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FORMULATION AND CHARACTERIZATION OF LIPOSPHERES OF BCS CLASS II DRUG LANSOPRAZOLE

Osama Uddin*. Dr. Satkar Prasad

Bhabha University, Bhopal (M.P.)

Corresponding Author mail id: usamak544@gmail.com

Abstract

This study focuses on the formulation and characterization of Lansoprazole-loaded lipospheres to enhance their solubility and bioavailability. Lipospheres were prepared using a melt dispersion technique, with varying ratios of lipid core components and surfactants. The formulations were evaluated for percentage yield, drug entrapment efficiency, particle size, zeta potential, flow properties, and drug release kinetics. Among the formulations tested, F2 exhibited the highest percentage yield (85.45% ± 0.32) and drug entrapment efficiency (84.65% ± 0.36). Microscopic analysis confirmed the spherical morphology and uniform distribution of lipospheres in F2, with a mean particle size of 156.30 nm. Zeta potential measurements indicated good stability and flow properties were suitable for further processing. The drug release profile of F2 followed First Order kinetics, demonstrating sustained release over 12 hours.

Keywords: Lansoprazole, lipospheres, melt dispersion technique, drug delivery, bioavailability, particle size, zeta potential, sustained release, first order kinetics.

Introduction

Lansoprazole, a proton pump inhibitor (PPI), is widely used for the treatment of gastric acidrelated disorders such as peptic ulcers, gastroesophageal reflux disease (GERD), and ZollingerEllison syndrome. Classified as a BCS Class II drug, Lansoprazole is characterized by its low solubility and high permeability, posing significant challenges

for its oral bioavailability (Shargel *et al.,* 2012). Improving the solubility and, consequently, the bioavailability of such drugs is a critical aspect of pharmaceutical formulation development.

Lipospheres have emerged as a promising delivery system for enhancing the solubility and

bioavailability of poorly water-soluble drugs. These systems are composed of a lipid core

surrounded by a surfactant layer, which can encapsulate both hydrophilic and lipophilic drugs, protecting them from degradation and enhancing their stability and bioavailability (Muller *et al.,* 2000). The lipid core, typically composed of solid lipids like stearic acid or cetyl alcohol, melts during the preparation process and encapsulates the drug, while the surfactant stabilizes the formulation and ensures uniform dispersion in the aqueous phase.

The melt dispersion technique is one of the most efficient methods for preparing lipospheres. This method involves melting the lipid core and dispersing the drug in the molten lipid, followed by emulsification with an aqueous phase containing a surfactant and stabilizer. The resulting oilin-water (o/w) emulsion is then rapidly cooled to form solid lipospheres, which can be isolated and characterized (Bhosale *et al.,* 2016).

The current study focuses on the formulation and characterization of Lansoprazole-loaded

lipospheres to enhance its solubility and bioavailability. Various batches were prepared using different ratios of lipid core components and surfactants, and their physical properties, drug entrapment efficiency, particle size, zeta potential, and drug release profiles were evaluated. The aim was to identify the optimal formulation with the best performance characteristics for potential therapeutic application.

Material and Methods

Material

The formulation of Lansoprazole-loaded lipospheres utilized various chemicals and excipients. Lansoprazole was provided by Bioplus Life Sciences Pvt. Ltd., Bangalore. Disodium hydrogen phosphate, potassium dihydrogen phosphate, and sodium chloride

were sourced from S. D. Fine Chem. Ltd., Mumbai. Methanol, ethanol, and chloroform were supplied by Qualigens Fine Chemicals, Mumbai. Sodium hydroxide came from Chempure Specialty Chemicals, Mumbai, and hydrochloric acid from Thomas Baker, Mumbai. Stearic acid and gelatin were obtained from HiMedia Laboratories, Mumbai, while cetyl alcohol was from Lobachemie, Mumbai, and Tween 80 from Thomas Baker, Mumbai.

Methods

Formulation and development of Liposphere

Lansoprazole encapsulated Liposphere were developed by melt dispersion technique (Bhosale *et al.,* 2016). The formulation of different batches is depicted in Table 1. Briefly, the lipid core was melted on a water bath maintained at 70-72°C. Finely powdered drug was dispersed into the molten lipidic phase. The aqueous phase was prepared by heating a blend of water and surfactant to 70-72°C with a stabilizer. The molten lipidic phase was slowly transferred to the hot aqueous phase (o/w emulsion) and the emulsification was assisted by stirring the content on a sonicator continuously. The milky dispersion was then rapidly cooled to 20°C by immersing the formulation in an ice bath without stopping the agitation to yield a uniform dispersion of lipospheres. The obtained lipospheres were then washed with water and isolated by filtration.

