CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
SJIF Impact Factor: 7.187
https://doi.org/10.5281/zenodo.22719293

Available online at: http://www.iajps.com Research Article

FORMULATION AND IN VITRO EVALUATION OF FLUCONAZOLE -LOADED SOLID LIPID NANOPARTICLES

I Naramada*[1], Are Nikhil[2], Kolukunda Sarikha[2], Harkesh Singh[2], Mohd Zareef Khan[2], Sonam Rai[2]

[1]Assistant Professor, Department of Pharmaceutics, St. Mary's College of Pharmacy, Hyderabad, Telangana.

[2]Students, Department of Pharmaceutics, St. Mary's College of Pharmacy, Hyderabad, Telangana.

Abstract:

The present study was aimed to formulate and evaluate Fluconazole loaded solid lipid nanoparticles (SLNs) for improved antifungal activity and controlled drug delivery. Fluconazole is a widely used antifungal agent, but its conventional formulations may show limited penetration and reduced therapeutic effectiveness. Solid lipid nanoparticles were developed to enhance drug stability, entrapment efficiency, and sustained drug release. The prepared formulations were evaluated for important physicochemical parameters such as particle size, entrapment efficiency, zeta potential, and in-vitro drug release studies. The results showed that the particle size of the formulations ranged within the nanometer range and demonstrated good entrapment efficiency and stability. The in-vitro drug release study showed a sustained release pattern over a period of 12 hours. Among all the formulations, F4 was found to be the optimized formulation due to its smaller particle size, higher entrapment efficiency, and better drug release profile. Stability studies indicated that the optimized formulation remained stable under different storage conditions. From the results, it can be concluded that solid lipid nanoparticles are a promising drug delivery system for improving the therapeutic efficacy of paclitaxel in anticancer therapy.

Keywords: *Fluconazole, Solid Lipid Nanoparticles, Antifungal activity, Drug Delivery System, Sustained Drug Release, Entrapment Efficiency.*

Corresponding author:

I Naramada,

Assistant Professor, St. Mary's College of Pharmacy, Hyderabad, Telangana 500025

QR CODE

Please cite this article in press ***I Narmada*** *et al.,* ***Formulation And In Vitro Evaluation Of Fluconazole - Loaded Solid Lipid Nanoparticles.,****. Indo Am. J. P. Sci, 2026; 13(09).*

INTRODUCTION:

Solid lipid nanoparticles (SLNs) are advanced colloidal drug delivery systems that have gained significant attention in pharmaceutical research due to their ability to improve drug stability, bioavailability, and therapeutic efficacy. SLNs were first introduced in the early 1990s as an alternative to traditional carrier systems such as liposomes, emulsions, and polymeric nanoparticles. They are composed of physiologically compatible lipids that remain solid at both room and body temperatures, stabilized by suitable surfactants 6.SLNs typically range in size from 50 to 1000 nm and consist of a solid lipid core matrix in which the drug is either dissolved or dispersed. This solid matrix enables controlled and sustained drug release while protecting the incorporated drug from chemical degradation. Due to their unique properties, SLNs are particularly suitable for delivering poorly water-soluble drugs, such as Paclitaxel, enhancing their solubility and bioavailability.One of the major advantages of SLNs is their biocompatibility and biodegradability, as they are prepared using physiological lipids such as triglycerides, fatty acids, and waxes. Additionally, SLNs avoid the use of toxic organic solvents in many preparation methods, making them safer for clinical applications. Their ability to provide targeted drug delivery, reduce systemic toxicity, and improve therapeutic outcomes has made them a promising approach in modern drug delivery systems.8 Furthermore, SLNs have shown great potential in various routes of administration, including oral, topical, parenteral, and pulmonary delivery. Their versatility, ease of large-scale production, and stability during storage contribute to their growing importance in pharmaceutical development. As a result, SLNs are widely explored for applications in anticancer therapy, gene delivery, and controlled drug release systems .

MATERIALS:

Fluconazole was procured from Synpharma Research Labs, Hyd, Glyceryl monostearate, Tween 80, Span 20 and Methanol were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY:

Preparation of solid lipid nanoparticle formulations of Fluconazole by hot homogenization method

The solid lipid (Glyceryl monostearate) was melted above its melting point. The drug (Fluconazole) was dissolved or dispersed in the molten lipid. An aqueous surfactant solution (Tween 40 and Span 80) was heated to the same temperature. The lipid phase was added to the aqueous phase under high-speed homogenization to form a coarse emulsion. The emulsion was subjected to ultrasonication for a specified time to reduce particle size.The nanoemulsion was cooled to room temperature to allow lipid solidification and formation of SLNs.

