Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 32s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Formulation and In-Vitro Evaluation of Fexofenadine HCl Nano Lipid Based Formulation

Fathima B[1], Chukka S[*1]

[1]Department of Pharmacy, Chaitanya (Deemed to be University), Himayathnagar, Moinabad, Hyderabad, Telangana, India

[*]**Corresponding author:**

Chukka S

Department of Pharmacy, Chaitanya (Deemed to be University), Himayathnagar, Moinabad, Hyderabad, Telangana, India

Email ID: sarithapuligilla28@gmail.com

Cite this paper as: Fathima B, Chukka S, (2025) Formulation and In-Vitro Evaluation of Fexofenadine HCl Nano Lipid Based Formulation. *Journal of Neonatal Surgery*, 14 (32s), 2796-2802.

ABSTRACT

Introduction: Nanostructured lipid carriers (NLC's) are second-generation lipid nanoparticles that are used as alternative colloidal drug carriers. Fexofenadine HCl, is a long-acting antihistamine that is used to treat annual hay fever, angioedema and chronic autoimmune hives.

Methods: Fexofenadine NLC was prepared using the ultra-sonication method followed by hot homogenization. Total six formulations were developed. All the formulations were evaluated for particle size analysis, encapsulation efficiency and drug release studies. The physical stability was conducted on optimized formulation for 3 months.

Results: The particle size of all the formulations was found in the range of 124± 0.12 to 231.4± 0.12 nm. The PDI was ranged between 0.204 ±0.002 to 0.273± 0.001. The zeta potential values for all the NLC formulations were found to be within the range of -22.21± 2.23 to -28.17± 1.31. Based on the physicochemical properties, F6 formulation was selected as the optimized formulation.

Conclusion: Fexofenadine NLC was developed using ultrasonication method and hot homogenization. The optimized formulation (F6) showed highest encapsulation efficiency, drug release and was stable for 3 months.

Keywords: *Fexofenadine, nanostructured lipid carriers, encapsulation efficiency, in vitro release***.**

1. INTRODUCTION

Lipid-based drug delivery systems have the capability to improve the solubility and bioavailability of orally administered poorly water-soluble and/or lipophilic drugs (O'Driscoll & Griffin, 2008; Avula *et al.,* 2023). Since smaller particles have a larger surface area, which increases medication solubility and dissolution speed as well as oral bioavailability, nanosized carriers have drawn a lot of interest (Sapavatu *et al.,* 2020). Lipids, which are solid at room temperature, make up the majority of solid lipid nanoparticles (SLNs), the first generation of lipid nanocarriers (Avula *et al.,* 2023). Second-generation lipid nanoparticles known as nanostructured lipid carriers (NLCs) are employed as substitute colloidal drug carriers. In order to create an unstructured matrix that enhances drug loading and decreases drug ejection from the matrix during storage, they combine a solid matrix with a liquid lipid (Togaru *et al.,* 2017). Both lipophilic and hydrophilic medicines exhibit substantial drug loading in NLCs, which also facilitate oral absorption of encapsulated medications through payer's patches or lymphatic selective uptake. (Fundaro *et al*., 2000; Chen *et al*., 2001).

NLC also showed sustained release of the drug from the lipid matrix which results in the prolongation of the drug concentration within the therapeutic window (Xie *et al*., 2011). Hence, NLC is becoming one of the best selected drug delivery system.

Fexofenadine HCl, is a long-acting antihistamine that is used to treat annual hay fever, angioedema, and chronic autoimmune hives (Sharaff *et al.,* 2024; Sapavatu and Jadi, 2019). It is less drowsy than first-generation histamine-receptor inhibitors. It has a 35% oral bioavailability in humans.

Therefore, the aim of the present work was to evaluate NLC for enhancement of the oral bioavailability of the drug. The prepared NLCs were characterized for *in vitro* physiochemical performance, solid-state compatibility and stability study.

2. MATERIAL AND METHODS

Materials

Fexofenadine was received as gift sample from Aurobindo Pharma Ltd, India. Dynasan-114, oleic acid, Egg lecithin E-80, Poloxamer-188 and dialysis membrane (70 dm) were purchased from Himedia chemicals (Hyderabad, India). All other reagents and chemicals obtained were of analytical grade.

