IJBPAS, June, 2023, 12(6): 2739-2759

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

COMPARATIVE STUDY OF N-ACETYL CYSTEINE LOADED FOUR TYPES OF NANOPARTICLES

MADUPOJU B[1, 2], RAJU RS[3], DESU PK[2*], GSN KOTESHWARA RAO[4], ALAVALA RR[3, 5], AMARA RD[6] AND CHAKRAVARTHI G[3]

1: Research Scholar, Department of Pharmacy, Koneru Lakshmaiah Education Foundation, Vaddeswaram, Guntur, Vaddeswaram, AP, India

2: Department of Pharmaceutics, Nalanda College of Pharmacy, Cherlapally, Nalgonda, Telangana, India. 508001

3: Department of Pharmacy, Koneru Lakshmaiah Education Foundation, Vaddeswaram, Guntur, Vaddeswaram, AP, India.

4: Department of Pharmacy, School of Medical and Allied Sciences, Galgotias University, Greater Noida 203201, India

5: Shobhaben Pratapbhai Patel School of Pharmacy & Technology Management, SVKM's NMIMS, V.L. Mehta Road, Vile Parle (W), Mumbai 400056, India

6: Department of Engineering English, College of Engineering, Koneru Lakshmaiah Education Foundation, Vaddeswaram, AP, India

***Corresponding Author: Dr. D Prasanna Kumar Desu: E Mail: prasanna.desu@gmail.com**

Received 10th July 2022; Revised 15th Sept. 2022; Accepted 10th Oct. 2022; Available online 1st June 2023

https://doi.org/10.31032/IJBPAS/2023/12.6.7197

ABSTRACT

The aim of the study was the optimization of N-Acetyl Cysteine (NAC) loaded solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in terms of physicochemical and biopharmaceutical properties, to develop effective and stable formulations. And characterize their physicochemical properties, *in-vitro* drug release behaviour parameter. Homogenization technique was the preferred method of preparation for nanoparticles. FTIR, DSC, XRD study results indicated no interactions between the drug and formulative ingredients, lipid structure and undisturbed structural nature of NAC in the formulations. The morphology of the prepared distinct types of nanoparticles was found to be approximately spherical in shape and to have a rough surface, according to SEM photographs. The mean particle size of the produced nanoparticles varied between

99.23±11.21 and 159.10±15.36nm depending on the formulation. The PDI ranged from 0.157±0.21 to 0.232±0.13 in this study. The developed formulation's entrapment efficiency was in the range of 62.56±1.25-86.32±1.24%. Among the four types of nanoparticles highest amount of release percentage i.e., 95.25% was found for solid lipid nanoparticles. Finally, among the four types of NAC loaded nanoparticles no statistically significant differences between NLCs and SLNs, were found, and they are deemed promising carriers for anti-oxidant drug delivery.

Keywords: NAC -N Acetylcysteine, SLN-Solid lipid nanoparticles-Nano lipid carriers, NDC-Nano drug conjugates, LPHNP-Lipid polymer hybrid nanoparticles

INTRODUCTION

Nanocarriers are at the forefront of nanotechnology's rapid growth, and they have a wide range of potential applications in drug delivery, clinical treatment, and research. SLNs (solid lipid nanoparticles) are at the cutting edge of nanotechnology's rapid advancement. The size of submicron SLNs varies from 50 to 1000 nm **[1]**. It has been discovered that using solid lipid rather than liquid lipid improves control over encapsulated substance release kinetics and the stability of chemically-sensitive lipophilic components **[2, 3]**. A new generation of nanostructured lipid carriers (NLCs) has been produced, consisting of a lipid matrix with a unique nanostructure. This nanostructure increases drug loading and ensures that the drug is firmly incorporated throughout storage **[4]**. NLCs (nanostructured lipid carriers) are new pharmaceutical formulations made up of physiological and biocompatible lipids, as well as surfactants and co-surfactants. Because of their unique features, nanoparticles have generated a lot of interest in recent years for a variety of medicinal applications. Surface modification of functionalized nanoparticles allows them to interact specifically with target molecules on the cell membrane or within the cell **[5]**. Nanostructured lipid carriers (NLC) are a delivery method in which partial-crystallized lipid particles with mean radii of less than 100 nm are disseminated in an aqueous phase including an emulsifier, as opposed to other colloidal carriers(s). NLC may have certain advantages as a potential delivery system in some scenarios. Lipid-based NPs are lipid-based and can be employed in a wide range of biomedical applications. A lipid NP is usually spherical in shape, with a diameter of 10 to 1000 nm. Lipid nanotechnology is a specialist field concerned with the design and production of lipid nanoparticles for a number of purposes, such as medication delivery and RNA release in cancer therapy **[6, 7]**. Lipid–drug conjugates are drug molecules that have been covalently modified with

lipids (LDCs). LDCs have several advantages, including higher oral bioavailability, greater tumour targeting, decreased toxicity, and improved drug loading into delivery carriers. LDCs based on the chemical structures of pharmaceuticals and lipids can be made using a variety of conjugation methods and chemical linkers **[8]**. Lipid–polymer hybrid nanoparticles (LPHNPs) are next-generation core–shell nanostructures inspired by both liposomes and polymeric nanoparticles (NPS), having a lipid coating encasing a polymer core.**[9]** N-acetylcysteine (NAC) has been used as a thiol-containing protective agent because its hepatoprotective characteristics have been demonstrated in various research. N-Acetylcysteine (NAC) is a powerful antioxidant that also has anti-inflammatory, mucolytic, and hepatoprotective properties **[10]**. Despite these benefits, NAC has a low bioavailability (between 6 and 8%), which limits its therapeutic usefulness. It happens because it combines plasmatic proteins and forms disulphide bridges once it enters the bloodstream. Nearly 30% of NAC is excreted in the urine when given intravenously, and excessive doses may cause blood pressure to rise **[11]**. As a result, while looking for innovative ways to increase NAC bioavailability, the creation of carriers to transport and stable it inside the body is a major concern.

This study was designed as a preliminary project to create four types of innovative NAC loaded lipid nanoparticles (SLN, NLC, NDC, LPHNP) and analyse their physicochemical properties, in-vitro drug release behaviour parameter, in order to improve the pharmacological properties of NAC.

MATERIALS

Arudavis labs private limited provided the N acetylcysteine (Tamilnadu, India). Vijaya chemicals, Hyderabad, and other chemicals provided Glyceryl monostearate, Soya lecithin, Span, and tweens, and the reagents utilised were analytical grade.

METHODOLOGY

Fourier Transform Infrared Spectroscopy (FTIR) [12]

The FTIR spectra were recorded in the 4,000–400 cm^1 scanning range using the KBr disc technique on an FTIR spectroscopy (PerkinElmer Spectrum One, Waltham, Massachusetts, USA).

Formulation development

Preparation of solid lipid nanoparticle formulations of N-acetyl cysteine by the hot homogenization method [13]

At 37 degrees Celsius above the melting point of specified lipids, the hot homogenization method was utilised to make solid lipid nanoparticles. The formulations incorporated lipophilic (Soya lecithin, Polysorbate-80) and hydrophilic (Soya lecithin, Polysorbate-80) surfactants

(Tween 40 and 80). At a temperature of 10°C over the lipid's melting point, sufficient amounts of lipid, active component (N-acetyl cysteine), and lipophilic surfactants were weighed and combined in a water bath. Water and the hydrophilic surfactant were heated to the same temperature in a separate beaker and swirled constantly. Drop by drop, the previously described lipid phase was added to the aqueous surfactant solution and agitated for a few hours at 2700 RPM. After being sonicated for 30-40 minutes, the dispersion was retained. It was possible to design a system that was thermodynamically stable.