Table -1: Composition of Fluconazole for preparation of solid lipid nanoparticles

F.no	Drug(mg)	Glyceryl monostearate (mg)	Tween 40 (mg)	Span 80 (mg)
F1	100	100	10	-
F2	100	150	20	-
F3	100	200	-	10
F4	100	250	-	20

Evaluation of Fluconazole loaded nanoparticles:

Particle size:

To measure the mean particle size and size distribution of Fluconazole -loaded solid lipid nanoparticles (SLNs), which is critical for stability, drug release, and bioavailability.

Zeta Potential:

The zeta potential values of the prepared formulations ranged from -18.4 mV to -25.8 mV. Negative zeta potential values indicate good stability of nanoparticles due to electrostatic repulsion between particles, which prevents aggregation. Among all formulations, F4 showed the highest zeta potential (-25.8 mV) indicating better stability of the nanoparticle system.

SEM analysis:

The surface morphology and shape of Fluconazole -loaded solid lipid nanoparticles were examined using scanning electron microscopy (SEM). A small amount of lyophilized SLN powder was mounted on metallic stubs using double-sided conductive adhesive tape and coated with a thin layer of gold to enhance conductivity and prevent charging. The samples were then observed under the SEM at appropriate accelerating voltages, and images were captured at various magnifications. SEM analysis revealed that the nanoparticles were predominantly spherical with a smooth surface and uniform distribution, confirming the successful formation of SLNs. These morphological observations were correlated with particle size measurements obtained

from dynamic light scattering, providing a comprehensive understanding of the nanoparticle characteristics.

Drug Entrapment efficiency:

The entrapment efficiency of Fluconazole in solid lipid nanoparticles was determined using the indirect method. Briefly, a known volume of SLN dispersion was centrifuged at high speed (e.g., 15,000–20,000 rpm) for 30–60 minutes to separate the free (unentrapped) drug in the supernatant from the nanoparticle pellet. The supernatant was carefully collected, and the concentration of unencapsulated Fluconazole was quantified using a validated UV-Visible spectrophotometric method.

$$\text{Entrapment Efficiency (\%)} = \frac{\text{Amount entrapped}}{\text{Total drug loaded}} \times 100$$

In-vitro drug release studies

The in-vitro release of Fluconazole from solid lipid nanoparticles was evaluated using the diffusion method. Briefly, a known quantity of SLN dispersion containing a predetermined amount of Fluconazole was placed into a pre-soaked dialysis membrane with an appropriate molecular weight cut-off (e.g., 12–14 kDa). The sealed dialysis bag was immersed in a dissolution medium, such as phosphate-buffered saline (PBS, pH 7.4) or simulated body fluid, maintained at 37 ± 0.5°C with continuous stirring at 100 rpm to mimic physiological conditions. At predetermined time intervals (e.g., 1, 2, 4, 6, 8 hours), aliquots of the dissolution medium were withdrawn and replaced with an equal volume of fresh medium to maintain sink conditions. The amount of Fluconazole released was quantified using a validated UV-Visible spectrophotometric method.

Percentage of drug release was determined using the following formula.

$$\text{Perentage drug release} = \frac{\text{Da}}{\text{Dt}} \times 100$$

Where, Dt = Total amount of the drug

Da = The amount of drug released

Stability studies:

The stability of Fluconazole -loaded solid lipid nanoparticles was evaluated to assess the formulation's physical and chemical integrity over time under different storage conditions. SLN samples were stored in tightly sealed containers at refrigerated (2–8°C), room temperature (25°C ± 2°C, 60% ± 5% RH), and accelerated conditions (40°C ± 2°C, 75% ± 5% RH) for a period of 3 months.

RESULTS AND DISCUSSION:

DRUG EXCIPIENT COMPATIBILITY STUDIES

FT-IR Spectra of Fluconazole and excipients were recorded. All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Drug and lipids. It also confirmed that the stability of drug during encapsulation process.

