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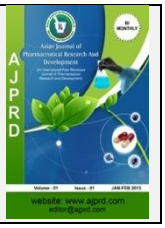

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Research Article

Formulation and Evaluation of Antifungal Nanocream for Topical Drug Delivery

Payal Mahendra Jadhav[1], Dr. Ajay Randhir Fugate[1], Dr. Vishweshwar Mahishankar Dharashive[1], Vaishnavi Laxmikant Havale[2]

[1]Shivlingeshwar College of Pharmacy, Almala, Tq-Ausa, Dist-Latur

[2]Dagadojirao Deshmukh D.Pharmacy College, Almala, Tq-Ausa, Dist-Latur

ABSTRACT

The objective of this study was to develop and optimize a nanostructured lipid carrier (NLC)-based nano cream loaded with Voriconazole for enhanced topical antifungal delivery. Voriconazole, a hydrophobic antifungal agent, exhibits poor aqueous solubility and variable bioavailability, making it a suitable candidate for lipid-based nano systems. Preformulation studies confirmed the drug's purity and solubility profile. Voriconazole was identified as a whitecrystallinepowderwithameltingpointof128–130°Canddemonstratedgoodsolubility in methanol, ethanol, and DMSO. FTIR analysis confirmed the absence of significant drug– excipient interactions.

NLCs were prepared via hot homogenization followed by ultrasonication, employing glyceryl monostearate and oleic acid as solid and liquid lipids, respectively, with Tween 80 and Poloxamer 188 as surfactants. A 3^2 factorial design was utilized to optimize formulations based on particle size and entrapment efficiency .Among the nine experimental batches, Batch F6 exhibited optimal characteristics,with a particle size of 182nm,PD Iof 0.22, zeta potential of –30 mV, entrapment efficiency of 89.41%, and drug loading of 31.8%.

Batch F6 was further incorporated into four nano cream formulations (F1–F4), varying in Carbopol 940 and stearic acid concentrations. Formulation F3 was identified as optimal, demonstrating excellent spreadability (6.1 gm.cm/sec), drug content (100.5%), and sustained drug release (79.5%over8hours). Anti fungal activity one of inhibition was found as 38mm. The optimized cream also maintained its physical stability, pH, and drug content under accelerated stability testing.

In conclusion, the developed Voriconazole-loaded NLC-based nano cream presents a promising and patient-compliant approach for effective topical antifungal therapy, offering improved drug delivery, stability, and therapeutic efficacy.

Keywords: Anti-fungal, Voriconazole, Nanocream, Carbopol 940, Topical drug delivery, statistical optimization.

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*Address for Correspondence:

Payal Mahendra Jadhav, Shivlingeshwar College of Pharmacy, Almala, Tq-Ausa,Dist-Latur

INTRODUCTION

Conventional drug delivery systems (CDDS) represent the traditional methods of administering pharmaceutical compounds for therapeutic purposes. These systems, often designed for oral, topical, or parenteral routes, rely on relatively simple mechanisms of drug release and absorption.

Mechanism and Types of Conventional Drug Delivery Systems

Conventional drug delivery involves administering the active pharmaceutical ingredient (API) in a form that releases the drug over a relatively short duration, typically without the use of advanced targeting or controlled release mechanisms. The most common forms include:

- **Oral tablets and capsules**: Suitable for systemic infections, but with limited specificity for skin fungal infections.
- **Topical creams, ointments, and gels**: Directly applied to the affected skin area and commonly used for dermal

fungal infections.

- **Parenteral injections**: Used when rapid or systemic drug delivery is necessary,though less frequently employed for skin infections. [1].

Topical drug delivery is advantageous in such cases due to:

Localized treatment, Reduced systemic exposure, Ease of use [2].

Limitations of Conventional Systems in Dermatological Use

- **Poor skin penetration**: Many antifungal agents have limited ability to penetrate the stratum corneum and reach deeper layers where fungal elements may reside [3].
- **Frequent reapplication**: Due to rapid clearance from the skin surface (via washing, sweating, or rubbing), patients must apply the medication multiple times daily.
- **Resistance development**: Sub therapeutic concentrations at the infection site may contribute to the development of resistant fungal strains.

Systemic side effects: In some cases, particularly with prolonged or large-area application, the drug may enter systemic circulation and cause adverse effects [4].

MATERIAL AND METHOD

Table1: List of Materials

Sr.No.	Material	SourceofProcurement
1.	Voriconazole	SwapnaroopAgency, India
2.	Glycerylmonostearate	ThomasBaker,Mumbai
3.	Oleicacid	ThomasBaker,Mumbai
4.	Tween80	MerckIndiaLimited,Mumbai
5.	Poloxamer188	ResearchlabFineChem,Mumbai
6.	Carbopol940	AmishiDrugs&ChemicalPvt.Ltd.
7.	Triethanolamine	Molychem,Mumbai
8.	Propyleneglycol	LobaChemie,Mumbai, India
9.	Stearic acid	ResearchlabFineChem,Mumbai
10.	Methylparaben	ThermoFisherScientificIndia,Mumbai
11.	Cetosterylalcohol	HiMediaLab.,India
12.	Ethanol	MerckIndiaLimited,Mumbai
13.	Methanol	MerckIndiaLimited,Mumbai
14.	Distilled water	Inhouse