Table 1: Formulation development of Solid Lipid Nanoparticles (SLN)

F.no	N-acetyl cysteine (mg)	Glyceryl monostearate (gms)	Soya lecithin (mg)	Polysorbate-80	Tween 40 (mg)	Tween 80 (mg)
SLNF1	50	0.25	50	100	50	100
SLNF2	50	0.5	100	50	100	50
SLNF3	50	0.75	50	100	50	100
SLNF4	50	1	100	50	100	50
SLNF5	50	1.25	50	100	50	100
SLNF6	50	1.5	100	50	100	50
SLNF7	50	1.75	50	100	50	100
SLNF8	50	2	100	50	100	50
SLNF9	50	2.25	50	100	50	100
SLNF10	50	2.5	100	50	100	50
SLNF11	50	2.75	50	100	50	100
SLNF12	50	3	100	50	100	50

Preparation of nanostructured lipid carrier nanoparticle formulations of N-acetyl cysteine by the hot homogenization method [14]

At a temperature over the melting point of specified lipids, the hot homogenization method was utilised to produce solid lipid nanoparticles. Lipids were used as lipophilic and hydrophilic surfactants in the formulations (Soya lecithin, Polysorbate-20) (Tween 40 and 80). At a temperature of 85°C above the lipid's melting point, sufficient amounts of lipid, active component (N-acetyl cysteine), and lipophilic surfactants were weighed and combined in a water bath. Water and the hydrophilic surfactant were heated to the same temperature in a separate beaker and swirled constantly. Drop by drop, the previously stated lipid phase was added to the aqueous surfactant solution and agitated for 30 minutes at 1200 RPM. After being sonicated for 30 minutes, the dispersion was retained. It was feasible to design a system that was thermodynamically stable.

Table 2: Formulation development of Nanostructured Lipid Carriers (NLC)

F.no	N-acetyl cysteine (mg)	Glyceryl monostearate (gms)	Soya lecithin (mg)	Polysorbate-20	Tween 20 (mg)	Tween 40 (mg)
NLCF1	50	0.5	50	100	50	100
NLCF2	50	1	100	50	100	50
NLCF3	50	1.5	50	100	50	100
NLCF4	50	2	100	50	100	50
NLCF5	50	2.5	50	100	50	100
NLCF6	50	3	100	50	100	50
NLCF7	50	3.5	50	100	50	100
NLCF8	50	4	100	50	100	50
NLCF9	50	4.5	50	100	50	100
NLCF10	50	5	100	50	100	50
NLCF11	50	5.5	50	100	50	100
NLCF12	50	6	100	50	100	50

Preparation of Lipid drug conjugate nanoparticle formulations of N-acetyl cysteine by the hot homogenization method [15]

For the manufacture of nanosuspensions, i.e., suspensions of drug nanoparticles, the high-pressure homogenization approach was applied as described. LDC nanoparticles combine the features of SLN and nanosuspension. The matrix substance is a lipidic molecule, similar to SLN. The matrix, like nanosuspensions, is made up of a drug. The bulk material was dispersed in Surfactants Tween 20 and Tween 80 solution containing Glyceryl monostearate to generate a pre-dispersion for the fatty acid–Soya lecithin nanoparticles. This predispersion was homogenised at 1500 bar in a homogenizer. If necessary, the sample was stored in ice between cycles to keep temperatures below 400°C. The generated LDC nanoparticle dispersions had a solids content of 5% and a surfactant content of 1%. (Tween 20 and 80).

Table 3: Formulation development of Lipid Drug Carriers (NDC)

F.no	N-acetyl cysteine (mg)	Glyceryl monostearate (gms)	Soya lecithin (mg)	Polysorbate-40	Tween 20 (mg)	Tween 80 (mg)
NDCF1	50	0.5	50	100	50	100
NDCF2	50	1	100	50	100	50
NDCF3	50	1.5	50	100	50	100
NDCF4	50	2	100	50	100	50
NDCF5	50	2.5	50	100	50	100
NDCF6	50	3	100	50	100	50
NDCF7	50	3.5	50	100	50	100
NDCF8	50	4	100	50	100	50
NDCF9	50	4.5	50	100	50	100
NDCF10	50	5	100	50	100	50
NDCF11	50	5.5	50	100	50	100
NDCF12	50	6	100	50	100	50

Table 4: Formulation development of Lipid Polymer Hybrid Nanoparticle (LPHN)

F.no	N-acetyl cysteine (mg)	Glyceryl monostearate (gms)	Soya lecithin (mg)	Polysorbate-60	Tween-40 (mg)	Tween- 80 (mg)
LPHNF1	50	0.5	50	100	50	100
LPHNF2	50	1	100	50	100	50
LPHNF3	50	1.5	50	100	50	100
LPHNF4	50	2	100	50	100	50
LPHNF5	50	2.5	50	100	50	100
LPHNF6	50	3	100	50	100	50
LPHNF7	50	3.5	50	100	50	100
LPHNF8	50	4	100	50	100	50
LPHNF9	50	4.5	50	100	50	100
LPHNF10	50	5	100	50	100	50
LPHNF11	50	5.5	50	100	50	100
LPHNF12	50	6	100	50	100	50

Preparation of Lipid polymer hybrid nanoparticle formulations of N-acetyl cysteine by the hot homogenization method [16]

At a temperature over the melting point of specified lipids, the hot homogenization method was utilised to produce solid lipid nanoparticles. Lipids were used as lipophilic and hydrophilic surfactants in the formulations (Soya lecithin, Polysorbate-60) (Tween 40 and 80). In a water bath at a temperature 40°C over the lipid's melting point, a suitable amount of lipid, active component (N-acetyl cysteine), and lipophilic surfactants were weighed and mixed. Water and the hydrophilic surfactant were heated to the same temperature in a separate beaker and swirled constantly. Drop by drop, the previously described lipid phase was added to the aqueous surfactant solution and agitated for 30 minutes at 11,000 RPM. After being sonicated for 60 minutes, the dispersion was retained. It was conceivable to create a system that was thermodynamically stable.

DSC study [17]

The compatibility research was completed using Differential Scanning Calorimetry (DSC Q10 V9.0 Build 275). DSC analysis was performed on the natural drug as well as additional excipients to evaluate whether they were compatible with the drug. The specific heat and enthalpies of transition are determined using a differential scanning calorimeter. The heat of transition is directly measured by the area beneath the acquiring curve. A differential scanning calorimeter with a heating rate of 15oC/min and a temperature range of 0 to 1000°C was used to make the thermograms. The design gets hermetically sealed in an environment.

XRD study[18]

The crystalline properties of the samples were examined using the D8 Advance X-ray Diffractometer (Bruker, Germany). XRD patterns for cholesterol oleate, Cur, physical mixture of Cur and NAPG50-NLC, blank NAPG50-NLC, and Cur-

NAPG50-NLC (as the representation of blank NAPG-NLC and Cur-loaded NAPG-NLC, respectively) were determined using a Cu Ka radiation (k 14 1.5406), 40 kV voltage, and 40 mA current. The scans were carried out at 3–40 for 2 hours, with a count time of 0.3 seconds and a step angle of 0.02.

Scanning electron microscopy [19]

To organise the samples for SEM analysis, the microspheres were sprinkled on one side of an adhesive stub. The microspheres were gold-coated prior to microscopy. Finally, the morphology and length of the microspheres were identified using a scanning electron microscope (FEI Quanta2 hundred MK2, Netherlands).

CHARACTERIZATION OF DRUG-LOADED SLN

Vesicle size measurement (VZ) [20]

A Malvern particle size analyzer was used to determine the average vesicle size (Malvern Mastersizer 2000 instruments Ltd., UK). In a glass beaker, 5 ml of each formulation was distributed in 500 ml of double-distilled water while gently stirring (600 rpm). All measurements were made in triplicate (mean standard deviation).

The Determination of the Polydispersity Index [21]

The particle size and polydispersity index (PDI) of all the produced Nanoparticles were measured using the dynamic light scattering (DLS) technique. Before the analysis, each sample was diluted with a suitable amount of distilled water to a concentration of 1 percent.

Determination of entrapment efficiency [22]

The percentage of active chemicals encapsulated in nanoparticles as a fraction of the initial pharmacological dose is the entrapment efficiency (EE) (percent). The EE of nanoparticles was calculated using a UV-Vis spectrophotometer. The unencapsulated medicine was extracted from the nanoparticles using centrifugation (at 22000 rpm for 45 minutes) and filtration. After that, the samples were diluted in methanol (1:9) and analyzed one by one. The sample absorbance was measured using 1 cm thick quartz cells that functioned at specific N-acetylcysteine wavelengths (). The EE % was computed in the following way:

(EE) (%)=gf/gi.100

Where

GF denotes the initial amount of progesterone employed and

gi denotes the amount of progesterone effectively entrapped in nanoparticles.

