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Dr. Poulami Gupta Banerjee
West Bengal Chemical Industries Ltd., Kolkata, India

Dr. Atanuka Paul
West Bengal Chemical Industries Ltd., Kolkata, India

Dr. Argha Chakraborty
West Bengal Chemical Industries Ltd., Kolkata, India

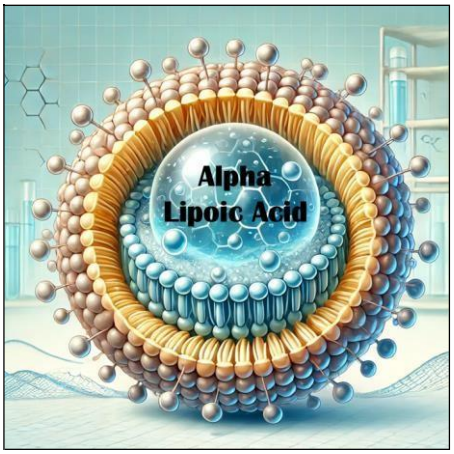
Subrata Kundu
West Bengal Chemical Industries Ltd., Kolkata, India

Correspondence
Dr. Poulami Gupta Banerjee
West Bengal Chemical Industries Ltd., Kolkata, India

Enhancing the stability and bioavailability of alpha-lipoic acid: Development and evaluation of a liposomal formulation by West Bengal Chemical Industries Ltd

Poulami Gupta Banerjee, Atanuka Paul, Argha Chakraborty and Subrata Kundu

Abstract
Alpha-Lipoic Acid (ALA), a naturally occurring antioxidant, is widely recognized for its ability to reduce oxidative damage, regenerate endogenous antioxidants, and serve as a free radical scavenger. Despite its numerous nutraceutical and therapeutic potentials, the clinical application of ALA remains limited due to its poor solubility, chemical instability, and low bioavailability. To overcome these challenges, West Bengal Chemical Industries Ltd. (WBCIL) developed a liposomal ALA formulation designed to enhance the stability, solubility, and therapeutic efficacy of ALA. This study aimed to evaluate the physicochemical properties, encapsulation efficiency, and bioavailability of WBCIL's liposomal ALA. The liposomal formulation produced uniform liposomes with a mean particle size of ~227 nm, as confirmed by Dynamic Light Scattering (DLS) and viewed under a Scanning Electron Microscope (SEM). The encapsulation efficiency of liposomal ALA was found to be within the range of 86% (± 3%) as confirmed using High-Performance Liquid Chromatography (HPLC) analysis, demonstrating its superior encapsulation efficiency while Differential Scanning Calorimetry (DSC) analysed the thermal stability of the encapsulated ALA. The results highlight the importance of liposomal ALA and WBCIL's technological advancement to develop a delivery system for enhancing the stability, bioavailability, and therapeutic efficacy of ALA. This novel formulation addresses critical challenges associated with traditional ALA administration, paving the way for more effective applications in nutraceutical and pharmaceutical contexts. Further clinical validation is warranted to confirm its potential for human health benefits.



Keywords: West Bengal Chemical Industries Ltd, ALA, human health benefits, bioavailability

1. Introduction
Liposomal alpha-lipoic acid (ALA) represents a significant advancement in antioxidant delivery, enhancing its stability, solubility, and bioavailability compared to conventional ALA formulations [1]. Encapsulating ALA within liposomes vesicular structures composed of phospholipid bilayers protects it from rapid degradation caused by environmental factors such as light, heat, and oxygen, ensuring improved absorption and controlled release at the target site [2, 3] This innovative delivery system enhances the effectiveness of ALA in therapeutic and cosmetic applications, where its ability to combat oxidative stress and support cellular health is well recognized [4].

In dermatology, liposomal ALA has demonstrated superior efficacy in reducing UV-induced erythema, preventing premature skin aging, and aiding in skin repair, making it a valuable ingredient in anti-aging and protective skincare formulations [3, 5]. Moreover, liposomal encapsulation enhances ALA's synergistic effects with other antioxidants, further amplifying its therapeutic potential [6, 7]. Given these benefits, the development and optimization of liposomal ALA formulations have become a focal point in research, paving the way for more effective clinical and commercial applications.

This article focuses on the liposomal alpha lipoic acid formulation manufactured by West Bengal Chemical Industries Ltd. (WBCIL). WBCIL has leveraged advanced pharmaceutical techniques to produce a stable and efficient delivery system for ALA. The study investigates the formulation's physicochemical properties, encapsulation efficiency, thermal stability, and overall suitability for pharmaceutical and cosmetic applications.

The aim of this research is to assess the performance of WBCIL's liposomal alpha lipoic acid in terms of its stability, encapsulation efficiency, and thermal properties. Through a comprehensive analysis involving Dynamic Light Scattering (DLS), Differential Scanning Calorimetry (DSC), High-Performance Liquid Chromatography (HPLC), Scanning Electron Microscopy (SEM) and Fourier Transform Infrared (FTIR) Spectroscopy, this article seeks to contribute valuable insights into the potential of liposomal formulations to enhance the therapeutic efficacy of ALA.

2. Liposomal Alpha-Lipoic Acid: Advances in Formulation, Stability, and Therapeutic Potential

Alpha-lipoic acid (ALA) is a potent endogenous antioxidant known for their ability to mitigate oxidative damage. These compounds play a critical role in reducing free radicals, regenerating endogenous antioxidants such as vitamins C and E, and serving as metal chelating agents [8-10]. Due to these properties, Alpha-lipoic acid (ALA) has been investigated for its therapeutic potential in various conditions, including diabetes, neurodegenerative diseases, and nephropathies [11-13]. More recently, ALA has demonstrated protective effects against cisplatin (CDDP)-induced ototoxicity, with increased glutathione concentration, lipid peroxidation inhibition, and enhanced antioxidant enzyme activity being key contributors to this effect [8, 14].