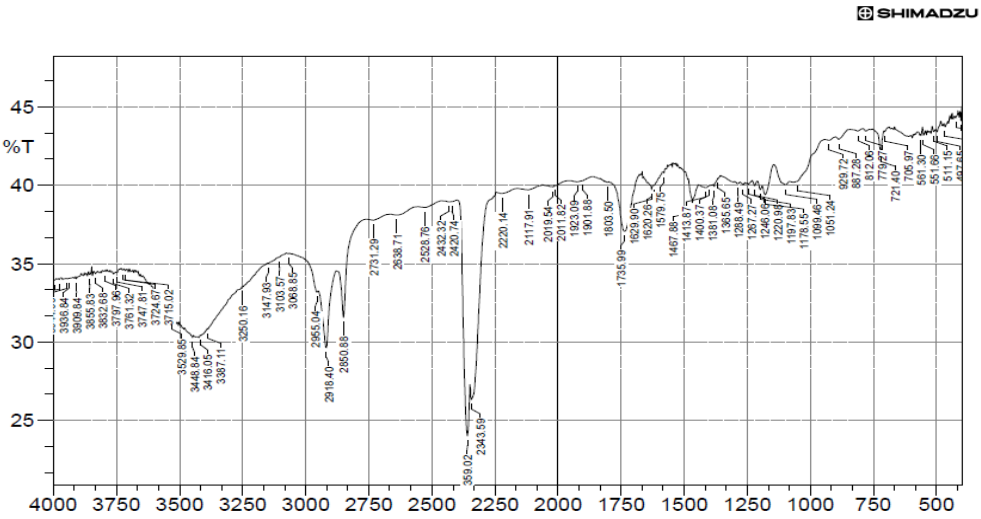

Fig-1: FTIR Spectra of Fluconazole

Table-2: Characteristic Peaks and frequency of Fluconazole

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3500	3902.75
2	OH Bending	1500-1000	1204.65
3	C-H stretching	3000-2500	2839.31
4	C=O stretching	2000-1500	1599.93

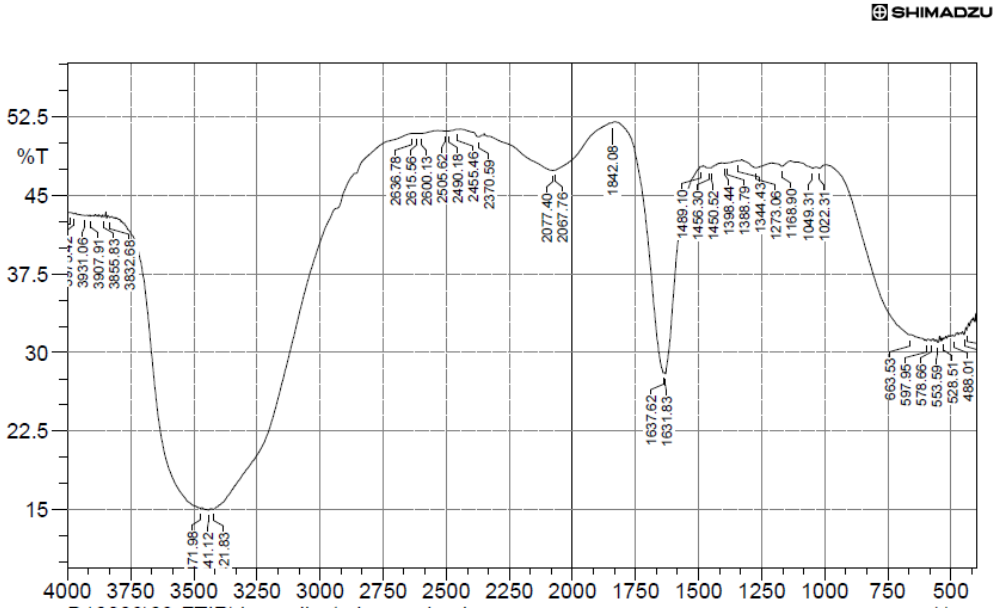

Fig-2: FTIR Spectra of Optimised Formulation

Table-3: Characteristic Peaks of Optimised Formulation

S. No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	4000-3750	3907.65
2	OH Bending	1500-1000	1481.39
3	C-H stretching	3000-2500	2633.85
4	C=O stretching	2000-1500	1635.73

EVALUATION PARAMETERS

Particle size:

With an increase in lipid concentration, the particle size increased. based on entrapment effectiveness and particle size distribution.

