Advances in Bioresearch
Adv. Biores., Vol 16 (5) September 2025: 410-419

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.16.5.410419

Advances in Bioresearch

ORIGINAL ARTICLE

Design and Development of Nanosuspension of Poorly Water-Soluble Lansoprazole for Solubility Enhancement

Malgundkar H.K[1]*, Nemade L.S[1], Pomaje M.D[1], Hingmire R.S[2]
[1]Department of Pharmaceutics, Govindrao Nikam College of Pharmacy, Sawarde, Maharashtra.
[2] Department of Pharmacy, Terna College of Engineering, Dharashiv, Maharashtra.
Corresponding Author: Malgundkar H.K
Email: rushikeshhingmire49@outlook.com

ABSTRACT
Nanosuspension involves dispersion of solid drug particles in dispersion phase leading to reduction in particle size of drug which eventually increases the solubility by increasing surface area. In this study, the attempt was made to enhance solubility and dissolution rate of a Lansoprazole which is BCS class II drug. Nanopure technique of preparation was implemented using methanol as solvent and system was stabilized by polyvinylpyrrolidone as a stabilizer. Screening of optimized formula was carried out using Box Behnken design (Quadratic model). Being a thermo labile drug Lansoprazole is unstable but freeze-dried formulation was stable under appropriate storage condition. Optimized freeze-dried Lansoprazole formulation showed enhancement in drug release and solubility was increased by 7-fold than that of pure Lansoprazole. Lansoprazole nanosuspension offers a novel formulation for delivery as it is stable and causes enhancement in dissolution and solubility and may consequently enhance its bioavailability and can be effectively used for treatment of gastric ulcer.
KEYWORDS: - *Nanosuspension, Lansoprazole, Lyophilization, Nanopure, PVP K-30, Box- Behnken design*

Received 23.07.2025 Revised 09.08.2025 Accepted 22.09.2025

How to cite this article:
Malgundkar H.K, Nemade L.S, Pomaje M.D, Hingmire R.S. Design and Development of Nanosuspension of Poorly Water-Soluble Lansoprazole for Solubility Enhancement. Adv. Biores., Vol 16 (5) September 2025: 410-419.

INTRODUCTION

Most of the drugs available in market are highly lipophilic in nature and more focus is put on research work to enhance their aqueous solubility. Nanotechnology is one of the important novel drug delivery systems which involves emphasis on solubility enhancement of poorly water-soluble drugs mainly categorized in BCS class II and BCS class IV. A pharmaceutical nanosuspension is defined as "very finely dispersed solid drug particles in an aqueous vehicle, stabilized by surfactants, for either oral and topical use or parenteral and pulmonary administration, with reduced particle size, leading to an increased dissolution rate and therefore improved bioavailability"(1). The particle size distribution of the solid particles in nanosuspension is usually less than one micron with an average particle size ranging between 200 and 600 nm. Nano sized particles, increases saturation solubility by increasing surface area and thus leading to enhancement in dissolution rate and solubility of poorly water soluble drugs(2). Lansoprazole is antiulcer agent generally known as proton pump inhibitor used to treat symptoms of gastro esophageal reflux disease (GERD), to eradicate Helicobacter pylori, and to treat hypersecretory conditions such as Zollinger-Ellison Syndrome. Mechanism of action usually involves inhibition of H,K-ATPase thus, inhibiting gastric acid secretion(3). Solubility of Lansoprazole is different in different solvent and while designing product development it should be considered as major factor(4). Along with the solubility, stability of Lansoprazole is another formulation consideration while designing product. Lansoprazole is highly thermo labile drug and conventional formulation approaches showed poor stability of Lansoprazole(5),(6). In this present study, nanosuspension was selected to be a promising solubility enhancement technique and Nanopure technique was implemented for nanosuspension preparation. Nanopure technology usually involved homogenization in non-aqueous media at 0°C or even below the freezing point. This method is also called as "deepfreeze" homogenization and thus, can be

effectively use for thermo labile drug such as Lansoprazole(7). After utilizing method of preparation, post production process like Lyophilization (freeze drying) is carried out to enable the desired stability of the product throughout the storage of the formulation(8). It has been reported in recent literature that, using a fast-freeze-drying technology for preparation of drug nanosuspension is beneficial to preserve the original particle size distribution. It has been previously reported that, the combined effect of steric stabilizer and cryoprotectant contributes to the nanosuspension formulation(9,10). In this present study, seventeen different drug nanosuspension formulation were studied by optimization technique using Box Behnken design (BBD) and product responses were recorded(11).

MATERIAL AND METHODS

Lansoprazole was purchased from Sigma – Aldrich Chemicals, Germany. PVP was purchased from Qualigens Fine Chemicals, Mumbai. Mannitol was purchased from UV Scientific, Hyderabad. Methanol was obtained from RANKEM, New Delhi. Membrane filter and Dialysis membrane was purchased from Sigma – Aldrich chemicals, Germany. All other chemicals and reagents were of analytical grade.