Table 2: List of Instruments and Equipment's

Sr. No.	List of Equipment	Model
1.	Analytical Balance	Aczet CY224
2.	Magneticstirrer	Remi
3.	pH Meter	Labman LMPH-10
4.	HighSpeedHomogenizer	IKA, Silverson Remi
5.	Melting Point Apparatus	Standard Steel MP01
6.	UV-spectrophotometer	Jasco550
7.	FTIR	IR Affinity-1,Shimadzu Japan
8.	BrookfieldViscometer	LVDV-EAmtech
9.	Ultrasonic bath sonicator	Bio Technics India12L300H
10.	Franz Diffusion Cell	Perme Gear, Hanson Research
11.	Particle size analyser	Malvern DLS

1. Formulation procedure for Voriconazole Nanostructured Lipid Carriers (NLCs):

The formulation of Voriconazole NLCs was done by Hot Homogenization and Ultrasonication method which include following steps:

a. *Preparation of the Lipid Phase*

- Weigh the required quantity of Voriconazole, Glyceryl Monostearate (GMS) (solid lipid), and Oleic Acid (liquid lipid) based on the selected formulation from the 3^2 factorial design.
- Transfer the lipids and drug into a clean beaker.
- Heat the mixture to 70–75°C in a water bath (above the melting point of GMS, which is ~58°C) to ensure complete melting of lipids and dissolution of Voriconazole.
- Stir the molten mixture gently to obtain a clear, homogeneous lipid phase.

b. *Preparation of the Aqueous Phase*

- In a separate beaker, accurately weigh Tween 80 (surfactant) and Poloxamer 188 (co-surfactant).
- Dissolve them in distilled water (quantity calculated based on total batch size) and heat the aqueous phase to the same temperature (70–75°C) as the lipid phase to avoid premature lipid solidification during mixing.

c. *Formation of Pre-emulsion (Hot Homogenization)*

- Slowly add the hot aqueous phase to the hot lipid phase under continuous high- speed stirring.
- Homogenize the mixture using a high-speed homogenizer at 15,000 rpm for 10 minutes.
- This process leads to the formation of a coarse oil-in-water emulsion, where lipid droplets are dispersed in the aqueous phase.

d. *Size Reduction by Ultrasonication*

- Transfer the coarse emulsion to an ultrasonicator and sonicate the emulsion at 40– 60% amplitude for 5–10 minutes, depending on equipment specifications.
- Sonication breaks down the large lipid droplets into nanometre-sized particles, forming a nano emulsion.

e. *Cooling and Solidification*

- After ultrasonication, allow the hot nano emulsion to

cool gradually to room temperature under gentle magnetic stirring.

- During cooling, the lipid phase solidifies, converting the nano emulsion into nanostructured lipid carriers (NLCs) with solid lipid cores.
- Store the formulation at 4 – 8 ^{0}C for further evaluation and stability studies.

2. Formulation procedure for Voriconazole Nano cream by using NLCs:

For the formulation of nano cream Emulation-based gel cream formulation using hot emulsification technique method was used as per following steps:

i. *Preparation of Carbopol gel base*

- Disperse Carbopol 940 in 60–70% of distilled water under gentle stirring.
- Allow to hydrate for 30–60 minutes.
- Adjust pH to 5.5–6.5 with Triethanolamine (TEA) to form a clear gel.

ii. *Preparation of Oil phase*

- In a separate beaker, melt and mix Stearic acid, Cetosteryl alcohol at 70–75°C until completely melted.

iii. *Incorporate NLC and Water-soluble Ingredients*

- Add propylene glycol and methyl paraben to the carbopol gel (or dissolve separately and add).
- Add Tween 80 and Optimized Voriconazole NLC (F6) to the gel base and mix thoroughly at room temperature.

iv. *Emulsification*

- Slowly add the hot oil phase into the gel base under mechanical stirring or homogenization (1000–1500 rpm) until uniform.

v. *Final Adjustment and Packaging*

- Check and adjust the pH to 5.5–6.5 if required.
- Allow to cool to room temperature
- Transfer into airtight, sterile cream container and store at room temperature or under refrigeration.

RESULT AND DISCUSSION

Preformulation study:

a. Drug Characterization

Drug characterization parameters such as colour, odour and appearance were analysed for the procured drug samples and the results were shown in table 8.

Table 3: Drug Characterization parameters

Colour	White
Odour	Odourless
Appearance	Crystallinepowder

a. Determination of melting point:

The melting point of Voriconazole was found to be in the range of **128-130^{0}C**.

b. *Solubilitystudy:*

The solubility study of Voriconazole was carried out by using different solvent systems as per the literature. The solubility results were shown in table 4.

Table 4: Results for solubility study

Sr. No	Solvent	Observation
1.	Methanol	Soluble
2.	Ethanol	Soluble
3.	Dimethyl sulfoxide(DMSO)	Soluble
4.	Acetone	Soluble
5.	Water	Insoluble

FT-IR of Voriconazole:

The IR spectrum of Voriconazole was recorded by using FTIR spectrometer. IR spectra were shown in figure 8. Characteristic functional groups were observed in FTIR spectrum as shown in table 6.