Table 1: Preparation of Liposphere of Lansoprazole

F. Code	Drug (mg)	Lipid core (mg)		Tween 80 as Surfactant (ml)	Gelatin or pectin as Stabilizer (mg)	Water (ml)
		Stearic acid (mg)	Cetyl alcohol (mg)			
F1	30	100	100	1.5ml	2	98
F2	30	150	200	1.5ml	2	98
F3	30	200	300	1.5ml	2	98
F4	30	100	300	1.5ml	2	98
F5	30	150	150	1.5ml	2	98
F6	30	200	100	1.5ml	2	98

Characterization of Lansoprazole encapsulated lipospheres

Percentage yield of Lipospheres

Yield of Lipospheres percent w/w was calculated according to the following formula:

$$\% \text{ Yield } \frac{\text{Weight of lipospheres}}{\text{Wt. of drug } + \text{ Wt. of excipients}} \text{X100}$$

Drug loading and Entrapment efficiency

The amount of Lansoprazole present in lipospheres was determined by taking the known amount of lipospheres in which 10mg of drug should be present theoretically. Then the lipospheres were crushed and the powdered microspheres was taken and dissolved in 10 ml of methanol and stirred for 15 minutes with an interval of 5 minutes and allowed to keep for 24 hours (Cherniakov *et al.,* 2012). Then the solution was filtered through whatmann filter paper. Then the absorbance after appropriate dilution was measured spectrophotometrically at 294nm by UV-visible spectrophotometer.

$$\text{Drug entrapment efficiency (\%)} = \frac{\text{Experimental drug content}}{\text{Initial drug content in the formulation}} \text{X100}$$

Microscopic Evaluation

An optical microscope (Cippon-Japan) with a camera attachment (Minolta) was used to observe the shape of the prepared microspheres for each drug: lipid ratio (Brown *et al.,* 2013).

Measurement of mean particle size

The mean size of the lipospheres was determined by Photo Correlation Spectroscopy (PCS) on a submicron particle size analyzer (Malvern Instruments) at a scattering angle of 90°. A sample (0.5mg) of the lipospheres suspended in 5 ml of distilled water was used for the measurement (Nasr *et al.,* 2008).

Determination of zeta potential

The zeta potential of the drug-loaded lipospheres was measured on a zeta sizer (Malvern zetasizer instruments) by determining the electrophoretic mobility in a micro electrophoresis flow cell. All the samples were measured in water.

Flow property determination of the Lipospheres

Bulk density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined (Newman, 1995). Accurately weighed amount of granules taken in a 50 ml capacity measuring cylinder was tapped for 100 times on a plane hard wooden surface and estimated the LBD and TBD, calculated by using following formula:

$$\textbf{LBD (Loose bulk density)} = \frac{\text{Mass of powder}}{\text{Volume of Packing}}$$

$$\textbf{TBD (Tapped bulk density)} = \frac{\text{Mass of powder}}{\text{Tapped Volume of Packing}}$$

Compressibility index: Percent compressibility of powder mix was determined by Carr's compressibility index, calculated by using following formula (Newman, 1995):-

$$\textbf{Carr's Index} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \text{X100}$$

Hausners ratio: It is determined by comparing tapped density to the bulk density by using following equation (Wells, 1998):-

$$\textbf{Housner's ratio} = \frac{\text{Tapped bulk density}}{\text{Loose Bulk density}}$$

***In-vitro* drug release studies**

The dissolution of Lansoprazole from the prepared lipospheres was monitored using USP XXV paddle II apparatus (Higuchi, 1963). The Amount of the lipospheres equivalent to 10mg of Lansoprazole was dispersed into the dissolution medium. The dissolution media was 900 ml of pH 1.2 buffers maintained at 37 ±0.5ºC and rotating at 50 ±1 rpm. The 5ml aliquots were withdrawn at pre-determined time intervals and the withdrawn samples were replaced with fresh dissolution medium. The samples were then analyzed spectrophotometrically at 294 nm for Lansoprazole content.

Results and Discussion

The percentage yields and drug entrapment efficiencies of the Lansoprazole-loaded lipospheres formulations (F1-F6) were evaluated to assess the preparation efficiency and drug encapsulation capabilities. The results are summarized in Tables 2 and 3. The percentage yields ranged from 74.45% to 85.45%, with F2 exhibiting the highest yield at 85.45% ± 0.32. This indicates that F2 was the most efficient in terms of

recovering the final product after formulation. The drug entrapment efficiencies ranged from 71.45% to 84.65%, with F2 again showing the highest efficiency at 84.65% ± 0.36. This suggests that F2 was effective in encapsulating Lansoprazole within the lipospheres, ensuring a high percentage of drug content in the final formulation. Microscopic observation and particle size analysis were performed to evaluate the physical characteristics of the optimized liposphere formulation, F2. The micrograph showed that the lipospheres in F2 were spherical and well-dispersed, indicating a uniform and stable formulation. The particle size analysis revealed that the optimized formulation F2 had a mean particle size of 156.30 nm. This small and uniform particle size is favorable for drug delivery systems, ensuring efficient drug release and biodistribution.

