LIPOKON™ Technology

Konark HERBALS & HEALTH CARE

Clinically-Backed Liposomal Delivery Platform

What is LIPOKON™

LIPOKON™ is a proprietary Liposomal delivery technology designed to significantly enhance the absorption, stability, and bioavailability of nutraceutical actives. It enables brands to deliver superior efficacy at lower doses with better consistency.

Now Scientifically Published

The LIPOKON™ Technology platform is now guaranteed by a peer-reviewed scientific publication, validating its formulation approach, physicochemical characteristics, and performance advantages.

Why LIPOKON™ Matters

- Enhanced bioavailability as compared to conventional powders
- Improved cellular uptake through Liposomal Encapsulation
- Better stability of sensitive actives
- Lower dose, higher impact formulations
- Clean-label compatible, scalable, and regulatory-aligned
- Gives competitive edge to the brand

What Brands Can Claim

Brands using LIPOKON™ technology can state:

- "Formulated using LIPOKON™ Technology"
- "Powered by a scientifically published Liposomal Delivery System"
- "Technology supported by peer-reviewed research"

Applicable across Multiple Actives under LIPOKON™ Technology, like:

- CoQ10
- Curcumin
- Berberine
- Glutathione
- Minerals
- Fat-soluble vitamins and selected botanicals and others

Brand advantage: Instead of relying only on ingredient-level studies, brands can now:

- Anchor their product story to a published delivery technology
- Offer value added ingredients
- Build trust with consumers, medical professionals and regulators
- Delivery decides efficacy

LIPOKON™

Now has technical paper published:
INTERNATIONAL JOURNAL of
VERSATILE RESEARCH & ANALYSIS (IJVRA)
ISSN: 2984-8903

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Lipokon™ Technology: An Industrially Scalable Approach to High-Performance Nutraceutical and Herbal Delivery

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Abstract:

Lipokon™ is an innovative technology platform delivers the enhancement of oral bioavailability, stability and protection across nutraceuticals with differing solubility and physicochemical profiles through molecular-level encapsulation and amorphization. This research applies the Lipokon™ platform for four nutraceutically diverse actives: berberine, caffeine, curcumin, and resveratrol, and comprehensively evaluates the resulting formulations with respect to solid-state behavior, colloidal properties, and in vitro performance. All formulations exhibited homogeneous appearance, physiologically compatible pH, and controlled moisture content, ensuring physical and chemical stability. Powder X-ray diffraction (XRD) and Differential Scanning Calorimetry (DSC) revealed a dramatic transition from crystalline raw materials to predominantly amorphous states. Particle size analysis revealed nanometric lipid assemblies with Z-average values ranging up to 200 nm. All formulations demonstrated high structural uniformity (Polydispersity Index (PdI): NMT 0.5) and maintained stable negative zeta potentials with lower negative values, ensuring colloidal integrity through effective electrostatic and steric stabilization. Field emission scanning electron microscopy (SEM) and transmission electron microscopy (TEM) showed morphological transformation from angular crystalline particles to uniform nanostructured spherical particles. Energy-dispersive X-ray spectroscopy confirmed molecular-level encapsulation through elevated oxygen content and persistent phospholipid signatures, indicating successful lipid matrix integration. Attenuated Total Reflectance Fourier Transform Infrared (ATR-FTIR) Spectroscopy validated amorphization while confirming chemical integrity without degradation. In vitro dissolution studies demonstrated superior and

nearly complete release performance for Lipokon™ Caffeine, which achieved in immediately, while Lipokon™ Resveratrol exhibited controlled biphasic release. These comprehensive findings establish Lipokon™ as a robust, scalable delivery platform capable of transforming crystalline actives into bioavailable formulations while maintaining adaptability across chemically diverse molecules, offering significant potential for enhanced therapeutic efficacy and clinical application.

Keywords: liposomal delivery, nutraceutical, amorphous, bioavailability, phospholipid matrix.

1. Introduction:

Liposomes are phospholipid bilayers that are self-assembled and most broadly used and applicable nanocarrier systems to deliver bioactive compounds in the pharmaceutical, nutraceutical, cosmetic, and functional foods industry (1). Their amphiphilic nature allows small-sized structures to encapsulate hydrophilic molecules internally and lipophilic molecules externally, offering greater solubility, chemical and enzymatic stability, with protection against environmental degradation, and controlled release characteristics of a wide variety of actives (2, 3). Despite these intrinsic benefits, traditional liposomes exhibit several limitations that hinder their translational and commercial applicability. Notably, they demonstrate lower target specificity, resulting in insufficient accumulation at the intended site of action and unintended distribution to non-target tissues (4). The mononuclear phagocytic system rapidly recognizes and clears circulating particles, thereby reducing the systemic circulation time and early leakage of encapsulated products (5,6). Consequently, conventional liposomes exhibit a short half-life and poor retention of encapsulated components (7). Despite advances in liposomal formulation science, maintaining high loading efficiency across structurally diverse molecules remains challenging (8). Small molecules with hydrophilic properties are likely to have poor encapsulation efficiency because they easily diffuse between the lipid bilayer or are weakly held by the hydrophilic aqueous core. On the other hand, with increasing concentration, highly lipophilic molecules can interfere with bilayer packing and vesicle integrity of the bilayers, which frequently causes rapid leakage or burst release (9,10). Traditional passive loading techniques, such as thin-film hydration, ethanol injection, and reverse-phase evaporation, are widely employed; however, they typically require a high lipid-to-drug ratio and suffer from limitations including poor drug retention, non-uniform structural stability, and limited reproducibility (11). Active or remote loading methods, including pH-gradient–mediated mechanisms, have improved the encapsulation of ionizable amphiphilic molecules; however, they are constrained by stringent physicochemical requirements, sensitivity to processing parameters, and applicability to a limited range of compound classes (12). These constraints are more imperative when it comes to commercial scale-up, where consistency in the manufacturing process, cost-effectiveness, and compliance with regulations are imperative.

Additionally, liposomal loading and stability are especially problematic in the nutraceutical industry, where active ingredients vary widely in terms of solubility and permeability properties (13). The Biopharmaceutics Classification System (BCS) can be used to explain these complexities in the above-

mentioned properties. The greatest formulation challenge, and consequently the highest potential benefit from liposomal encapsulation, is associated with molecules exhibiting both low aqueous solubility and low membrane permeability (BCS Class IV), where delivery systems must simultaneously address solubilization, physicochemical stability, membrane interaction, and controlled release. Compounds characterized by low solubility but adequate permeability (BCS Class II) also strongly benefit from lipid-assisted solubilization strategies, which improve dissolution and bioavailability. In contrast, hydrophilic and poorly permeable molecules (BCS Class III) primarily require structural shielding and membrane-interactive carriers to enhance transport across biological barriers (14). Even highly soluble and highly permeable active compounds (BCS Class I) may warrant encapsulation when tissue protection, prolonged residence time, or controlled release is desired (15). As modern nutraceutical formulations increasingly incorporate multiple BCS classes within a single product, the need for sophisticated delivery systems capable of overcoming physicochemical barriers while maintaining industrial manufacturability has become increasingly critical.

Hence, there has been a persistent need to advance lipid composition engineering, optimize vesicle size distribution, implement appropriate surface modifications, and fine-tune processing parameters to prevent vesicle fusion, aggregation, and drug leakage (16). A major unresolved and open-ended challenge remains the translation of laboratory-scale innovations into commercially viable, cost-effective, and reproducible manufacturing systems suitable for real-world nutraceutical products.

To address these unmet needs, the present research proposes 'Lipokon™', a state-of-the-art and commercially viable liposomal platform (Konark Herbal and Healthcare Pvt. Ltd) designed to enable high-performance, consistent, and effective encapsulation of nutraceutical actives across all four BCS classes (17). Four model compounds were chosen to reflect varied solubility and permeability values: Caffeine (BCS Class I), Resveratrol (BCS Class II), Berberine hydrochloride (BCS Class III), and Curcumin (BCS Class IV) (18–21). Hence, the use of these molecules in combination represents the full spectrum of challenges encountered in the modern development of nutraceutical products.

