric method. This approach was selected for its simplicity and reproducibility in assessing polymeric coatings. The results (Table 5, Fig. 6) demonstrated that the coating efficiency increased proportionally with chitosan concentration. Formulation F-II achieved an optimal coating level of approximately 10%, providing a suitable balance between gastric protection and controlled drug release. Higher polymer levels in F-III and F-IV (13–17%) improved acid resistance but may delay drug release, whereas the lower coating in F-I (<8%) offered inadequate protection under gastric conditions.

Table 5: Percentage coating of formulations.

Formulation Code	Chitosan (g)	Coated weight (g)	% Coating (wt. gain)
F-I	0.40	5.40	**7.4%**
F-II	0.60	5.60	**10.7%**
F-III	0.80	5.80	**13.8%**
F-IV	1.00	6.00	**16.7%**

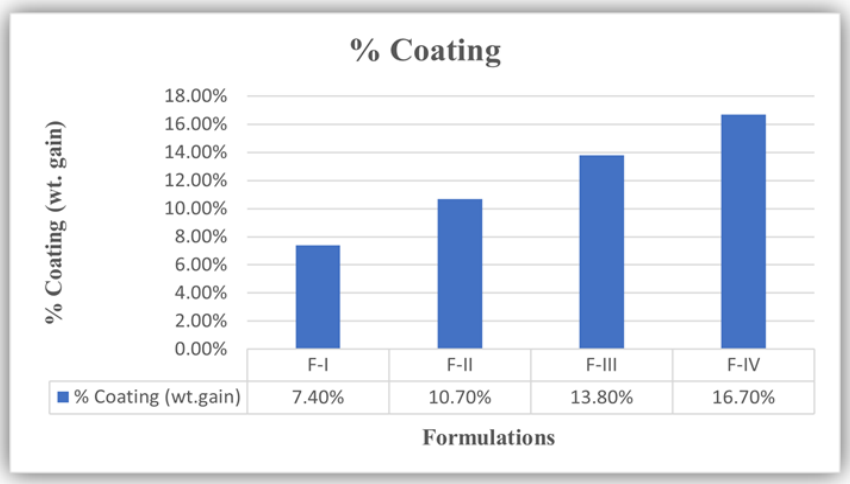

Fig. 6: Graphical representation of Percentage coating of formulations.

Determination of Percentage Drug Content

Table 6: Percentage drug content of formulations.

Formulation Code	Label claim (mg ALA / g coated)	Assayed ALA (mg/g) ± SD	% Drug content ± % RSD
F-I	925.93	916.67 ± 12.96	99.0 ± 1.4%
F-II	892.86	883.93 ± 12.50	99.0 ± 1.4%
F-III	862.07	851.72 ± 10.34	98.8 ± 1.2%
F-IV	833.33	820.83 ± 12.50	98.5 ± 1.5%

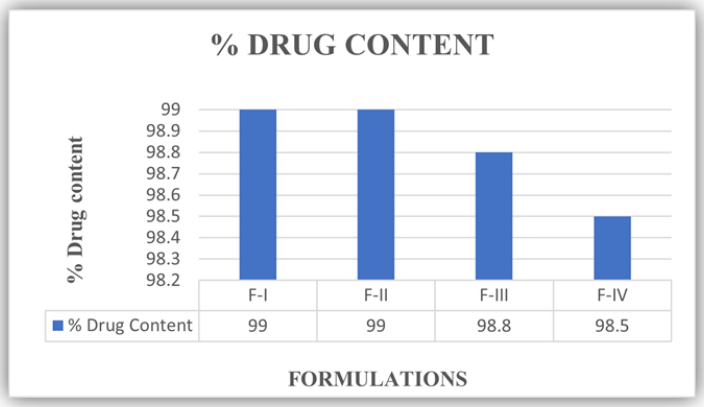

Fig. 7: Graphical representation of Percentage drug content of Formulations.

The drug content determination results confirmed that all coated formulations-maintained ALA levels close to the theoretical label claim, indicating minimal loss of drug during the coating and drying processes. As shown in Table 6, the assayed values for all batches were within a narrow range of 98.5–99.0% of the label claim, with low variability (%RSD ≤ 1.5%), demonstrating good reproducibility of the method. Specifically, formulations F-I, and F-II each showed 99.0 ± 1.4% drug content, while F-III and F-IV exhibited slightly lower but still acceptable values of 98.8 ± 1.2% and 98.5 ± 1.5%, respectively. These findings confirm that the coating process did not significantly alter the active drug content, thereby ensuring the therapeutic integrity of Alpha Lipoic Acid in all tested batches.