CALIBRATION CURVE

50 mg of drug was taken in a 50 ml of volumetric flask. A stock solution was prepared by adding methanol as co- solvent and the volume was made with phosphate buffer pH 7.4. Stock solution ranged from 2-40µg/ml prepared and absorbance recorded at 281nm(12,13).

PREPARATION OF LANSOPRAZOLE NANOSUSPENSION

Freeze drying and nanosuspension formation were carried out in combination by freezing the solutions containing Lansoprazole, Solvent (Methanol), PVP (stabilizer) and Mannitol with slight water (to avoid rehydration) in the 2 mL 2R borosilicate glass vials, which were submerged into liquid nitrogen(14). The shelf temperature was held at −25 °C while the vials were being loaded to prevent melting of the frozen solutions. Drying was performed using a BioBase freeze Drier (NRI technologies). The vials were equilibrated for 5 min and the primary drying cycle was initiated by decreasing the chamber pressure to 65mTorr and decreasing the temperature to −25 °C for 24 h, followed by this, secondary drying was performed at 20 °C. Thus, combined effect of Lyophilization and stabilizer is utilized for stable formulation.

FORMULATION AND OPTIMIZATION

Optimization was carried by using Box Behnken design using Design of Expert® software(12). Three different independent factors and two dependent factors were selected(13).

CHARACTERIZATION OF NANOSUSPENSION

1] FTIR analysis: Compatibility study of Lansoprazole with stabilizers PVP and Mannitol was studied by using Perkin Elmer FTIR instrument [17].

2] Thermal analysis (DSC): The possible interaction between drug and excipients was performed by using Mettler Toledo, Switzerland instrument(15).

3] X-Ray Diffraction analysis: Optimized nanosuspension was analyzed with the help of XRD 7000, Shimadzu. X-ray diffraction. XRD analysis of freeze dried nanosuspension were recorded by x- ray diffractometer (16,17).

4] Scanning Electron Microscopy (SEM): Surface morphology of the specimen will be determined by using a scanning electron microscopy (SEM), JEOL, JSM -6701 F, Japan (18)·(19).

5] Polydispersity index (PI): In this present work, particle size distribution is ascertained by scattering light intensity method(18).

6] Zeta potential (Surface charge): Zeta potential or surface charge can be used to predict long term stability and in case of combined electrostatic and steric stabilization, a minimum zeta potential of ± 20mV is desirable (20,21).

7] Solubility determination: Excess amount of drug is shaken on rotary shaker (Royal scientific RSW, Mumbai) and absorbance were recorded using UV visible spectrophotometer (Shimadzu UV-1601**)** (22,23).

8] In vitro drug release study: In vitro drug release studies were performed using USP Type- I apparatus using rotating basket. Freeze dried nanosuspension was filled in capsule size 0 and subjected to dissolution using phosphate buffer (7.4) as dissolution medium. Absorbances were recorded at 281 nm and percent cumulative drug release was then calculated(22).

9] Stability study: Long term stability studies were conducted in a humidity chamber with specification as per ICH guideline 25°C/60% RH. The drug content was calculated for minimum 6 months(14).

10] Drug Content: The drug content in the freeze-dried product was analyzed using UV spectrophotometer, the amount of drug was determined at 281nm(13).

11] Moisture content: Measurement of residual moisture in lyophilized products is usually performed using coulometric Karl Fisher titration method (24).

RESULT AND DISCUSSION

Solubility of optimized formulation was found to be 3.17 mg/10 ml. While solubility of pure drug was found to be 0.31 mg/10 ml in distill water and 0.49 mg/10 ml in phosphate buffer pH 7.4. Thus, from obtained results, it was concluded that the, solubility of Lansoprazole was enhanced by 7 folds in phosphate buffer pH 7.4 by formulating as freeze-dried Lansoprazole nanosuspension as compared to Lansoprazole drug. FTIR, DSC and XRD studies confirmed that drug was well compatible with other excipients. Polydispersity value obtained was greater than "one" i.e., ***1.777***; this indicates greater heterogeneous dispersion in mass. Particle size observed between 171 nm to 338 nm when observed by scanning electron microscopy. XRD data supports the DSC studies which indicated the decreased crystallinity of drug in the prepared formulation by exhibiting lower values of melting points. The result of zeta potential displayed -12.6 mV (mean) zeta value and confirmed quite stable in dispersed medium. In obtained result, pure drug release after 120 minutes is 47.28±4.7 % and drug release from optimized freeze-dried formulation is 99.73±3.1%. Thus, it can be concluded that there is enhancement in dissolution rate of Lansoprazole by using nanosuspension (lyophilization) technique. From stability studies, it was concluded that freeze dried Lansoprazole formulation was stable under appropriate storage condition. Thus, along with solubility enhancement, stability of Lansoprazole is also enhanced and quite maintained.

