IMPROVEMENT OF ORAL BIOAVAILABILITY OF DRUGS USING NANOSTRUCTURED LIPID CARRIERS

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Abstract

The goal of this work was to create solid lipid nanoparticles that contained 13 mg of both doxorubicin and curcumin per ml of the SLN dispersion. Size, zeta potential, entrapment efficiency (EE), and drug loading (DL) were used to characterize the SLN after they were synthesized using a hot homogenization procedure. The characterization of the created formulation enabled for the conclusion to be made that the SLNs were successfully synthesized and amorphous, showing that curcumin and doxorubicin were present in a solubilized condition. Furthermore, compared to free curcumin's first order release, the generated Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles displayed a zero order release, illuminating the controlled release property of the substance.To the best of our knowledge, it is the most potent combination of high drug loading and the largest increase in curcumin and doxorubicin solubility in an aqueous medium (1.4×10^6times increase compared to 11 ng/ml in water for free curcumin).The results showed that the LOD and LOQ were 1.95 ng/ml and 19 ng/ml, respectively. Total recovery was 85% or more. At LQC, MQC, and HQC, individual recoveries were 80.18, 87.18, and 84.42%, respectively.The intra-day accuracy for QC samples with a precision of less than 2% was 99.43-102.21%, while the inter-day accuracy was 99.47-106.83%.

Introduction

Lipid drug conjugates (LDC), solid lipid nanoparticles (SLN), and nanostructured lipid carriers (NLC) have all recently been researched as carrier systems for a variety of purposes. Due to the β modification of solid lipid, SLN have a lot of issues with drug loading and drug ejection when kept for an extended period of time.The first lipid nanoparticle manufacturing efforts were carried out at academic laboratories in 1990. The lipid nanoparticles were created concurrently by M. R. Gasco in Turin, Italy, R. H. Muller in Berlin, Germany, and J. S. Lucks in Kiel, North

Germany. These unique carriers particle matrix was made of a solid lipid, so to distinguish them from fluid liposomes and nanoemulsions, they were given the name solid lipid nanoparticles (SLN). The second generation of lipid nanoparticles, known as nanostructured lipid carriers (NLC), was created in 1999. In these particles, the matrix is made up of a mixture of solid and liquid lipid oil, rather than just one single solid lipid.[1][2].To address the issues of SLN, NLC have been developed. They are regarded as belonging to the second generation of lipid nanoparticles.By mixing a liquid lipid with the solid lipid, a greater particle drug loading can be produced compared to SLN, and this allows NLC to exhibit a better loading capacity for active drugs. As a result, the NLC have a higher drug loading capacity than the SLN, and there is less risk of drug expulsion during storage.[3][4][5]

Combinatorial chemistry, high-throughput screening, and genomics have created a technological platform that generates a significant number of novel chemical entities (NCEs) with therapeutic promise each year in today's drug development world. The pharmaceutical medication delivery industry is projected to expand at a compound annual growth rate of 7.5 percent from $1048.1 billion in 2015 to $1504.7 billion in 2020. Even though a large number of new pharmacological compounds have been created, only a handful have been successful in gaining commercial acceptance. Because finding and developing a medication is a time-consuming and expensive process that may take up to 13 years and cost up to $900 million, according to current estimates. In addition, lack of effectiveness (which accounted for 30% of failures), safety (which accounted for 30% of failures), poor bioavailability, and an unfavorable pharmacokinetics profile (which accounted for 40% of failures) were the leading causes of clinic attrition. As a result, more medication candidate molecules are removed before they can be tested in humans. [6].[7][8]

Furthermore, the newly found medicines identified throughout the research and development procedures are not appropriate for oral administration. Because new chemical entities characteristics changed toward greater molecular weight and increased lipophilicity. As a result, lipophilic compounds low water solubility has become a persistent issue in drug discovery as well as the early and late stages of pharmaceutical development. Furthermore, it was estimated that up to 70% of presently developed compounds and 40% of already commercialized medicines are water-insoluble. As a consequence, an inadequate quantity of medication enters the systemic circulation, followed by the site of action, resulting in poor bioavailability and a