Assay of Alpha Lipoic Acid by HPLC Method

The assay of Alpha Lipoic Acid (ALA) was performed using a validated HPLC method for accurate quantification in the formulations. Optimized chromatographic conditions ensured sharp, well-resolved peaks with no interference from excipients. The method proved to be precise, reliable, and suitable for routine analysis of ALA content.

Standard Calibration plot

A stock solution of Alpha Lipoic Acid (ALA) was prepared in methanol (100 µg/mL) and diluted to obtain working standards of 2–10 µg/mL. Each solution was injected (20 µL) into the HPLC system under optimized conditions, and peak areas were recorded at 330 nm. A calibration curve of peak area versus concentration was plotted to determine the regression equation and correlation coefficient.

Table 7: Standard plot of Alpha lipoic acid.

Concentration (µg/mL)	Peak Area (µV)
2	162,000 ± 0.012
4	295,000 ± 0.007
6	421,000 ± 0.011
8	547,000 ± 0.005
10	672,000 ± 0.009

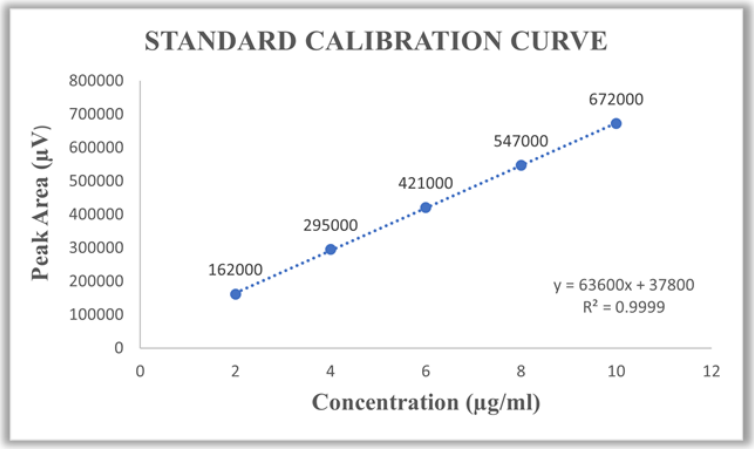

Fig. 8: Standard calibration curve of Alpha lipoic acid.

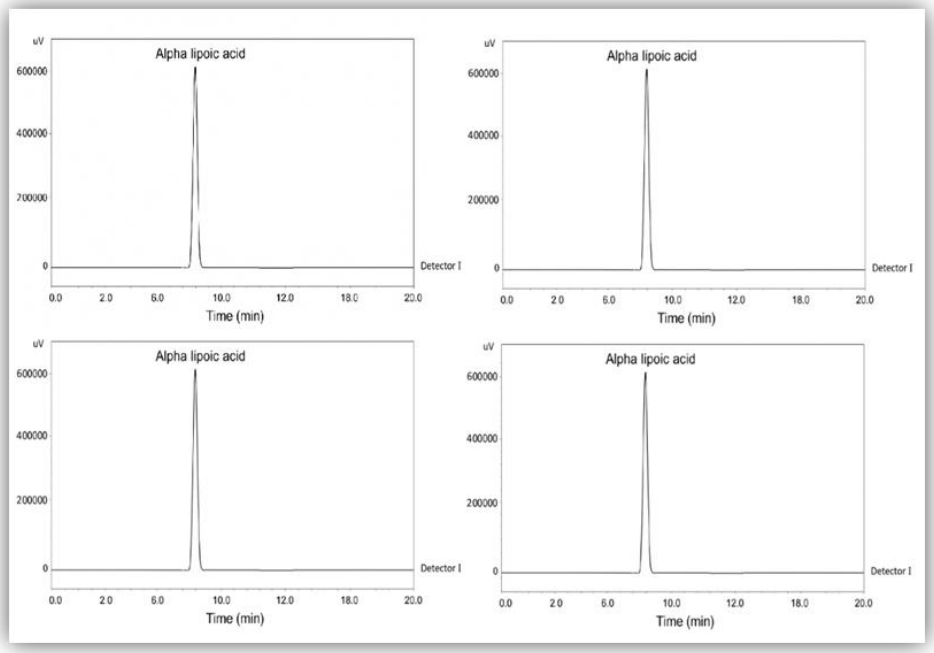

Fig. 9: HPLC Chromatogram of Formulations F-I, F-II, F-III, F-IV.