In general, ALA is known as a naturally occurring antioxidant for its ability to protect cells from oxidative damage, support energy production, and promote overall health. However, when taken in its regular form, ALA is not easily absorbed by the body, limiting its effectiveness. Liposomal encapsulation solves this problem by protecting ALA from degradation in the digestive system, ensuring better absorption and higher bioavailability. This means that liposomal ALA can reach the bloodstream more efficiently, allowing the body to maximize its benefits in various health applications [8, 9].

Despite these promising findings, the clinical application of ALA remains limited due to its poor solubility and chemical instability, particularly under acidic conditions and during systemic circulation [8-9, 15-16]. To address these limitations, researchers have explored various delivery mechanisms, including nano-formulations. Liposomes, which closely mimic biological membranes, have emerged as favourable carriers for bioactive agents like ALA due to their high biocompatibility and ability to encapsulate poorly soluble materials [17].

One of the key advantages of liposomal ALA is its powerful antioxidant properties. ALA is unique because it works in both water and fat-soluble environments, allowing it to neutralize harmful free radicals throughout the body. Additionally, it helps regenerate other antioxidants like Vitamin C, Vitamin E, and Glutathione, enhancing the body's natural defence system against oxidative stress. These antioxidant properties make ALA particularly beneficial in preventing neurodegenerative diseases, reducing inflammation, and supporting overall cellular health [10, 11].

Liposomal ALA also plays a vital role in energy production by supporting mitochondrial function. It aids in the Krebs cycle, a fundamental process that generates ATP, the body's main source of energy. This makes it an excellent supplement for individuals experiencing chronic fatigue or those seeking to improve physical endurance and overall energy levels. By boosting cellular energy, ALA helps combat tiredness and enhances overall well-being [12, 13].

In addition to its energy-boosting effects, liposomal ALA has shown promise in protecting brain health. One of its unique features is its ability to cross the blood-brain barrier, allowing it to protect neurons from oxidative damage and inflammation. This neuroprotective effect makes ALA valuable in managing conditions such as Alzheimer's and Parkinson's disease. Studies suggest that ALA can improve cognitive function, enhance memory, and even aid in nerve repair, making it a powerful tool in brain health support [14, 15].

Liposomal ALA also plays a crucial role in metabolic health, particularly in blood sugar regulation. It has been found to improve insulin sensitivity, making it beneficial for people managing diabetes or metabolic disorders. Additionally, it protects pancreatic cells from oxidative stress, supporting glucose metabolism and reducing the risk of diabetic complications. For individuals suffering from diabetic neuropathy, ALA helps alleviate nerve inflammation, reducing symptoms such as tingling or numbness in the extremities [16, 17].

Cardiovascular health is another area where liposomal ALA proves beneficial. By improving endothelial function, ALA promotes healthy blood circulation and reduces the risk of heart disease. It also protects lipids from oxidative damage, helping lower inflammation and prevent atherosclerosis, a condition characterized by the buildup of fatty deposits in the arteries. These heart-protective properties make ALA an important supplement for maintaining cardiovascular wellness [18, 19].

Beyond internal health benefits, liposomal ALA supports detoxification and liver health by aiding in the recycling of glutathione, a key detoxifying agent. This helps the liver eliminate toxins more effectively while reducing inflammation, making it particularly beneficial for individuals dealing with fatty liver disease or toxin overload. Additionally, emerging research suggests that ALA may provide support during pregnancy by reducing oxidative stress, which helps protect both the mother and the developing baby from cellular damage [20-22].

Liposomal ALA is also gaining popularity in skincare due to its ability to combat premature aging. When applied

topically, ALA reduces the impact of oxidative stress caused by UV radiation, helping prevent fine lines, wrinkles, and other signs of aging. It also promotes skin healing, reducing the appearance of scars and blemishes, making it a valuable addition to skincare routines focused on maintaining youthful, healthy skin [23].

Overall, liposomal ALA is a versatile and highly effective supplement that enhances daily health and wellness. Its superior absorption and wide range of benefits make it an excellent choice for individuals looking to improve energy levels, support brain function, regulate blood sugar, protect the heart, and promote radiant skin. Whether taken as a dietary supplement or used in skincare, liposomal ALA offers a natural and scientifically backed approach to achieving better health and vitality.

However, liposomal systems also face challenges, including poor structural stability, degradation upon storage, and a short systemic half-life [15-16, 18-19]. Hybrid nano-systems that incorporate polymeric counterparts with lipid formulations have been proposed to overcome these limitations, improving the structural stability and bioavailability of liposomal formulations [17-19].

Recent advancements in liposomal ALA systems offer promising solutions for addressing the solubility and stability issues associated with ALA. A study by Halder *et al*. (2023) demonstrated the potential of an ALA-loaded liposomal system (LIP/ALA) to enhance nutraceutical properties. Using a solvent injection method, researchers developed uniform liposomes with a mean particle size of approximately 150 nm.[15] The liposomal encapsulation protected ALA from degradation under acidic conditions (pH 1.2) and facilitated its release under physiological conditions with lipase activity (pH 6.8).[15] An in vivo study showed a 2.8-fold and 5.8-fold increase in systemic exposures of ALA and DHLA, respectively, following oral administration of LIP/ALA [18]. Moreover, LIP/ALA demonstrated significant hepatoprotective effects in a rat model of acute hepatic injury, outperforming free ALA in reducing plasma alanine aminotransferase and aspartate aminotransferase levels [15, 16, 18].

Despite these advancements, several research gaps remain. While liposomal systems effectively enhance ALA's stability and bioavailability, concerns about their structural stability during storage and their relatively short systemic half-life persist [15-16, 18-19]. Furthermore, hybrid lipid-polymer nano-systems show promise, but their complexity and potential biocompatibility issues require further exploration.