Table 1. Physicochemical parameters of lansoprazole

Characteristics	Observations
Colour	White (Brownish colour)
Odour	Odourless
Melting point	176 °C

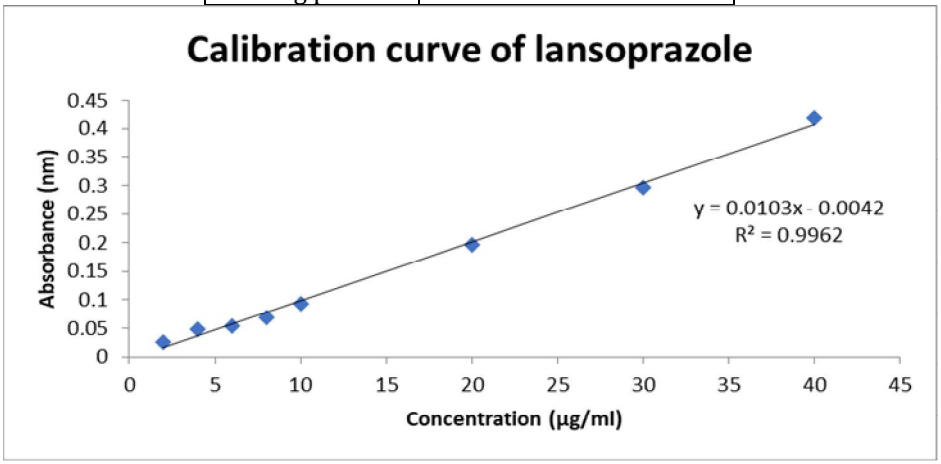


Figure 1. Calibration curve

Table 2. Formulation table suggested by Box-Behnken design (Quadratic model for Response 1- Drug content)

	Factor 1	Factor 2	Factor 3	Response 1
Run	A: Mannitol	B: PVP	C: Secondary drying temp	Drug Content
	mg	mg	degree centigrade	%
1	12.5	5	20	61
2	15	7.5	25	68
3	12.5	7.5	22.5	70
4	15	5	22.5	63
5	12.5	7.5	22.5	65
6	10	10	22.5	77
7	10	7.5	25	72
8	12.5	10	25	75
9	12.5	7.5	22.5	69

10	10	5	22.5	65
11	12.5	7.5	22.5	70
12	12.5	5	25	69
13	12.5	7.5	22.5	68
14	10	7.5	20	71
15	12.5	10	20	78
16	15	10	22.5	79
17	15	7.5	20	73

Table 3. Formulation table suggested by Box-Behnken design (Quadratic model for Response 2- Moisture content)

	Factor 1	Factor 2	Factor 3	Response 2
Run	A:Mannitol	B:PVP	C:Secondary drying temp	Moisture content
	mg	mg	degree centigrade	% (w/w)
1	12.5	5	20	2.8
2	15	7.5	25	3.2
3	12.5	7.5	22.5	3.2
4	15	5	22.5	2.9
5	12.5	7.5	22.5	3.1
6	10	10	22.5	4.2
7	10	7.5	25	3.5
8	12.5	10	25	3.9
9	12.5	7.5	22.5	3.3
10	10	5	22.5	3
11	12.5	7.5	22.5	3.3
12	12.5	5	25	3.1
13	12.5	7.5	22.5	3.2
14	10	7.5	20	3.4
15	12.5	10	20	4.5
16	15	10	22.5	4.1
17	15	7.5	20	3.7

Table 4. ANOVA for Quadratic model (Response 1: Drug Content)

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	391.52	9	43.50	9.84	0.0032	significant
A-Mannitol	0.5000	1	0.5000	0.1131	0.7465	
B-PVP	325.13	1	325.13	73.53	< 0.0001	
C-Secondary drying temp	0.1250	1	0.1250	0.0283	0.8712	
AB	4.00	1	4.00	0.9047	0.3732	
AC	9.00	1	9.00	2.04	0.1967	
BC	30.25	1	30.25	6.84	0.0346	
A^2	8.55	1	8.55	1.93	0.2070	
B^2	5.81	1	5.81	1.31	0.2892	
C^2	5.81	1	5.81	1.31	0.2892	

Table 5. ANOVA for Quadratic model (Response 2: Moisture Content)

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	3.72	9	0.4137	81.58	< 0.0001	significant
A-Mannitol	0.0050	1	0.0050	0.9859	0.3538	
B-PVP	3.00	1	3.00	591.80	< 0.0001	
C-Secondary drying temp	0.0612	1	0.0612	12.08	0.0103	
AB	0.0000	1	0.0000	0.0000	1.0000	
AC	0.0900	1	0.0900	17.75	0.0040	
BC	0.2025	1	0.2025	39.93	0.0004	
A^2	0.0442	1	0.0442	8.72	0.0213	
B^2	0.2179	1	0.2179	42.97	0.0003	
C^2	0.0684	1	0.0684	13.50	0.0079	