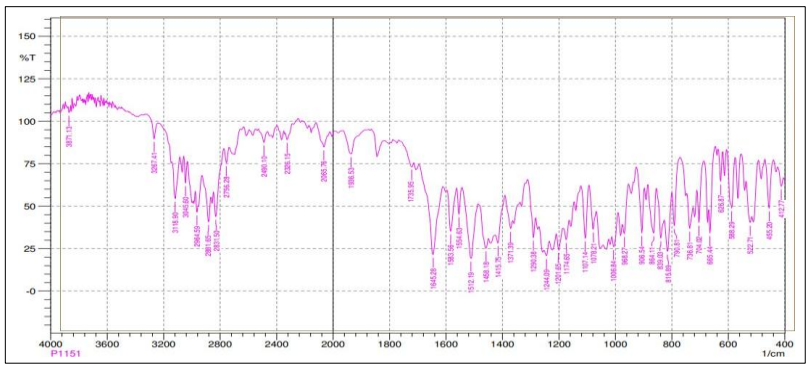

Figure 1: IR of Voriconazole

Table 5: IR frequencies of Voriconazole functional group

Functional group	Observed Frequency	Reported Frequency
O-H stretching (Hydroxylgroup)	3267.41	3500 - 3200
C-H stretching (Aromaticgroup)	2964.59	3000 - 2800
C=O stretching (Carbonylgroup)	1735.95	1750 - 1650
C=N stretching (Imidazolering)	1583.56	1650 - 1570
C-Fstretching (Fluoro group)	1371.39	1400 - 1000
C-O stretching (Ether stretching)	1244.09	1300 - 1050

Drug excipients compatibility study:

The FTIR Spectra of Voriconazole in pure form and their physical mixture was observed; the result showed that there is no interaction between drug, polymer and excipients

Table 6: Factorial Design Model Parameters

Independent variables	Name	Unit	Levels		
			Low(-1)	Middle	High(+1)
X1	Glyceryl monostearate	%	3	4	5
X2	Oleicacid	%	1	2	3

Table 7: Formulation strategy

Sr.no.	Ingredients	Quantity(%w/v)								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1.	Voriconazole	1	1	1	1	1	1	1	1	1
2.	Glyceryl monostearate	3	3	3	4	4	4	5	5	5
3.	Oleicacid	1	2	3	1	2	3	1	2	3
4.	Tween80	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
5.	Poloxamer188	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
6.	Distilled water	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Total		1 gm batch								

Figure 2: Voriconazole NLCs

Evaluation of Nano structured Lipid Carrier batches:

Particle size (nm):

The particle size analysis of all nine batches of Voriconazole-loaded nanostructured lipid carriers (NLCs) revealed a size range between 170 nm and 280 nm, indicating successful nanoscale formulation. Batch F9 exhibited the smallest particle size (170 nm), which is favorable for enhanced cellular uptake, skin permeation, and sustained drug release. Conversely, Batch F1 recorded the largest particle size (280nm), which may contribute to reduced surface area and relatively slower drug diffusion. The consistently small particle sizes across all batches suggest effective emulsification during the hot homogenization and ultra sonication process, and confirm the suitability of the selected lipid and surfactant system for achieving stable and efficient NLC formulations. These particle size values also support optimal drug encapsulation and controlled topical delivery, essential for the desired therapeutic efficacy of the nanocream.

Table 8: Particle size analysis (nm)

Batches	Particlesize(nm)
F1	280 ± 5
F2	268 ± 4
F3	254 ± 4
F4	215 ± 3
F5	196 ± 3
F6	182 ± 2
F7	192 ± 3
F8	175 ± 4
F9	170 ± 3

Figure17: Voriconazole NLCs

Evaluation of Nano structured Lipid Carrier batches:

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Table 9: Particle size analysis (nm)

Batches	Particlesize(nm)
F1	280 ± 5
F2	268 ± 4
F3	254 ± 4
F4	215 ± 3
F5	196 ± 3
F6	182 ± 2
F7	192 ± 3
F8	175 ± 4
F9	170 ± 3

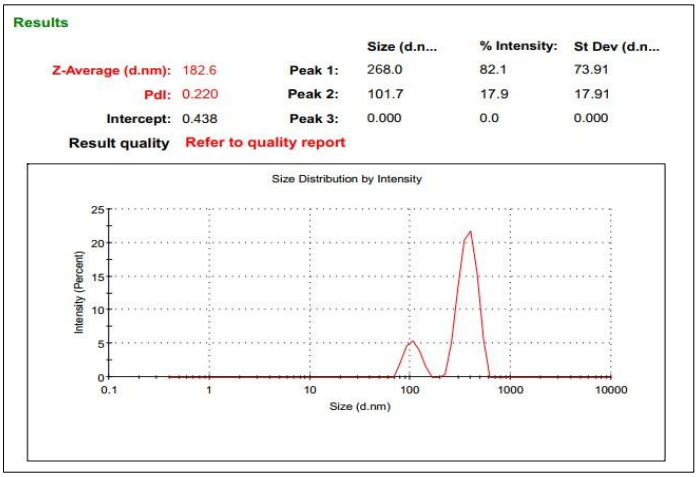

Figure 18: Particle size and PDI Report

Polydispersity Index (PDI):

The PDI values for all 9 batches ranged from 0.210 to 0.340, reflecting acceptable to excellent particle size uniformity across formulations. Batch F6 demonstrated the lowest PDI value (0.220), indicating highly uniform and mono disperse nano particle distribution, which contributes significantly to the physical stability, reproducibility, and consistent drug release of the formulation.