Methods

Formulation of Fexofenadine NLCs

Fexofenadine NLC was prepared by hot homogenization followed by ultra-sonication method. Take the required quantity of drug, solid lipid, liquid lipid and egg lecithin and dissolved in 10 ml of chloroform and methanol (1:1) mixture. The organic solvent was evaporated by rotary evaporator. Lipid phase was heated at above 5º C of its melting point for drug embedment. Then the aqueous phase was prepared by dissolving the poloxamer-188 in sufficient double distilled water to produce 10 ml and heated at same temperature. Hot aqueous phase was then added to molten lipid phase and homogenized for 5 min at 12,000 rpm. The resulted coarse hot oil in water emulsion was ultrasonicated to get nanoemulsion using probe sonicator for 20 min. The nanoemulsion was cooled at room temperature to obtain Fexofenadine NLCs (Abdel hameed *et al.,* 2022).

Characterization of Fexofenadine NLC

Determination of particle size, PDI and ZP

The prepared nanostructured lipid carrier formulations were diluted in 1:50 ratio with double distilled water and particle size, PDI and ZP of Fexofenadine NLCs were determined by photon correlation spectroscopy using Malvern Zetasizer (Chettupalli *et al.,* 2025; Abdel hameed *et al.,* 2022).

Encapsulation efficiency

The encapsulation efficiency (EE) of NLCs was determined as the amount of drug, Fexofenadine encapsulated in per cent related to the total amount of drug added to the system. The encapsulation efficiency was determined by centrifugation technique. A known volume of Fexofenadine -NLCs dispersion was subjected for centrifugation at 10000 rpm (Remi centrifuge, Mumbai, India) for 30 min. Then the supernatant was separated, filtered using membrane filter, and was diluted appropriately. The amount of drug was assayed at 220 nm using a spectrophotometer and encapsulation efficiency calculated using the equation below (Chettupalli *et al.,* 2025):

$$\mathbf{EE} = W_{total} - W_{free} / W_{total} * 100$$

In vitro release kinetics

Drug release studies were conducted on all the Fexofenadine - NLCs formulations using dialysis method in 0.1 N HCl (pH1.2) for 2 hrs followed by pH 6.8 phosphate buffers for 22 hrs. During *in vitro* release studies, dialysis membrane (Molecular weight 12,000 - 14,000 Da) was used.

Before the study, the dialysis membrane was soaked in double distilled water for overnight. In donor compartment, about 2 ml of formulation was taken for release study, which consisted of a boiling tube with opening at the one end and tied with dialysis membrane at the other end. A beaker of 250 ml capacity was used as receptor compartment with 100 ml release medium and maintained at the temperature of 37 ± 0.5º C. About 2 ml of samples was withdrawn from receiver compartment and was replaced with fresh medium periodically at predetermined time intervals and analyzed for drug content using UV-visible spectrophotometer at 220 nm (Komati *et al.,* 2019).

The analyzed data were fitted into different kinetic models such as zero order, first order, Higuchi, Hixson–Crowell, and Korsmeyer–Pappas model (1983), and best fit model was determined on the basis of regression coefficient (R^2) value.

Differential scanning calorimetry

Drug-excipient interaction study was conducted to determine the possibility of any interaction between Fexofenadine and excipients by carrying out thermal analysis of the formulation using DSC (Perkin Elmer, Germany). Each sample was weighed accurately and kept in aluminium pans and scanned between 30 ºC and 400 ºC at a heating rate of 10 ºC/min. and cooling rate of 40ºC/min under nitrogen. An empty aluminium pan was used as reference in the study (Chettupalli *et al.,* 2023; Sapavatu and Jadi, 2020; Pandala *et al.,* 2019).

Stability studies

Stability study was conducted on Fexofenadine loaded optimized NLCs (F6) were stored at room temperature and refrigerated temperature (25 ± 2°C and 4°C) for 3 months. The changes in the formulation were observed by measuring the particle size, PDI, ZP, assay and EE periodically after 1 day, 1 month and 3 months after the storage (Liu D *et al*., 2011)

Lyophilisation of Fexofenadine -NLCs

The optimized Fexofenadine-NLCs containing 10% w/v trehalose as cryoprotectant were prepared and kept at deep freezer at -40º C for overnight. Then, the frozen samples of the formulations were transferred into freeze-dryer (Lyodel, India). Vacuum was applied and sample was subjected to drying for about 48 h to get powdered lyophilized product (Muller RH *et al.,* 1996). The powdered formulation is used for further studies,