This research presents the formulation, optimization, and characterization of Lipokon™ formulations for each model compound, along with a systematic evaluation of encapsulation efficiency, vesicle morphology, particle size distribution, bilayer integrity, release kinetics, and physicochemical stability. This work is expected to enhance scientific understanding as well as the commercial translation of liposomal technologies by establishing a unified, industrially scalable liposomal delivery platform capable of delivering structurally diverse nutraceuticals. These results will support next-generation nutraceutical, functional food, and wellness products requiring high stability, efficacy, and consumer-ready performance in line with current therapeutic and nutritional needs.

2. Materials and Methods:

2.1. Materials

Curcumin (≥95% purity) and Berberine (≥95% purity) were utilized from Konark Herbal and Healthcare Pvt. Ltd., while Resveratrol (≥95% purity) were procured from SMR Biotech and Caffeine (≥95% purity) from Ahimsa natural. Sunflower Lecithin AmiLife® Standard Sunflower Lecithin) and Soya Phosphatidyl Choline (AmiLife® Soya Phosphatidyl Choline) were purchased from Amitex Agro Product Pvt. Ltd. The modified starch–based encapsulating agents were procured from Ingredion. All materials utilized in the study were of pharmaceutical grade.

2.2. Methodology for the preparation of Lipokon™ products

Konark Herbal and Healthcare Pvt. Ltd has developed a novel lipid-based multicomponent formulation incorporating Curcumin, Resveratrol, Caffeine, and Berberine to enhance bioavailability, stability and protection of nutraceuticals. The lipid carrier system consisted of Sunflower Lecithin and Soya Phosphatidyl Choline. Briefly, the bioactive compounds were dispersed in an aqueous phase under controlled thermal conditions to ensure uniform dissolution and compatibility. This phase was gradually incorporated into the phospholipid matrix under high-shear mixing at elevated temperature to promote homogeneous dispersion and lipid–active interactions. Encapsulation and stabilization of the lipid assemblies were achieved using modified starch–based encapsulating agents. The resulting dispersion underwent mechanical size reduction using horizontal bead milling (Jay Instruments and Systems Pvt Ltd (JISL) Rotamate II-lab horizontal bead mill), followed by spray drying (ABV Engineering spray dryer Nozzle Type) to obtain a free-flowing powder. All materials employed were of nutraceutical grade.

2.3. Evaluation / Characterization of Lipokon™ Products

2.3.1. Physical Assessment and pH Determination

The physical characteristics of the Lipokon™ formulations were evaluated through visual inspection to assess colour, homogeneity, and overall appearance. Each formulation was examined under adequate lighting to ensure uniformity and the absence of visible particulates or phase separation.

For pH determination, a 1% w/v dispersion of each Lipokon™ product was prepared in distilled water. The pH of the resulting solution was measured using a calibrated digital pH meter (Siena Instruments Digital pH meter). Before analysis, the instrument was standardized using certified buffer solutions at pH 4.0, 7.0, and 10.0. Measurements were performed in triplicate at room temperature, and the mean value was recorded (23).

2.3.2. Moisture Content

Moisture content of the Lipokon™ formulations was determined using the standard AOAC gravimetric method. Accurately weighed samples were placed in a moisture analyzer (MB25 Moisture Analyzer, MB25) maintained at 105 °C and dried until a constant weight was obtained. The percentage moisture

content was calculated on a dry weight basis, expressed as grams of water per 100 g of dried sample. All measurements were performed in triplicate, and the mean values were reported (24).

2.3.3. Attenuated Total Reflection Fourier Transform Infrared Spectroscopy (ATR-FTIR)

The chemical compatibility and possible interactions between Lipokon™ components were evaluated using attenuated total reflection Fourier transform infrared spectroscopy (ATR-FTIR). Spectra were recorded on a Jasco FTIR/4600 spectrometer (Jasco Co., Tokyo, Japan) equipped with a ZnSe ATR crystal and a TGS detector. Sample 10 mg was placed directly onto the ATR prism, and gentle pressure was applied to ensure optimal contact. Each spectrum was collected over a wavenumber range of 4000–400 cm^{-1}, with appropriate resolution and scan accumulation settings. The raw spectra were processed and corrected using the ATR correction mode in Jasco Spectra Manager Version 2. The corrected spectra were analyzed to identify characteristic functional groups and detect any shifts or changes indicative of molecular interactions or structural modifications.

2.3.4. Powder X-Ray Diffraction (p-XRD)

The crystallinity of the Lipokon™ formulations and raw materials was assessed via a Brucker D2 Phaser 2nd Generation X-ray diffractometer (Karlsruhe, Germany) operating at a voltage of 30 kV, a current of 10 mA, a scanning rate of 15.00°/min, and a 2θ range of 5.002°–60.990°, with an angular accuracy of ±0.02° 2θ, and it was further analyzed via the DIFFRAC. SUITE MEASUREMENT CENTER 21 CRF Part 11 V7.5. (25).

2.3.5. Differential Scanning Calorimetry (DSC)

Thermal behavior and solid-state properties of the Lipokon™ formulations were evaluated using a DSC-60 differential scanning calorimeter (Shimadzu, Kyoto, Japan). Accurately weighed 5 mg samples of the raw nutraceutical and optimized formulations were sealed in standard aluminium pans, while an empty pan served as the reference. All analyses were performed under a nitrogen purge at 100 mL/min to prevent oxidative degradation during heating. The samples were heated from 30 °C to 360 °C at a constant heating rate of 10 °C/min, and the resulting thermograms were recorded. The obtained DSC curves were examined to determine melting transitions, glass transition temperature (Tg), recrystallization events, and any changes in thermal behavior indicative of possible interactions or amorphization within the formulation matrix.

2.3.6. Particle Size, Polydispersity Index, and Zeta Potential

The particle size (PS) and polydispersity index (PDI) of liposomes were measured by dynamic light scattering (DLS) using Litesizer 100 (Anton Paar, Austria). The scattering data were recorded at a 90° angle. The zeta potential (ZP) of them was measured with the Zetasizer, Malvern instrument Ltd. device

by applying laser Doppler velocimetry (LDV). The dispersions were diluted more than a hundred times with PBS and analyzed six times (26).

2.3.7. Polarized Light Microscopy

Polarized light microscopy was employed to assess the structural features and birefringence patterns of the Lipokon™ formulations. 1 mg/mL sample was prepared in aqueous medium, placed on a clean glass microscope slide, and gently spread to form a thin, uniform layer. A coverslip was carefully positioned over the sample to minimize air entrapment and ensure proper visualization. The prepared slide was examined under a polarized light microscope (LEXT® OLS 5000, Mumbai, India) equipped with crossed polarizers. Images were captured to observe optical anisotropy, lamellarity, crystallinity, and any phase-separated structures within the formulation. All observations were conducted at ambient room temperature, and representative micrographs were recorded for documentation and analysis (27).

2.3.8. Field Emission Scanning Electron Microscopy (FE-SEM) and Energy-Dispersive X-ray Spectroscopy (EDX)

The surface morphology and elemental composition of the spray-dried Lipokon™ powders were evaluated using scanning electron microscopy (SEM) coupled with energy-dispersive X-ray spectroscopy (EDX) (FEI Quanta 200 FEG model equipped with a 15 kV accelerating voltage). Before analysis, samples were gently sprinkled onto a double-sided carbon adhesive tape mounted on an aluminium platform. Excess, loosely bound particles were removed by gentle tapping to ensure stable sample adherence. The mounted samples were then sputter-coated with a thin layer of gold under vacuum to enhance surface conductivity and prevent charging during imaging. SEM micrographs were obtained using an SEM instrument equipped with an EDX detector, operated at an accelerating voltage appropriate for high-resolution imaging.

The SEM analysis provided information on particle shape, surface texture, and structural uniformity of the liposomal microparticles. Elemental composition and distribution were further assessed using EDX spectroscopy, where characteristic X-ray emission peaks were recorded and used to confirm the presence of formulation components, including phospholipids and excipient elements (28). Images and spectra were acquired at 1000X magnification and regions to ensure representative characterization of the samples.