On the other hand, Batch F1 exhibited the highest PDI (0.340), suggesting a wider particle size distribution, which could potentially affect the stability and homogeneity of the system.

However, since all batches maintained PDI values below 0.4, the formulations are considered to be within acceptable limits for NLC systems, ensuring good colloidal stability and suitability for topical delivery.

The results were expressed in table.

Table 10: Polydispersity index (PDI)

Batches	PDIvalue
F1	0.34
F2	0.31
F3	0.28
F4	0.30
F5	0.26
F6	0.22
F7	0.25
F8	0.23
F9	0.22

Zeta Potential (mV):

Zeta potential is an important indicator of the surface charge and electrostatic stability of nanoparticles. The zeta potential values across all batches ranged from –21.6mV to –35.7 mV, indicating moderate to good physical stability of the NLC dispersions. Batch F6 exhibite dazeta potential of –30 mV, signifying strong repulsive forces between particles, which help in preventing aggregation and maintaining dispersion stability.

Generally, a zeta potential value above ±30 mV is considered ideal for stable colloidal systems. The results confirm that the developed NLC spossess sufficient surface charge to remain stable during storage and application. Results were shown in table 11.

Table11: Zeta potential

Batches	ZetaPotential(mV)
F1	-21.6
F2	-22.7
F3	-24.2
F4	-26.0
F5	-28.5
F6	-30.0
F7	-32.8
F8	-34.7
F9	-35.7

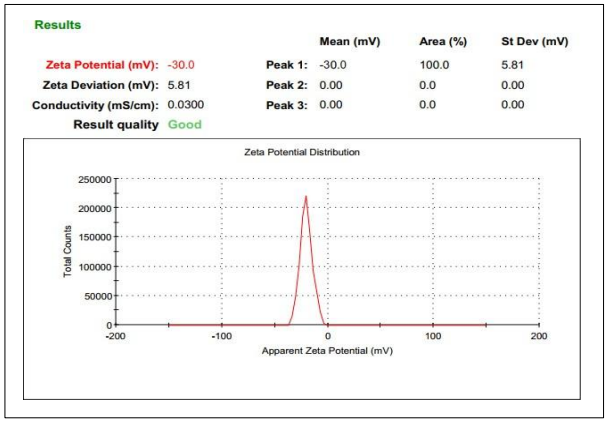

Figure 19: Zeta Potential Report

Entrapment Efficiency (%EE):

Entrapment efficiency is a key parameter that determines the capacity of lipid matrices to encapsulate and retain the active drug. The % EE values for the formulated NLCs ranged from 72.25 % to 89.41 %, with a notable trend of increased entrapment at higher concentrations of Oleic Acid, the liquid lipid. This can be attributed to the enhanced solubilization of Voriconazole within the oily matrix, thereby reducing the amount of free drug. The maximum entrapment efficiency was achieved in BatchF6 (89.41±1.9%), which had a balanced ratio of solid and liquid lipids, providing an optimal microenvironment for drug retention. On the other hand, Batch F1 recorded the lowest % EE (72.25 ± 1.1 %), reflecting suboptimal lipid composition for efficient drug encapsulation. These findings suggest that formulation factors significantly influence drug entrapment characteristics in NLC systems. The results for entrapment efficiency were shown in table 12.

Table 12: Entrapment Efficiency

Batches	Entrapment Efficiency (%)
F1	72.25 ± 1.1
F2	79.44 ± 1.4
F3	82.94 ± 1.5
F4	76.23 ± 1.2
F5	84.81 ± 2.3
F6	89.41 ± 1.9
F7	79.91 ± 1.8
F8	86.61 ± 1.1
F9	86.54 ± 2.0

Determination of Drug loading (%DL):

Drug loading (DL%) is a critical parameter that reflects the efficiency with which the lipid matrix accommodates the active pharmaceutical ingredient relative to the total lipid content. The results showed that the drug loading of Voriconazole in NLCs ranged from 22.5% to 32.0%, indicating excellent drug incorporation within the lipid phase. The highest drug loading was observed in Batch F6 (31.8%), attributed to the optimal ratio of Glyceryl Monostearate and Oleic Acid, which provided a suitable lipid environment for solubilizing and entrapping the hydrophobic drug. Conversely, Batch F1 demonstrated the lowest DL% (22.5%), likely due to lower lipid concentration and suboptimal lipid-drug compatibility. These findings confirm the efficiency of the hot homogenization– ultra sonication method and underscore the significance of lipid composition in maximizing drug loading for effective topical delivery of nano cream. The results were expressed in table 13.