lack of pharmacological effect. This is a topic that formulation scientists are concerned about. As a result, low water solubility remains a barrier to effective medication research, design, and optimization. As a result, there is a critical need for an alternate method to improve solubility in pharmaceutical development programs. Because the medication's solubility is one of its most significant physicochemical characteristics in terms of drug release and absorption, it plays a crucial role in its bioavailability, particularly for orally given drugs. Furthermore, the orally given drug's bioavailability is determined not only by its solubility in the GIT but also by its permeability across cell membranes. As a result, drug molecules must be present in dissolved form to be carried through biological membranes. In addition, all processes except endocytosis need that medication to be present in an aqueous solution before it may be absorbed. This, in turn, is determined by the drug's aqueous solubility (absolute or intrinsic solubility) and dissolving rate in water.[9][10].Doxorubicin is one of the most commonly prescribed chemotherapeutic drugs, however due to its cardiotoxic effects and drug resistance, its clinical use is still restricted. Combinations of chemotherapy treatments with various medications have been proposed to increase the therapeutic effectiveness of the anthracycline doxorubicin.[11].Doxorubicin's anticancer activity has been demonstrated to be enhanced when combined with curcumin.Even though combination chemotherapy frequently exhibits enhanced antitumor activity, adverse effects might occasionally worsen. Chemotherapies could therefore be coloaded in a nanocarrier to get around these restrictions and regulate the pharmacokinetics of medications. Various lipid nanoparticle types have been employed to deliver anticancer medications, but solid lipid nanoparticles (SLN) have drawn more interest recently.[12][13].

SLN are incredibly alluring nanocarriers that stop the active ingredients from degrading chemically and boost their bioavailability. The development of an ion pairing with a lipophilic counter-ion has been suggested as an alternative to boost the doxorubicin encapsulation because the efficiency of the entrapment of hydrophilic medicines like doxorubicin into SLN is low. Designing SLN with doxorubicin loaded by using a lipophilic anion that also exhibits anticancer action is an appealing possibility.[14][15].From the plant curcuma longa (turmeric), curcumin (Cur) is a hydrophobic polyphenol with minimal intrinsic toxicity. Numerous pharmacologic effects, including antibacterial, anti-inflammatory, antioxidant, and anticancer activities, have been linked to it. Although curcumin is extremely hydrophobic, its instability and low

bioavailability are significant obstacles to its continued use in medicine. Therefore, it is necessary to develop innovative methods to enhance the physicochemical characteristics and therapeutic effectiveness of curcumin.[16]

The objective of the present study is to develop solid lipid nanoparticles-based oral delivery system for Curcumin and Doxorubicin for chronic therapy. The underlying hypothesis for this investigation is that both the drugs suffer from the disadvantage of being poorly 3% bioavailable when given orally. Nanotechnology has been reported to be an efficient tool for enhancing the permeability of medications. The specific aims for this investigation are,development and validation of an HPLC method for quantification of Curcumin and Doxorubicin,Formulation and characterization of Curcumin and Doxorubicin loaded solid lipid nanoparticles using LIPOID S 75 as stabilizer as solid lipids and Optimization and characterization of Developed SLNs

MATERIAL AND METHODS

Chemicals and Materials

From Sunpure Extracts Pvt. Ltd. in New Delhi, India, curcumin was purchased. From Sun Pharmaceuticals Industries Ltd doxorubicin was purchased. Compritol® 888 ATO and Glyceryl Monostearate (GMS) was acquired from Gattefosse India Pvt. Ltd, and phospholipon 90G was obtained from Fisher Scientific and β- glucuronidase from Sigma Aldrich. Tween 80 and polyethylene glycol 600 were procured from nearby merchants (CDH, New Delhi, India). Product CurcuWIN was bought from OmniActive Health Technologies.

From Fisher Scientific acetonitrile (ACN), chloroform, and methanol (HPLC grade) was purchased and syringe filters was purchased from Waters India Pvt. Ltd. The research also used several reagents, all of which were of analytical quality.