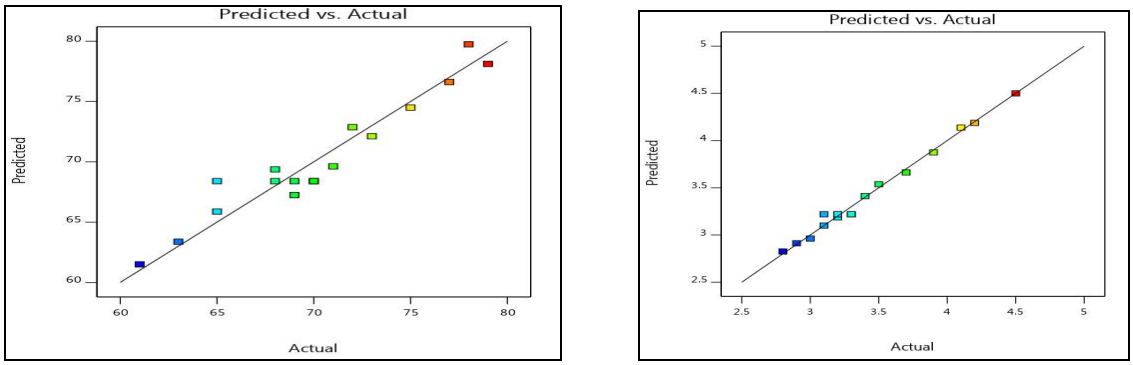


Figure 2. Predictive Vs actual response

a. Response-1 **b. Response-2**

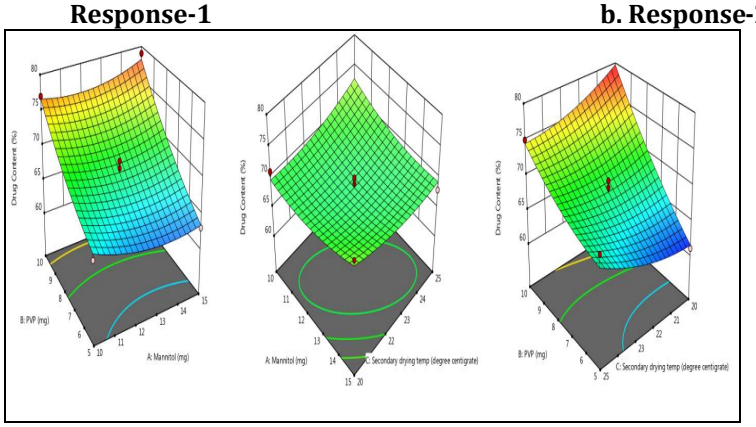


Figure 3. (a), (b) and (c)

(a): 3D response surface for response 1(Drug content) plotted between A Vs B;
(b) 3D response surface plotted between A Vs C
(c) 3D response surface plotted between B Vs C.

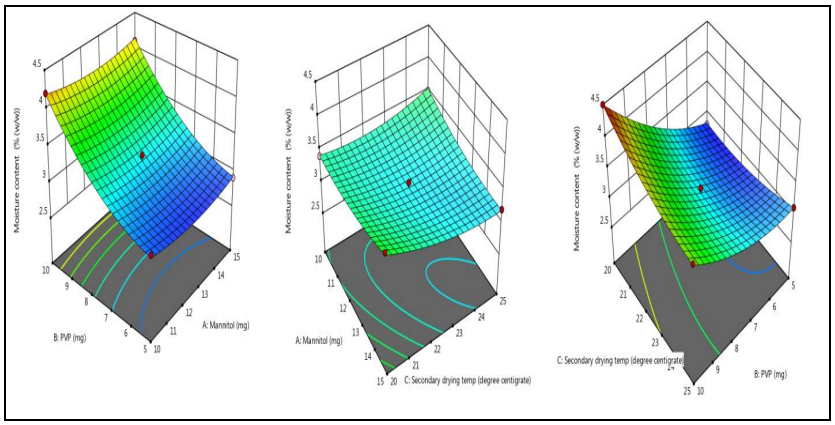
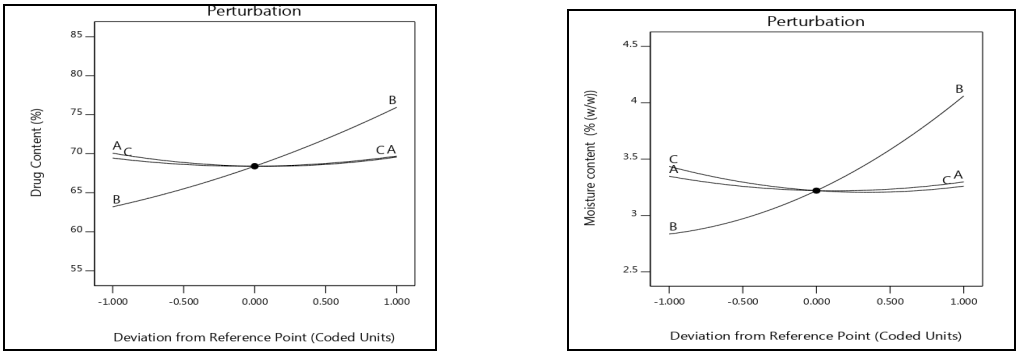


Figure 4. (a), (b) and (c)

(a): 3D response surface for response 2 (Moisture content) plotted between A Vs B;
(b) 3D response surface plotted between A Vs C
(c) 3D response surface plotted between B Vs C.