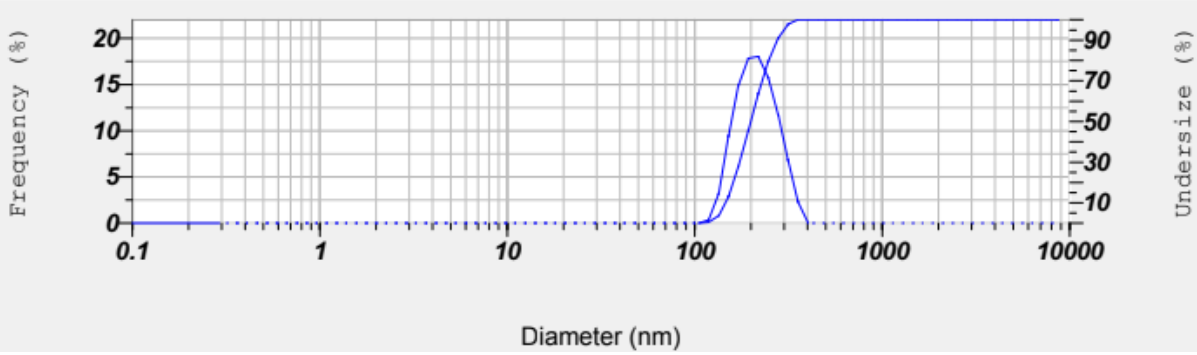

Fig-3: Particle size analysis of Optimized formulation

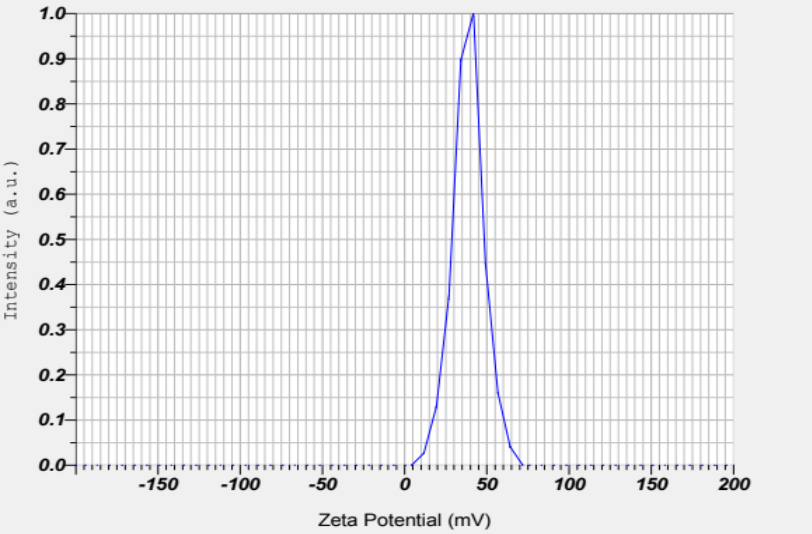

Fig-4: Zeta potential of Optimized formulation

Drug entrapment efficiency:
Optimizing the lipid concentration to be used in the creation of solid lipid nanoparticles was the first step of the work plan. Based on the particle size and entrapment effectiveness of the discovered solid lipid nanoparticles, the lipid content was optimized.

Table-4: Evaluation Studies of Prepared solid lipid nanoparticles: Entrapment Efficiency and Particle size

Batch No	Particle size (nm)	Zeta potential (mV)	Entrapment Efficiency (%)
F1	164	-18.4	72.5
F2	144	-21.6	78.2
F3	121	-23.2	81.4
F4	119	-25.8	85.6

Particle Size:
The particle size of the prepared solid lipid nanoparticles ranged from 119nm to 164 nm**.** It was observed that particle size decreased from F1 to F4**,** which indicates better homogenization and stabilization of nanoparticles. Smaller particle size improves drug absorption, stability**,** and targeting efficiency. Among all formulations, F4 showed the smallest particle size (168 nm) indicating better nanoparticle formation.

Zeta Potential:
The zeta potential values of the prepared formulations ranged from -18.4 mV to -25.8 mV. Negative zeta potential values indicate good stability of nanoparticles due to electrostatic repulsion

between particles, which prevents aggregation. Among all formulations, F4 showed the highest zeta potential (-25.8 mV) indicating better stability of the nanoparticle system.

Entrapment Efficiency (EE):
Entrapment efficiency of the prepared SLNs ranged from 72.5% to 85.6%. The results showed that entrapment efficiency increased from F1 to F4, indicating better drug incorporation within the lipid matrix. Higher entrapment efficiency suggests effective drug loading and reduced drug loss during formulation. The highest entrapment efficiency was observed in F4 (85.6%), which indicates better drug encapsulation.