Preparation of Curcumin and Doxorubicin Loaded Solid Lipid Nanoparticles

A high-pressure hot homogenization process was used to prepare solid lipid nanoparticles that were loaded with doxorubicin and curcumin. Tween 80, phospholipon 90G, and water were combined to create the aqueous phase, which was then heated to about 80°C. At 70–75 °C, lipid [Compritol®888 ATO and GMS (4:1)] was melted, and curcumin in polyethylene glycol 600 solution was added. To create a coarse emulsion, the resulting lipid mixture was added to the

aqueous phase while being homogenised at high speed (8000 rpm for 8 min). The latter was subsequently passed through a high pressure homogenizer three times at 500 psi, and the resulting dispersion was cooled to room temperature to create the SLNs.

To achieve a 1.3% w/v curcumin and 1.3% w/v doxorubicin in the SLN dispersion, several formulations will be prepared using different types and quantities of the lipid and by the concentration of phospholipon 90G.[17][18][19][20]

CHARACTERIZATION

Assay of the "Total Drug Content (TDC)" of Doxorubicin and Curcumin in Dispersion

Methanol: chloroform (1:1) was selected as the solvent for dissolving the SLNs based on the solubility of Compritol®888 ATO and GMS. The chloroform:methanol solvent system was used to appropriately dilute 1 ml of the dispersion to 5000 times. Using the appropriate blank and the resulting solution, a spectrophotometric analysis was performed at max 425 nm. TDC was calculated using the formula below:

$$\text{Total drug content (\%)} = \frac{\text{observed drug content}}{\text{Theoretical drug content}} \times 100$$

Entrapment Efficiency (EE) Calculation

The dialysis membrane method was used to calculate the EE of solid lipid nanoparticles that were loaded with the drugs doxorubicin and curcumin. Before use, the membrane (cut off at 7 kDa MW) was submerged in double-distilled water for an entire night. One millilitre of the dispersion was dialyzed for 45 minutes at room temperature against 100 millilitres of methanol using a pre-soaked dialysis bag that was knotted at both ends. Following suitable dilution (5000 times) with methanol: chloroform (1:1), the amount of drug still present in the dialysis bag was analysed spectrophotometrically to determine the amount of drug trapped inside the SLNs.

EE was calculated using the formula below:

$$\text{Entrapment Efficiency (\%)} = \frac{\text{Entrapped drug}}{\text{Total drug content}} \times 100$$

Zeta Potential, Polydispersity Index (PDI), and Particle Size Analysis

After the proper dilution (20 times) using double-distilled water, the mean diameter, PDI, and zeta potential of the dispersion were calculated using the DelsaTM Nano C Particle Analyzer.

Field Emission Scanning Electron Microscopy (FESEM)

The FESEM was used to examine the solid lipid nanoparticles that were loaded with the drugs doxorubicin and curcumin for uniformity in size, shape, and physical stability characteristics, such as aggregation or irregularity. The narrow probing beams used in FESEM at low and high electron energies improve spatial resolution while causing the least amount of sample damage. It offers ion-free images with topography data at magnifications of 250–1,000,000X. A drop of the sample was applied to the copper grid with carbon coating to create a thin layer. Samples were examined using a FESEM after the grid had been air dried.[21]

DSC, or a Differential Scanning Calorimeter

On a Q20 differential scanning calorimeter, thermograms of curcumin, Doxorubicin,Curcumin and Doxorubicin Loaded Solid Lipid Nanoparticles, blank SLNs, and a lipid mixture (Compritol R 888 ATO and GMS (4:1)) were taken. In the nitrogen environment, samples were heated at a predetermined rate of 10°C/min over the temperature range of 30–300°C in aluminium hermetic pans.

Infrared Fourier Transform (FTIR)

Curcumin, Doxorubicin ,Doxorubicin Loaded Solid Lipid Nanoparticles, blank SLNs, and lipid mixture [Compritol R 888 ATO and GMS (4:1)] Fourier transform infrared spectra were captured using a 60 MHz Varian EM 360 (PerkinElmer,) and the KBr pellet technique. The acquired peaks were compared to look for any notable changes.

Diffraction of X-rays from powder (PXRD)

Measurements was made with an X-ray diffractometer using X-rays to determine the crystalline or amorphous nature of SLNs. By subjecting the samples to Cu K α radiation (45 kV, 40 mA) and scanning from 5° to 50°, 2θ at a step size of 0.017◦ and scan step length of 25 s, PXRD experiments were carried out.

