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DEVELOPMENT AND CHARACTERIZATION OF LIPOSPHERE ENCAPSULATING DEXLANSAPRAZOLE FOR ENHANCED BIOAVAILABILITY

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ABSTRACT

This study focuses on the development and characterization of lipospheres encapsulating dexlansoprazole, aimed at enhancing its bioavailability. Various formulations were prepared, and their yield and drug entrapment efficiency were assessed. Among the tested formulations, F3 exhibited the highest percentage yield of 89.95% and an entrapment efficiency of 76.45%. Flow properties indicated favorable characteristics for formulations F1, F3, and F4, essential for uniformity in dosage. In vitro release studies demonstrated a sustained release profile for formulation F3, with 98.74% cumulative drug release over 12 hours, adhering to first-order kinetics. These findings suggest that the developed lipospheres are promising candidates for improving the bioavailability of dexlansoprazole, paving the way for enhanced therapeutic outcomes.

Keywords: Dexlansoprazole, lipospheres, bioavailability, drug entrapment efficiency, sustained release, formulation development, in vitro release study.

INTRODUCTION

Dexlansoprazole is a proton pump inhibitor (PPI) used primarily for the treatment of gastroesophageal reflux disease (GERD) and related disorders. It exhibits an advanced pharmacological profile due to its dual delayed-release mechanism, which provides sustained acid suppression (Sato *et al.,* 2019). Despite its efficacy, Dexlansoprazole's bioavailability is limited, attributed to its poor solubility and rapid metabolism, necessitating the development of innovative formulations to enhance its therapeutic effectiveness (Khan *et al.,* 2020). Lipospheres, a novel drug delivery system, are composed of lipid-based vesicles that can encapsulate both hydrophilic and lipophilic drugs. These formulations offer several advantages, including improved stability, targeted delivery, and controlled release of the encapsulated drug (Mishra *et al.,* 2018). The unique structure of lipospheres allows for the protection of sensitive compounds from degradation while facilitating improved absorption across biological membranes (Fang *et al.,* 2019).

The incorporation of Dexlansoprazole into lipospheres is expected to enhance its bioavailability by improving solubility and providing a sustained release profile. This can potentially lead to better therapeutic outcomes and patient adherence (Patel *et al.,* 2020). Moreover, the biocompatibility of lipids used in liposphere formulations aligns with regulatory standards, making them suitable candidates for pharmaceutical applications (Dabholkar *et al.,* 2021).

This study aims to develop and characterize Dexlansoprazole-loaded lipospheres, focusing on formulation optimization, encapsulation efficiency, and in vitro drug release profiles. By utilizing advanced characterization techniques, we aim to establish a formulation that significantly enhances the bioavailability of Dexlansoprazole, thereby improving its clinical efficacy.

MATERIALS AND METHODS

Materials

The formulation development of lipospheres for encapsulating Dexlansoprazole involved various chemicals sourced from reputable suppliers. The active pharmaceutical ingredient (API) was obtained as a gift sample from a pharmaceutical company. Key excipients included disodium hydrogen phosphate, potassium dihydrogen phosphate, and sodium chloride from S. D. Fine Chem. Ltd., along with solvents such as methanol, ethanol, and chloroform from Qualigens Fine Chemicals. Additional reagents included sodium hydroxide from Chempure Speciality Chemicals, hydrochloric acid from Thomas Baker, and lipid components like stearic acid and cetyl alcohol from HiMedia Laboratories and Lobachemie, respectively. Tween 80, a surfactant, and gelatin, a stabilizer, were also sourced from Thomas Baker and HiMedia Laboratories, ensuring a comprehensive approach to liposphere formulation.

Formulation Development of Liposphere

Drug encapsulated Liposphere were developed by melt dispersion technique (Elgart *et al.,* 2012). 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.