2.1 Factors Leading to Reduced ALA Synthesis

Although the body has the capability to synthesize ALA, several factors can contribute to a decline in its production [21]. One of the primary reasons is aging. Research shows that as individuals age, mitochondrial function declines, leading to a reduction in ALA synthesis. This decline is associated with increased oxidative stress and reduced energy metabolism, making supplementation beneficial for older adults [22]. Nutritional deficiencies also play a significant role in reducing ALA production. Since ALA synthesis depends on essential nutrients such as sulphur-containing amino acids (e.g., cysteine and methionine), inadequate dietary intake of these compounds can impair its formation. Additionally, a diet deficient in B vitamins, particularly biotin and thiamine, can hinder the enzymatic reactions required for ALA synthesis [23].

Chronic health conditions, such as diabetes, liver disease, and neurodegenerative disorders, can further deplete ALA levels in the body. Studies indicate that oxidative stress caused by these conditions increases the demand for antioxidants like ALA, leading to a faster depletion rate [24]. Similarly, exposure to environmental toxins, including heavy metals and pollutants, can reduce ALA availability by increasing oxidative burden and impairing mitochondrial efficiency [24]. Given these factors, supplementation with liposomal ALA can help restore optimal levels, ensuring its benefits are fully realized. Liposomal delivery enhances absorption and bioavailability, allowing for greater cellular uptake compared to traditional ALA supplements [24].

2.2 Addressing Research Gaps with WBCIL Formulated Liposomal Alpha-Lipoic Acid

Despite its endogenous synthesis, the amount of ALA produced by the body is relatively small and primarily used for essential cellular processes [19]. It functions as a cofactor for mitochondrial dehydrogenase enzymes, which help break down carbohydrates and amino acids for energy production. Unlike other antioxidants that can be stored for future use, ALA is quickly utilized, and its production does not generate surplus amounts for broader physiological benefits [20]. Therefore, obtaining ALA through diet or supplementation becomes necessary to harness its full potential, especially for antioxidant and anti-inflammatory functions [20]. The liposomal alpha-lipoic acid (ALA) developed by West Bengal Chemical Industries Ltd. (WBCIL) aims to address these limitations by leveraging innovative formulation techniques. The WBCIL liposomal ALA is designed to enhance the stability, solubility, and bioavailability of ALA, overcoming its rapid degradation and poor absorption. By incorporating advanced liposomal technologies, this formulation holds the potential to achieve prolonged systemic circulation, improved storage stability, and superior therapeutic efficacy. Unlike traditional liposomal systems, WBCIL's approach emphasizes optimizing encapsulation techniques and improving structural integrity, making it a promising alternative for developing stable and effective ALA-based therapeutic protocols.

3. Materials and Methods

3.1 HPLC Method for Quantifying Alpha-Lipoic Acid in Nutraceuticals

Instrumentation and Chromatographic Conditions

The quantification of alpha-lipoic acid was carried out using high-performance liquid chromatography (HPLC) with a Zorbax SB C18 column (Agilent, USA) [21]. The mobile phase consisted of a mixture of methanol, buffer solution, and acetonitrile, adjusted to a specific pH using monobasic potassium phosphate. The buffer solution was prepared by dissolving monobasic potassium phosphate in distilled water. The flow rate was maintained, and detection was carried out using a UV detector set to a specific wavelength. These chromatographic conditions ensured high resolution and reproducibility of the alpha-lipoic acid peaks.

3.2 Determination of assay percentage of liposomal alpha-lipoic acid

For the determination of the assay percentage, liposomal alpha-lipoic acid sample was diluted with methanol and the

mixture was sonicated for specific time followed by passing through a filter. The filtered sample was analysed further using HPLC (Agilent, USA) [21]. The peak area of ALA in the sample chromatogram was compared to the peak area of the standard chromatogram to calculate the percentage assay of the compound in the liposomal formulation.

3.3 Determination of Encapsulation Efficiency (EE) of Liposomal Alpha-Lipoic Acid

Definition and Calculation

Encapsulation efficiency (EE) is a critical parameter in evaluating the effectiveness of liposomal formulations, as it indicates the proportion of the active compound successfully entrapped within the liposomal vesicles relative to the total amount used during the formulation [21]. It was calculated using the formula:

$$\%EE = \frac{\text{Amount of Encapsulated Drug}}{\text{Total Amount of Drug}} \times 100$$

3.4 Fourier Transform Infrared (FTIR) Spectroscopy

The FTIR spectra were recorded using an FTIR spectrometer (Agilent, USA) within the range of 4000-400 cm^{-1} using Attenuated Total Reflectance (ATR) mode. ATR mode is a sampling technique in Fourier Transform Infrared (FTIR) spectroscopy that enables direct analysis of solid, liquid, or gel samples without extensive preparation. In ATR mode, an infrared beam is directed onto a high-refractive-index crystal, where it undergoes internal reflection, creating an evanescent wave that penetrates a few micro-meters into the sample, allowing for efficient spectral acquisition with minimal interference from sample thickness or surface irregularities [21].

3.5 Differential Scanning Calorimetry (DSC) Analysis

The thermal properties of the liposomal alpha lipoic acid sample were analyzed using Differential Scanning Calorimetry (DSC). This analysis was performed at Sapala Organics (Secunderabad, India) [21]. The sample was prepared by placing it in a standard aluminium pan, and an empty aluminium pan was used as the reference. The analysis began at an initial temperature of 40°C, with a constant heating rate of 10°C/min, up to a final temperature of 500°C. The DSC thermogram was recorded to observe melting points, phase transitions, and thermal stability of the sample.

3.6 Dynamic light scattering analysis of Alpha Lipoic Acid

Dynamic Light Scattering (DLS) is a widely employed analytical technique for evaluating the size distribution of nanoparticles or macromolecules in solution. This method relies on detecting fluctuations in the intensity of scattered light caused by particles undergoing Brownian motion [21]. Smaller particles exhibit faster fluctuations due to their higher rate of motion, allowing DLS to provide accurate particle size measurements [22].