(a) Drug content **(b) Moisture content**

Figure 5. Perturbation plot showing the deviation from the reference point

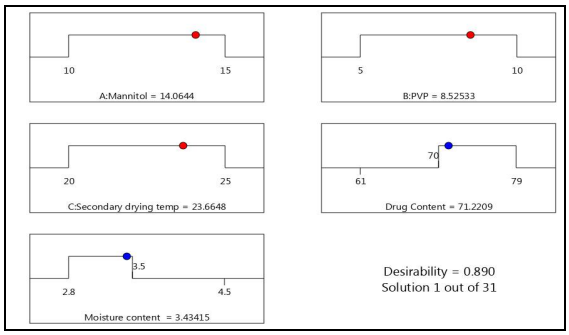


Figure 6. Numerical method of finding the value for optimized formulation

Table 7. Coefficients of all variable included in Box-Behnken study

	Intercept	A	B	C	AB	AC	BC	A^2	B^2	C^2
Drug Content	68.4	-0.25	**6.375**	0.125	1	-1.5	**-2.75**	1.425	1.175	1.175
p-values		0.7465	**< 0.0001**	0.8712	0.3732	0.1967	**0.0346**	0.2070	0.2892	0.2892
Moisture content	3.22	-0.025	**0.6125**	**-0.0875**	1.40	**-0.15**	**-0.225**	**0.1025**	**0.2275**	**0.1275**
p-values		0.3538	**< 0.0001**	**0.0103**	1.0000	**0.0040**	**0.0004**	**0.0213**	**0.0003**	**0.0079**

Table 8. Optimized concentration level of freeze dried product.

Factor	Name	Level	Low Level	High Level	Std. Dev.	Coding
A	Mannitol	14.06	10.00	15.00	0.0000	Actual
B	PVP	8.53	5.00	10.00	0.0000	Actual
C	Secondary drying temp	23.66	20.00	25.00	0.0000	Actual

Table 9. Measured responses observed of optimized formula

Response	Predicted Mean	Predicted Median	Observed	Std Dev	SE Mean	95% CI low for Mean	95% CI high for Mean	95% TI low for 99% Pop	95% TI high for 99% Pop
Drug Content	71.2209	71.2209	73.27	2.10272	1.02631	68.7941	73.6478	59.5427	82.8992
Moisture content	3.43415	3.43415	3.18	0.071214	0.0347585	3.35196	3.51634	3.03863	3.82966

Table 10. Estimated parameters of optimized formula

Parameter	Estimated values
Solubility	3.17 mg/10 ml (phosphate buffer pH 7.4)
Drug content	73.27 %
Moisture content	3.18 %(w/w)

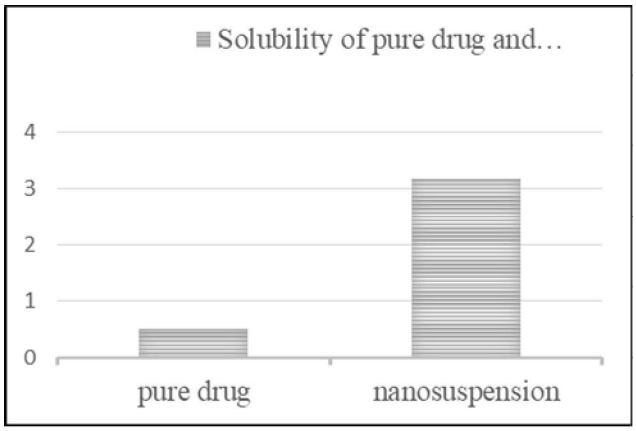
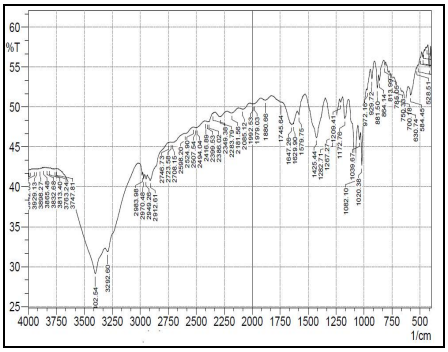
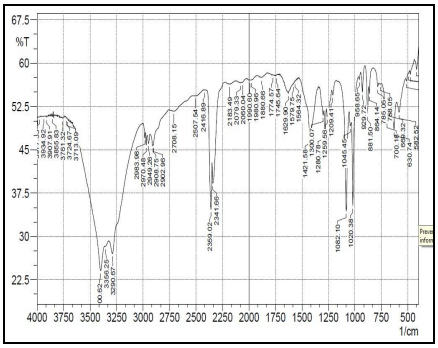


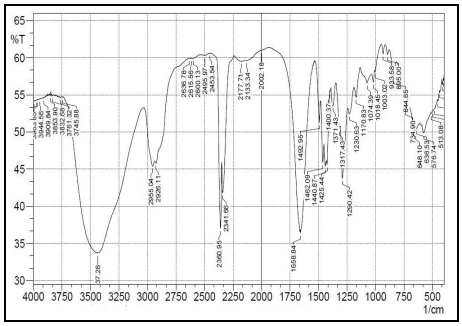
Figure 7. Solubility of pure drug and nanosuspension (mg/10mL)