Morphology by SEM

Fexofenadine freeze-dried NLCs were suitably diluted to 100 times with double distilled water and from this a drop of NLC formulation was placed on sample holder and air dried. Then, the sample was observed at 15,000 volts at various magnifications by mounted in SEM (Eslavath *et al.,* 2019; Ramasamy T *et al*., 2012)

RESULTS AND DISCUSSION

The Fexofenadine NLCs was developed using hot homogenization followed by ultra-sonication method. Oleic acid and dynasan-114 were used as liquid lipid and solid lipid respectively for the preparation of Fexofenadine-NLCs. Egg lecithin and poloxamer-188 were used as surfactant and co-surfactant. Total 6 formulations were developed. The homogenization and sonication time of 4 min (12,000 rpm) and 20 min, respectively, were selected for the preparation of Fexofenadine NLCs.

Table 1: Composition of Fexofenadine NLC formulation

Ingredients (mg)	F1	F2	F3	F4	F5	F6
Fexofenadine	30	30	30	30	30	30
Oleic acid (ml)	0.08	0.09	0.08	0.09	0.08	0.09
Dynasan-114	150	100	-	-	-	-
Dynasan-116	-	-	150	100	-	-
Dynasan-118	-	-	-	-	150	100
Egg lecithin	80	80	80	80	80	80
Solvent(ml)(1:1) (Chloroform : Methanol	10	10	10	10	10	10
Poloxamer-188	150	150	200	200	250	250
Double distilled water (ml)	10	10	10	10	10	10

Table 2: Physical characters of Fexofenadine NLC formulations

Formulation	Size (nm)	PDI	ZP (mV)	Assay (%)	EE (%)
F1	231.4 ± 1.10	0.215±0.002	-22.21±2.23	98.57±0.02	71.10±0.12
F2	208.1 ± 2.01	0.211±0.003	-24.10±1.03	99.03±0.01	77.21±0.23
F3	142.3± 2.11	0.262±0.001	-25.02±2.31	98.31±0.03	90.01±0.15
F4	195.2 ± 0.15	0.273±0.001	-26.10±1.21	98.32±0.03	89.13±0.12
F5	214.1 ± 2.13	0.256±0.003	-27.05±2.03	98.10±0.03	91.03±0.16
F6	124.0± 0.12	0.204±0.002	-28.17±1.31	99.53±0.14	95.41±0.27

Differential scanning calorimetry

The DSC thermograms were recorded for pure drug, Dynasan 114 and physical mixture is shown in Figure 1-3. The pure drug and solid lipid showed an endothermic peak at 61.28º C and 142.21º C, respectively.

Particle size analysis

The mean size of all the formulations was found in the range of 124± 0.12 - 231.4± 0.12 nm (Table 2). The particle size statistics show that the variation in particle size depends on the amount of lipid in the formulation. The PDI of all the Fexofenadine NLC formulations were ranged between 0.204 ±0.002 - 0.273± 0.001 and showed within the acceptable limits

for all the formulations. Usually, a small value of PDI indicates a homogenous population, while a larger PDI means a high heterogeneity in particle size. The zeta potential values for all the NLC formulations were found to be within the range of -22.21± 2.23-28.17± 1.31. However, all the formulations have a zeta potential less than -30 mV, which indicated that all the dispersions were electro statistically stable.

Encapsulation efficiency

An important parameter with respect to NLCs as drug carriers is their capacity for drug encapsulation. As summarized in Table 2, Formulation (F1) shows lowest entrapment of 71.10 ± 0.12% whereas highest in the formulation (F6) 95.41 ± 0.27 as compared to the rest of the formulations. The higher encapsulation was observed by increasing oil content, the percentage of encapsulated drug increases as the drug shows more solubility in lipid blend. The high EE% values observed in this study indicate that the lipid and surfactant compositions employed were satisfactory. The total drug content in all the NLCs formulations was determined and to be ranged between 98.10 ± 0.03 to 99.53 ± 0.14%.

***In vitro* release kinetics**

The drug release from Fexofenadine NLC was shown in Figure 4. Drug release from Fexofenadine NLC was biphasic showing burst release followed by sustained drug release. The initial burst release could be occurred due to the presence of the free Fexofenadine drug in the external phase and on the surface of the NLC. The burst release rate was affected by the change of concentration of lipid and surfactant in external phase. When the lipid concentration increased, the initial burst release rate decreased this may be due to the higher concentration of drug presence in the inner core (Priyanka & Sathali, 2012; Tsukamoto *et al.,* 2013). The lipophilic nature of the Fexofenadine could be the reason for sustained release of the drug from internal lipid phase after initial burst release.