Table 7: HPLC peaks showing a retention time of Formulations and Pure drug.

SI.No.	DRUG	RT*	Area (µV)	Height	Theoretical Plate	Tailing Factor
1.	Alpha lipoic acid	8.175	7598517	5282	11506.858	1.003
2.	F-I	8.243	7498920	618275	11156.337	0.999
3.	F-II	8.198	7315450	642686	11392.055	1.000
4.	F-III	8.087	7276899	635210	11368.675	1.002
5.	F-IV	8.032	7246112	628954	11297.342	1.004

The content of Alpha Lipoic Acid in all formulations was found in the range of **98% to 99%** which was within the acceptable limits.

In-Vitro Drug Release Studies

Table 8: % Cumulative drug release of Alpha lipoic acid Formulations (F-I to F-IV).

Time (min)	Percentage Drug Release (%)			
	% Cumulative drug release in 0.1N HCl			
	F-I	F-II	F-III	F-IV
0	0	0	0	0
15	10.17	3.51	1.17	0.32
30	18.59	8.73	4.23	1.87
60	27.91	15.67	9.89	4.79
120	43.87	27.51	15.43	10.17
% Cumulative drug release in Phosphate buffer Ph 7.4				
150	59.92	41.39	28.73	17.81
180	81.77	62.11	41.29	29.77
240	-	81.51	61.12	48.23
360	-	98.79	84.76	67.48

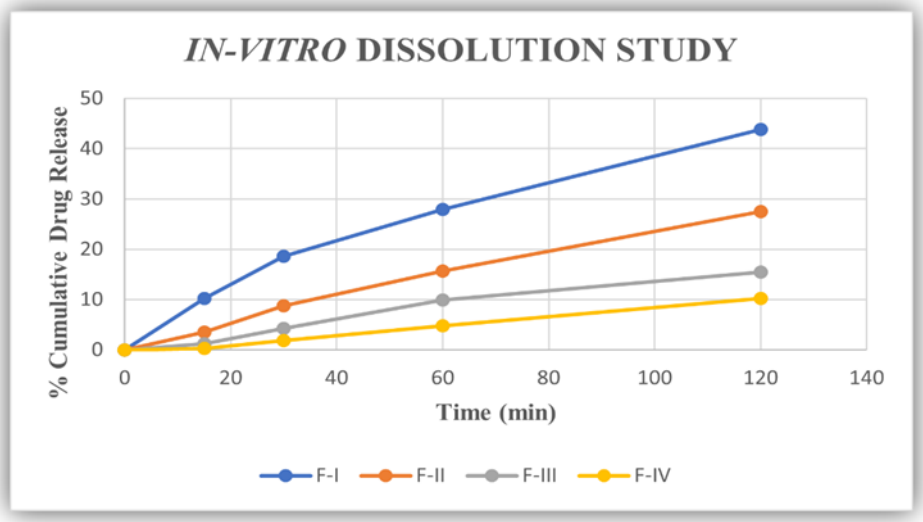

Fig. 10: % Cumulative drug release of Alpha Lipoic Acid Formulations in 0.1N HCl.