Surface morphology:
According to scanning electron microscopy (SEM), the solid lipid nanoparticles were round, smooth, and free of any aggregation.

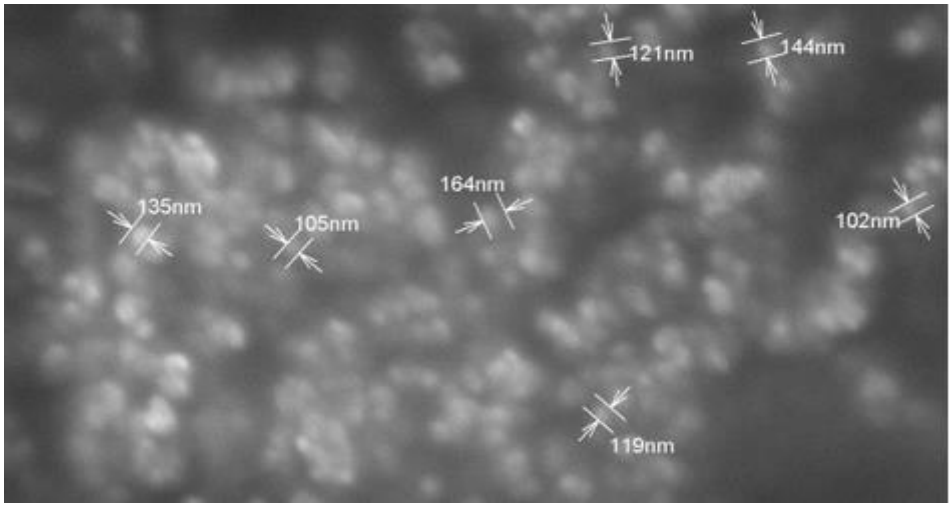

Fig-5: SEM analysis of Optimized Solid lipid nanoparticle

In vitro drug release studies

Table-5: In vitro drug release profiles of SLN (F1-F4)

Time	F1	F2	F3	F4
0	0	0	0	0
1	14.63	15.93	16.83	17.35
2	23.28	25.50	24.58	23.60
3	34.57	35.76	33.21	34.51
4	45.30	44.97	46.58	47.75
6	59.86	66.58	63.28	65.35
8	68.43	74.12	72.15	73.28
10	79.82	81.20	83.25	82.35
12	89.56	91.25	93.57	94.55

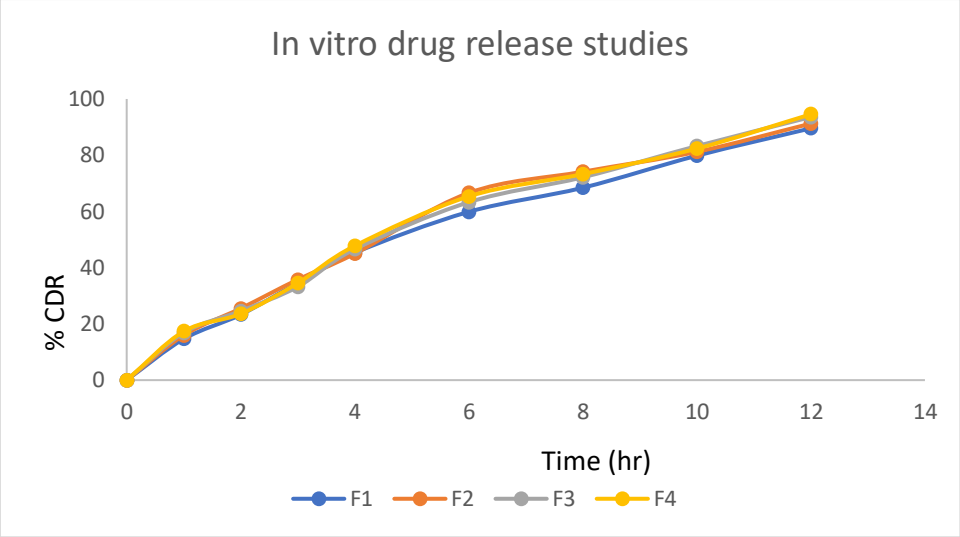

Fig-6: Drug release for (F1-F4) formulations

Observation:
The in-vitro drug release study of SLN formulations (F1–F4) showed a gradual and sustained release pattern over 12 hours. Drug release increased with time for all formulations. Among them, F4 showed the highest cumulative drug release (94.55%), followed by F3 (93.57%), F2 (91.25%), and F1 (89.56%) at 12 hours, indicating better drug release behavior and suggesting F4 as the optimized formulation.