2.3.9. Transmission Electron Microscopy (TEM)

Microstructural properties of Lipokon™ liposomes were demonstrated with the aid of transmission electron microscopy (TEM). The lyophilized liposomal powder was reconstituted in phosphate-buffered saline (PBS, pH 7.4) and appropriately diluted to obtain a suitable particle density. A small aliquot was mounted on a carbon-coated copper grid, negatively stained with phosphotungstic acid, air-dried, and evaluated by transmission electron microscope (Tecnai T20, 200 kV, FEI)for morphology and structural integrity of nanostructured particles (29).

2.3.10. High-Performance Liquid Chromatography (HPLC) Method Development

Active nutraceuticals in Lipokon™ formulations quantitative analysis were analysed with a validated HPLC system (Shimadzu) with a C18 column (packing L1). Chromatographic conditions were finely tuned for each analyte to guarantee the sensitivity and resolution of the results. Berberine was investigated at 345 nm with a mobile phase of monobasic potassium phosphate and sodium lauryl sulfate in water with acetonitrile (1:1 v/v) at a flow rate of 1.0 mL/min, column temperature of 40 °C. Curcuminoids were detected at 420 nm in a mobile phase of tetrahydrofuran and citric acid solution after solvent extraction with acetone. Resveratrol was quantified at 303 nm with a mobile phase of acetonitrile and phosphate buffer (pH 3.0) in a 40:60 v/v ratio, at a flow rate of 1.0 mL/min and a column temperature of 35 °C; samples were prepared by solvent extraction and properly diluted with the corresponding mobile phase before injection.Caffeine quantification was performed at 275 nm using the same C18 column. The mobile phase consisted of acetonitrile, tetrahydrofuran, and sodium acetate buffer (0.82 g/L, pH 4.5 adjusted with glacial acetic acid) in a 25:20:55 v/v/v ratio. The system was operated at a flow rate of 1.0 mL/min, with the column oven maintained at 30 °C.

2.3.11. Product Yield

The product yield of the spray-dried Lipokon™ formulations was determined by comparing the mass of the dried powder collected after spray drying with the total mass of solid materials initially fed into the spray dryer. Before processing, the total solid content of the feed solution was accurately recorded. Following spray drying, the dry powder obtained from the collection chamber and cyclone separator was carefully weighed (30).

The percentage product yield was calculated using the following equation:

$$Product\ Yield\ (\%) = \frac{Final\ mass\ of\ dried\ product\ (gm)}{Initial\ mass\ of\ solid\ material\ (gm)}\ x\ 100$$

2.3.12. Assay and % Encapsulation Efficiency

Assay measurement was achieved with accurate weighing of formulation samples, dissolution in the respective mobile phase or extraction solvent, and HPLC of the solutions under validated conditions. The entrapment efficiency of the Lipokon™ formulations was quantified using an indirect ultracentrifugation method. Following liposome preparation, 1 mL of the dispersion was transferred into a centrifuge tube and centrifuged at 30,000 rpm (RCF ≥ 50,000 × g) for 10 min at room temperature to separate the unencapsulated (free) drug present in the external aqueous phase. The resulting supernatant was collected and analyzed for free drug content using an HPLC Instrument.

The percentage of entrapment efficiency (EE%) was calculated using the following equation:

$$\%\ Encapsulation\ Efficiency = \frac{Total\ conc.of\ product - Non\ encapsulated\ conc.of\ product}{Total\ conc.of\ product} x\ 100$$

2.3.13. Dissolution study

The in vitro release profiles of Lipokon™ formulations (Curcumin, Resveratrol, Berberine, and Caffeine) were evaluated using a USP Type II dissolution apparatus at 37 ± 0.5 °C. Based on the physicochemical properties of each analyte, the following dissolution media and conditions were employed: Curcumin in phosphate-buffered saline (PBS, pH 7.4) containing 0.1% surfactant at 100 rotation per minute (rpm) (31); Resveratrol in PBS (pH 7.4) with 0.5% surfactant at 75 rpm (32); Berberine in PBS (pH 6.8) at 100 rpm (33,34); and Caffeine in PBS (pH 7.4) at 50 rpm (34).At predetermined intervals over 24 hours, 5 mL aliquots were withdrawn, replaced with fresh medium, filtered (0.45 µm), and analyzed by HPLC at 425, 306, 345, and 273 nm, respectively. The methods were applied with minor variations, as indicated in the respective references.

3. Results and discussion:

3.1. Physical Assessment and pH Determination

Lipokon™ formulations of berberine, curcumin, resveratrol, and caffeine demonstrated high physical stability and uniformity. Upon visual inspection, all products exhibited a consistent, homogeneous appearance, with coloring properties characteristic of such formulations (a vibrant yellow color for curcumin and berberine, and an off-white to translucent color for resveratrol and caffeine). There was no evidence of phase separation or grit formation. The pH values of 1% w/v aqueous dispersions were within the physiologically compatible range, ensuring minimal irritation upon oral administration (Table 1). These values are favourable for phosphatidylcholine-based lipid matrices, which generally have a near-neutral microenvironment. Observed pH stability is crucial, as it determines the ionization state of the active ingredients and the overall chemical stability of the liposomal bilayer for storage.

Table 1. Represented product appearance, color, and pH of solution

Product	Appearance	Color	pH (mean ± SD)*
Lipokon™ Caffeine	Free Flowing Powder	Off-white	5.60 ± 0.03
Lipokon™ Resveratrol	Free Flowing Powder	Cream	4.65 ± 0.04
Lipokon™ Berberine	Free Flowing Powder	Yellow	5.58± 0.05
Lipokon™ Curcumin	Free Flowing Powder	Yellowish orange	5.73 ± 0.08

*Values represent mean ± standard deviation (n=3) of 1% w/v aqueous dispersions

3.2. Moisture Content

The moisture content of lipid-based formulations of Lipokon™ was selected with a view to either long-lasting maintenance or resistance to microbial growth. Moisture contents for all formulations were between 0.76% and 4.18%. The actual mean values recorded for, in particular: Berberine (4.18% ±0.12 %), Curcumin (0.76% ±0.09 %), Resveratrol (1.40% ±0.15%), and Caffeine (1.98% ±0.11%). Water concentrations observed at the experimental range had major impacts on lipid bilayers, as increased amounts led to phospholipid hydrolysis or a leaky state containing the active ingredient. Overall, these results indicate that the drying process was effective and the moisture content was reduced to a range that ensures physical and chemical stabilities without clumping or caking.