Zeta Potential [23]

The zeta potential of a particle represents the total charge of the particle as well as the stability of the formulation. The differential light scattering (DLS) technique was utilised to measure the zeta potential using the Zeta sizer Nano-ZS90, Malvern

Instrument Ltd., UK. Nanoparticle samples were scattered using Milli-Q water. At 25 °C, all measurements were done in triplicate.

***In vitro* release studies and release kinetics [24]**

Using a USP-II dissolution apparatus (paddle apparatus) at 50 pm, an in vitro profile of drug-loaded nanoparticle formulation was created. The test was carried out in 700 mL 0.1 N HCl for the first 2 hours, then 200 mL tri-sodium hydrogen phosphate was added to keep the pH at 7.4. The dissolving media was held at 37 0.5 °C in thermostatically regulated water. At present time intervals, 5 ml of the sample was taken and replaced with an equal volume of fresh medium to maintain the sink condition. The materials were evaluated using the UV spectrophotometric method at a wavelength of 290 nm. The experiment was repeated three times, with the percentage of medication utilised calculated.

RESULTS AND DISCUSSION

Fourier Transform Infrared Spectroscopy

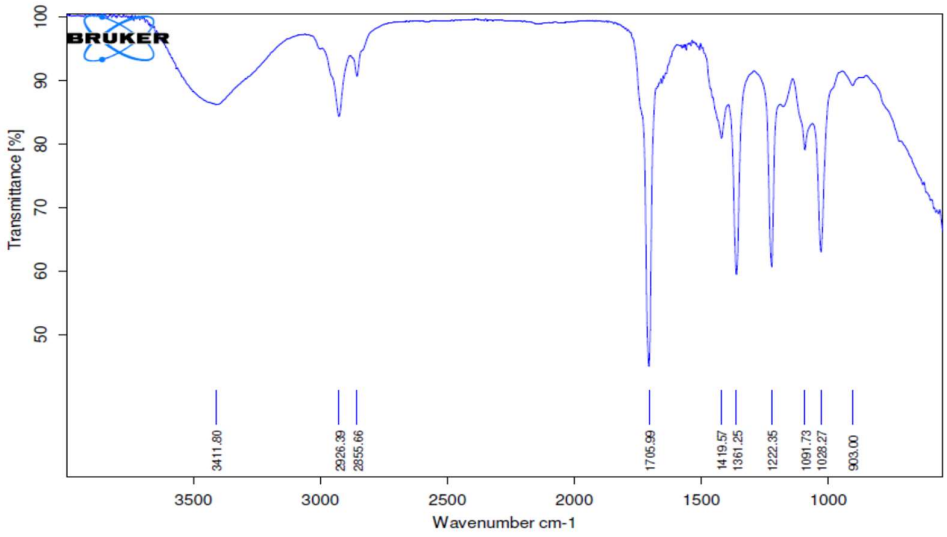

Figure 1: FTIR spectra of N-Acetyl cysteine

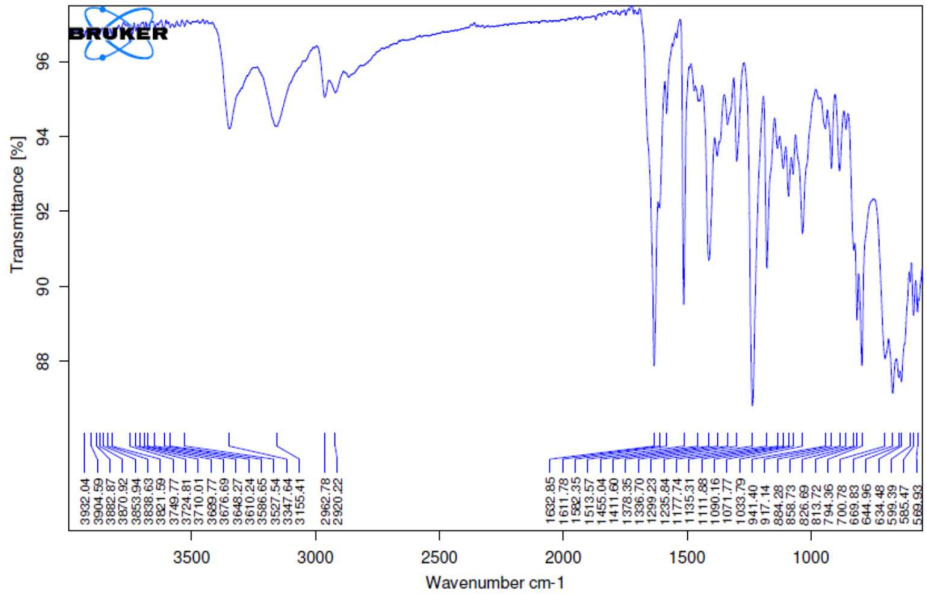

Figure 2: FTIR spectra of a physical drug-excipient mixture (Solid lipid nanoparticles(SLN))

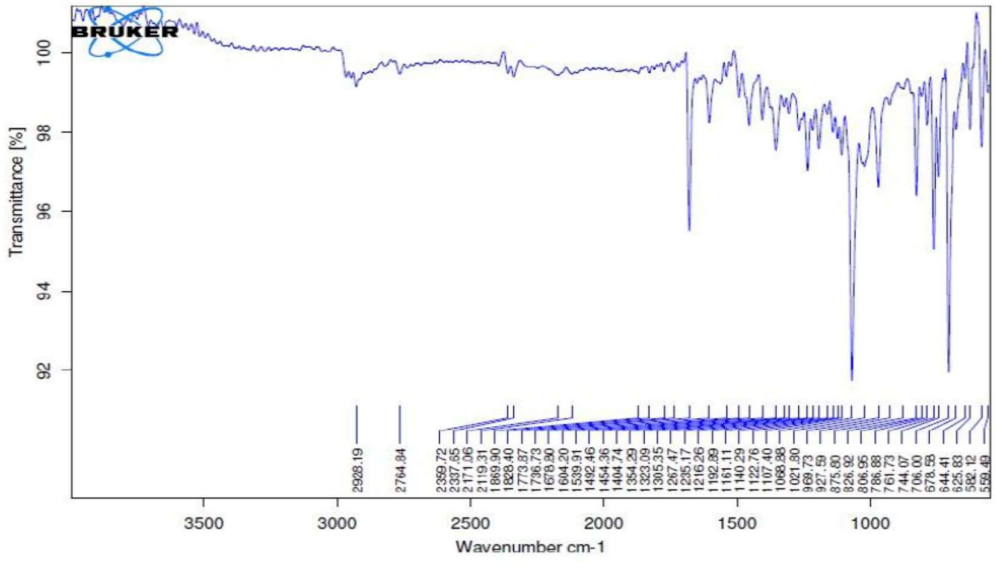

Figure 3: Physical combination of medication and excipients (Nanostructure lipid carrier (NLC)) FTIR spectra

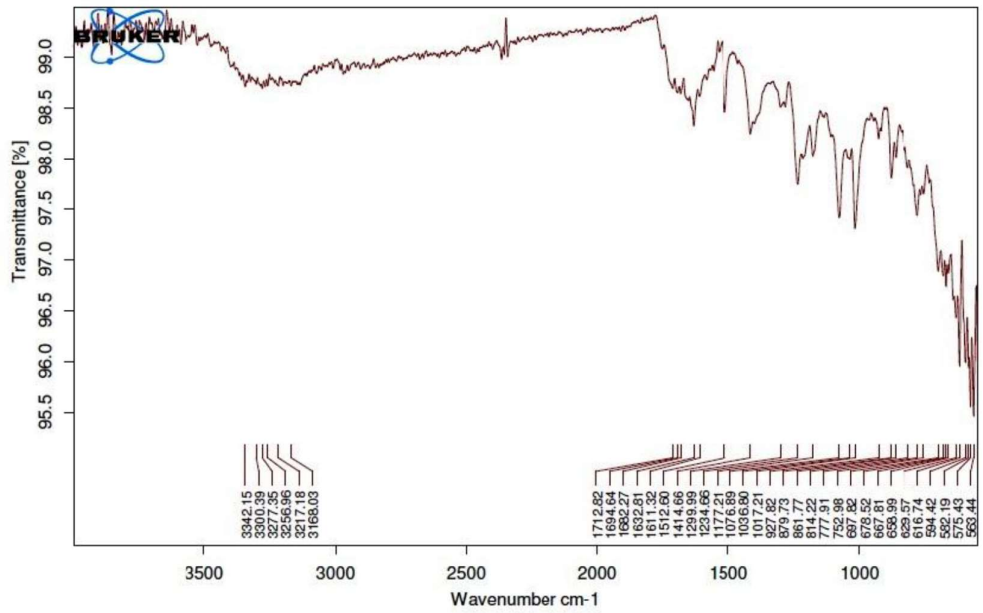

Figure 4: Physical combination of drug and excipients (Lipid Drug Conjugate nanoparticles (LDC)) FTIR spectra