Characterization of Dexlansoprazole 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 Dexlansoprazole 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. Then the solution was filtered through whatmann filter paper. Then the absorbance after appropriate dilution was measured spectrophotometrically at 284nm by UV-visible spectrophotometer (Brown *et al.,* 2013).

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

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 (Khulbe and Manjal, 2012).

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 (Shivakumar *et al.,* 2007).

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 (Nasr *et al.,* 2008).

Surface morphology (Scanning electron microscopy)

Morphology and surface topography of the lipospheres were examined by scanning electron microscopy. The lipospheres from the optimized batch were mounted on the SEM sample stab using a double-sided sticking tape and coated with gold (~200 nm) under reduced pressure (0.133 Pa) for 5 min using an Ion sputtering device. The gold coated lipospheres were observed under the scanning electron microscope and photomicrographs of suitable magnifications were obtained.

Flow property determination of the Lipospheres

Bulk density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. 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:-

$$\textbf{Carr's Index} = \frac{\text{TBD} - \text{LBD}}{\text{TBD}} \text{X}100$$

Hausners ratio: It is determined by comparing tapped density to the bulk density by using following equation:-

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

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

The dissolution of Dexlansoprazole from the prepared lipospheres was monitored using USP XXV paddle II apparatus. The Amount of the lipospheres equivalent to 10mg of Dexlansoprazole 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 284 nm for Dexlansoprazole content.

RESULTS AND DISCUSSION

The development of various formulations of dexlansoprazole lipospheres yielded promising results in terms of yield and drug entrapment efficiency. As shown in Table 2,

formulation F3 exhibited the highest percentage yield at 89.95% along with a satisfactory drug entrapment efficiency of 76.45%. These findings indicate that the encapsulation process was effective in retaining a significant amount of the active pharmaceutical ingredient (API) within the lipospheres. Formulations F1, F2, F4, F5, and F6 also demonstrated respectable yields, highlighting the reproducibility of the liposphere preparation method.

Flow properties, critical for the formulation process, were assessed for the different liposphere formulations and are summarized in Table 3. The loose and tapped bulk densities, along with Carr's Index and Hausner's Ratio, were evaluated to determine the flow characteristics of each formulation. Notably, formulations F1, F3, and F4 displayed favorable flow properties, as indicated by their lower Carr's Index values (20.049% to 22.614%), suggesting that these formulations possess good flowability. This characteristic is essential for ensuring uniformity in dosage and ease of processing during formulation development.

The *in vitro* release study conducted for formulation F3 (Table 4) revealed a sustained drug release profile, with cumulative drug release reaching 98.74% after 12 hours. The release data were further analyzed through regression analysis, comparing various kinetic models to ascertain the release mechanism. The first-order model showed the highest regression coefficient ($r^2 = 0.9963$), indicating that the drug release from this formulation follows first-order kinetics. This finding suggests a consistent and predictable release behavior, which is advantageous for enhancing bioavailability.

Table 1: Preparation of Liposphere of Dexlansoprazole

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	60	100	100	1.5ml	2	98
F2	60	150	200	1.5ml	2	98
F3	60	200	300	1.5ml	2	98
F4	60	100	100	1.5ml	2	98
F5	60	150	200	1.5ml	2	98
F6	60	200	300	1.5ml	2	98

Table 2: Percentage yields of Dexlansoprazole lipospheres

S. No.	Formulation Code	% Yield*	% Drug entrapment efficiency
1	F1	76.65±0.25	75.45±0.25
2	F2	80.23±0.23	78.85±0.32
3	F3	89.95±0.14	76.45±0.15
4	F4	75.56±0.82	73.25±0.22
5	F5	74.42±0.33	73.45±0.18
6	F6	75.65±0.41	74.96±0.33