In order to propose the possible release mechanism, the release data were evaluated for various kinetic models (Higuchi, 1963; Korsmeyer, 1983; Peppas, 1985).

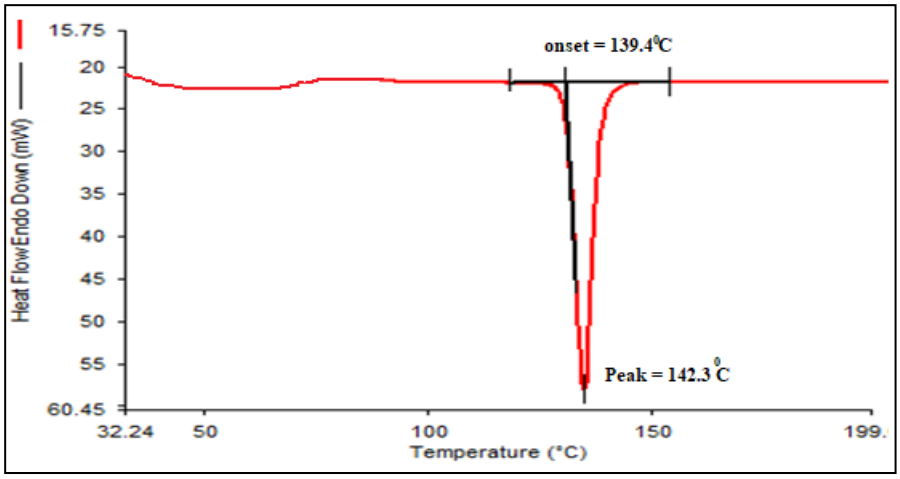

Figure 1: DSC thermogram for pure drug

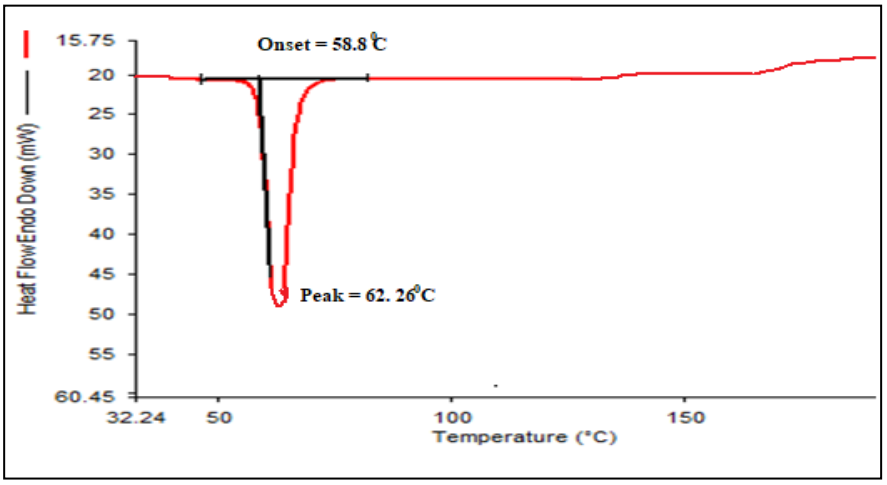

Figure 2: DSC thermogram of lipid

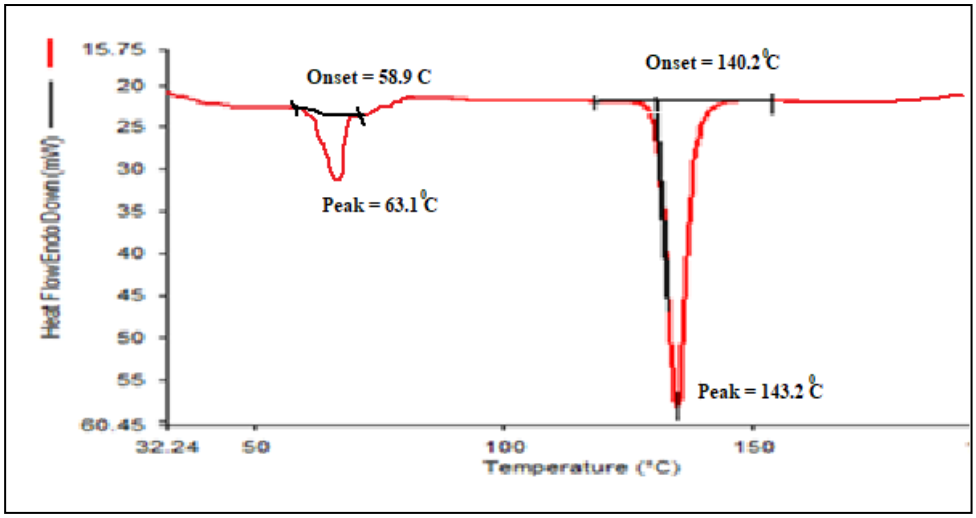

Figure 3: DSC thermogram of physical mixture

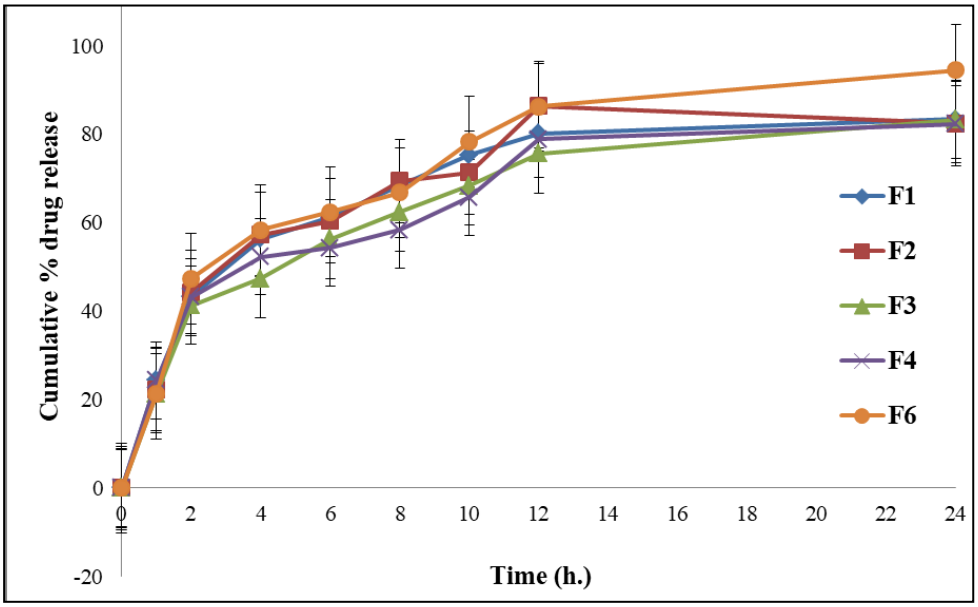

Figure 4: Dissolution profiles of Fexofenadine NLCs formulations (F1-F6)

3. CONCLUSION

Fexofenadine NLCs were successfully formulated by hot homogenization followed by ultrasonication method using Dynasan 114 and oleic acid as the solid lipid and liquid lipid respectively. The formulated NLCs with lowest particle size and highest encapsulation efficiency, loading efficiency, and drug release were selected as optimized formulation (F6) and used for further study. The stability study was conducted on optimized formulation and was stable for 3 months.

REFERENCES