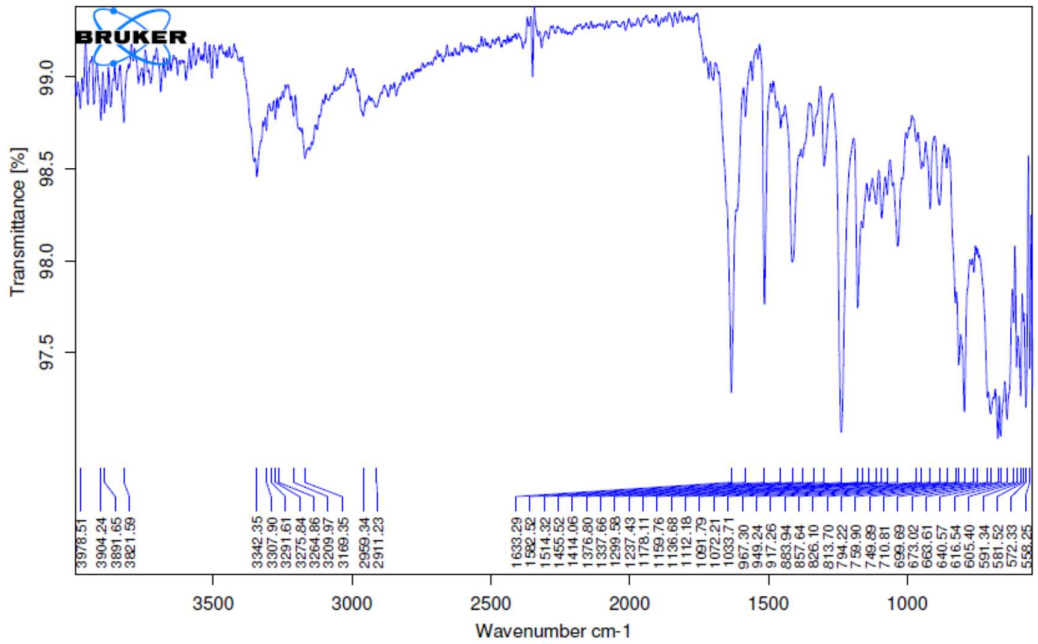

Figure 5: Physical combination of medication and excipients (Lipid polymer hybrid nanoparticles (LPHP)) FTIR spectroscopy

The FTIR peak matching approach was used to assess the drug's compatibility with the specified lipid and other excipients. Peaks did not emerge or disappear in the drug-lipid mixture, indicating that there was no chemical interaction between the drug, lipid, and other constituents.

DSC Analysis

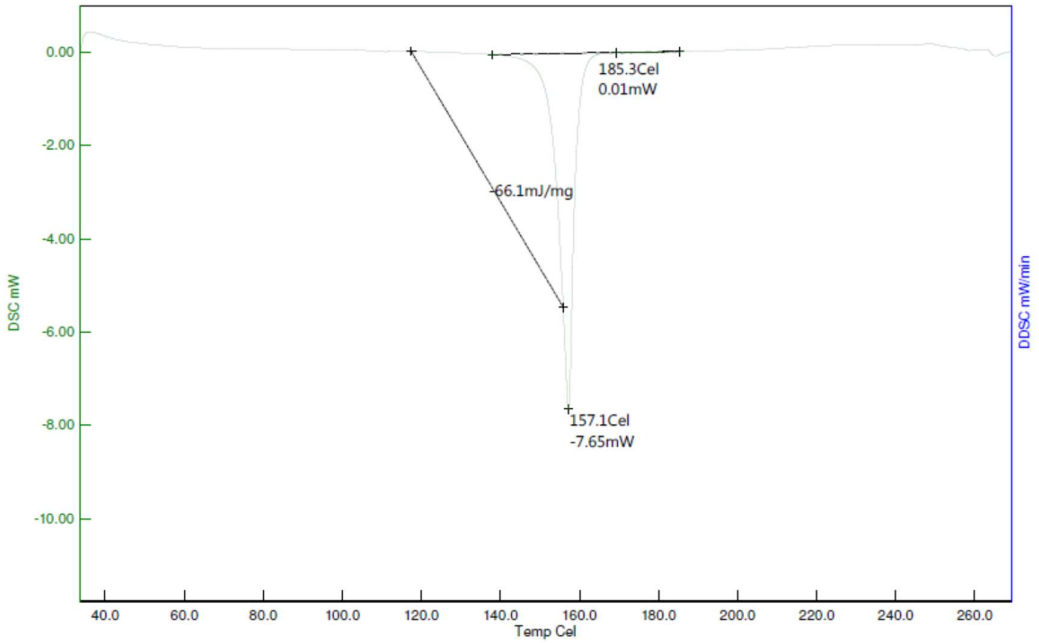

Figure 6: DSC Analysis of Acetyl cysteine

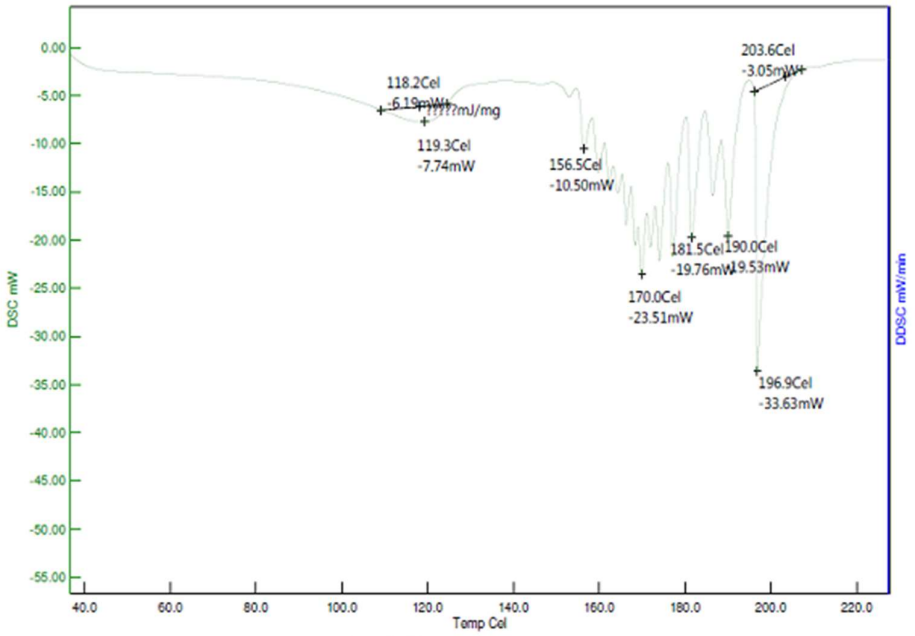

Figure 7: DSC Analysis of Optimized Solid lipid nanoparticles formulation (SLNF10)