By applying the Bragg's equation nλ = 2d sin, where λ is the wavelength of the incident X-ray beam and n is the order of the interference, the instrument calculates the interlayer spacing d from the scattering angle. To determine the typical drugs peak intensity, obtained XRD patterns were compared.

Studies on photostability

According to ICH guidelines, the photostability tests on free curcumin (curcumin dispersion in 1% CMC) and curcumin, free doxorubicin,Doxorubicin Loaded Solid Lipid Nanoparticles were carried out. Clear glass and amber-colored containers were used to store free curcumin and Curcumin, Doxorubicin,Doxorubicin Loaded Solid Lipid Nanoparticles, respectively. The samples were positioned in the photostability chamber and subjected to light for 10 days at a minimum illumination of 1.2 million lux hours. Free curcumin's total drug content (assay) was assessed after 10 days, and Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles total drug content, entrapment effectiveness, particle size, zeta potential, and PDI were assessed.

Variation in Particle Size With regard to pH and duration

Curcumin, Doxorubicin Loaded Solid Lipid was diluted (20 times) with pH 1.2, 6.8, and 7.4 buffers before being incubated at 37°C. To establish the stability of Curcumin, Doxorubicin,Doxorubicin Loaded Solid Lipid Nanoparticles on oral administration, samples were taken at various time intervals, and their particle size was measured.

VALIDATION OF BIOANALYTICAL METHOD

Following U.S. Food and Drug Administration criteria, the method was developed and validated for the determination of curcumin and Doxorubicin in plasma. The method was validated for sensitivity, linearity ,system suitability, precision,specificity, recovery andaccuracy.By adding 40µl of blank plasma to 10µl of each appropriate working dilution of curcumin and Doxorubicin

to produce concentrations of 25–500 ng/ml of curcumin and Doxorubicin , a five point calibration curve of curcumin and Doxorubicin was created.In order to validate the results, samples of high quality control (HQC: 500 ng/ml), medium quality control (MQC: 200 ng/ml), and low quality control (LQC: 25 ng/ml) were prepared in a similar manner.

Chromatographic Prerequisites

Utilising a UPLC system (waters, Acquity UPLC H class), curcumin and Doxorubicin was determined. In this a reversed phase Accucore C18 column (100 mm 4.6 mm, 2.6 m)was utilized. Acetonitrile: Water (1:1, isocratic) was used as the mobile phase, and 0.1% acetic acid was used to bring the pH value down to 3. The analytical column was maintained in a thermostatic oven at 35°C while the elution was carried out at a flow rate of 0.10 mL/min. A Waters Photodiode Array Detector was used to find curcumin at a predetermined wavelength of 425 nm.

RESULT AND DISCUSSION

Solid lipid nanoparticles with added curcumin and Doxorubicin

As detailed in Table 1, many formulations containing 10-13 mg (1–1.3%) of curcumin and Doxorubicin per ml of curcumin and Doxorubicin dispersion were prepared. However, upon keeping, the majority of these SLN systems demonstrated the settling of curcumin and doxorubicin crystals at the bottom of the SLN curcumin and Doxorubicin formulation within 24 hours of manufacture.

The drugs were settled in every batch made with Compritol R 888 ATO, with concentrations ranging from 4 to 10% w/w. When Precirol ATO 5 R was utilised as the lipid component (FF4 and FF5), however, no settling was noticed.However, the FF5 formulation had a particle size of ≥1 μ (1000 nm), therefore three batches of the F4 were made and its TDC, entrapment effectiveness, and particle size were assessed.The chosen formulation FF4's particle size was also >700 nm. In the following section of the investigation, various stirring speeds and HPH cycles were used to try to reduce the particle size of the formulations FF4 and FF5.It was noted that increasing the HPH cycles and stirring speed did not result in particles smaller than 700 nm. Additionally, F4 and F5 were disqualified after lengthier storage (>2 weeks) revealed curcumin and doxorubicin settling.

The following method was to construct Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles formulation by mixing Compritol 888 ATO R and GMS (lipid mixture) in various

ratios. The formulations were then tested to see if curcumin and doxorubicin settled after being added.In the next batch of curcumin SLN formulations, combine GMS with Compritol 888 ATO R. The generated formulations (FF8-FF13) were assessed for drug assay/TDC, entrapment effectiveness, particle size, and PDI because there was no evidence of the drug settling.