Samples were sent to Indian Association for Cultivation of Science (IACS), Kolkata, India for DLS analysis. The DLS analysis provides information on size of the particles, their polydispersity in solution and zeta potential. Particle size is represented by the hydrodynamic radius of the particles in the solution, offering insight into their size and distribution. Polydispersity Index (PDI) indicates the uniformity of the particle size distribution. A lower PDI suggests a more uniform sample, while a higher PDI points to the non-uniform particle size or a broader distribution.[23] Zeta Potential measures the surface charge of the particles, which is crucial for evaluating their stability in suspension. Zeta potential values less than -30 mV and higher than +30 mV imply less chances of particle agglomeration. Thereby indicating their stability in solution.

3.7 Scanning electron microscopy and energy dispersive x-ray analysis of liposomal alpha lipoic acid

In this study, Scanning Electron Microscopy (SEM) and Energy Dispersive X-ray Analysis (EDAX) analysis was conducted to investigate the surface characteristics and morphological differences between the ALA active pharmaceutical ingredient (API) and the liposomal ALA formulation. Samples were sent to S. N. Bose Innovation Centre, Kalyani University, India for SEM & EDAX analysis.

4. Results and Discussion

4.1 HPLC Analysis of Liposomal Alpha-Lipoic Acid

The chromatogram of the alpha-lipoic acid standard exhibited a sharp and well-defined peak with a retention time suitable for accurate quantification under the specified chromatographic conditions. The method demonstrated high precision and reproducibility, with minimal variation in retention time and peak area across multiple injections.

The retention time remained consistent across multiple injections, indicating the method's reliability for routine quantification of alpha-lipoic acid in liposomal formulations. This precision is critical for ensuring accurate assay and encapsulation efficiency calculations, making this method suitable for quality control and analytical validation.

4.2 Assay of Liposomal Alpha-Lipoic Acid

The assay of the liposomal alpha-lipoic acid sample was determined using the standard curve generated from the alpha-lipoic acid standard as seen from figure 1a. The analysis revealed that the percentage assay of the active compound in the liposomal formulation was 35.66%, figure 1b.

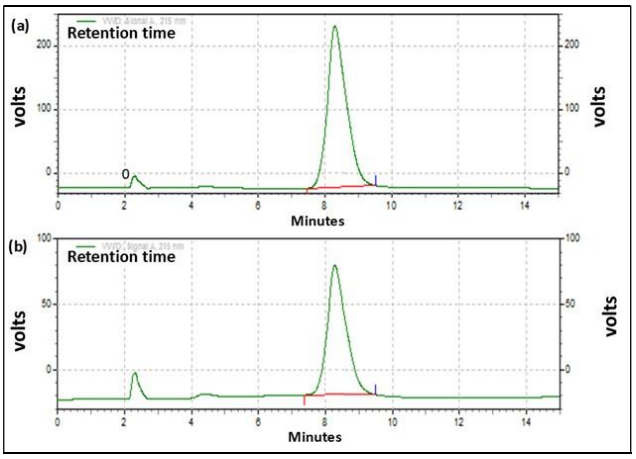


Fig 1: A Chromatogram of (a) Alpha-Lipoic Acid standard and (b) Liposomal Alpha-Lipoic Acid to determine the Assay percentages of Alpha Lipoic acid

This result suggests that the liposomal encapsulation

technique employed by WBCIL effectively retained the alpha-lipoic acid content without significant loss or degradation during preparation. The consistency between the claimed and measured assay values further validates the formulation's reproducibility, a critical aspect for large-scale manufacturing.

4.3 Encapsulation Efficiency (EE) of Liposomal Alpha-Lipoic Acid: The encapsulation efficiency of the liposomal alpha-lipoic acid formulation was calculated based on the amount of encapsulated and unencapsulated drug. The analysis revealed an encapsulation efficiency of 83% ±3%, indicating that a significant proportion of the alpha-lipoic acid was successfully entrapped within the liposomal vesicles. This high EE value highlights the efficiency of the liposomal formulation technique in enhancing nutraceutical entrapment and stability.

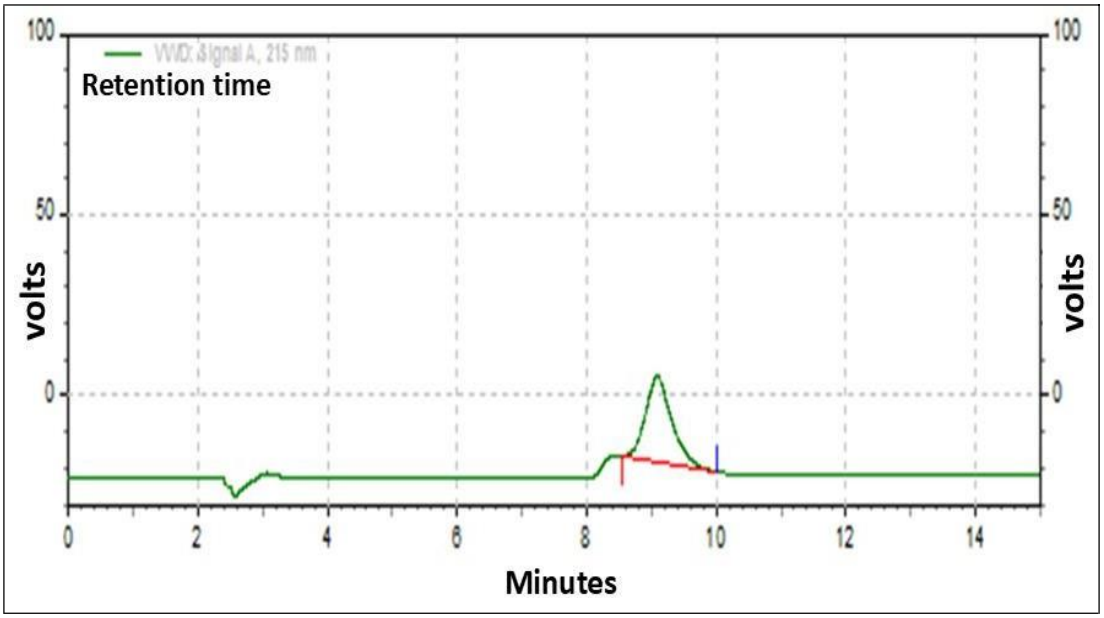


Fig 2: This chromatogram shows encapsulated alpha-lipoic acid in liposomes

A high EE value is essential for maintaining the therapeutic efficacy of liposomal formulations, as it ensures that a significant proportion of the active compound is available for controlled release. The high EE observed in this study indicates minimal drug loss during the encapsulation process, confirming an optimal formulation protocol. This efficiency also ensures enhanced stability and bioavailability, addressing the common limitations of alpha-lipoic acid, such as poor solubility and rapid degradation [24, 25].