[1] Abdel hameed A.H., Abdelhafez W.A., Saleh K., Mohamed M.S. (2022) Formulation, optimization, and *in vivo* evaluation of nanostructured lipid carriers loaded with Fexofenadine HCL for oral delivery. J. Drug Deliv. Sci. Technol. 74, 103607.

[2] Abdelhameed A.H., Abdelhafez W.A., Saleh, K.I., Hamad, A.A., Mohamed M.S. (2023) Formulation and optimization of oral fast dissolving films loaded with nanosuspension to enhance the oral bioavailability of Fexofenadine HCL. J. Drug Deliv. Sci. Technol. 85, 104578.

[3] Avula, P. R., Chettupalli, A. K., Chauhan, V., & Jadi, R. K. (2023). Design, formulation, in-vitro and in-vivo

pharmacokinetic evaluation of Nicardipine-nanostructured lipid carrier for transdermal drug delivery system. Materials today: Proceedings.

[4] Beloqui A, Solinis MA, Gascon AR. (2013). Mechanism of transport of saquinavir-loaded nanostructured lipid carriers across the intestinal barrier. J Control Release 166:115–23.

[5] Chakraborty S, Shukla D, Jain A. (2009). Assessment of solubilization characteristics of different surfactants for carvedilol phosphate as a function of pH. J Colloid Interface Sci 335:242–9.