3.3. Attenuated Total Reflection Fourier Transform Infrared Spectroscopy (ATR-FTIR)

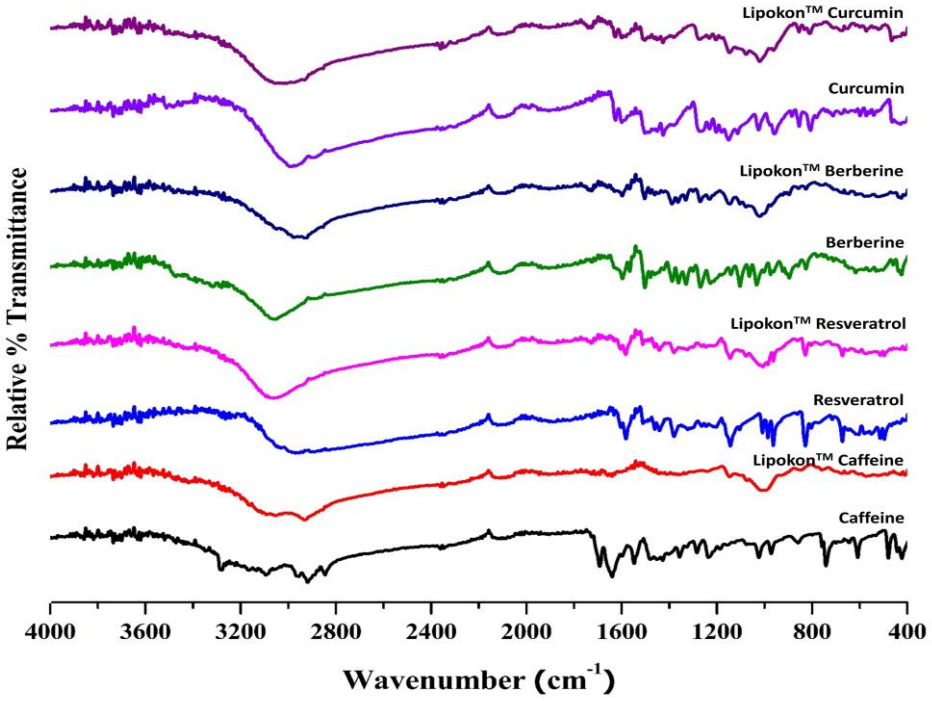


Figure 1. FTIR images of active ingredients and Lipokon™ products

Raw berberine exhibited sharp absorption bands characteristic of its alkaloid structure, including N-H and O-H stretching (3600-3000 cm^{-1}), aromatic C=C stretching (1600-1500 cm^{-1}), and C-O/C-N stretching (1200-800 cm^{-1}). Lipokon™ Berberine showed broadened and reduced-intensity bands across these regions, indicating molecular interactions with the lipid matrix while preserving chemical integrity. Raw caffeine displayed sharp peaks at 1700-1400 cm^{-1} (C=O and C=N stretching), while Lipokon™ Caffeine exhibited peak broadening consistent with molecular dispersion. Raw curcumin showed intense peaks at 3000-2800 cm^{-1} (C-H stretching), 1600-1500 cm^{-1} (aromatic C=C and C=O), and 1200-900 cm^{-1} (C-O and aromatic C-H bending). Lipokon™ Curcumin demonstrated reduced intensity across all functional groups, indicating strong lipid matrix interactions. Raw resveratrol displayed characteristic O-H stretching (3600-3200 cm^{-1}), aromatic C=C (1600-1500 cm^{-1}), and C-O stretching (1200-900 cm^{-1}), while Lipokon™ Resveratrol showed significant peak broadening, particularly in hydroxyl and aromatic regions.

All Lipokon™ formulations demonstrated systematic peak broadening and intensity reduction compared to raw materials, reflecting universal molecular-level encapsulation across all actives (Figure 1). The absence of new characteristic peaks indicated that no chemical degradation had occurred. Preservation of fingerprint region peaks (1200-400 cm^{-1}) in all Lipokon™ formulations indicated intact molecular skeletal structures. The broad absorption band at 3000-3500 cm^{-1} in all Lipokon™ formulations is consistent with O-H and N-H stretching of phospholipids and glycerol excipients. These findings support that the Lipokon™ technology achieves molecular-level encapsulation through non-covalent interactions, maintaining chemical integrity while facilitating amorphization observed in p-XRD analysis and enabling enhanced bioavailability through intimate dispersion within the lipid matrix.

3.4. Powder X-Ray Diffraction (p-XRD)

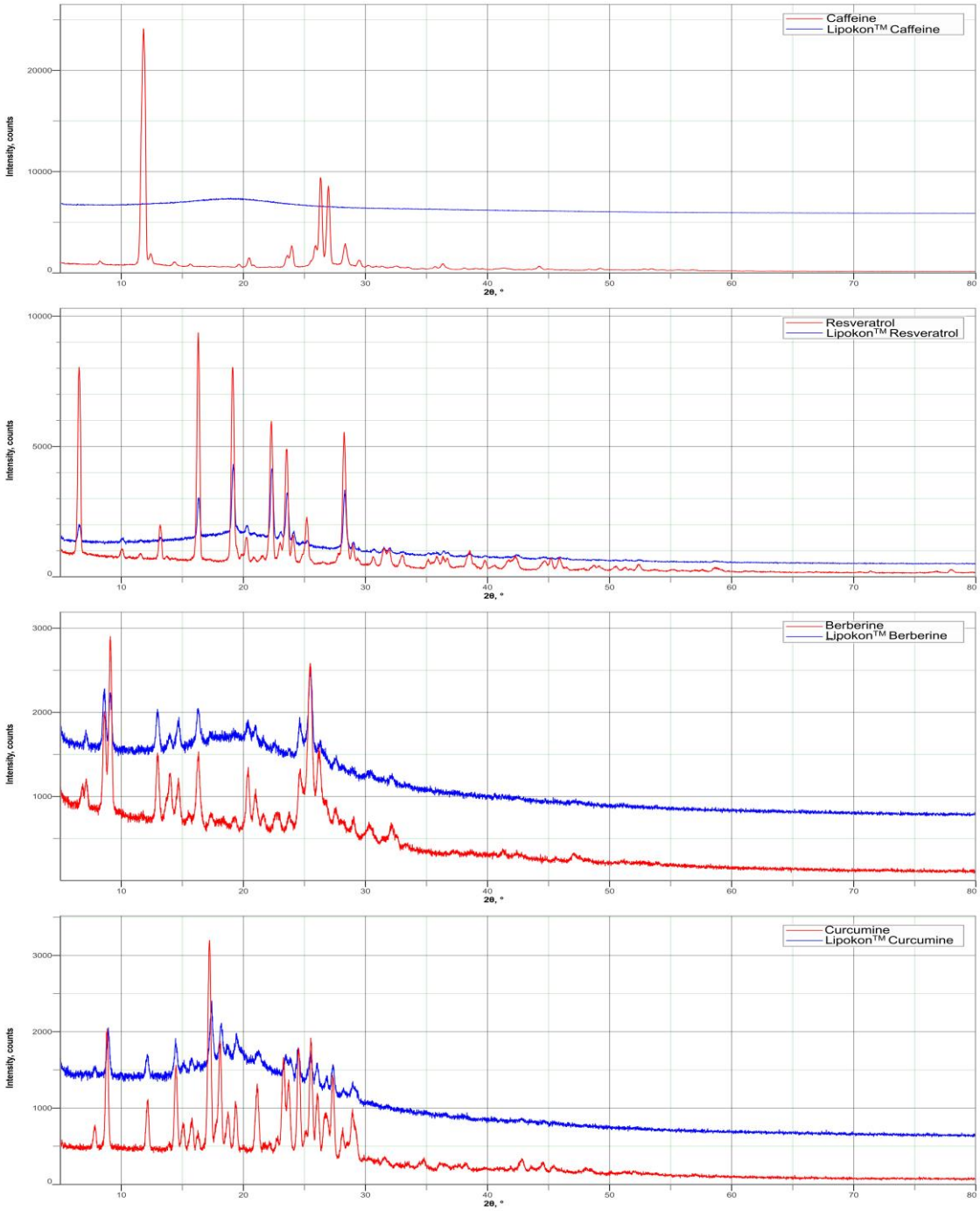


Figure 2. p-XRD graphs of active ingredients with overlapped Lipokon™ products

X-ray diffraction (XRD) patterns (Figure 2) confirmed the successful transition of the active ingredients from a crystalline state to a predominantly amorphous or molecularly dispersed state within the Lipokon™

matrix. For raw caffeine, resveratrol, berberine, and curcumin, crystalline diffractograms showed numerous sharp, high-intensity Bragg reflections demonstrating their stable crystalline nature. In contrast, the Lipokon™ formulations displayed a dramatic reduction in peak intensity and the emergence of broad amorphous halos. The significant decrease in peak intensity observed for all formulations suggests that the Lipokon™ technology successfully overcomes the lattice energy of pure drugs by entrapping them within the lipid framework. This structural change is an important indication of the system's ability to enhance dissolution and oral bioavailability.