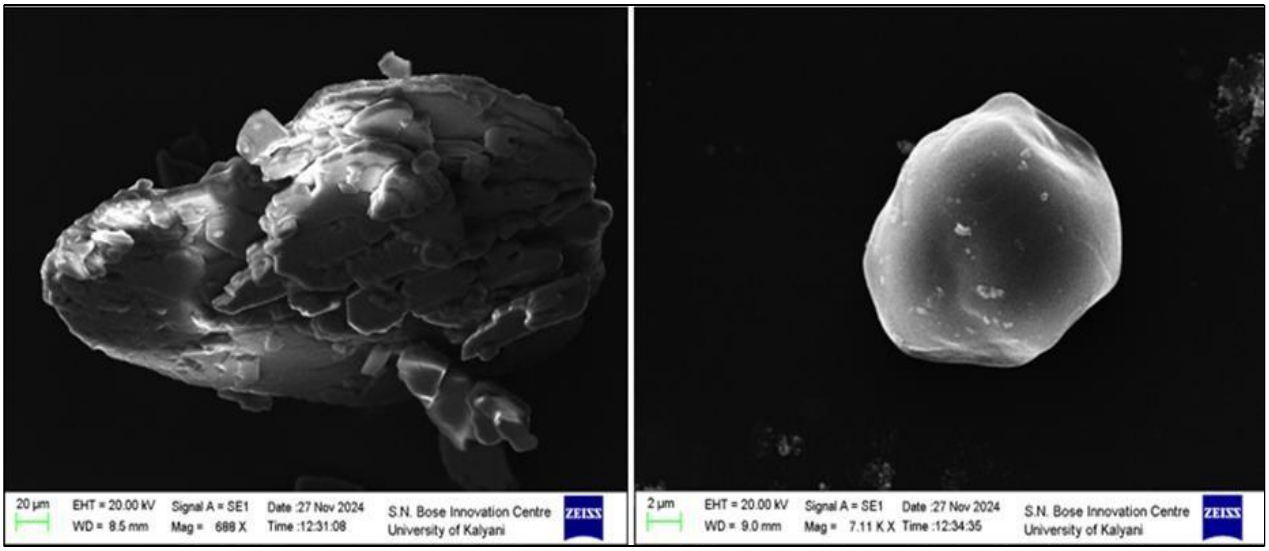
4.4 Dynamic light scattering analysis of alpha lipoic acid
Liposomal ALA demonstrates superior characteristics compared to the non-liposomal ALA. The encapsulation process reduces particle size, enhances size uniformity, and improves stability, making it a more promising formulation for drug delivery and therapeutic applications.

Table 1: Comparative analysis using dynamic light scattering of non-liposomal ALA and Liposomal ALA

Name of the Sample	Zeta potential (mV)	Interpretation of zeta potential	Particle size (nm)	Interpretation of particle size	Polydispersity Index (PDI)	Interpretation of PDI
Non-Liposomal ALA	-26.35	Moderate or low stability due to lack of surface stabilization.	370.3	Typically, larger due to crystalline or aggregated forms of raw ALA. [23]	0.4699	Higher PDI, indicating non-uniformity and the presence of larger aggregates.
Liposomal ALA	-30.79	Higher zeta potential, providing enhanced colloidal stability due to liposomal structure [24]	227.3	Smaller, uniform particles (~227.3 nm) due to encapsulation in liposomes.	0.3329	Lower PDI, reflecting a well-defined and homogeneous size distribution.
Acceptance criteria	Greater than (>) +30 & less than (<) -30 mV (for encapsulated Liposomal products)		500-2000 for liposomal products		<1 for liposomal products	

DLS was used to determine the particle size distribution and polydispersity index of formulations, including ALA. The results, summarized in the Table 1 provide insights into the size and stability of the formulations. The non-liposomal ALA exhibited a particle size of 370.3 nm with a PDI of 0.4699, indicating a moderately polydisperse sample. The liposomal ALA formulation had a particle size of 227.3 nm with a PDI of 0.3329 suggesting greater uniformity in particle distribution. The acceptance criteria for coated liposomal products suggest an optimal particle size range of 200 to 2000 nm with a PDI of less than 1. Overall, these results highlight the importance of formulation parameters in achieving the desired particle size and stability, which are crucial for optimizing bioavailability and performance in liposomal drug delivery systems.