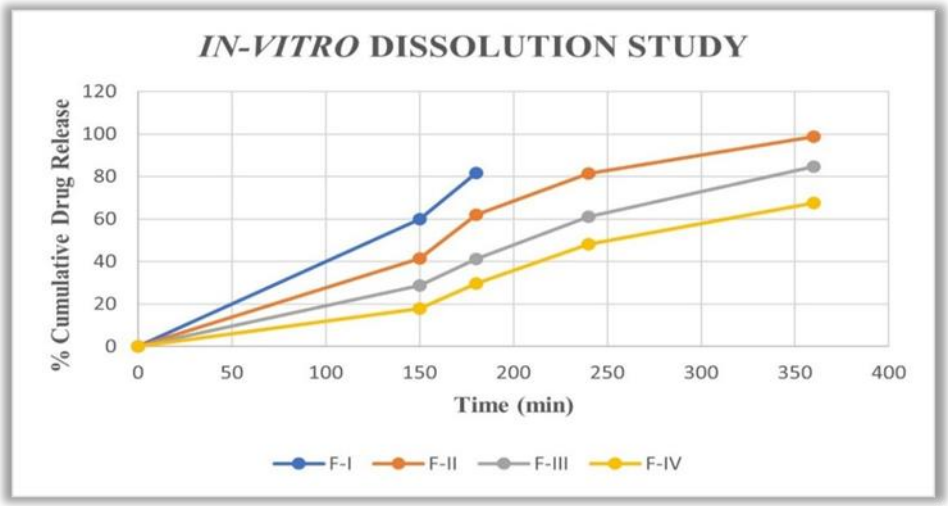

Fig. 11: % Cumulative drug release of Alpha Lipoic Acid Formulations in Phosphate buffer pH 7.4.

The *in-vitro* drug release study of formulations F-I, F-II, F-III, and F-IV was conducted in 0.1 N HCl for 2 hours followed by phosphate buffer pH 7.4 up to 6 hours. In the acidic medium, all formulations released some amount of drug, indicating that none of them were completely gastric resistant. F-I showed the highest release (43.87% at 120 min), confirming poor acid resistance, while F-II, F-III, and F-IV released comparatively lower amounts (27.51%, 15.43%, and 10.17% at 120 min, respectively), suggesting partial gastric protection with increasing polymer concentration. After shifting to pH 7.4 buffer, the cumulative drug release increased significantly for all formulations. F-I showed complete drug release by 240 min, while F-II and F-III reached 98.79% and 84.76% at 360 min, respectively. F-IV provided the slowest and most controlled release, with 67.48% at 360 min. These results indicate that increasing polymer concentration reduced premature drug release in acid and provided more sustained release in intestinal conditions, with F-IV showing good gastric resistance and the most prolonged, controlled release profile.

Drug Release Kinetics

The *in-vitro* drug release data of Alpha lipoic acid formulations were subjected to various mathematical models to understand the release kinetics. The results of these analyses are summarized in Table 9. The selection of the most appropriate release model was based on the regression coefficient (R^2), with values closer to 1 indicating a better fit. An R^2 value equal to 1 signifies a perfectly linear relationship, meaning the drug is released at a constant rate as

time progresses. Among all tested models, formulations F-IV (R^2 = 0.9844) exhibited the highest.

R^2 values in the Korsmeyer-Peppas model, indicating that the drug release followed non-Fickian (anomalous) diffusion involving a combination of diffusion and polymer relaxation (erosion) mechanisms. The Zero-order kinetics with a high R^2 value also suggested a nearly constant release rate, suitable for sustained release formulation. Overall, the release behavior of the F-IV formulation demonstrated controlled and predictable drug release characteristics. The subsequent graphs illustrate the plots used for determining drug release kinetics.