3.5. Differential Scanning Calorimetry (DSC)

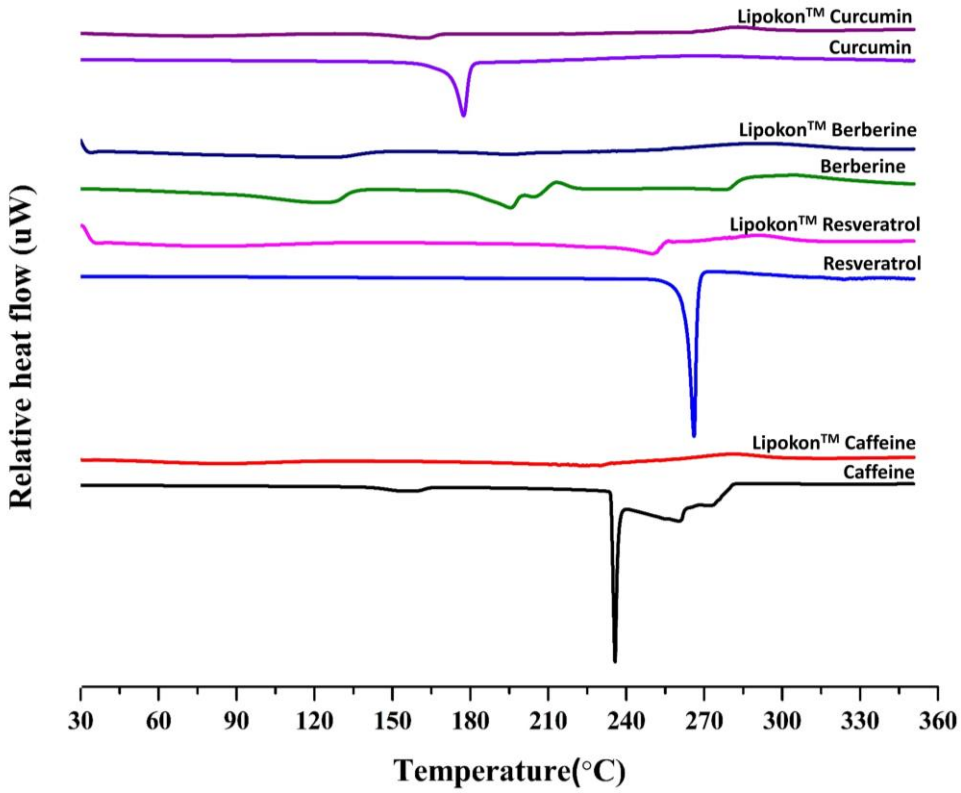


Figure 3. DSC thermograms of active ingredients and Lipokon™ products

Differential Scanning Calorimetry: DSC was used to check for the thermal behaviour of the Lipokon™ Product (Figure 3). The endothermic peaks in the thermograms of the pure nutraceuticals were sharp and corresponded to their respective melting points: Caffeine at 236°C, Resveratrol at 267°C, Berberine at 192°C, and Curcumin at 183°C. In the Lipokon™ formulations, these crystalline endotherms were either absent or markedly reduced in intensity, with pronounced broadening and significant peak shifts. The disappearance of these signature melting peaks signifies that the drugs are no longer in a crystalline state, but rather are molecularly spread out all over the lipid matrix. This amorphous phase is crucial so that the fast and prolonged release profiles seen for oral delivery applications are achieved, because it dispels any energy required to dissolve the crystal lattice once in dissolution.

3.6. Particle Size and Polydispersity Index and Zeta Potential

The physicochemical properties of Lipokon™ formulations, as seen in Z-average particle size, polydispersity index (PdI), and zeta potential, illustrate the multipurpose nature of the lipid matrix for the encapsulation of different molecules with different physicochemical characteristics (Figure 4). The physicochemical properties of Lipokon™ formulations exhibited strong performance, as evidenced by average particle sizes from 119.3 nm to 154.0 nm, which reflect the formation of nanometric lipid assemblies by the high-shear mixing and size reduction process. The smallest size obtained was with Lipokon™ Berberine at 119.3 nm (PdI: 0.250), followed by Lipokon™ Caffeine at 125.2 nm (PdI: 0.271), Lipokon™ Curcumin at 126.4 nm (PdI: 0.267), and Lipokon™ Resveratrol at 154.0 nm (PdI: 0.392). Negative zeta potential values confirmed the colloidal stability, as Lipokon™ Resveratrol and Lipokon™ Curcumin showed superior electrostatic stabilization, -44.8 mV and -36.9 mV, respectively. Lipokon™ Berberine showed a stable surface charge (-21.9 mV), while that of Lipokon™ Caffeine (-11.9 mV) suggested that the stability of the latter is effectively supported by the steric stabilization provided by the phospholipid matrix and modified starch encapsulating agents. These results confirm the development of homogeneous and stable lipid-active delivery systems. The entire particle size area and surface charge profiles of the four compounds all confirmed the stable Lipokon™ delivery system development, giving a technically sound foundation for enhanced cellular uptake and bioavailability of Lipokon™.

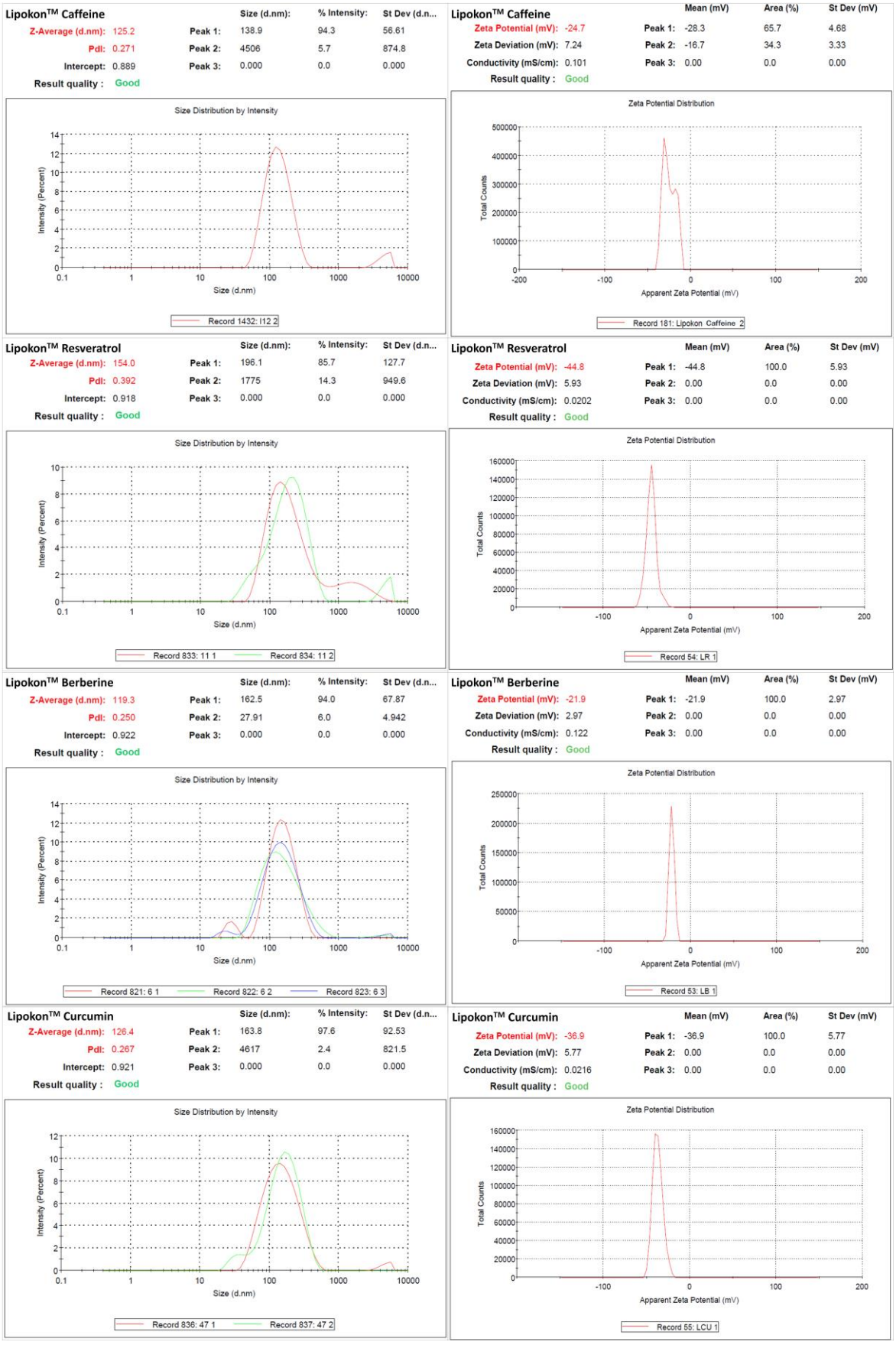
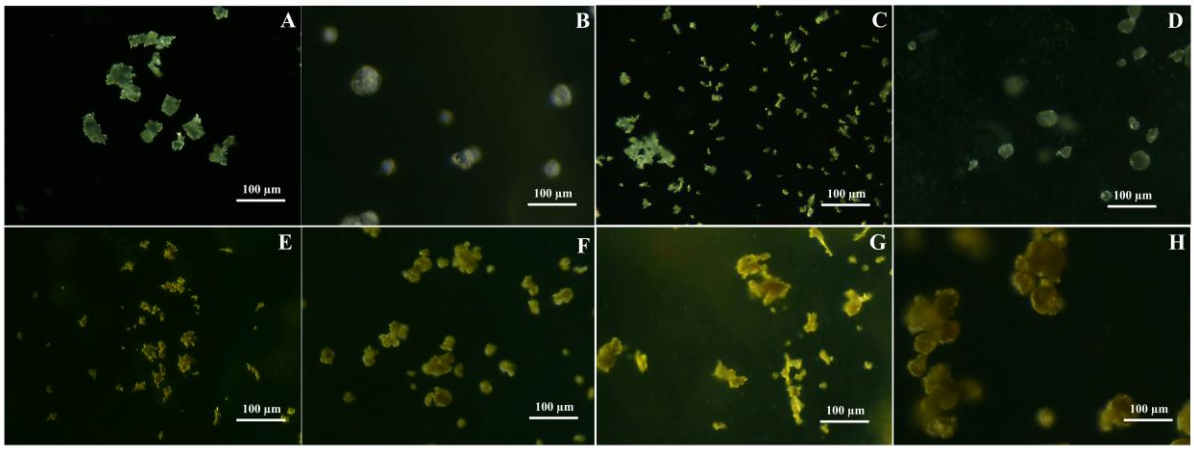