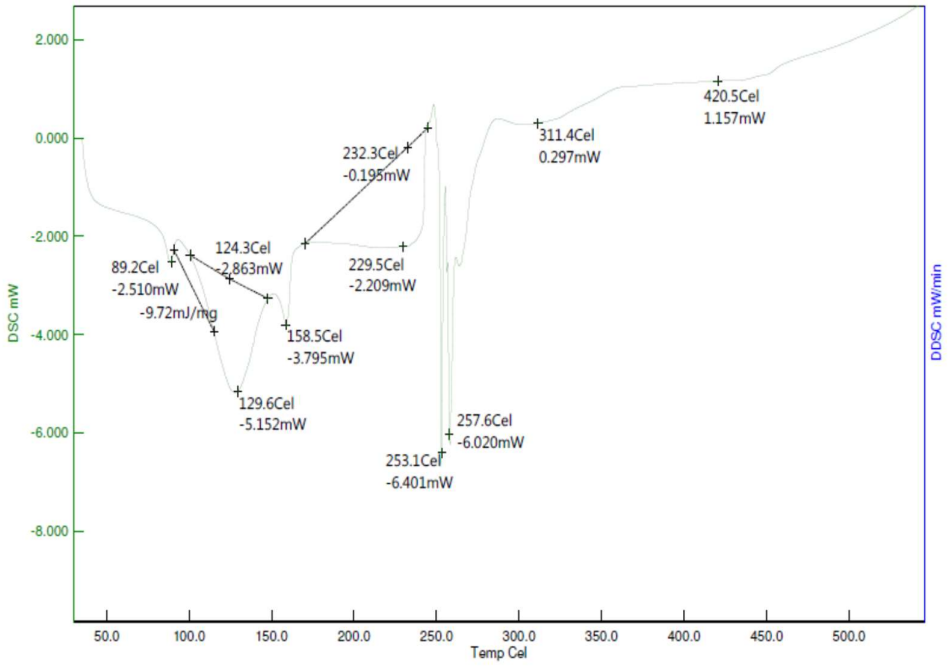

Figure 8: DSC Analysis of Optimized Nano structure lipid carrier nanoparticles formulation (NLCF11)

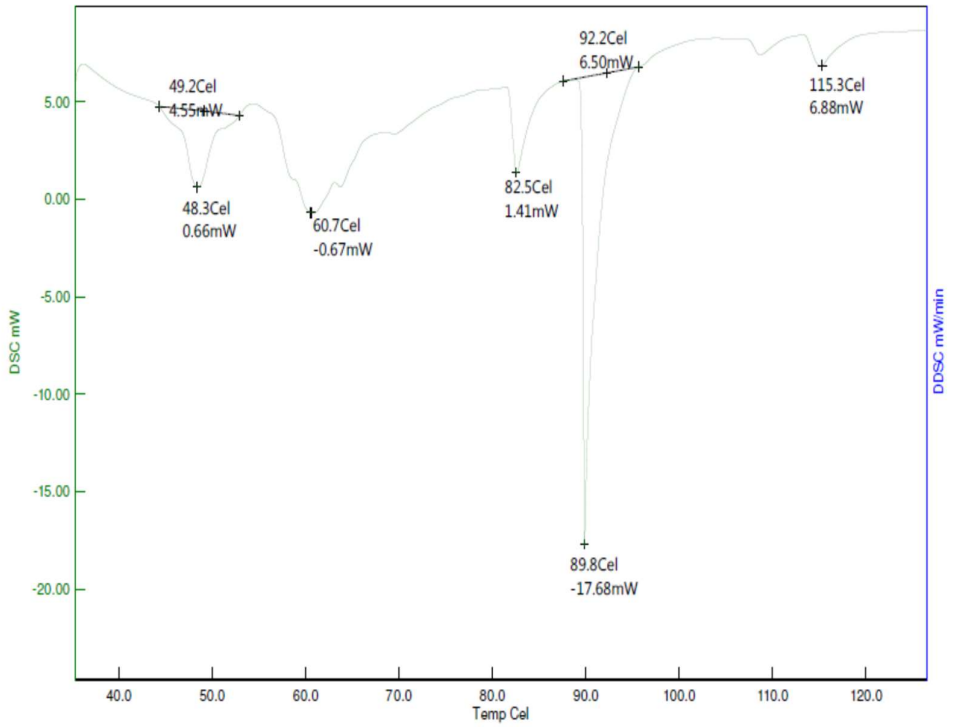

Figure 9: DSC Analysis of Optimized Lipid drug conjugate nanoparticles formulation (NDCF11)

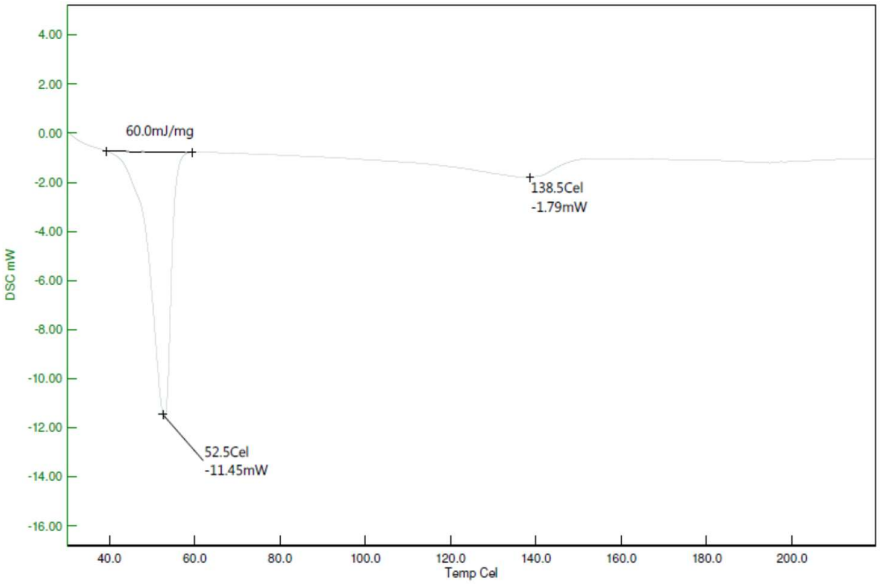

Figure 10: DSC Analysis of Optimized Lipid polymer hybrid nanoparticles formulation (LPHPF9)

The DSC thermograms of pure n- acetyl cysteine and loaded nanoparticles showed a pronounced endothermic peak at 118°C, which corresponded to its melting temperature. The huge endothermic peak of the pure drug was a bit smaller and relocated to 349.8°C in the physical mixture, demonstrating its unchanged nature. This means the medication has no chemical or physical interaction with the lipid structure.

X-ray diffraction (XRD) study

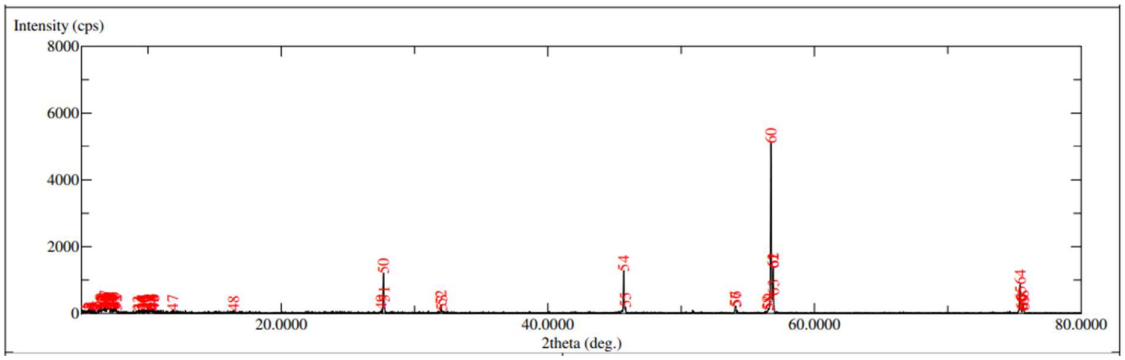

Figure 11: XRD Analysis of optimized formulation Solid lipid nanoparticles (SLNF10)

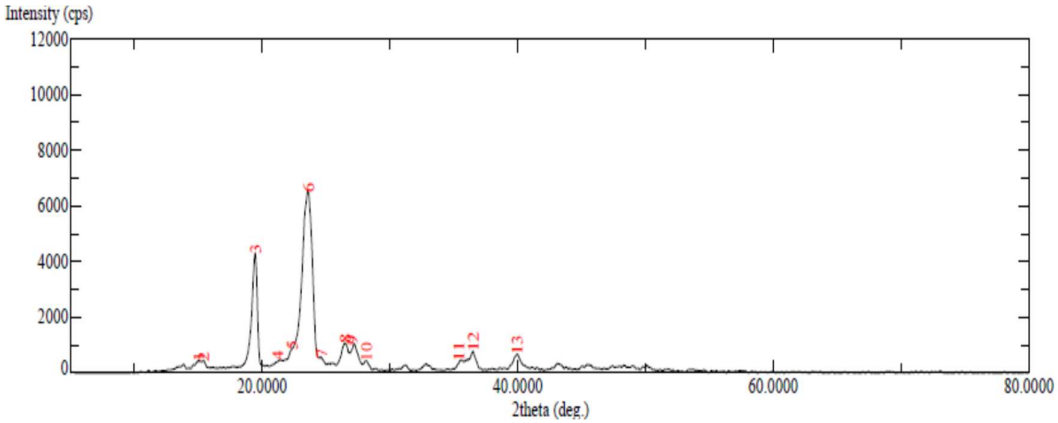

Figure 12: XRD Analysis of optimized Nano structure lipid carrier formulation (NLCF11)