4.5 Scanning Electron Microscopy of Alpha Lipoic Acid

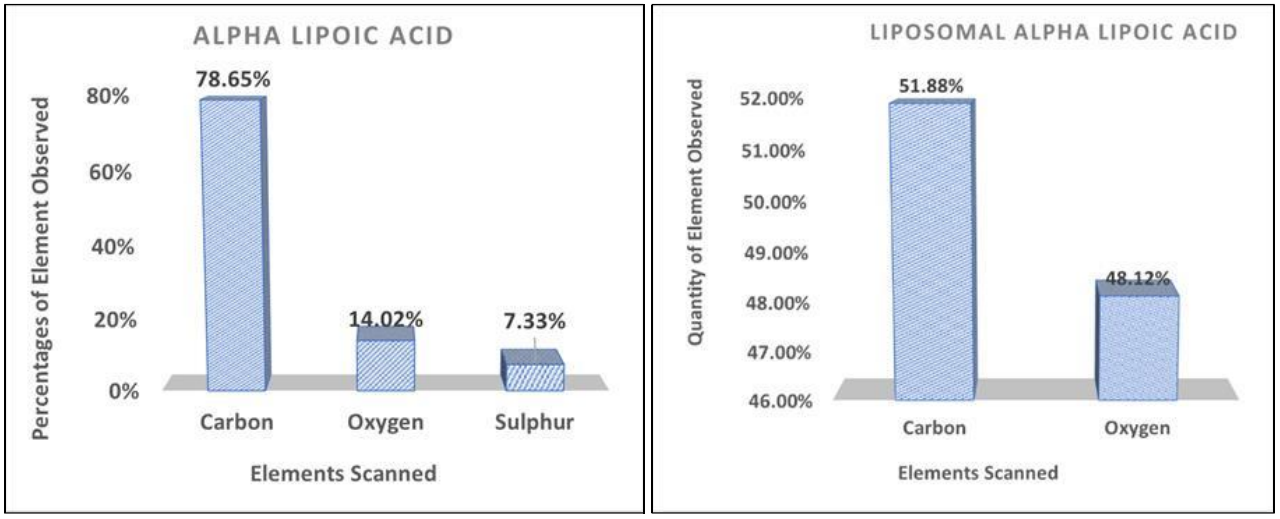


(a) (b)

Fig 3: (a) An irregularly shaped non liposomal ALA and (b) A round shaped particle of liposomal ALA is observed under a Scanning Electron Microscope

Scanning Electron Microscopy (SEM) is employed to examine the surface morphology and microstructural features of liposomal Alpha-Lipoic Acid (ALA). This method provides high-resolution images by scanning the surface of the sample with a focused beam of electrons [26]. SEM images presented in Figure 3 provides a detailed view of the ALA particle, revealing its overall shape, texture, and surface features. The sample exhibited a smooth and round shaped morphology, with a relatively well-defined outer structure. The absence of sharp crystalline edges suggests encapsulation of the sample. The smooth surface texture indicates proper encapsulation. Non-liposomal ALA displayed crystalline and irregular structures, while the liposomal ALA was found to exhibit spherical or smooth morphologies indicative of successful encapsulation.[25] This method allowed for the direct comparison of the microstructural differences between the two forms of ALA, providing valuable information about the impact of the liposomal encapsulation process on the physical characteristics of the formulation.

Furthermore, EDAX analysis of ALA and Liposomal ALA indicates that the ALA API is encapsulated with the liposomes, as Sulphur, a characteristic element of ALA, is found to be completely absent in Liposomal ALA indicated in Figure 4. Highlighting the efficiency of encapsulation of ALA within the liposomes.



(a) (b)

Fig 4: EDAX analysis of (a) Alpha Lipoic Acid and (b) Liposomal Alpha Lipoic Acid showing the quantity of elements observed

4.6 FTIR Spectroscopy

The FTIR spectrum of the liposomal alpha-lipoic acid formulation is shown above. Key observations and interpretations are as follows:

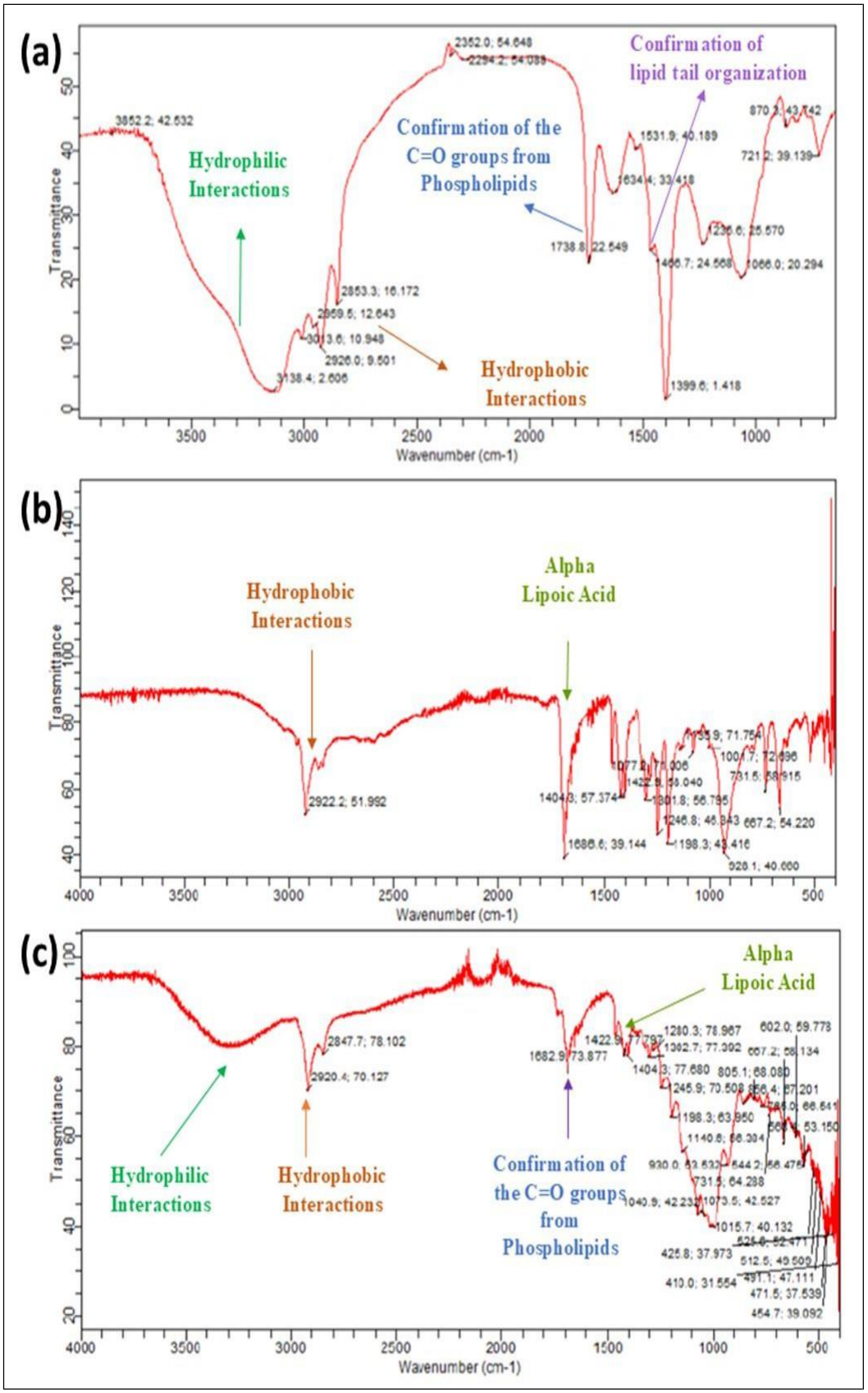


Fig 5: FTIR Spectrum of (a) empty liposome (b) ALA (c) Liposomal ALA

FTIR spectroscopy plays a crucial role in the characterization of liposomal formulations by providing detailed information about the chemical structure and molecular interactions within the system [18]. It enables the identification of functional groups present in the ALA formulation, helping to confirm the chemical composition and structural integrity of the encapsulated active compound. The obtained spectrum was analysed to identify characteristic peaks corresponding to various functional groups present in the liposomal alpha-lipoic acid formulation. Specific wavenumbers were matched with known functional group absorption ranges to confirm the presence of alpha-lipoic acid and any potential interactions between the drug and liposomal excipients.

The FTIR spectral analysis of the liposomal alpha-lipoic acid formulation revealed key functional group vibrations, confirming the presence of characteristic molecular components. A broad absorption band at 3399.3 cm^{-1} corresponds to the O-H stretching vibration, indicating the presence of hydroxyl groups and possible hydrogen bonding within the liposomal matrix. Peaks at 2918.5 cm^{-1} and 2850 cm^{-1} are associated with the symmetric and asymmetric C-H stretching vibrations of aliphatic lipid chains, characteristic of the liposomal structure. A sharp peak at 1705.3 cm^{-1} represents the C=O stretching vibration, confirming the presence of the carbonyl group from alpha-lipoic acid. Additionally, a peak at 1356.8 cm^{-1} corresponds to C-H bending vibrations, commonly found in fatty acid components of liposomes. Broad peaks in the 1100-1000 cm^{-1} range indicate C-O stretching vibrations, likely from ester or ether groups in the ALA, while signals in this region may also correspond to S-S stretching vibrations from disulfide bonds, verifying the structural integrity of alpha-lipoic acid. C=O Peak Shift (~1738 to 1682 cm^{-1}) confirms the presence of ALA surrounded by phospholipids, supporting encapsulation. FTIR analysis was carried out to identify the functional groups and confirm the chemical structure of the liposomal ALA formulation.

The FTIR spectrum provides clear evidence of the successful encapsulation of alpha-lipoic acid within the liposome. The absence of significant peak shifts or loss of functional group signals indicates that no strong chemical interactions occurred between alpha-lipoic acid and the liposome, preserving the nutraceutical's integrity. This stability is critical for ensuring consistent therapeutic performance and shelf life of the formulation [27, 28].

Table 2: Allotment of FTIR peaks in empty liposome, ALA and Liposomal ALA

Parameter	Empty Liposome	Alpha Lipoic Acid	Liposomal Alpha Lipoic Acid
Confirmation of OH Groups	Broad peak near 3370-3340 cm^{-1} (due to lipid hydration) [28]	Broad OH stretch near 3500-3200 cm^{-1}	Retention of broad OH stretch near 3500-3300 cm^{-1} confirming encapsulation with hydration stability
Confirmation of C=O Groups	Peak near 1730 cm^{-1} (ester carbonyl from phospholipids) [27]	Strong peak near 1700 cm^{-1} indicating C=O from API	Peak shift near 1725-1740 cm^{-1} indicating interaction of API with lipid bilayer
Hydrophobic Interactions	CH_2 symmetric and asymmetric stretch at 2920-2850 cm^{-1} [29]	Less prominent hydrophobic CH stretches	Distinct CH_2 and CH_3 stretches at 2920-2850 cm^{-1} confirming lipid tail organization around API
Hydrophilic Interactions	PO_4^- stretching at 1024 cm^{-1}, confirming phospholipid head groups. [30]	Presence of C=O stretching (~1650 cm^{-1}) from carboxyl groups of ALA	Both C=O (ALA) and PO_4^- (Liposome) peaks retained but slightly shifted. Confirms strong interaction between hydrophilic ALA groups and liposome polar heads.
Encapsulation Stability	Stable peaks for CH2, CH3, and phosphate groups [31]	Strong ALA peaks ~1688 cm^{-1}, 1402 cm^{-1}.	Retention of both lipid and API peaks, confirming successful encapsulation
Lipid Tail Organization	Ordered lipid bilayer peaks (e.g., CH2 at 2850-2920 cm^{-1}) [32]	Not applicable	Similar CH2 peaks but reduced sharpness, indicating lipid rearrangement post-encapsulation