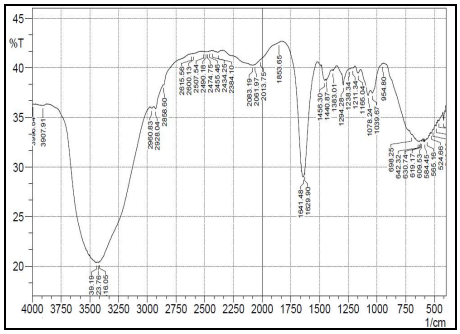
(a) FTIR spectra of lansoprazole



(b) FTIR spectra of Mannitol

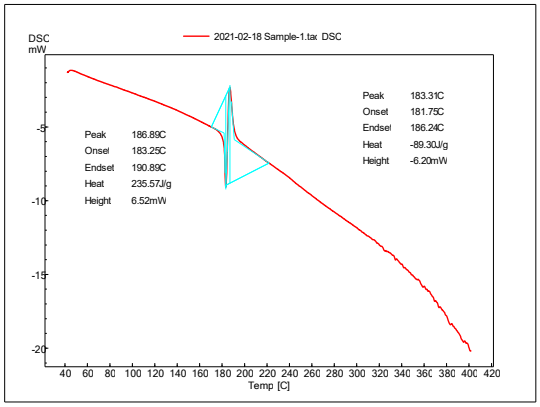


(c) FTIR spectra of PVP

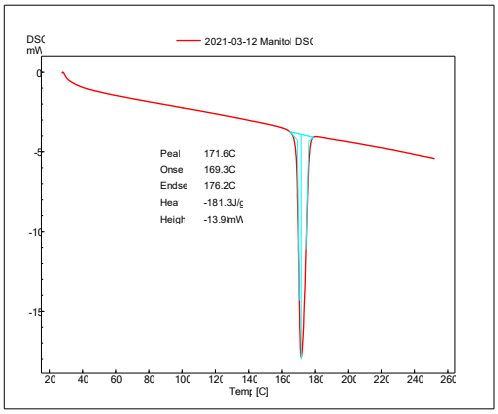


(d) FTIR of optimized nanosuspension

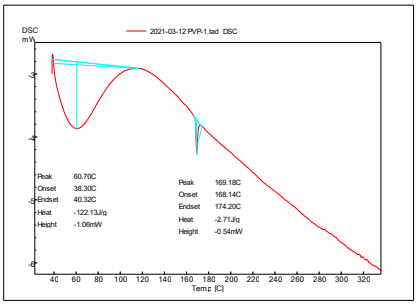
Figure 8. FTIR spectra a, b, c, d.