Table 13: Drug Loading

Batches	Drug Loading (%DL)
F1	22.5 ± 0.6
F2	24.3 ± 0.5
F3	26.1 ± 0.7
F4	24.7 ± 0.6
F5	27.8 ± 0.5
F6	31.8 ± 0.4
F7	25.5 ± 0.6
F8	29.3 ± 0.6
F9	32.0 ± 0.5

Drug Content (%):

Drug content analysis was conducted to assess the uniformity and accuracy of Voriconazole incorporation within the NLC formulations. The results showed that all nine batches exhibited drug content in the range of 94.2% ± 0.6 to 99.4% ± 0.3, confirming minimal drug loss during formulation and efficient entrapment within the lipid matrix. The highest drug content was observed in Batch F6 (99.4% ± 0.3), validating its status as the optimized formulation. This high drug content may be attributed to the effective solubilization of Voriconazole within the combined solid and liquid lipid system and the use of optimized surfactant concentrations. In contrast, Batch F1 showed the lowest drug content (94.2%±0.6),which could be linked to lower lipid and surfactant levels, leading to slight drug loss during processing. All formulations demonstrated drug content values above 94%, indicating excellent uniformity, reproducibility, and suitability for further development into a topical nano cream formulation.

Table 14: Drug content (%)

Batches	Drug Content (%)
F1	94.2 ± 0.6
F2	95.5 ± 0.4
F3	96.8 ± 0.5
F4	95.0 ± 0.6
F5	97.6 ± 0.4
F6	99.4 ± 0.3
F7	95.8 ± 0.5
F8	98.5 ± 0.3
F9	99.0 ± 0.4

Optimization of Voriconazole NLCs:

To study the effect of independent variables on responses Design Expert 7.0 soft ware was used. Experimental design layout developed for 9 possible batches of Voriconazole NLCs is shown in table. Out of the various models such as Linear, 2FI, Quadratic and Cubic which fit well was suggested by software and was tested for analysis of variance (ANOVA). Regression polynomials were calculated for the individual dependent variables and then one factor and perturbation graphs were obtained for each individual dependent variable.

Table 15: The layout of the Actual Design

Runs	Factor1 A:%GMS	Factor2 B: % Oleicacid	Response1 Particlesize (nm)	Response2 EE%
1	5	3	170	86.54
2	4	3	182	89.41
3	5	1	192	79.91
4	3	3	254	82.94
5	4	1	215	76.23
6	3	2	268	79.44
7	3	1	280	72.25
8	4	2	196	84.81
9	5	2	175	86.61

Results for the Particle size:

Fit Summary: After entering the data in Design-Expert software, fit summary applied to the data after which the" Quadratic vs 2FI"was suggested by the software. Data was expressed in table 16.

Table 16: Fit summary table for particle size

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob>F	
Meanvs Total	414736.00	1	414736.00			
Linearvs Mean	12797.67	2	6398.83	28.22	0.0009	
2FIvs Linear	4.00	1	4.00	0.01	0.9081	
Quadratic vs 2 FI	1313.00	2	656.50	45.45	0.0057	Suggested
Cubic vs Quadratic	43.33	2	21.67	63660000.00	<0.0001	Aliased
Residual	0.00	1	0.00			
Total	428894.00	9	47654.89			

1. ANOVA for Particle size:

The analysis of variance (ANOVA) was performed to identify significant and insignificant factors. The results of ANOVA for the particle size are as following table 17.

Table 17: ANOVA table for a particle size

Source	Sum of Squares	df	Mean Square	F Value	p-value Prob > F	
Model	14098.17	3	4699.39	392.7065924	<0.0001	significant
A-GMS	11704.17	1	11704.17	978.06	<0.0001	
B-Oleic acid	1093.50	1	1093.50	91.38	0.0002	
A^2	1300.50	1	1300.50	108.68	0.0001	
Residual	59.83	5	11.97			
C or Total	14158.00	8				

The Model F-value of 392.71 implies the model is significant.There is only a 0.01% chance that a "Model F-Value" this large could occur due to noise.

Values of " Prob > F "less than 0.0500 indicate model terms are significant. In this case A, B and A^2 are significant model terms.

2. Fit Statistics for particle size

Table 18: Fit Statistics for particle size

Std. Dev.	3.46	R-Squared	0.9958
Mean	214.67	Adj R-Squared	0.9932
C.V. %	1.61	PredR-Squared	0.9855
PRESS	205.69	Adeq Precision	50.010

The "Pred R-Squared" of 0.9855 is in reasonable agreement with the "Adj R-Squared" of 0.9932. "Adeq Precision" measures the signal to noise ratio.A ratio greater than 4 is desirable.

ratio of 50.010 indicates an adequate signal.This model can be used to navigate the design space.

3. Final Equation in Terms of coded Factors for particle size:

Table 19: Final equation in terms of coded factor for particle size

Particle size	=
+197.67	
-44.17	* A
-13.50	* B
+25.50	*A^2

The equation in terms ofcoded factors can be used to make predictions about the response for given levels of each factor.