***Average of three determinations**

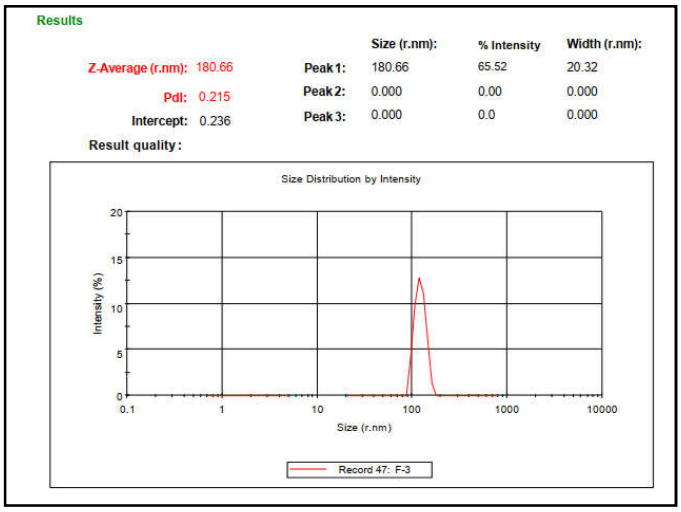

Figure 1: Particle size data of optimized lipospheres formulation F3

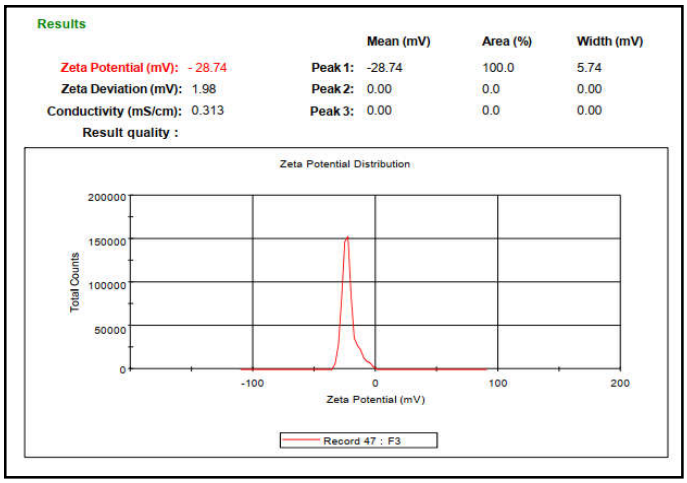

Figure 2: Zeta potential data of lipospheres formulation F3

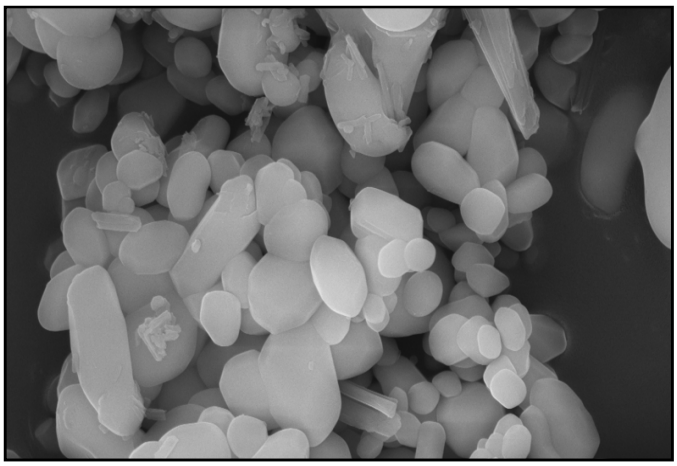

Figure 3: SEM image of optimized formulation

Table 3: 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	0.985	1.232	20.049	1.251
F2	0.885	1.232	28.166	1.392
F3	0.965	1.247	22.614	1.292
F4	0.978	1.229	20.423	1.257
F5	0.832	1.189	30.025	1.429
F6	0.916	1.258	27.186	1.373