Stability studies:

Table-6: Results of stability studies of optimized formulation F-4

Formulation Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-4	**25^{0}C/60%RH**	94.55	93.82	92.74	91.63	**Not less than**
F-4	**30^{0}C/75% RH**	94.55	93.40	92.15	90.84	**Not less than**
F-4	**40^{0}C/75% RH**	94.55	92.96	91.48	90.12	**Not less than**

The stability study results showed that the optimized formulation F4 remained stable for 3 months under different storage conditions, with only a slight decrease in drug content. The values remained within the acceptable limit (NLT 90%), indicating good stability of the SLN formulation.

CONCLUSION:

The present study was carried out to formulate and evaluate Fluconazole loaded solid lipid nanoparticles (SLNs) for enhanced antifungal activity. Fluconazole SLNs were prepared using suitable lipids and surfactants by an appropriate formulation method. Different formulations (F1–F4) were developed and evaluated for important parameters such as particle size, entrapment efficiency, zeta potential, and in-vitro drug release. The results showed that all the prepared formulations had acceptable nanoparticle characteristics and demonstrated a sustained drug release pattern. Among the formulations, F4 showed smaller particle size, higher entrapment efficiency, and better stability compared to other formulations.From the overall evaluation studies, it can be concluded that Fluconazole loaded solid lipid nanoparticles are a promising drug delivery system

for anticancer therapy. The optimized formulation F4 exhibited desirable physicochemical properties and sustained drug release behavior, indicating improved drug delivery potential. The stability studies also confirmed that the optimized formulation remained stable under different storage conditions. Therefore, the developed SLN formulation may enhance the therapeutic effectiveness of Fluconazole while reducing systemic side effects, making it a suitable approach for enhanced antifungal activity.

REFERENCES:

1. World Health Organization (WHO). *Cancer Fact Sheet*, 2023.
2. Bray F, et al. *Global cancer statistics 2020: GLOBOCAN estimates*. CA Cancer J Clin. 2021;71(3):209–249.
3. Kalyanaraman B. *Teaching the basics of cancer metabolism*. Free Radic Biol Med. 2017.
4. Chabner BA, Roberts TG. Chemotherapy and the war on cancer. Nat Rev Cancer. 2005.
5. Siegel RL, Miller KD, Jemal A. Cancer statistics. CA Cancer J Clin. 2020.
6. Mehnert W, Mäder K. Solid lipid nanoparticles: production, characterization and applications. Adv Drug Deliv Rev. 2001;47:165–196.
7. Müller RH, Mäder K, Gohla S. Solid lipid nanoparticles (SLN) for controlled drug delivery. Eur J Pharm Biopharm. 2000;50:161–177.
8. Mukherjee S, Ray S, Thakur RS. Solid lipid nanoparticles: a modern formulation approach. Indian J Pharm Sci. 2009;71(4):349–358.
9. Souto EB, Müller RH. Lipid nanoparticles: effect on bioavailability and pharmacokinetics. Int J Pharm. 2010.
10. Pardeike J, Hommoss A, Müller RH. Lipid nanoparticles (SLN, NLC) in drug delivery. Int J Pharm. 2009.
11. Bhongiri B, Ramachandran V, Kumar RS. Preformulation studies of S-Equol. Journal of Pharmaceutical Negative Results. 2022;13(4):1020-9.
12. Ekambaram P, Sathali AA, Priyanka K. Solid lipid nanoparticles: a review. Sci Revs Chem Commun. 2012;2(1):80–102.
13. Wissing SA, Kayser O, Müller RH. Solid lipid nanoparticles for parenteral drug delivery. Adv Drug Deliv Rev. 2004;56:1257–1272.
14. Das S, Chaudhury A. Recent advances in lipid nanoparticle formulations. J Control Release. 2011;146:1–10.
15. Ganesan P, Narayanasamy D. Lipid nanoparticles for drug delivery. Int J Pharm Investig. 2017;7(3):111–120.
16. Beloqui A, et al. *Nanostructured lipid carriers for oral delivery*. Nanomedicine. 2016;12:143–161.
17. Parveen R, Baboota S, Ali J, Ahuja A, Vasudev SS, Ahmad S. Preparation and evaluation of SLNs. AAPS PharmSciTech. 2009.
18. Shah R, Eldridge D, Palombo E, Harding I. Lipid nanoparticles: production and applications. Springer, 2015.