4. Graphical Presentation: Diagnostics of particle size

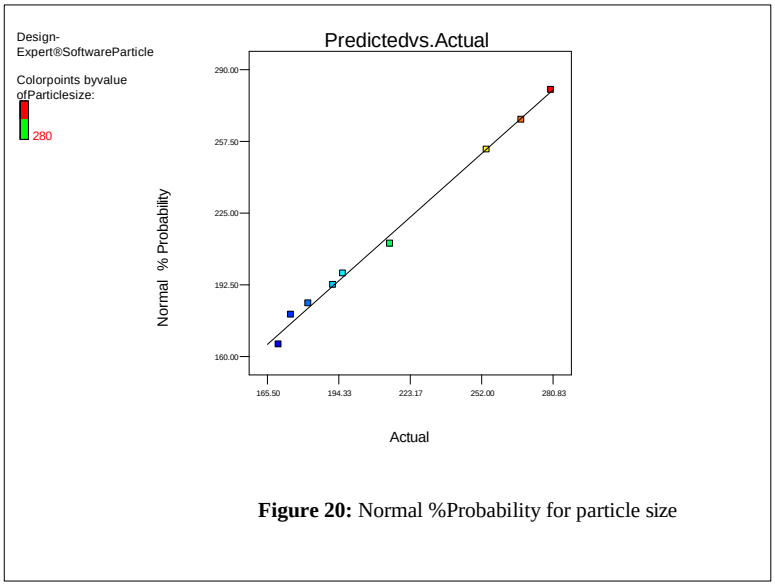

Figure 20: Normal %Probability for particle size

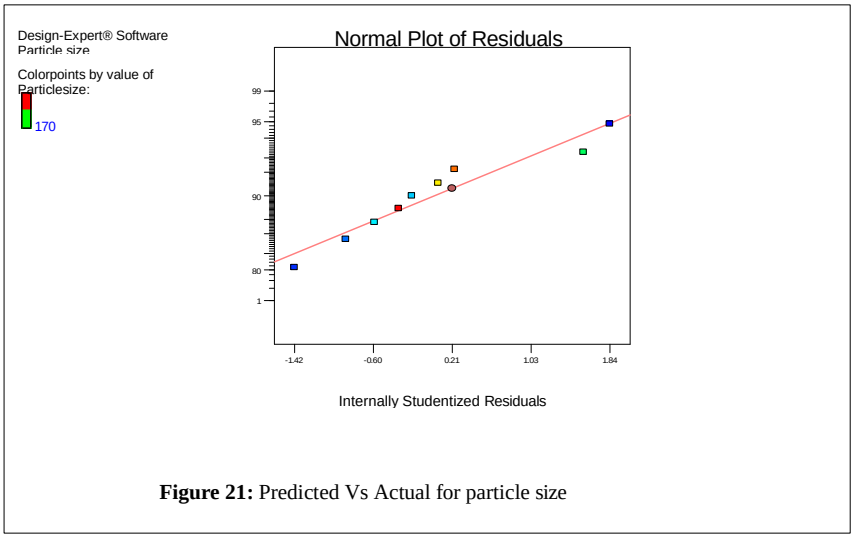

Figure 21: Predicted Vs Actual for particle size

5. Model Graphs of particle size: One-factor Graphs of particle size:

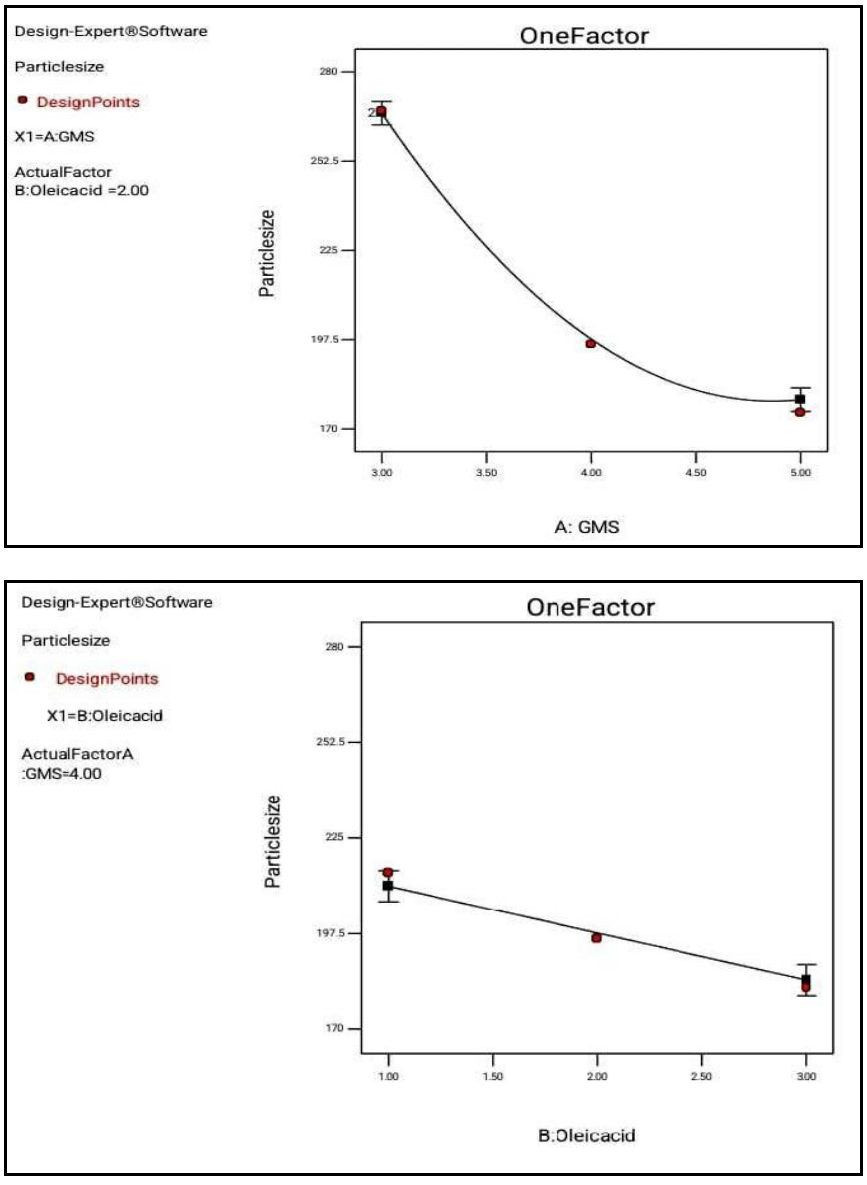

Figure 22: Effect of % GMS on particle size

CONCLUSION

It was successfully demonstrated that the feasibility of incorporating Voriconazole into NLCs and formulating them into a nano cream for enhanced topical delivery. Batch F6 was identified as the optimized NLC formulation due to its superior physical, chemical, and encapsulation properties. Furthermore, when integrated into a nano cream (F3), it showed ideal viscosity, spreadability, high drug content, and sustained drug release over 8 hours. These findings suggest that nanostructured lipid-based topical formulations hold significant promise for the effective management of dermal fungal infections, ensuring enhanced drug stability, penetration, and patient compliance.

REFERENCES

1. Jaiswal P, Gidwani B and Vyas A: Nanostructured lipid carriers and their current application in targeted drug delivery. Artificial Cells Nano medicine and Biotechnology 2016; 44(1):27-40.
2. Sharma A and Baldi A: Nano structured lipid carriers: A review. Journal of Developing Drugs 2018; 7(2):1000191.
3. Nandvikar NY, Lala RR and Shinde A S: Nanostructured lipid carrier: the advanced lipid carriers. Int J Pharm Sci Res 2019; 10(12):5252-65.
4. Patel DK, Kesharwani R and Kumar V: Lipid nanoparticle topical and transdermal delivery: a review on production, penetration mechanism to skin. International Journal of Pharmaceutical Investigation 2019; 9(4): 148-53.
5. Shah R, Eldridge D, Palombo E and Harding I: Lipid nanoparticles: Production, characterization and stability. New York, NY, USA: Springer International Publ 2015.
6. Boskabadi M, Saeedi M, Akbari J, Morteza-Semnani K, Hashemi SM and Babaei A: Topical gel of vitamin A solid lipid nanoparticles: A hopeful promise as a dermal delivery system. Advanced Pharmaceutical Bulletin 2021; 11(4): 663.
7. Jenning V and Gohla S: Comparison of wax and glyceride solid lipid nanoparticles (SLN®). International Journal of Pharmaceutics 2000; 196(2): 219-22.
8. Mishra V, Bansal K K ,Verma A,YadavN,Thakur S, Sudhakar K and Rosenholm JM: Solid lipid nanoparticles: Emerging colloidal nano drug delivery systems. Pharmaceutics 2018; 10(4): 191.
9. Müller RH, Radtke M and Wissing SA: Nanostructured lipid matrices for improved microencapsulation of drugs. International J of Pharmaceutics 2002; 242(1-2): 121-8.
10. Jaiswal P, Gidwani B and V yas A: Nanostructured lipid carriers and their current application in targeted drug delivery. Artificial Cells Nanomedicine and Biotechnology 2016; 44(1): 27-40.
11. Khosa A, Reddi S and Saha RN: Nanostructured lipid carriers for site-specific drug delivery. Biomedicine & Pharmacotherapy 2018; 103: 598-613.
12. Soni K, Kukereja BK, Kapur M and Kohli K: Lipid nanoparticles: future of oral drug delivery and their current trends and regulatory issues. Int J Curr Pharm Rew Res2015; 7(1): 1-8.
13. Sharma A and Baldi A: Nanostructured lipid carriers: A review. Journal of Developing Drugs 2018; 7(2):1000191.
14. Joshi M and Patravale V: Formulation and evaluation of nanostructured lipid carrier (NLC)–based gel of Valdecoxib. Drug Development and Industrial Pharmacy 2006; 32(8): 911-8.