Figure 4. Z-average particle size, polydispersity index (PdI), and zeta potential for all Lipokon™ Products.

3.7. Polarized Light Microscopy

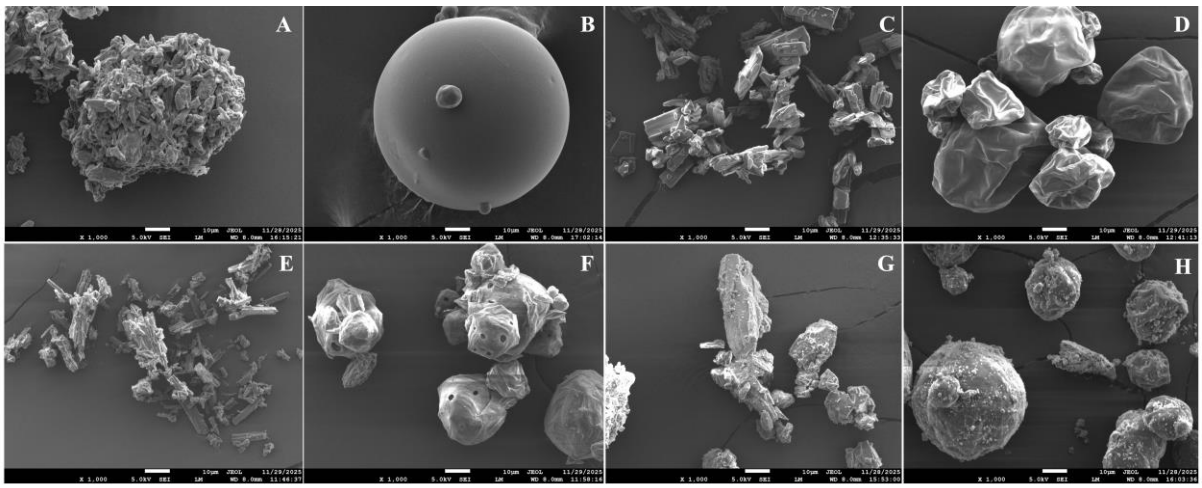


A=Caffeine , B=Lipokon™ Caffeine, C=Resveratrol, D=Lipokon™ Resveratrol, E=Berberine, F=Lipokon™ Berberine, G=Curcumin, H=Lipokon™ Curcumin

Figure 5: Polarizing light microscopy (PLM) images of the active ingredients and Lipokon™ Products

Figure 5 (A–H) shows morphological transitions from pure bioconstituents to Lipokon™ formulations (PLM). The pure caffeine (A), resveratrol (C), berberine (E), and curcumin (G) showed characteristic crystalline birefringence morphology and angular and flake-like shape, confirming their crystalline state. The associated Lipokon™ formulations, Lipokon™ Caffeine (B), Lipokon™ Resveratrol (D), Lipokon™ Berberine (F), and Lipokon™ Curcumin (H), exhibited subsided birefringence. Micrographs showed spherical or irregularly shaped glass-like particles without strong patterns of light interference in the materials. The lack of crystallinity indicates that the active compounds either have been converted into an amorphous state or are molecularly dispersed in the lipid matrix. The lack of crystal-like structures in the Lipokon™ batches indicates that encapsulation processes are effective in inhibiting recrystallization and in achieving a mix at the molecular level, necessary for increased dissolution and bioavailability of these molecules.

3.8. Field Emission Scanning Electron Microscopy (FE-SEM) and Energy-Dispersive X-ray Spectroscopy (EDX)



A=Caffeine , B=Lipokon™ Caffeine, C=Resveratrol, D=Lipokon™ Resveratrol, E=Berberine, F=Lipokon™ Berberine, G=Curcumin, H=Lipokon™ Curcumin