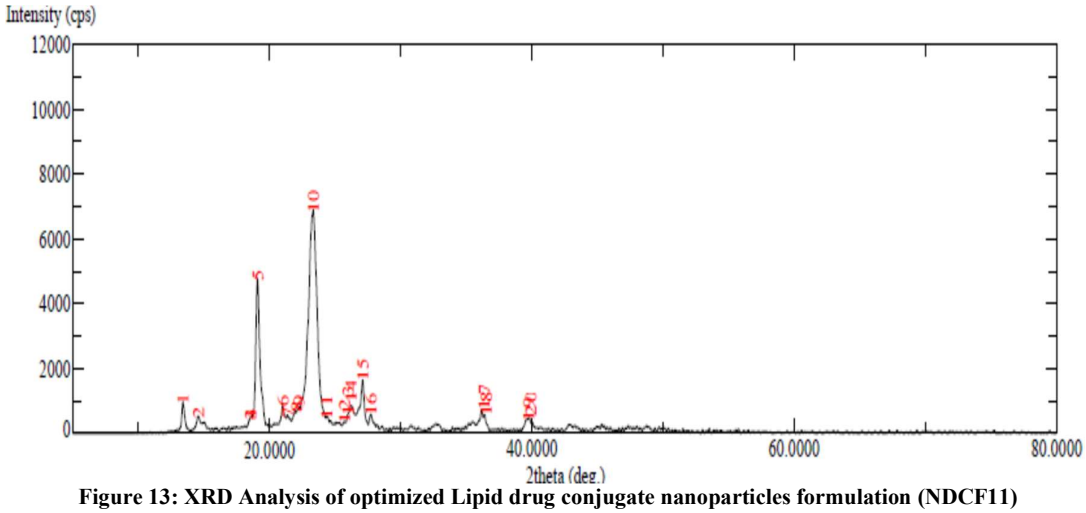

Figure 13: XRD Analysis of optimized Lipid drug conjugate nanoparticles formulation (NDCF11)

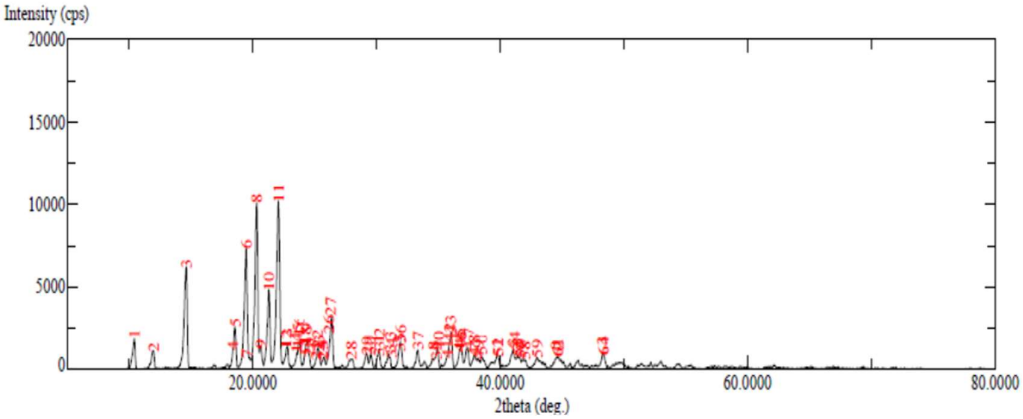

Figure 14: XRD Analysis of optimized Lipid polymer hybrid nanoparticles formulation (LPHPF9)

The XRD analysis was used to determine whether N acetyl cysteine was amorphous or crystalline in various types of nanoparticles and to reveal the crystalline

form of the lipid, which is especially important for lipid-based formulations because lipids frequently undergo polymorphic transitions that result in drug expulsion and recrystallization.

SEM analysis

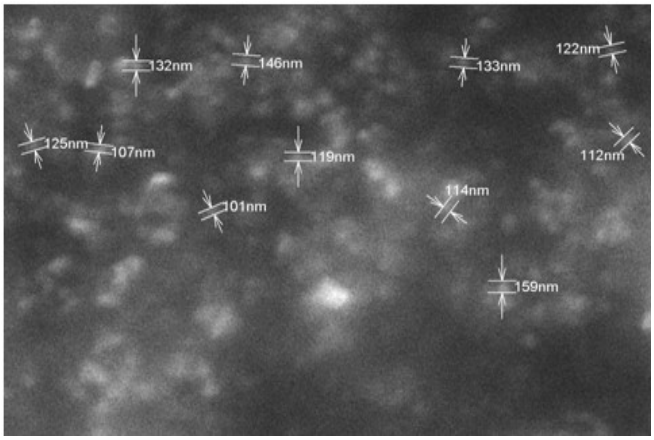

Figure 15: SEM Analysis of optimized Solid lipid nanoparticles formulation (SLNF10)

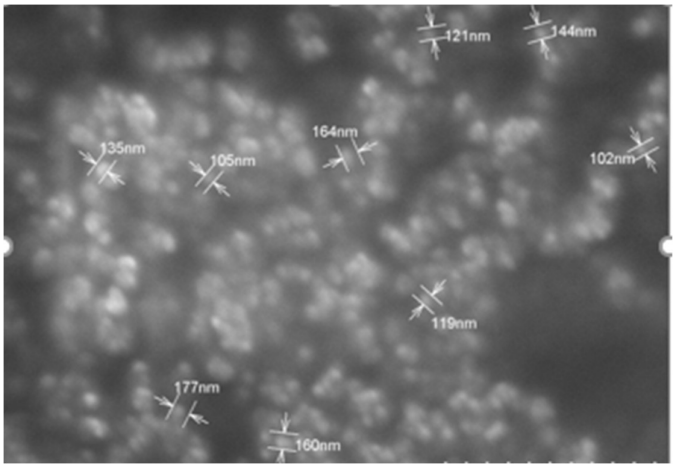

Figure 16: SEM Analysis of optimized Nano structure lipid carrier nanoparticles formulation (NLCF11)

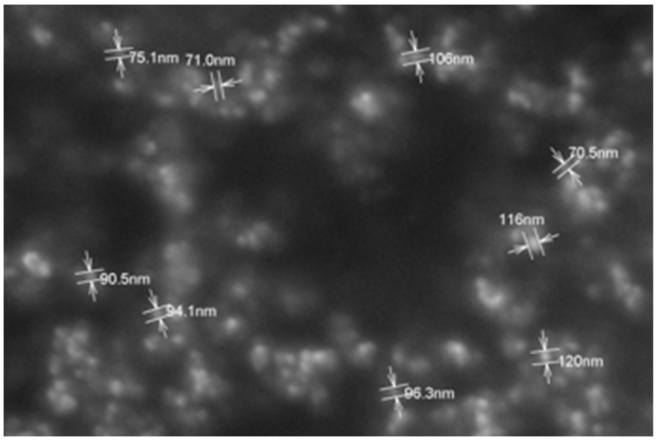

Figure 17: SEM Analysis of optimized Lipid drug conjugate nanoparticles formulation (NDCF11)

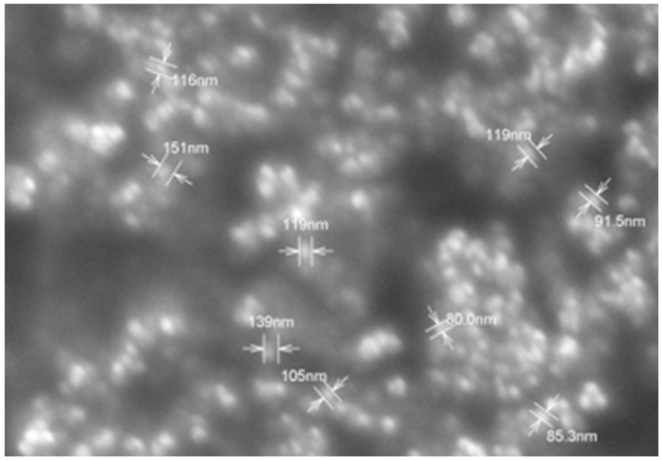

Figure 18: SEM Analysis of optimized Lipid polymer hybrid nanoparticles formulation (LPHPF9)

The morphology of the prepared diverse types of nanoparticles was found to be virtually spherical in shape and have a rough surface, as illustrated in SEM photomicrographs of the nanoparticles in **Figures 15-18**.