15. Subramaniam B, Siddik ZH and Nagoor NH: Optimization of nanostructured lipid carriers: Understanding the types, designs, and parameters in the process of formulations. Journal of Nanoparticle Research 2020; 22(6): 1-29.
16. Ahmad J, Rizwanullah M, Amin S, Warsi MH, Ahmad MZ and Barkat M: Nanostructured lipid carriers (NLCs): Nose-to-brain delivery and theranostic application. Current Drug Metabolism 2020; 21(14): 1136-43.
17. Elmowafy M and Al-Sanea M M: Nanostructured lipid carriers (NLCs) as drug delivery platform: Advances in formulation and delivery strategies. Saudi Pharmaceutical Journal 2021; 29(9): 999-1012.
18. PurohitDK:Nano-lipidcarriersfortopicalapplication:Currentscenario.AsianJournal of Pharmaceutics (AJP): Free full text articles fromAsian J Pharm 2016; 10(1).
19. Radtke M, Souto EB and Müller RH: Nanostructured lipid carriers:a novel generation of solid lipid drug carriers. Pharm Technol Eur 2005; 17(4): 45-50.
20. Fang CL, A Al-Suwayeh S and Fang JY: Nanostructured lipid carriers (NLCs)for drug delivery and targeting. Recent Patents on Nanotechnology 2013; 7(1): 41-55.
21. Thirupathi G, Swamy SK and Ramesh A: Solid lipid nanocarriers as alternative drug delivery system for improved oral delivery of drugs. Journal of Drug Delivery and Therapeutics 2020; 10(6): 168-72
22. Torchilin V: Editor Handbook of Materials for Nanomedicine: Polymeric Nanomaterials. CRC Press 2020; 16Verma, D. D., et al. (2003). Particle size of liposomes influences dermal delivery of substances. *International Journal of Pharmaceutics*, (258(1-2):141-151.
23. Lopes, L.B.(2007).Overcoming the cutaneous barrier with micro emulsions *Pharmaceuticals*,3(2),147–165.
24. Pathan, I. B., & Setty, C. M. (2009). Chemical penetration enhancers for transdermal drug delivery systems. *Tropical Journal of Pharmaceutical Research*, 8(2):173–179.
25. Barry, B.W. Novel mechanisms and devices to enable successful transdermal drug delivery. *European Journal of Pharmaceutical Sciences*, 2001; 14(2):101–114.
26. Benson, H.A. Transdermal drug delivery: Penetration enhancement techniques .*Current Drug Delivery*, 2005; 2(1):23–33.
27. Prausnitz, M. R., & Langer, R. Transdermal drug delivery. *Nature Biotechnology*, 2008; 26(11):1261–1268.
28. Williams, A. C., & Barry, B. W. Penetration enhancers. *Advanced Drug Delivery Reviews*, 2004;56(5):603–618.
29. Zhang, L., et al.. Nanoparticles in medicine: Therapeutic applications and developments. *Clinical Pharmacology & Therapeutics*, 2008; 83(5), 761–769.
30. Souto, E. B., & Müller, R. H. Cosmetic features and applications of lipid nanoparticles (SLN®,NLC®).*International Journal of Cosmetic Science*,2008; 30(3),157– 165.
31. Prow,T.W.,etal.Nanoparticlesandmicroparticlesforskindrugdelivery. *Advanced Drug Delivery Reviews* 2011; 63(6):470–491.
32. Honeywell-Nguyen, P.L., & Bouwstra, J.A.Vesiclesin topical drug delivery: Skin penetration and barrier recovery. *Advanced Drug Delivery Reviews*, 2005; 57(4):411– 435.
33. Ventola, C. L. The nanomedicine revolution. *Pharmacy and Therapeutics*, 2012; 37(9):512–525.
34. Sahoo, S. K., et al. Nanotechnology in drug delivery. *Drug Discovery Today*, 2007; 12(21–2):865–873.
35. Nair, R., et al. Nanoparticulate drug delivery system for bioavailability enhancement of poorly water-soluble drugs. *Current Nanoscience*, 2010; 6(3):193–206.
36. Müller, R.H.,etal. Solid lipid nanoparticles (SLN) for controlled drug delivery – A review of the state of the art. *European Journal of Pharmaceutics and Biopharmaceutics*, 2000; 50(1):161–177.
37. Pardeike, J., et al. Lipid nanoparticles (SLN, NLC) in dermal drug delivery: Concepts, recent advances, and future challenges.