Figure 6: SEM images of active ingredients with Lipokon™ Products

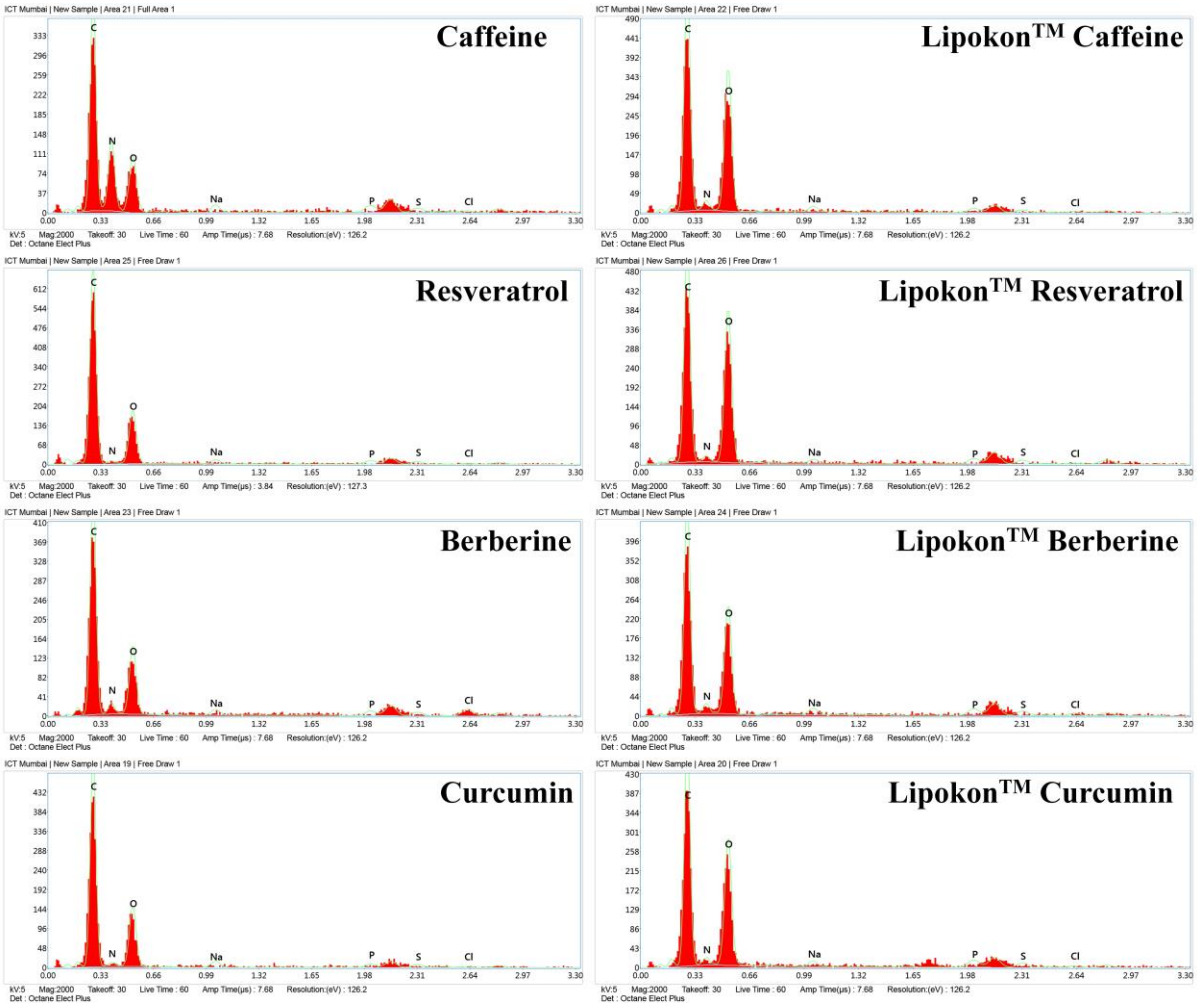


Figure 7: EDX images of active ingredients and Lipokon™ Products

The surface morphologies of the pure active nutraceutical ingredients and their Lipokon™ formulations were characterized by scanning electron microscopy (SEM) as indicated in Figure 6 (A–H). The pure ingredients (caffeine (A), resveratrol (C), berberine (E), curcumin (G)) were in crystalline structure; irregularly distributed, angular, needle-like, or flake-like. These properties characterize the extreme crystallinity of the raw compounds. Lipokon™ formulations, Lipokon™ Caffeine (B), Lipokon™ Resveratrol (D), Lipokon™ Berberine (F), and Lipokon™ Curcumin (H), on the other hand, showed a complete transformation in particle architecture. In the case of the caffeine formulation (B), a perfectly smooth, spherical, glass-like particle was obtained, indicating an ideal amorphous state and successful molecular integration in the lipid-carrying system. The resveratrol (D), berberine (F), and curcumin (H) formulations had mostly spherical or oval arrangements. Since no visible crystal structures or surface-adhered drug crystals were observed in the Lipokon™ batches, this indicates molecular dispersion of the active agents within the lipid matrix. This morphological change from crystalline to amorphous, spherical particles is an essential marker of the technology's capability of recrystallization deterrence, which directly underlies the larger dissolution and potentially bioavailability reported in the performance studies.

The morphological transformation indicated by the SEM imaging was validated by the EDX analysis and yielded specific elemental signatures showing the successful encapsulation of pure ingredients and Lipokon™ formulations (Figure 7 and Table 2). Both EDX and SEM have performed well as

complementary methods to characterize pharmaceutical formulations, offering qualitative and quantitative mapping of drug and excipient distribution. (36)

The transition from crystalline, needle-like structures to spherical structures is chemically confirmed by a large rise in oxygen content in all formulations (13.22% to 32.57% for Caffeine, 18.32% to 34.42% for Resveratrol, 15.25% to 25.03% for Berberine, and 19.47% to 28.23% for Curcumin a trend corresponding to the oxygen-rich lipid environment surrounding drug molecules (37). The persistent detection of phosphorus (between 4.13% and 6.41%) in the Lipokon™ batches is an unequivocal chemical indication of the phospholipid-based delivery system. Moreover, the rapid decrease of various drug-specific elements, such as, for example, nitrogen of Caffeine decreased from 22.59% to 3.19% and chlorine concentration of Berberine from 13.41% to 5.11%, further affirms that the nutraceuticals are molecularly scattered in the lipid matrix as opposed to surface-constrained crystals (38). These elemental profiles confirm SEM visualizations showing a complete transformation from a crystalline to an amorphous state, which is important for improving the dissolution and potential bioavailability of these compounds.

Table 2. EDX data of active ingredients and Lipokon™ products

Sample	Carbon (C)	Oxygen (O)	Nitrogen (N)	Phosphorus (P)	Chlorine (Cl)
Caffeine	48.34	13.22	22.59	5.83	2.84
Lipokon™ Caffeine	51.09	32.57	3.19	4.13	3.64
Resveratrol	64.91	18.32	1.77	4.81	3.51
Lipokon™ Resveratrol	49.96	34.42	2.03	5.05	2.37
Berberine	57.50	15.25	3.87	4.04	13.41
Lipokon™ Berberine	52.36	25.03	3.48	6.18	5.11
Curcumin	63.50	19.47	1.84	4.34	2.95
Lipokon™ Curcumin	52.29	28.23	2.43	6.41	3.47

3.9. Transmission Electron Microscopy (TEM)

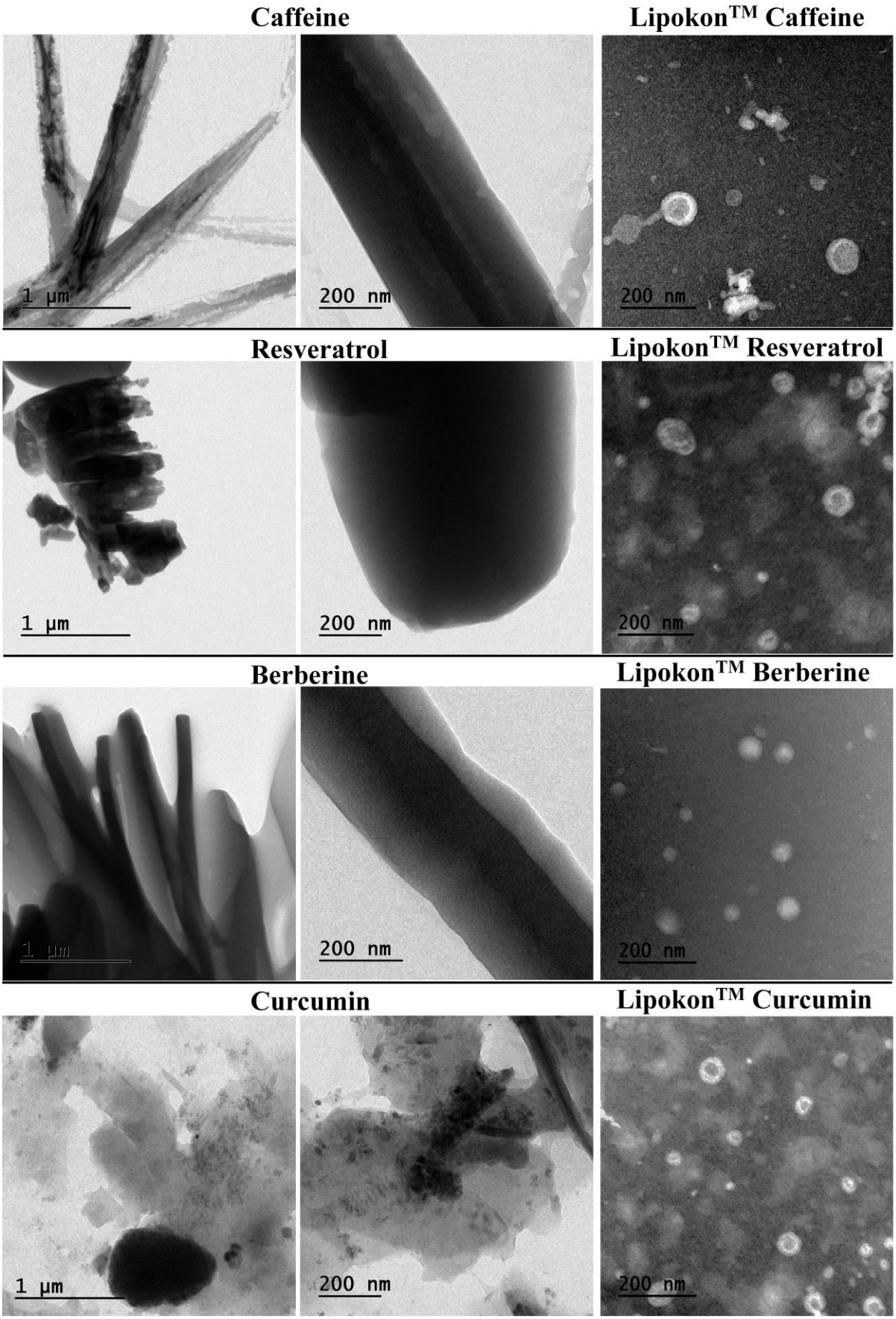


Figure 8. TEM images of active ingredients and Lipokon™ products

The surface morphology of the pure nutraceuticals and their Lipokon™ formulations were characterized through TEM (Figure 8). The pure nutraceuticals, Caffeine, Resveratrol, Berberine, and Curcumin, showed