Determination of Particle size

Table 5: Comparatives studies of Particle size of four types of NAC-loaded nanoparticles (F1-F12)

F.no	Solid lipid nanoparticles (SLN)	Nanostructure lipid carrier (NLC)	Lipid drug conjugate nanoparticles (NDC)	Lipid polymer hybrid nanoparticles (LPHP)
F1	96.23±9.98	85±2.38	93±7.91	101±4.36
F2	100.36±10.2	91±3.79	86±6.92	86±3.15
F3	99.23±11.21	88±3.78	90±4.85	131±4.32
F4	125.12±11.8	73±4.50	58±6.48	201±2.38
F5	149.56±10.8	102±3.27	63±5.34	87±5.12
F6	132.16±14.89	118±4.32	115±2.88	135±4.20
F7	98.69±9.67	123±2.27	201±8.25	140±6.27
F8	135.40±8.93	182±5.20	128±6.38	138±4.35
F9	120±10.78	99±6.22	130±7.55	125±2.05
F10	159.10±15.36	56±7.12	163±6.82	119±5.52
F11	149±13.85	164±5.21	116±5.30	98±4.50
F12	96.23±9.98	78±6.21	98±4.30	86±5.55

The mean particle size of the generated nanoparticles varied between 99.23±11.21 and 159.10±15.36nm, with the particle size increasing as the lipid and surfactant ratio increased, as indicated in the formulations with the greatest lipid ratio.

Determination of polydispersity index

PS and PDI were nearly constant, however, when the drug concentration was increased to 10%, PDI increased significantly from 0.157±0.21 to 0.232±0.13, respectively.

Table 6: Comparatives studies of polydispersity index of four types of NAC loaded nanoparticles (F1-F12)

F.no	Solid lipid nanoparticles (SLN)	Nano structure lipid carrier (NLC)	Lipid drug conjugate nanoparticles (NDC)	Lipid polymer hybrid nanoparticles (LPHP)
F1	0.189±0.22	0.246±0.32	0.181±0.95	0.212±0.32
F2	0.215±0.85	0.185±0.71	0.168±0.52	0.182±0.15
F3	0.182±0.46	0.237±0.55	0.162±0.73	0.127±0.12
F4	0.213±0.62	0.152±0.24	0.154±0.50	0.275±0.28
F5	0.156±0.50	0.298±0.75	0.247±0.23	0.185±0.12
F6	0.221±0.01	0.234±0.42	0.263±0.20	0.124±0.18
F7	0.232±0.13	0.231±0.22	0.169±0.47	0.179±0.25
F8	0.163±0.24	0.189±0.21	0.203±0.35	0.165±0.35
F9	0.157±0.21	0.176±0.18	0.154±0.55	0.172±0.04
F10	0.189±0.24	0.168±0.22	0.247±0.35	0.146±0.55
F11	0.201±0.28	0.154±0.28	0.168±0.29	0.164±0.42
F12	0.212±0.82	0.128±0.17	0.174±0.30	0.154±0.52

Drug entrapment efficiency

Table 7: Comparatives studies of drug entrapment efficiency of four types of NAC-loaded nanoparticles (F1-F12)

F.no	Solid lipid nanoparticles(SLN)	Nanostructure lipid carrier (NLC)	Lipid drug conjugate nanoparticles(NDC)	Lipid polymer hybrid nanoparticle(LPHP)
F1	71.25±1.25	58.93±1.36	58.50±1.98	61.21±1.35
F2	63.59±1.89	50.32±1.75	49.37±1.93	53.69±1.15
F3	82.35±1.42	53.86±1.58	63.21±1.85	50.31±1.32
F4	75.25±1.63	58.58±1.36	60.17±1.48	59.44±1.38
F5	73.18±1.50	62.31±1.83	57.45±5.39	63.34±1.12
F6	78.95±2.01	58.36±1.38	67.12±1.87	60.50±1.20
F7	68.93±0.99	60.25±1.23	69.34±1.25	64.36±1.27
F8	62.56±1.25	59.63±1.25	70.22±1.34	72.35±1.34
F9	80.69±1.32	63.39±1.20	71.50±1.52	68.93±2.05
F10	86.32±1.24	65.93±1.18	63.95±1.31	67.36±1.52
F11	84.36±1.24	72.34±1.21	71.24±1.28	68.93±1.48
F12	80.21±1.86	68.42±1.19	66.9±1.30	67.35±1.56

The developed formulation's entrapment efficiency was in the range of 62.56±1.25 - 86.32±2.24 percent. The entrapment efficiency rose as the lipid concentration increased, possibly due to the creation of bigger nanoparticles that entrapped a greater amount of drug. With an entrapment efficacy of 86 percent, solid lipid nanoparticles were determined to be the best of all.

In vitro drug release studies

Solid lipid nanoparticles had the highest percentage of release of any of the four types of nanoparticles, at 95.25 percent. The cumulative drug release profile shows that increasing the concentration of glyceryl monostearate results in a longer persistent effect, which could be attributable to the production of bigger nanoparticles, which in turn increases the diffusional path length, delaying the rate of drug release.

Table 8: *In-vitro* drug release experiments of four types of NAC loaded nanoparticles were compared.

Time (hrs)	Solid lipid nanoparticles (SLN)	Nano structure lipid carrier (NLC)	Lipid drug conjugate nanoparticles (NDC)	Lipid polymer hybrid nanoparticles (LPHP)
0	0	0	0	0
1	16.12±0.25	10.34±0.18	8.56±0.22	10.32±0.16
2	25.18±0.46	23.18±0.21	23.28±0.17	23.84±0.20
3	40.17±0.37	40.17±0.16	28.93±0.23	37.24±0.13
4	51.28±0.42	48.76±0.24	40.48±0.19	45.68±0.23
5	63.74±0.46	61.86±0.20	49.86±0.20	56.28±0.22
6	78.25±0.53	75.25±0.17	59.35±0.23	67.99±0.19
7	87.32±0.57	88.31±0.22	69.18±0.19	76.92±0.26
8	95.25±0.46	92.12±0.24	83.69±0.22	85.24±0.21