Formulas (F8-F10) revealed that curcumin was present observed under a light microscope, the drug appears as crystals, showing that it is present in an undispersed or undissolved form and was therefore rejected. FF13 was chosen above the three remaining formulations (FF11, FF12, and FF13) because it had the highest drug concentration (13 mg/ml).

In the current study, creation of a curcumin and Doxorubicin encapsulated lipidic SLN with a high drug loading (13% with respect to lipid matrix) and containing 13 mg of curcumin and Doxorubicin per ml was done To the best of our knowledge, it is the biggest increase in curcumin and Doxorubicin solubility in an aqueous medium (1.4×10^6 times increase compared to 11 ng/ml in water for free curcumin) combined with high drug loading.[22][23]

Table 1: Solid lipid nanoparticles with high curcumin and Doxorubicin concentrations (1–1.3%) and their composition.

Formulation code	Lipid (%)	Tween 80 (%)	PEG 600 (%)	Phospholipon 90 G (%)	Curcumin and doxurubicin (%)	Drug settling
FF1	4	11	7	0.50	1	✓
FF2	5	11	7	0.50	1	✓
FF3	5	11	7	0.78	1	✓
FF4*	5	11	7	0.50	1	x
FF5*	5	11	7	0.50	1.3	x
FF6	7	11	7	0.78	1	✓
FF7	9	11	7	0.78	1	✓

Table 2: Characterisation of FF4 formulation

FF4	TDC	Entrapment efficiency	Particle size (nm)
1	92.3%	77.53%	> 700

2	91.7%	78.66%	> 700
3	94.3%	77.88%	> 700

Characterization of curcumin and Doxorubicin encapsulated lipid

TDC/ Assay was established to be 14.33 ± 0.14 mg/ml (98.46 ± 0.01%) (n = 6) of curcumin and Doxorubicin encapsulated lipidic SLN. The average particle size was 546.2± 43.1 nm (n = 6), and the entrapment efficiency was 89.74± 0.87%. Blank SLNs had an average particle size of 328.6 nm. Curcumin and Doxorubicin loading results in substantially higher particle sizes, suggesting that it is likely surface loaded in addition to being integrated into the SLNs' core. The latter may be brought on by curcumin's and Doxorubicin high solubility in the surfactant layer around the SLNs. Curcumin and Doxorubicin has a high solubility in both PEG and Tween 80, which are currently utilised as the surfactant and solvent, respectively. PEG is also renowned for supporting surfactants.The PDI of the Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles was 0.288± 0.062 (n = 6) while that of the blank SLNs was 0.343. PDI of ≤ 0.3 is regarded as being very monodisperse, but values of 0.3–0.4 are regarded as just somewhat polydisperse.Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles and blank SLNs had zeta potentials of -9.89±3.88 mV (n = 6) and -0.62 mV, respectively.[24][25][26]

Field emission scanning microscopy(FESEM)

The stability of the particles was demonstrated by the Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles FESEM, which revealed that they were almost spherical in shape and existed as distinct entities rather than agglomerates.The surfactant layer gives the particles stability and prevents them from aggregating.

X-ray diffraction studies

Curcumin, Doxorubicin ,Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles, blank SLNs and lipid mixture X-ray diffraction patterns in powder are presented in Figure 1. Curcumin's and Doxorubicin crystalline structure could be seen in the PXRD pattern, which showed peaks at 2 scattered angles of 16.31^0, 8.91^0, 26.62^0, and 25.64^0.Again confirming its crystalline structure, the PXRD pattern of the lipid mixture showed strong peaks at 2 dispersed angles 22.32^0, 23.97^0, 4.57^0, and 19.64^0.

The spectra of curcumin and the lipid mixture were different from those of Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticlesand blank SLNs, though. At 2θ dispersed angles of 22.2^0, 19.5^0, and 24.6^0 in the case of Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles and 19.43^0, 22.23^0, and 23.94^0 in the case of blank SLNs, certain characteristic peaks that do match to the lipid mix have been found.[23]

DSC, or differential scanning calorimetry

By measuring the variations in the amount of heat needed to keep the sample and reference at the same temperature as a function of temperature and time, differential scanning calorimetry is a thermoanalytical technique. Pure curcumin showed a melting endotherm at 181.18°C, which corresponded to its reported melting point of 180–183°C.