4.7 Differential Scanning Calorimetry analysis

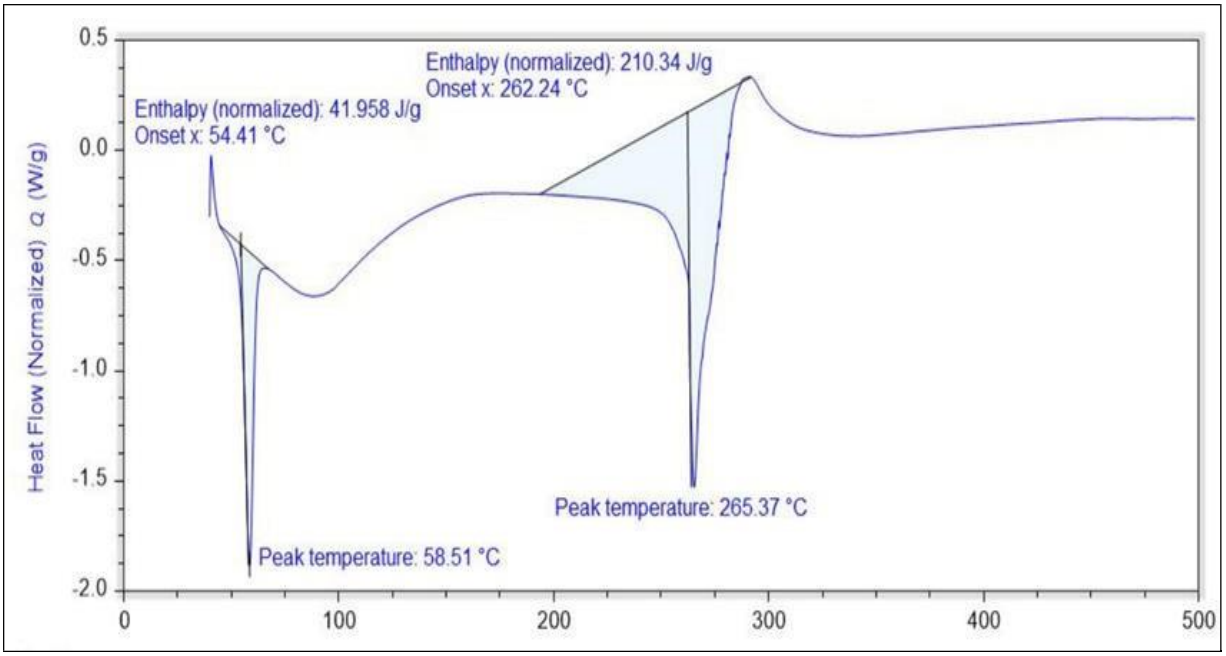


Fig 6: A Thermogram of Liposomal ALA from DSC analysis

The sample demonstrated thermal stability up to 200°C, beyond which an exothermic event occurred, indicative of degradation of the liposomal alpha lipoic acid. The absence of significant weight loss or degradation prior to this temperature suggests good stability under moderate heating conditions. The thermogram showed additional thermal events between 150°C and 250°C, likely due to interactions between the liposomal matrix and the encapsulated alpha lipoic acid. These transitions suggest structural reorganization or degradation of the lipid bilayer. Beyond

250°C, a sharp exothermic peak was observed, signalling the complete thermal decomposition of the sample.

The DSC thermogram, corresponding to the liposomal formulation, exhibits significant shifts in thermal behavior. The melting peak of ALA shifts to 58.51°C (onset: 54.41°C), indicating molecular interactions between the API and the lipid bilayer. The degradation peak appears at 265.37°C (onset: 262.24°C), which suggests a change in thermal stability due to encapsulation. Additionally, a broad endothermic region between these peaks indicates lipid phase transitions, confirming successful incorporation of ALA into the liposomal matrix. The enthalpy values (41.958 J/g for melting and 210.34 J/g for degradation) further support these structural modifications.

The encapsulation of ALA within liposomes significantly enhances its thermal stability, as evidenced by the broader transitions and reduced enthalpy compared to pure ALA. [33] This protective effect is crucial in preventing thermal degradation, ensuring prolonged functional stability. The lipid bilayer acts as a barrier against environmental stressors such as heat, thereby maintaining the bioactivity of ALA. [34] Furthermore, the presence of a lipid-associated phase transition peak at approximately 265°C highlights the stability of the liposomal structure under elevated temperatures. This structural integrity is essential for ensuring the sustained release of ALA and optimizing its therapeutic efficacy.[35] The reduction in enthalpy further supports the stable interaction between ALA and the lipid components, reinforcing the suitability of liposomal encapsulation for thermosensitive compounds.[36, 37] Thus, DSC analysis confirms that liposomal formulation not only facilitates the successful encapsulation of ALA but also enhances its thermal stability and functional performance, making it a promising delivery system for improved bioavailability and controlled release [38, 39].

5. Conclusion

Liposomal alpha-lipoic acid (ALA) represents a significant milestone in the development of nutraceutical and therapeutic agents, addressing the long-standing challenges of poor solubility, rapid degradation, and limited bioavailability of Alpha-lipoic acid. By leveraging the unique properties of liposomal delivery systems, such as biocompatibility, enhanced encapsulation efficiency, and protection against harsh environmental conditions, the formulation developed by West Bengal Chemical Industries Ltd. (WBCIL) holds promise for overcoming these limitations. Studies have demonstrated the potential of liposomal ALA to stabilize the compound under acidic conditions, improve its systemic bioavailability, and ensure a controlled release in physiological environments. Moreover, its therapeutic efficacy, as evidenced in preclinical models, highlights its potential for addressing oxidative stress-related disorders, including diabetes, neurodegeneration, and hepatic injuries. Despite the advancements, challenges such as structural stability during storage and scalability for large-scale production remain to be fully addressed. Future research should focus on optimizing the liposomal formulation for prolonged shelf life and conducting extensive clinical trials to validate its safety and efficacy in human populations. The WBCIL liposomal alpha-lipoic acid formulation demonstrates remarkable potential as a robust delivery platform, capable of improving the therapeutic profile of ALA. Its application could pave the way for more effective nutraceutical and pharmaceutical interventions, further solidifying the role of liposomal technologies in advancing health and wellness solutions. The future implications of liposomal Alpha-Lipoic Acid (ALA) are vast, spanning pharmaceuticals, nutraceuticals, and cosmetics. Its enhanced stability, bioavailability, and controlled release offer promising advancements in managing oxidative stress-related diseases such as diabetes, neurodegenerative disorders, and cardiovascular conditions. In the nutraceutical sector, liposomal ALA can be integrated into functional foods and dietary supplements for improved antioxidant support. Additionally, its potential in dermatological applications, particularly for anti-aging and skin protection, makes it an attractive candidate for skincare formulations. Future research should focus on optimizing liposomal compositions, conducting clinical trials to validate efficacy, and exploring novel delivery systems for targeted and sustained release, ultimately expanding its therapeutic and commercial potential.

6. References

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