Zeta potential measurements were conducted to assess the stability of the lipospheres formulation F2. The zeta potential of F2 was found to be -29.4 mV. This value indicates good stability of the lipospheres in suspension, with reduced risk of particle aggregation.

The flow properties of the different liposphere formulations (F1-F6) were evaluated to determine their suitability for further processing and manufacturing. The results are summarized in Table 4. All formulations exhibited good flow characteristics, as indicated by their loose bulk density, tapped bulk density, Carr's Index, and Hausner's Ratio values.

The drug release profile of the optimized formulation F2 was studied over a period of 12 hours. The results are presented in Table 5. The release study showed a sustained drug release pattern from F2, with an initial burst release followed by a prolonged and controlled release phase. The cumulative drug release reached 98.45% at 12 hours. The release kinetics of the formulations were analyzed using different mathematical models, and the regression coefficients (r^2) were compared to select the optimized formulation. The results are summarized in Table 6. The First Order model exhibited the highest r^2 value of 0.9976, indicating that the drug release from F2 followed First Order kinetics. This suggests a concentration-dependent release rate, which is advantageous for maintaining therapeutic drug levels.

Table 2: Percentage yields of lipospheres

S. No.	Formulation Code	% Yield*
1	F1	74.45±0.15
2	F2	85.45±0.32
3	F3	79.85±0.38
4	F4	80.65±0.45
5	F5	76.65±0.36
6	F6	75.45±0.15

Table 3: % Drug entrapment efficiency of prepared Lansoprazole lipospheres formulation

S. No.	Formulation Code	% Drug entrapment efficiency
1.	F1	71.45±0.25
2.	F2	84.65±0.36
3.	F3	78.98±0.14
4.	F4	80.32±0.41
5.	F5	77.41±0.36
6.	F6	75.65±0.22