[6] Charman WN. (2000). Lipids, lipophilic drugs and oral drug delivery- some emerging concepts. J Pharm Sci 89:967–78

[7] Chettupalli, A. K., Ajmera, S., Amarachinta, P. R., Manda, R. M., & Jadi, R. K. (2023). Quality by Design approach for preparation, characterization, and statistical optimization of naproxen sodium-loaded ethosomes via transdermal route. Current Bioactive Compounds, 19(10), 79-98.

[8] Chettupalli, A. K., Kakkerla, A., Jadi, R. K., Uppu, P., Ghazwani, M., Hani, U., ... & Haque, M. A. (2025). Design, development, and preclinical evaluation of pirfenidone-loaded nanostructured lipid carriers for pulmonary delivery. Scientific Reports, 15(1), 11390.

[9] Chettupalli, A. K., Unnisa, A., Peddapalli, H., Jadi, R. K., Anusha, K., & Amarachinta, P. R. (2025). Development and evaluation of empagliflozin-loaded solid lipid nanoparticles: Pharmacokinetics and pharmacodynamics for oral delivery. Intelligent Pharmacy.

[10] Choudhury A, Laskar RE, Deka D, Sonowal K, Saha S, Dey BK. (2021) A review on nanoparticle: types, preparation and its characterization. Res J Pharm Technol. 14(3):1815-22.

[11] D and Bielory L. (2008) Fexofenadine hydrochloride in the treatment of allergic disease: a review. Journal of Asthma and Allergy 1: 19-29.

[12] Eedara B.B., Nyavanandi D., Narala, S., Veerareddy P.R., Bandari S. (2021) Improved Dissolution Rate and Intestinal Absorption of Fexofenadine Hydrochloride by the Preparation of Solid Dispersions: *In vitro* and in situ Evaluation. Pharmaceutics 13, 310.

[13] Eslavath, R. N., Bakshi, V., & Jadi, R. K. (2019). Formulation Development and In Vitro Release Studies of Tenofovir-containing Microsponges. INNOSC Theranostics and pharmacological sciences, 2(2), 16-24.

[14] Kaur IP, Bhandari R, Bhandari S, Kakkar V. (2008). Potential of solid lipid nanoparticles in brain targeting. J Control Release 127: 97–109.

[15] Komati, S., Dasi, V., Jadi, R. K., & Padala, N. R. (2019). Formulation Development and Characterization of Atazanavir Sulphate Controlled Release Non-Effervescent Floating Matrix Tablets. Journal of Drug Delivery & Therapeutics, 9.

[16] Korsmeyer RW, Gurny R, Doelker EM, (1983). Mechanism of solute release from porous hydrophilic polymers. Int J Pharm 15: 25–35.

[17] Kumar MNR. (2000). Nano and microparticles as controlled drug delivery devices. J Pharm Sci 3:234–58.

[18] Liu D, Liu Z, Wang L, (2011). Nanostructured lipid carriers as novel carrier for parenteral delivery of docetaxel. Colloids Surf B Biointerfaces 85:262–9.

[19] M.G. Shah, M. Tajmal, R. Karki. (2020) Formulation and evaluation of fexofenadine hydrochloride loaded chitosan nanoparticles. Int. J. Pharm. Sci. Res. 11(6): 2969-2975.

[20] Muller RH, Maassen S, Weyhers H, Mehnert W. (1996). Phagocytic uptake and cytotoxicity of solid lipid nanoparticles (SLN) sterically stabilized with poloxamine 908 and poloxamer 407. J Drug Target 4: 161–70.

[21] Muller RH, Mader K, Gohla S. (2000). Solid lipid nanoparticles (SLN) for controlled drug delivery – a review of the state of the art. Eur J Pharm Biopharm 50:161–77.

[22] Muller RH, Petersen RD, Hommoss A, Pardeike J. (2007). Nanostructured lipid carriers (NLC) in cosmetic dermal products. Adv Drug Deliv Rev 59:522–30.

[23] Nasr A.M., Qushawy M.K., Elkhoudary M.M., Gawish, A.Y., Elhady, S.S., Swidan, S.A. (2020) Quality by Design for the Development and Analysis of Enhanced In-Situ Forming Vesicles for the Improvement of the Bioavailability of Fexofenadine HCl *in vitro* and *in vivo*. Pharmaceutics, 12, 409.