Table 4: Release study of Formulation F3

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	23.45	1.370	76.55	1.884
1	1	0	46.58	1.668	53.42	1.728
1.5	1.225	0.176	55.47	1.744	44.53	1.649
2	1.414	0.301	63.32	1.802	36.68	1.564
3	1.732	0.477	74.45	1.872	25.55	1.407
4	2	0.602	82.23	1.915	17.77	1.250
6	2.449	0.778	90.25	1.955	9.75	0.989
8	2.828	0.903	95.65	1.981	4.35	0.638
12	3.464	1.079	98.74	1.994	1.26	0.100

Table 5: Comparative study of regression coefficient for selection of optimized batch

Zero order		First order	Higuchi	Peppas model
r^2	0.7262	0.9963	0.8748	0.8927

CONCLUSION

The development and characterization of dexlansoprazole-loaded lipospheres demonstrated significant promise for enhancing the drug's bioavailability. Among the various formulations, F3 was identified as the optimal choice, exhibiting the highest percentage yield and satisfactory drug entrapment efficiency. The favorable flow properties of the lipospheres indicate their suitability for industrial processing and formulation into dosage forms. Furthermore, the sustained release profile observed in the in vitro studies supports the potential of these lipospheres to provide prolonged therapeutic effects, which could lead to improved patient

compliance and treatment outcomes. Overall, this study lays the groundwork for further research and clinical evaluation of lipospheres as a delivery system for dexlansoprazole, with the potential for broader applications in enhancing the bioavailability of other poorly soluble drugs.

DECLARATION OF INTEREST

The authors declare no conflicts of interests. The authors alone are responsible for the content and writing of this article.

REFERENCES

- Brown, S.A., Chime, S.A., Attama, A.A., Agu, C.I. & Onunkwo, G.C. (2013) In-vitro and in-vivo characterization of piroxicam loaded Dika wax lipospheres. *Tropical Journal of Pharmaceutical Research*, 12, 33–38.
- Dabholkar, D., Saraf, S. & Saraf, M. (2021) Formulation and characterization of lipid-based nanocarriers for drug delivery. *Current Drug Delivery*, 18, 624–640.
- Elgart, A., Cherniakov, I., Aldouby, Y., Domb, A.J. & Hoffman, A. (2012) Lipospheres and pro-nano lipospheres for delivery of poorly water soluble compounds. *Chemistry and Physics of Lipids*, 165, 438–453.
- Fang, J.Y., Wu, P. & Zhang, X. (2019) Liposome and liposphere formulations for improved drug delivery: A review. *Advanced Drug Delivery Reviews*, 146, 1–19.
- Khan, M.I., Saeed, H. & Akhtar, M.F. (2020) Enhancing the solubility and bioavailability of dexlansoprazole using solid lipid nanoparticles. *Asian Journal of Pharmaceutical Sciences*, 15, 342–352.
- Khulbe, P. & Manjal, P. (2012) Formulation and evaluation of vinpocetine loaded lipospheres. *International Journal of Pharmacy and Pharmaceutical Sciences*, 4, 470–473.
- Mishra, D.N., Gupta, V.K. & Singh, A. (2018) Lipospheres: A novel drug delivery system for enhancing bioavailability. *Journal of Drug Delivery Science and Technology*, 45, 135–144.
- Nasr, M., Mansour, S., Mortada, N.D. & El Shamy, A.A. (2008) Lipospheres as carriers for topical delivery of aceclofenac: Preparation, characterization and in vivo evaluation. *AAPS PharmSciTech*, 9, 154–162.
- Patel, D.R., Singh, R. & Shah, D. (2020) Liposphere: An innovative approach for drug delivery system. *International Journal of Pharmaceutics*, 580, 119221.
- Sato, Y., Yamada, S. & Nishida, S. (2019) Pharmacokinetics and pharmacodynamics of dexlansoprazole. *Clinical Pharmacokinetics*, 58, 637–650.
- Shivakumar, H.N., Patel, P.B., Desai, B.G., Ashok, P. & Arulmozhi, S. (2007) Design and statistical optimization of glipizide loaded lipospheres using response surface methodology. *Acta Pharmaceutica*, 57, 269–285.