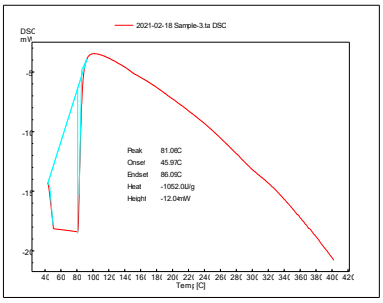


(a) DSC Curve of lansoprazole



(b) DSC curve of Mannitol





(c) DSC curve of PVP **(d) DSC curve of optimized formulation**

Figure 9. DSC curve a, b, c, d

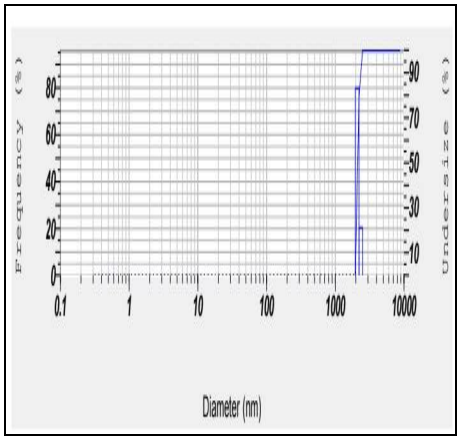


Figure 10: Particle size distribution of drug

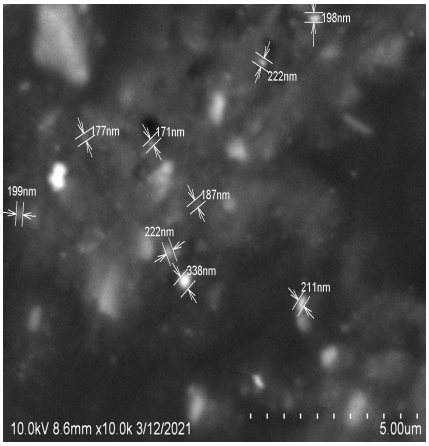


Figure 11.SEM image of optimized nanosuspension

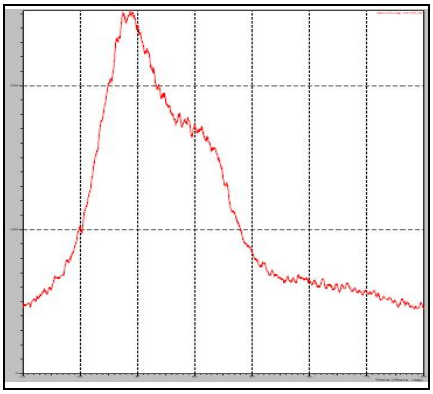


Figure 12. XRD

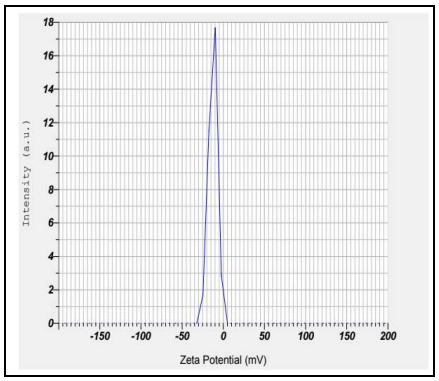


Figure 13. Zeta potential

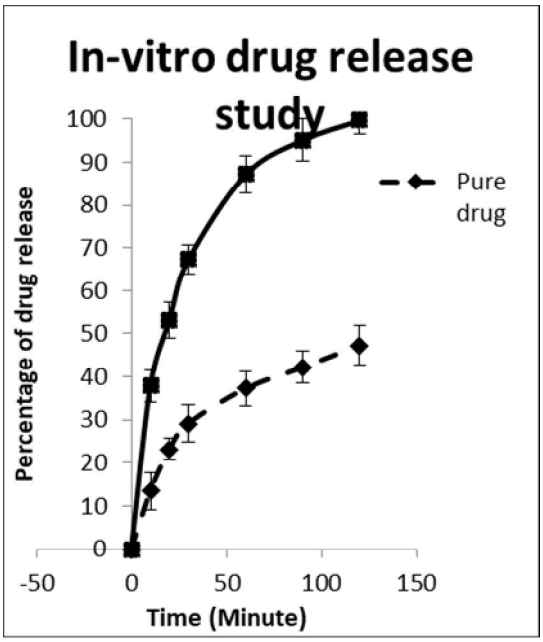


Figure 14. %CDR data

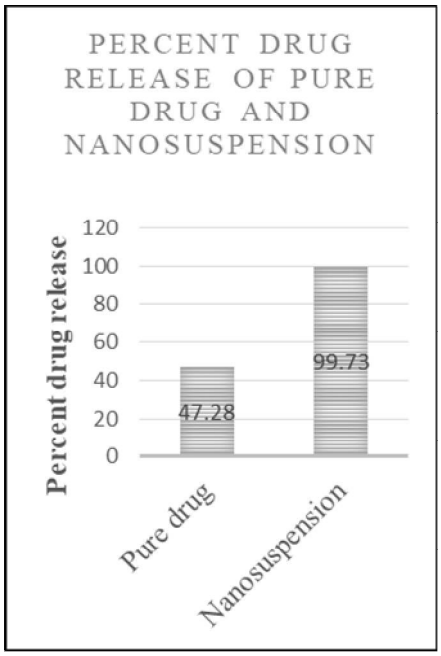


Figure 15. %CDR of pure drug and nanosuspension

Table 20. Stability studies

Storage condition	0 month	3 month	6 month
Drug content (%)	73.27±2.45	72.19±3.17	70.15±1.89
Percent Drug release (%)	99.73	98.73	96.99

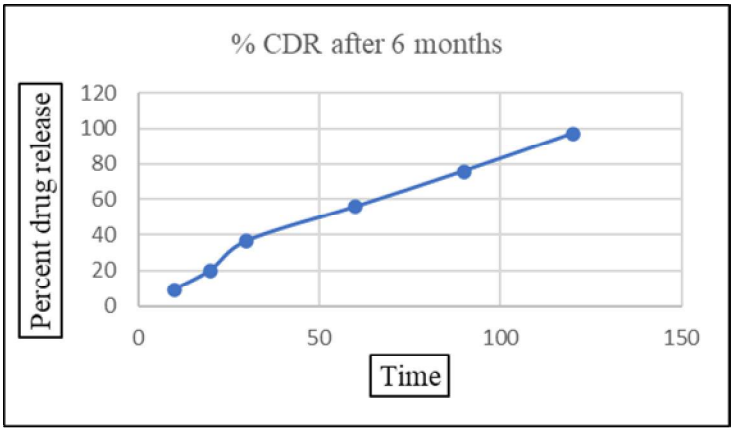


Figure 16. Percent drug release of freeze dried nanosuspension after 6 months

ACKNOWLEDGEMENT

I would like to acknowledge my guide Mr. Madan Pomaje and my co guide Ms. Lalita Nemade for their constant guidance and advice to complete this project. I would like to thanks Principal of Govindrao Nikam College of Pharmacy, Sawarde Mr. Anil Battase for encouraging me to complete this work. I would also like to thanks my colleagues, all staff members for directly or indirectly supporting me till the last moment of completion. I would like to thanks my parents and my husband for supporting and encouraging me and continuous understanding me throughout this project work. I also like to thanks Mr. Mrunal Karanjkar for helping me time to time. Last but not the least, I would like to thank God for blessing me always.

Conflict of interest: All authors confirmed there is no any conflict of interest.