clear and very distinct crystalline arrangements with irregular, angular, needle-shaped, or flake-shaped shapes. All of these properties are due to the high crystallinity of the raw material. In particular, Caffeine and Berberine presented elongated, needle-shaped crystals, whereas Curcumin had dense, irregular flakes. Differently, Lipokon™ (Caffeine, Resveratrol, Berberine, and Curcumin) formulations undergo a significant alteration in particle architecture. All formulations changed to a largely spherical or oval vesicular arrangement, with sizes remarkably smaller to the nanometer scale (less than 200 nm). There were no visible crystal lattice structures on Lipokon™ batches, as well as no surface-adhered drug crystals, evidence of successful molecular dispersion of the nutraceuticals into the lipid matrix. This morphological transition from crystalline to amorphous spherical structures is an important sign of the ability of the system to deter recrystallisation and is a key requirement for improved dissolution & bioavailability.

3.10. Product Yield

Lipokon™ product showed a consistent product yield of approximately 75–80% for all, indicating efficient powder recovery includes Lipokon™ Caffeine - 76.12±0.18 %, Lipokon™ Berberine – 75.98±0.09 %, Lipokon™ Resveratrol - 78.35±0.10 %, Lipokon™ Curcumin - 81.46±0.77%. The optimized spray-drying parameters, with appropriate solid content, minimized material loss and wall deposition. The lipid-based formulation aided effective particle formation, resulting in acceptable yields that demonstrate good process reproducibility and scalability of the spray-drying method.

3.11. Assay and % Encapsulation Efficiency

The drug loading of the Lipokon™ formulations was notably high, as demonstrated in the assay results. Lipokon™ Berberine showed an assay value of 31.98±0.15 %, Lipokon™ Resveratrol a value of 35.12±0.09 %, and Lipokon™ Curcumin (total curcuminoids) a value of 29.63±0.12 %. Lipokon™ Caffeine demonstrated a comparable total drug loading of 30.12 ±0.10 %, aligning with the platform's high-capacity delivery standards for both lipophilic and hydrophilic molecules. Involvement of the bioactives in lipid–polymer system confirmed through entrapment efficiency analysis; namely, curcumin and resveratrol showed entrapment efficiencies of 97.8 ± 1.2% and 96.9 ± 1.5%, respectively. Berberine possessed an entrapment efficiency of 92.4 ± 2.1% and caffeine an entrapment efficiency of 68.6 ± 3.4%.

3.12. Dissolution study

In vitro release profiles revealed a constant and controlled delivery mode for the four formulations over 24 h. Lipokon™ Caffeine produced the fastest release, with 39.41±0.19 % achieved within one hour and near-completion of release (99.1±0.92 %) occurred in 24 h (Figure 9). The biphasic release patterns were more retarded for the lipophilic resveratrol. Lipokon™ Curcumin and Lipokon™ Berberine had cumulative releases of 88.4±0.29 % and 93.6±0.48 % at 24 hours, respectively. Lipokon™ Resveratrol had the same long-term profile with a time-point of 91.2±1.08 % release. The peak burst release by all formulations (ranging from 4.2±0.09 % to 18.4±1.02 % at 0.5 hours) can possibly result from drug molecules adjacent

to the vesicle surface being released, and a sustained diffusion-controlled stage following that through the lipid core. These findings confirm that the Lipokon™ system can adequately stabilize a variety of bioactive compounds and provide a reliable mechanism for prolonged oral delivery.

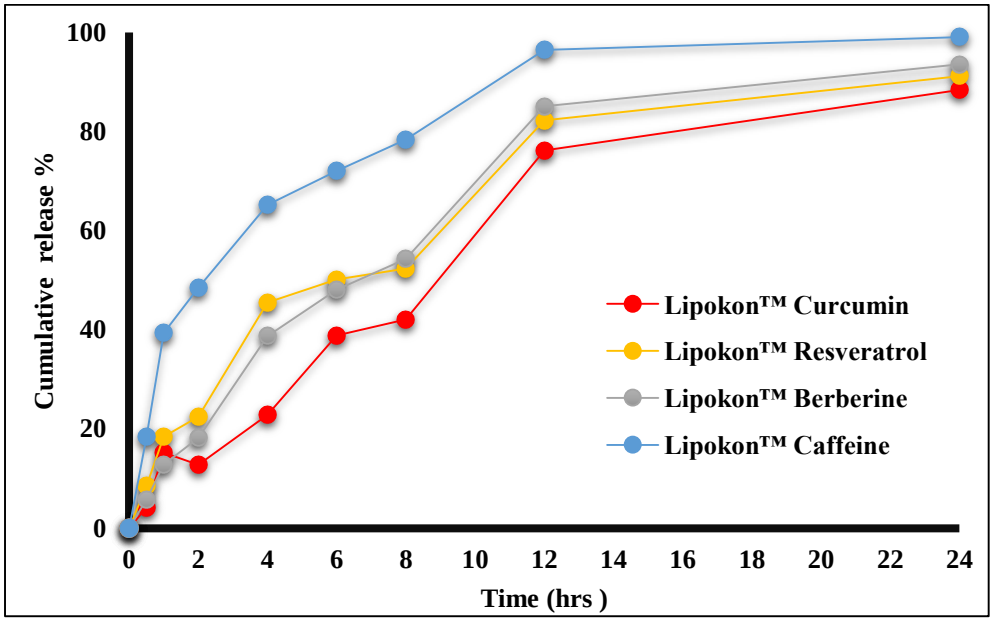


Figure 9. Dissolution Study for all Lipokon™ Products

4. Conclusion:

This study presents that Lipokon™ is an effective and versatile lipid-based delivery platform for nutraceuticals with diverse physicochemical properties. Comprehensive characterization confirmed the successful transformation of crystalline caffeine, resveratrol, berberine, and curcumin into amorphous, molecularly dispersed forms within a phospholipid matrix, resulting in enhanced stability and dissolution. Optimized particle size, stable negative zeta potentials, and uniform nanoscale vesicular morphology indicate strong colloidal stability and formulation robustness. In vitro dissolution studies further validated performance, showing near-complete release of caffeine and sustained release of resveratrol over 24 hours.

Overall, Lipokon™ effectively addresses key bioavailability challenges associated with poorly soluble actives and demonstrates adaptability across both hydrophilic and lipophilic compounds. These findings position Lipokon™ as a scalable and promising platform for advanced oral delivery applications with the potential to improve therapeutic efficacy and product performance.

5. Conflict of Interest:

Dr. Praful Patil, Dr. Saraswati Gupta, Mr. Ajay Pathak, and Mr. Vedant Gupta are employees of Konark Herbal and Healthcare Pvt. Ltd., the sponsor of the study.

Mr. Vedant Gupta is a Director of Konark Herbal and Healthcare Pvt. Ltd.

Madhuri Kshirsagar and Prof. Purnima Amin, declares no competing financial or non-financial interests related to this study.

6. Acknowledgement:

The authors and the Director of Konark Herbal and Healthcare Pvt. Ltd. sincerely acknowledge the research team for their valuable contributions and extend their kind appreciation to Prof. Amin for his strong support in the analysis and characterization of the research work.

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