[24] Nisharani S, Ranpise NS, Korabu SS, Ghodake VN. (2014). Second generation lipid nanoparticles (NLC) as an oral drug carrier for delivery of lercanidipine hydrochloride. Colloids Surf B Biointerfaces 116:81–7.

[25] O'Driscoll CM, Griffin BT. (2008). Biopharmaceutical challenges associated with drugs with low aqueous solubility- the potential impact of lipid-based formulations. Adv Drug Deliv Rev 60: 617–24.

[26] Pandala, S., Bakshi, V., & Jadi, R. K. (2019). Formulation Development and in vitro characterization of

zolmitriptan controlled release drug delivery systems. INNOSC Theranostics Pharmacol. Sci, 2(1), 6-11.

[27] Patel, S., Bhandari, R., & Kumar, P. (2019). Development and validation of a UV spectrophotometric method for the determination of Fexofenadine Hydrochloride in bulk and tablet formulations. Research Journal of Pharmacy and Technology, 12(2), 879-883.

[28] Peppas NA. (1985). Analysis of Fickian and non-Fickian drug release from polymers. Pharm Acta Helv 60:110–11.

[29] Priyanka K, Sathali AA. (2012). Preparation and evaluation of montelukast sodium loaded solid lipid nanoparticles. J Young Pharm 4:129–37.

[30] Raj R, Mongia P, Ram A, Jain NK. (2015). Enhanced skin delivery of aceclofenac via hydrogel-based solid lipid nanoparticles. Artif Cells Nanomed Biotechnol. [Epub ahead of print]. DOI: 10.3109/ 21691401.2015.1036997.

[31] Ramasamy T, Khandasami US, Ruttala H, Shanmugam S. (2012). Development of solid lipid nanoparticles enriched hydrogels for topical delivery of anti-fungal agent. Macromol Res 20:682–92.

[32] Ranpise NS, Korabu SS, Ghodake VN. (2014). Second generation lipid nanoparticles (NLC) as an oral drug carrier for delivery of lercanidipine hydrochloride. Colloids Surf B Biointerfaces 116:81–7.

[33] Sapavatu, S. N., & Jadi, R. K. (2019). Formulation development and characterization of gastroretentive drug delivery systems of loratadine. Int. J. Appl. Pharm, 11, 91-99.

[34] Sapavatu, S. N., & Jadi, R. K. (2020). Development of floating drug delivery system for loratadine: in vitro and in vivo evaluation. International journal of pharmaceutical sciences and research, 11, 3021-2.

[35] Sapavatu, S. N., Chinthala, R., & Jadi, R. K. (2020). An overview on pharmacokinetics of polymeric nanoparticles intended for oral delivery. Journal of Young Pharmacists, 12(3)

[36] Sharaff, C. S., Renukuntla, P., Peddapalli, H., Kuchukuntla, M., Bakshi, V., & Jadi, R. K. (2024). Formulation, development, and characterization of loratadine emulgel. Journal of Applied Pharmaceutical Research, 12(2), 42-50.

[37] Sultan A.A., El Nashar N.F., Ashmawy S.M., El Maghraby G.M. (2022) Cubosomes for Enhancing Intestinal Absorption of Fexofenadine Hydrochloride: In situ and *in vivo* Investigation. Int. J. Nanomed. 17, 3543–3560.

[38] Togaru, V., Venisetty, R. K., Bakshi, V., & Jadi, R. K. (2017). Formulation Development and In Vitro Evaluation of Propranolol Hydrochloride Extended Release Matrix Tablets. Emergent Life Sciences Research, 3, 38-47.

[39] Wen X, Tan F, Jing Z, Liu Z. (2004). Preparation and study the 1:2 inclusion complex of carvedilol with beta-cyclodextrin. J Pharm Biomed Anal 34:517–23.

[40] Xie S, Zhu L, Dong Z, (2011). Preparation, characterization and pharmacokinetics of enrofloxacin-loaded solid lipid nanoparticles: influences of fatty acids. Colloids Surf B Biointerfaces 83:382–7.

[41] Zhang L, Han L, Sun X, (2012). The use of PEGylated liposomes to prolong the circulation lifetime of salvianolic acid B. Fitoterapia 83: 678–89.

[42] Zhuang CY, Li N, Wang M, (2010). Preparation and characterization of vinpocetine loaded nanostructured lipid carriers (NLC) for improved oral bioavailability. Int J Pharm 394:179–85.