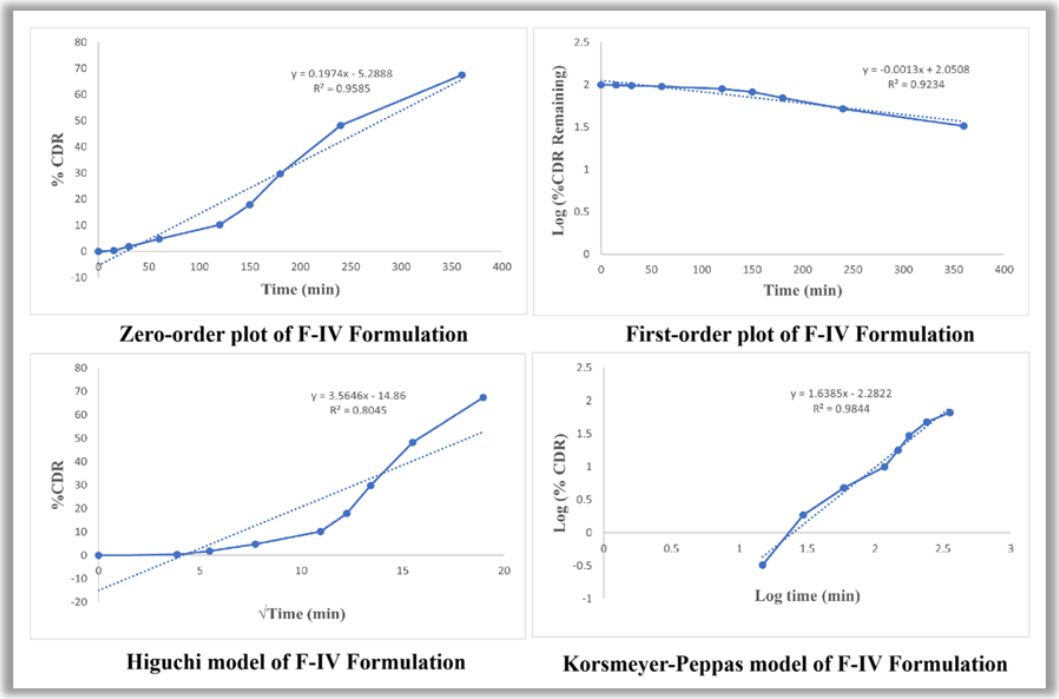

Fig. 12: Graphical representation of *in-vitro* Drug Release Kinetics of F-IV Formulation.

Table 9: Drug release kinetics data for F-IV.

Formulation	Correlation Coefficient (R^2)			
	Zero order	First order	Higuchi	Korsmeyer's
F-IV	0.9585	0.9234	0.8045	0.9844

Stability studies

Table 10: Stability study data of Formulations stored at 40±2ºC/75%±5% RH.

SI. No.	Tests			Initial Period	1st Month	2nd Month	3rd Month
1.	Physical Appearance			Pale yellow to yellow crystalline powder.	Complies	Complies	Complies
2.	Average Weight (g)			160.50	160.35	160.27	160.25
3.	*In Vitro* Dissolution Study	Acid Medium- 60 mins (NMT 10%)	F- I	27.91	27.13	26.92	26.77
			F- II	15.67	15.42	15.19	14.69
			F-III	9.89	9.57	9.31	8.95
			F-IV	4.79	4.41	4.09	3.89
4.		Alkaline medium (at the end of 60 mins) (%)	F- I	81.77	81.41	81.05	80.78
			F- II	62.11	61.97	61.81	61.31
			F-III	41.29	41.06	40.93	40.75
			F-IV	29.77	29.51	29.18	28.84
5.	Assay % (Limit: 98 to 99)			99	99	98.7	98.2

Stability studies revealed that there were no significant changes found in physical appearance, *in-vitro* drug release and assay during the period of three months even after stored at 40±2ºC/75%±5% RH. The study revealed that the formulation F- I to F-IV was stable at 40±2ºC/75%±5% RH even after stored for three months.

CONCLUSION

The present study demonstrated that chitosan is a promising coating polymer for developing gastro-resistant and sustained-release formulations of alpha-lipoic acid (ALA). Chitosan-coated ALA granules exhibited good physicochemical stability, high drug content uniformity (98.5–99%), and excellent micromeritic flow properties. Increasing polymer concentration effectively reduced premature drug release in acidic conditions while enabling sustained intestinal delivery. The optimized formulation (F-IV) showed the most controlled release profile, following non-Fickian diffusion kinetics, and maintained stability under accelerated conditions. Overall, chitosan coating enhanced ALA's protection against gastric degradation and improved its release control.

ACKNOWLEDGEMENT

I would like to express my heartfelt gratitude to my Guide, the Management, Principal, Head of the Department, and the Teaching and Non-Teaching staff of Sarada Vilas College of

Pharmacy, Mysuru, for their unwavering support, insightful guidance, and valuable suggestions throughout the duration of this research work.