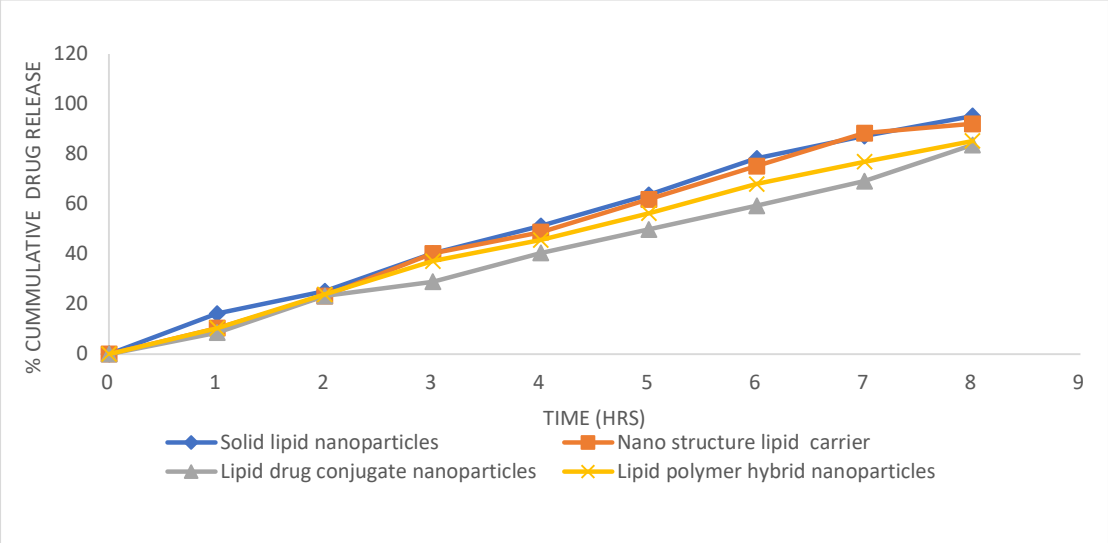

Figure 19: Comparatives studies of In-vitro drug release study

CONCLUSION

Finally, among the four types of NAC loaded nanoparticles no statistically significant differences between NLCs and SLNs, were found, and they are deemed promising carriers for anti-oxidant drug delivery. However, the solid lipid nanoparticles-based matrix system outperforms other nanoparticles in terms of percentage drug loading and percentage drug release. As a result, we find that optimized solid lipid nanoparticle formulations outperformed other nanoparticles in vitro in terms of physicochemical performance. The nanoscale co-encapsulation of both drugs prolonged their release and enhanced the chemical stability of N- Acetylcysteine. In the case of SLN, only solid lipids were utilized, whereas, in the case of NLC, both solid and liquid lipids were utilized. As an emulsion preparation, the SLN and NLC forms are distributed.

Acknowledgements

The authors are thankful to the authority of Konerul Lakshmaiah Education Foundation and Nalanda College of Pharmacy and Management for providing the necessary facilities.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest

REFERENCES

[1] Burns, A.A., Vider, J., Ow, H., Herz, E., Penate-Medina, O., Baumgart, M., Larson, S.M., Wiesner, U., Bradbury, M. Fluorescent Silica Nanoparticles with Efficient Urinary Excretion for Nanomedicine. Nano Lett., 9, 2009, 442–448.

[2] Lee, J.E., Lee, N., Kim, T., Kim, J., Hyeon, T. Multifunctional mesoporous silica nanocomposite nanoparticles for theranostic applications. Acc. Chem. Res., 44, 2011, 893–902.

[3] Cha, W., Fan, R., Miao, Y., Zhou, Y., Qin, C., Shan, X., Wan, X., Li, J. Mesoporous Silica Nanoparticles as Carriers for Intracellular Delivery of Nucleic Acids and Subsequent Therapeutic Applications. Molecules, 22(5), 2017, 782-794.

[4] Li, Z., Barnes, J.C., Bosoy, A., Stoddart, J.F., Zink, J.I. Mesoporous silica nanoparticles in biomedical applications. Chem. Soc. Rev., 41, 2012, 2590–2605.

[5] Slowing, I.I., Vivero-Escoto, J.L., Wu, C.W., Lin, V.S.Y. Mesoporous silica nanoparticles as controlled release drug delivery and gene transfection carriers. Adv. Drug Deliv. Rev., 60, 2008, 1278–1288.

[6] Popat, A., Hartono, S.B., Stahr, F., Liu, J., Qiao, S.Z., Lu, G.Q. Mesoporous silica nanoparticles for bioadsorption, enzyme immobilisation, and delivery carriers. Nanoscale, 3, 2011, 2801–2818.

[7] Tao, C., Zhu, Y., Xu, Y., Zhu, M., Morita, H., Hanagata, N. Mesoporous silica nanoparticles for enhancing the delivery efficiency of immune-stimulatory DNA drugs. Dalton Trans., 2014; 43,2014, 5142–5150.

[8] Grün, M., Lauer, I., Unger, K.K. The synthesis of micrometer- and sub-micrometer size spheres of ordered mesoporous oxide MCM-41. Adv. Mater., 1997; 9: 254–257. [CrossRef]

[9] Nalini, K. S., Madhu, S.S., Podilapu, S.R., and Goutam, G. Validation of stability indicating RP-HPLC method for the estimation of Mesalamine in bulk and tablet dosage form. Pharmaceutical Methods, 2013; 4, 2013, 56-61.

[10] Balaji, Y. M., Gyati, S.A., Abhay, A. Formulation and Development of Polysaccharide based Mesalamine

Nanoparticles. Int. J. of Pharm. & Clin. Res., 2016; 8(7), 2016, 676-684.

[11] Sundblom, A., Oliveira, C.L.P., Palmqvist, A.E.C., Pedersen, J.S. Modeling In Situ Small-Angle X-ray Scattering Measurements Following the Formation of Mesostructured Silica. J. Phys. Chem. C., 113,2009, 7706–7713.

[12] Hollamby, M.J., Borisova, D., Brown, P., Eastoe, J., Grillo, I., Shchukin, D. Growth of Mesoporous Silica Nanoparticles Monitored by Time-Resolved Small-Angle Neutron Scattering. Langmuir, 28, 2012, 4425–4433.

[13] Balaji, M., Ramyakrishna, N., Hanumanaik, M. Formulation Development and Characterization of Enteric Coated Tablets of Lansoprazole. Der Pharm Let., 12 (3), 2020, 22-38.

[14] Singh, S., Kotla, N.G., Tomar, S., Maddiboyina, B., Webster, T.J., Sharma, D., Sunnapu, O. A nanomedicine-promising approach to provide an appropriate colon-targeted drug delivery system for 5-fluorouracil. Int. J. of Nanomed., 10, 2015, 7175-7182.

[15] Singh, S., Vardhan, H., Kotla, N.G., Maddiboyina, B., Sharma, D., Webster, T.J. The role of surfactants in the formulation of elastic liposomal gels containing a synthetic opioid analgesic. Int. J. of Nanomed., 11, 2016, 1474-1482.

[16] Balaji, M., Abhay, A., Gyati, S.A., Sima, S., Ramya, K.N., Omprakash, S., Niranjan, K. Formulation and Characterization of Polycarbophil Coated Mucoadhesive Microspheres of Repaglinide. J. Pharm. Sci. & Res., 7(11), 2015, 972-977.

[17] [17] Kotla, N.G., Singh, S., Maddiboyina, B., Sunnapu, O., Webster, T.J. A novel dissolution media for testing drug release from a nanostructured polysaccharide-based colon-specific drug delivery system: an approach to alternative colon media. Int. J. of Nanomed., 11, 2016, 1089-1095.

[18] Ana, R.S., Karen, W., Adrian, C., Whitwood, J.H., Clark, C.F. Amine-Functionalised Hexagonal Mesoporous Silica as Support for Copper (II) Acetylacetonate Catalyst. Eur. J. Inorg. C., 6, 2006, 1275-1283. A. Dalpiaz, F. Sacchetti, A. Baldisserotto et al., "Application of the "in-oil nanoprecipitation" method in the encapsulation of hydrophilic drugs in PLGA nanoparticles," Journal of Drug Delivery Science and Technology, vol. 32, pp. 283–290, 2016.

[19] acobs C, Müller RH. Production and characterization of a budesonide

nanosuspension for pulmonary administration. Pharma Res. 19, 2002, 189–194.

[20] Sahib MN, Darwis Y, Peh KK, Abdul ameer SA, Tze Y, Tan F. Rehydrated sterically stabilized phospholipid nanomicelles of budesonide for nebulization: physicochemical characterization and in vitro, in vivo evaluations. Int J Nanomed. 6, 2011, 2351–2366.

[21] Qushawy, M.; Nasr, A.; Abd-Alhaseeb, M.; Swidan, S. Design, Optimization and Characterization of a Transfersomal Gel Using Miconazole Nitrate for the Treatment of Candida Skin Infections. Pharmaceutics 10, 2018, 26.

[22] W.S. Cheow, K. Hadinoto, Factors affecting drug encapsulation and stability of lipid–polymer hybrid nanoparticles Colloids Surf. B, 85, 2011, 214-220.

[23] Rahman H. S., Rasedee A., How Chee Wun, Abdul A. B., Zeenathul N. A., Othman H. H., Saeed M. I., Yeap S. K., Int J Nanomedicine. 8, 2013, 2769–2781.

[24] Rohan M. Shah, Daniel S. Eldridge, Enzo A. Palombo, JanH. Harding, "Microwave- assisted microemulsion technique for production of Miconazole nitrate and econazole nitrate loaded solid lipid nanoparticles", European Journal of pharmaceutics and biopharmaceutics , 1, 2017, 141-150.