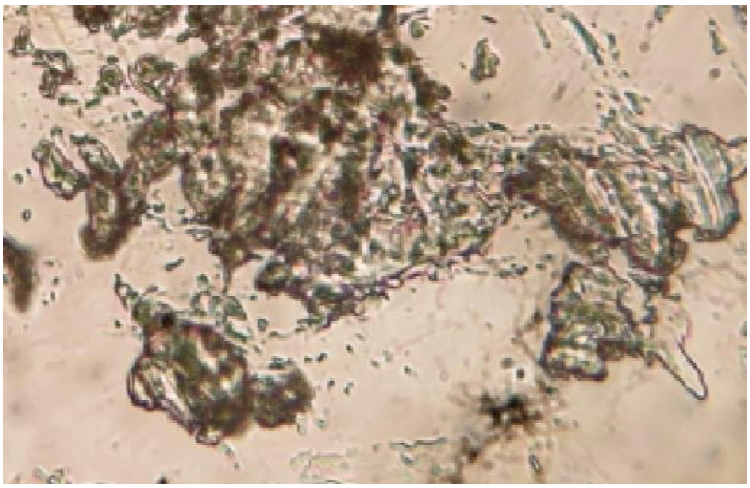

Figure 1: Microscopic observation of prepared liposphere formulation F2

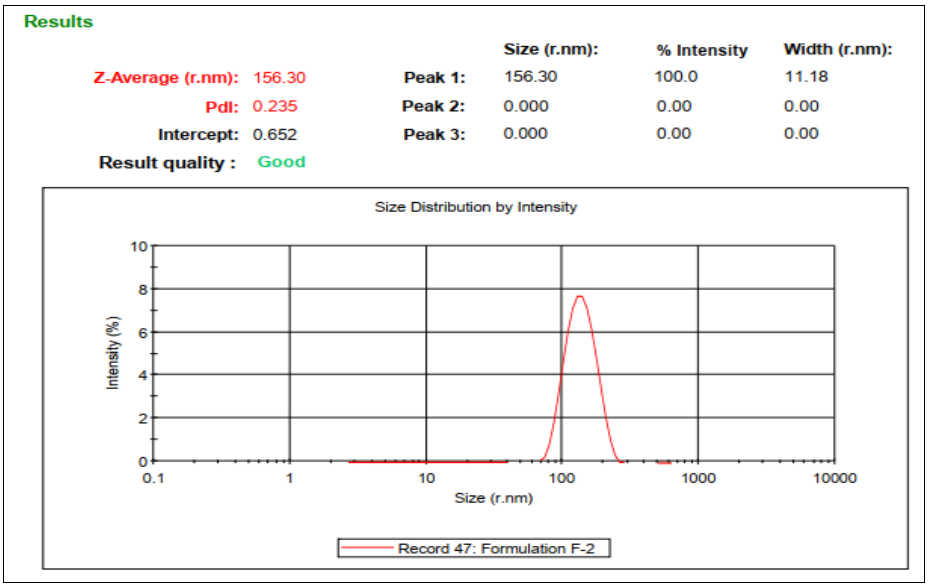

Figure 2: Particle size data of optimized lipospheres formulation F2

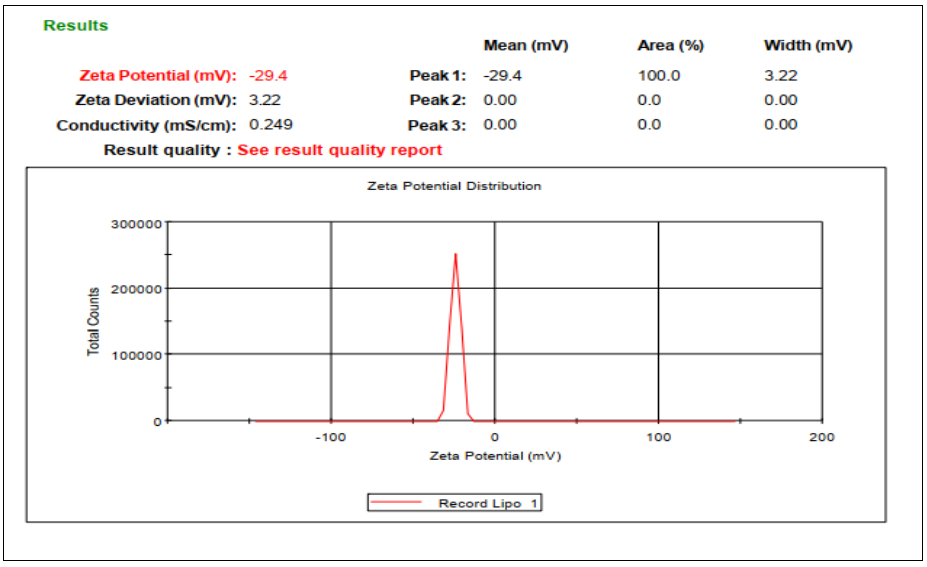

Figure 3: Zeta potential data of lipospheres formulation F2

Table 4: Result of flow properties of different liposphere formulation

Formulation code	Parameters			
	Loose Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio
F1	0.658	0.765	13.99	1.163
F2	0.689	0.795	13.33	1.154

F3	0.675	0.782	13.68	1.159
F4	0.693	0.799	13.27	1.153
F5	0.674	0.785	14.14	1.165
F6	0.688	0.792	13.13	1.151

Table 5: Release study of optimized formulation F2

Time (h)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
0.5	0.707	-0.301	25.65	1.409	74.35	1.871
1	1	0	33.25	1.522	66.75	1.824
1.5	1.225	0.176	45.65	1.659	54.35	1.735
2	1.414	0.301	58.98	1.771	41.02	1.613
3	1.732	0.477	69.98	1.845	30.02	1.477
4	2	0.602	76.65	1.885	23.35	1.368
6	2.449	0.778	88.85	1.949	11.15	1.047
8	2.828	0.903	93.32	1.970	6.68	0.825
12	3.464	1.079	98.45	1.993	1.55	0.190

Table 6: Comparative study of regression coefficient for selection of optimized batch

Zero order		First order	Higuchi	Peppas model
r^2	0.7862	0.9976	0.9160	0.9502

Conclusion

The formulation and characterization of Lansoprazole-loaded lipospheres have demonstrated promising results. Formulation F2 showed the highest percentage yield and drug entrapment efficiency, indicating efficient drug encapsulation and recovery.

Microscopic observation confirmed the uniformity and stability of the lipospheres, while particle size analysis revealed a small and uniform size suitable for drug delivery. The zeta potential measurement indicated good stability, and the flow properties were conducive to further processing. The drug release study revealed a sustained release profile fitting First Order kinetics, which is advantageous for controlled drug delivery. Overall, formulation F2 has shown optimal characteristics among the tested formulations, making it a promising candidate for further development as a pharmaceutical dosage form to enhance the bioavailability of Lansoprazole.

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