Funding Sources: Nil

REFERENCES

1. Savjani KT, Gajjar AK, Savjani JK.(2012): Drug Solubility: Importance and Enhancement Techniques. ISRN Pharm. (100 mL):1–10.
2. Sanjaymitra, P.V & GNK, Ganesh. (2018). Dissolution And Solubility Enhancement Strategies: Current And Novel Prospectives. Journal of Critical Reviews. 5. 1. 10.22159/jcr.2018v5i3.23451.
3. Motka U, Dabhi M, Sheth N, Dudhrejiya A. (2017): Formulation And Optimization Of Nanosuspension Prepared By Media Milling Technique To Enhance The Solubility Of Isradipine. Int J Pharm Sci Drug Res. 7(04):169–77.
4. Liu D, Xu H, Tian B, Yuan K, Pan H, Ma S.(2012): Fabrication of carvedilol nanosuspensions through the anti-solvent precipitation-ultrasonication method for the improvement of dissolution rate and oral bioavailability. AAPS PharmSciTech. 13(1):295–304.
5. Pathak P, Meziani MJ, Desai T, Sun YP. (2004): Nanosizing drug particles in supercritical fluid processing. J Am Chem Soc.9;126(35):10842–3.
6. Savant M. (2020): Nanosuspension : an Emerging Method of Drug Delivery. 6(11):101–3.
7. Yadollahi R, Vasilev K, Simovic S. (2015): Nanosuspension technologies for delivery of poorly soluble drugs. J Nanomater. (2):59–66.
8. Sutradhar KB, Khatun S, Luna IP. (2013): Increasing possibilities of nanosuspension. J Nanotechnol. 年;2013.
9. Geetha G, Poojitha U, Arshad K, Khan A. (2014): Various Techniques for Preparation of Nanosuspension-A Review. Int J Pharma Res Rev IJPRR.;3(39):30–7.
10. Ujwala K, Babu PRS. (2017): Solubility enhancement of paroxetine hydrochloride by hydrotropy. Indian J Pharm Sci.;79(4):591–8.
11. Pankaj P, Kailash B, Rao PRT, Kumud P, Ajit S, Singh KP.(2010): Micronization : An Efficient Tool For Dissolution Enhancement of Dienogest. International Journal of Drug Development & Research ;3(2):329–33.
12. Shelke V, Mutha S. (2020): Formulation and evaluation of lansoprazole sublingual tablet. J Res Pharm.;24(2):264–76.
13. Balaji M, Ramyakrishna N, Hanumanaik M. (2020): Formulation Development and Characterization of Enteric Coated Tablets of Lansoprazole. Der Pharm Lett.;12(3):22–38.
14. Emami F, Vatanara A, Park EJ, Na DH. (2018): Drying technologies for the stability and bioavailability of biopharmaceuticals. Pharmaceutics.;10(3):1–22.
15. Jain V, Kare P, Jain D, Singh R. (2011): Development and characterization of mucoadhesive nanosuspension of ciprofloxacin. Acta Pol Pharm - Drug Res.;68(2):273–8.
16. Priyanka KA, Nigar MK, Sachin NA. (2016): Formulation and Evalution of Solid Dispersion of Lansoprazole. Indian J Drugs.4(4):183–92.
17. Haddad F, Sawalha M, Khawaja Y, Najjar A, Karaman R. (2017). Dopamine and Levodopa Prodrugs for the Treatment of Parkinson's Disease. Molecules. 25;23(1):40. doi: 10.3390/molecules23010040. PMID: 29295587; PMCID: PMC5943940.
18. Yeom DW, Chae BR, Son HY, Kim JH, Chae JS, Song SH.(2017): Enhanced oral bioavailability of valsartan using a polymer-based supersaturable selfmicroemulsifying drug delivery system. Int J Nanomedicine. 2年;12:3533–45.
19. Araya-Sibaja AM, Vega-Baudrit JR, Guillén-Girón T, Navarro-Hoyos M, Cuffini SL.(2019): Drug solubility enhancement through the preparation of multicomponent organic materials: Eutectics of lovastatin with carboxylic acids. Pharmaceutics. 11(3):1–16.
20. Sande L, Sanchez M, Montes J, Wolf AJ, Morgan MA, Omri A.(2012): Liposomal encapsulation of vancomycin improves killing of methicillin-resistant Staphylococcus aureus in a murine infection model. J Antimicrob Chemother. 67(9):2191–4.
21. Patel P, Patel H, Mehta T, Panchal S. (2013): Self micro-emulsifying drug delivery system of tacrolimus: Formulation, in vitro evaluation and stability studies. Int J Pharm Investig. 3(2):95.
22. Nakarani M, Misra A, Patel J, Vaghani S.(2010): Itraconazole nanosuspension for oral delivery: Formulation, characterization and in vitro comparison with marketed formulation. Acta Pharm Sci. 年;52(3):305–14.
23. Shukla, Sandeep & Jain, Roli & Pandey, Archna. (2015). Nanosuspension formulation to improve the dissolution rate of Clonazepam.. international journal of advance research 2320-5407. 3. 588-591.
24. Lad S, Narkhede S, Luhar S, Prajapati A. (2022): Review On Moisture Content : A Stability Problem In Pharmaceuticals EPRA International Journal of Research and Development (IJRD). ;7838:27–33.