REFERENCES

1. Quester K, Rodríguez-González S, González-Dávalos L, Lozano-Flores C, González-Gallardo A, Zapiain-Merino SJ, Shimada A, Mora O, Vazquez-Duhalt R. Chitosan nanoparticles containing lipoic acid with antioxidant properties as a potential nutritional supplement. Animals, 2022 Feb 10; 12(4): 417.
2. Capece U, Moffa S, Improta I, Di Giuseppe G, Nista EC, Cefalo CM, Cinti F, Pontecorvi A, Gasbarrini A, Giaccari A, Mezza T. Alpha-lipoic acid and glucose metabolism: A comprehensive update on biochemical and therapeutic features. Nutrients, 2022 Dec 21; 15(1): 18.
3. Tripathi AK, Ray AK, Mishra SK, Bishen SM, Mishra H, Khurana A. Molecular and therapeutic insights of alpha-lipoic acid as a potential molecule for disease prevention. Revista brasileira de farmacognosia, 2023 Apr; 33(2): 272-87.
4. Salehi B, Berkay Yılmaz Y, Antika G, Boyunegmez Tumer T, Fawzi Mahomoodally M, Lobine D, Akram M, Riaz M, Capanoglu E, Sharopov F, Martins N. Insights on the use of α-lipoic acid for therapeutic purposes. Biomolecules, 2019 Aug; 9(8): 356.
5. Prasad S, Venkatesh, Kulkarni P K, Nagendra R, Joshi H. Development and evaluation of 90% alpha lipoic acid coated with suitable polymers. Int. j. res. pharm. pharm. sci., 2023; 4(8): 10-16.
6. Wikipedia Contributors. Chitosan. Wikipedia. Wikimedia Foundation; 2019. Available from: https://en.wikipedia.org/wiki/Chitosan.
7. Mawazi SM, Kumar M, Ahmad N, Ge Y, Mahmood S. Recent applications of chitosan and its derivatives in antibacterial, anticancer, wound healing, and tissue engineering fields. Polymers., 2024 May 10; 16(10): 1351.
8. Puttipipatkhachorn S, Nunthanid J, Yamamoto K, Peck GE. Drug physical state and drug–polymer interaction on drug release from chitosan matrix films. Journal of controlled release., 2001 Jul 10; 75(1-2): 143-53.
9. Boonsongrit Y, Mitrevej A, Mueller BW. Chitosan drug binding by ionic interaction. European journal of pharmaceutics and biopharmaceutics, 2006 Apr 1; 62(3): 267-74.
10. (PDF) AN Overview on Preformulation Studies [Internet]. [cited 2023 Jun 14]; Available from:

https://www.researchgate.net/publication/330193840_AN_OVERVIEW_ON_PREFORMUATION_STUDIES

11. The United States Pharmacopeia, the National Formulary. Google Books. 2025. Available from: https://books.google.co.in/books/about/The_United_States_Pharmacopeia_the_Natio.
12. Kumar S, Singh P. Various techniques for solubility enhancement: An overview. The Pharma Innovation, 2016; 5(1, Part A): 23.
13. Patni M, Rawat S. Analytical method development and validation for estimation of alpha lipoic acid in bulk and pharmaceutical dosage form by UV spectrometric method. J. Biol. Chem. Chron., 2018; 4(1): 67-70.
14. Prasad PR, Bhuvaneswari K, Rajani K. Quantitaive determination of Domperidone and Paracetamol in combined dosage form by FTIR spectroscopy. J Chem. Pharm. Res., 2012; 4(1): 180-185
15. Wikipedia Contributors. Differential scanning calorimetry. Wikipedia. Wikimedia Foundation; 2025.
16. Beakawi Al-Hashemi HM, Baghabra Al-Amoudi OS. A review on the angle of repose of granular materials. Powder Technol., 2018; 330: 397–417.
17. Amidon GE, Secreast PJ, Mudie D. Particle, Powder, and Compact Characterization. Developing Solid Oral Dosage Forms: Pharmaceutical Theory and Practice, 2009; 163–8.
18. Piao ZZ, Lee KH, Kim DJ, Lee HG, Lee J, Oh KT, Lee BJ. Comparison of release-controlling efficiency of polymeric coating materials using matrix-type casted films and diffusion-controlled coated tablet. AAPS Pharm. Sci. Tech., 2010 Jun; 11(2): 630-6.
19. Ta PL, Bernat-Just L, Alambiaga-Caravaca AM, Rodilla V, López-Castellano A, Bosch-Morell F. Optimization and Validation of a High-Performance Liquid Chromatography (HPLC-UV) Method for Quantification of α-Lipoic Acid in Cyclodextrins Complex for Ocular Delivery. Biomedical Chromatography., 2025 Jul; 39(7): e70133.
20. Anwar Bakr R, Kotta S, Aldawsari HM, Ashri LY, Badr-Eldin SM, Eltahir H, Ahmed SA, Alahmadi YM, Abouzied M. Improvement of solubility, dissolution, and bioavailability of phenytoin intercalated in Mg-Al layered double hydroxide. Frontiers in Pharmacology, 2024 Aug 2; 15: 1440361.