However, the Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles displayed a broad endotherm from 63 to 117 degrees Celsius, with a strong peak at 108.99 degrees Celsius The amorphous nature of Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles is indicated by the broadening of peaks, and its nanoscale is indicated by the change in temperature from higherto lower.The Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles sample lacked the strong peak that the lipid mixture had at 71.58 C. This might be because the lipid in the SLN formulation changed to a fully amorphous form.

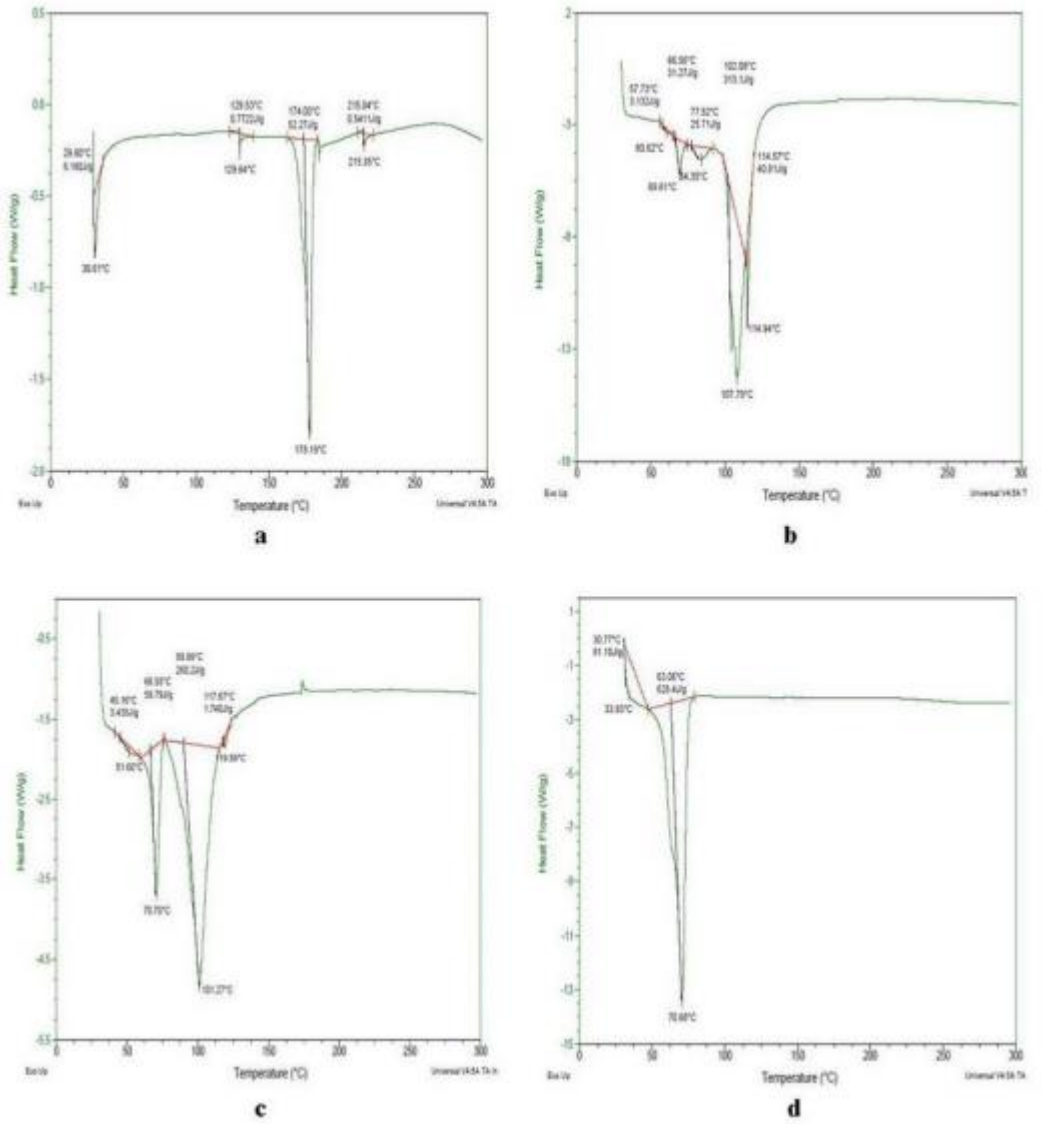

Fig.1 DSC endotherm

Validation of Bioanalytical Methods

In plasma samples, a calibration curve for curcumin and Doxorubicin has been determined to be linear from 14 to 501 ng/ml and 12 to 478 ng/ml. As no peak was seen in the chromatograms of blank plasma samples, the system was proven to be suitable, selective, and specific for the measurement of curcumin and doxorubicin under the optimised chromatographic conditions.LOD and LOQ were discovered to be 1.95 ng/ml and 19 ng/ml for curcumin,and 1.23 ng/ml and 13 ng/ml,for doxorubicin respectively. Over 85% of the recovery was overall. Individual recoveries were 80.18, 87.18, and 84.42% at LQC, MQC, and HQC for curcumin and 86.22, 81.98, and 74.33% for doxorubicin respectively.For QC samples with a precision of less

than two percent, the intra-day accuracy was 99.43–102.21%, and the inter-day accuracy was 99.47–106.83%.

Variation in Particle Size with time and pH

Particle size at the physiological pH was assessed with pH and Time Variation at times that corresponded to their residence times in these areas of the gastrointestinal tract (g.i.t.). At pH 1.25 and 7.1, no significant ($p \leq 0.05$) change in size and PDI was seen, confirming Curcumin,doxorubicin, Doxorubicin Loaded Solid Lipid Nanoparticles stability after incubation at these pH levels. This guarantees that Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles will enter the gut in its nano form. Furthermore, only a 6.6% increase in size was seen at pH 7.4 following a 24-hour incubation period.

Thus, it can be said that Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles maintain their integrity and stability under certain physiological circumstances.

Photostability Studies