Advanced Drug Delivery Reviews, 2009; 61(6):427–443.

38. Radtke, M., et al. Nanostructured lipid carriers (NLC):A novel generation of solid lipid drug carriers. *Pharmaceutical Technology Europe*, 2005; 17(4), 45–50.
39. Mehnert, W., & Mäder, K. Solid lipid nanoparticles: Production, characterization and applications. *Advanced Drug Delivery Reviews*, 2012; 64:83–101.
40. Wissing, S. A., & Müller, R. H. The influence of the crystallinity of lipid nanoparticles on the occlusive properties. *International Journal of Pharmaceutics*, 2003; 242(1–2):377–379.
41. Jenning,V.,etal.Solidlipidnanoparticlesforparenteraldrugdelivery.*AdvancedDrugDeliveryReviews*,2000; 47(2–3):229–245.
42. Müller, R. H., et al. Nanostructured lipid matrices for improved microencapsulation ofdrugs. *International Journal of Pharmaceutics*, 2002; 242(1–2):121– 128.
43. Beloqui, A., et al. Nanostructured lipid carriers: Promising drug delivery systems for future clinics. *Nanomedicine: Nanotechnology, Biology and Medicine*, 2016; 12(1):143–161.
44. Doktorovova, S., et al. Preclinical safety of solid lipid nanoparticles and nanostructured lipid carriers: Current evidence from in vitro and in vivo studies. *Nanomedicine*, 2014; 9(5):673–692.
45. Muller, R. H., et al. (2007). Nanostructured lipid carriers (NLC) in cosmetic dermal products. *Advanced Drug Delivery Reviews*, 2007; 59(6):522–530.