The goal of the study was to determine the degree of photoprotection curcumin and Doxorubicinreceived from the lipid matrix of Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles. It totally prevented photodegradation of the curcumin and Doxorubicinthat was encapsulated. However, when free curcumin and Doxorubicinwas stored in amber-colored containers, there was a degradation of 22.8%, which rose to 37% in transparent containers. Even after being stored in transparent containers, Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles did not degrade (TDC/assay remained unaltered). The particle size did, however, grow larger when exposed to light. This might be explained by the fact that more particles are colliding since light has given them kinetic energy.

CONCLUSION

The regulating action of curcumin on NF-kB and its lethal effect on cancer cell lines have been demonstrated in earlier studies by several investigators. The availability of curcumin and Doxorubicin to trigger a therapeutic response in the physiological system was the only limiting element. The curcumin and Doxorubicin formulation that is being presented effectively addresses this. With improved solubility, stability, permeability, and bioavailability, solid lipid

nanoparticles that were loaded with doxorubicin and curcumin may one day be investigated for treatment of different illnesses associated with inflammation and oxidative stress, including cancer.The goal of this study was to formulate Curcumin, Doxorubicin Loaded Solid Lipid Nanoparticles with 13 mg of curcumin and Doxorubicin per ml of the SLN dispersion. The developed formulation's characterization allowed to draw the conclusion that the SLNs were successfully synthesized and amorphous, demonstrating the presence of curcumin and Doxorubicin in a solubilized state. Additionally, Curcumin, Doxorubicin loaded Solid Lipid Nanoparticles showed a zero order release in comparison to free curcumin's first order release, demonstrating the controlled release property of the produced Curcumin, Doxorubicin loaded solid lipid nanoparticles. The stability of Curcumin, Doxorubicin loaded solid lipid nanoparticlesand curcumin encapsulated within the lipid matrix has been confirmed by stability experiments, including photostability.In the current study, a nanostructured lipid carrier has been developed in an effort to increase the bioavailability of a poorly soluble medication. SLN with excellent entrapment efficiency and sustained drug release for up to 36 hours have been developed using the solvent diffusion approach at 70 °C. The drug's crystal nature is confirmed to have transformed by DSC and XRD into an amorphous structure, which is crucial for increasing absorption rate and therefore bioavailability. Particle size analysis supports discrete, spherical globules with smooth surfaces that are nano-sized

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