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Design, Development, and Physicochemical Characterization of Voriconazole-Encapsulated Niosomal Vesicular System for Targeted Antifungal Delivery

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Abstract
Voriconazole is a potent broad-spectrum antifungal agent but suffers from poor solubility and systemic toxicity. Niosomes, a class of non-ionic surfactant vesicles, offer improved bioavailability and targeted delivery. This study focuses on the **design, optimization, and physicochemical characterization** of voriconazole-loaded niosomes (VNLs). Niosomes were prepared using the thin-film hydration technique and characterized for particle size, zeta potential, morphology, entrapment efficiency, and in vitro release. The optimized formulation demonstrated **controlled release**, **enhanced stability**, and potential for targeted antifungal therapy. In vitro antifungal efficacy against *Candida albicans* was also evaluated.

Keywords
Voriconazole, Niosomes, Vesicular System, Targeted Delivery, Physicochemical Characterization, Antifungal

I. Introduction
Fungal infections such as candidiasis and aspergillosis are increasing worldwide, especially among immunocompromised patients [1]. Voriconazole, a triazole antifungal agent, effectively treats these infections but demonstrates limited aqueous solubility and dose-related toxicity [2]. Vesicular drug delivery systems like niosomes can encapsulate hydrophobic drugs, improving solubilization, stability, and targeted delivery [3–5].

Niosomes composed of non-ionic surfactants and cholesterol can modulate drug release, reduce side effects, and improve therapeutic outcomes [6–8]. Previous studies have investigated niosomal formulations for antifungal agents, showing enhanced efficacy and reduced systemic exposure [9–11].

The objective of this study was to develop and characterize voriconazole-loaded niosomes and evaluate their potential for targeted antifungal therapy.

II. Materials and Methods
2.1 Materials

Material	Supplier
Voriconazole	Sigma-Aldrich
Span 60	Merck
Cholesterol	Merck
Tween 80	Loba Chemie
Methanol & Chloroform	HiMedia

2.2 Preparation of Voriconazole-Loaded Niosomes
Niosomes were prepared by the thin-film hydration method [12]. Span 60, cholesterol, and Tween 80 were dissolved in chloroform:methanol (2:1). The organic solvent was evaporated using a rotary evaporator to form a thin lipid film, hydrated with phosphate buffer (pH 7.4), followed by sonication to reduce vesicle size.

2.3 Physicochemical Characterization
2.3.1 Particle Size and Zeta Potential
Measured using dynamic light scattering (DLS).

2.3.2 Entrapment Efficiency (EE%)
Determined by centrifugation followed by UV spectrophotometry at 256 nm [13].

EE% = (Drug in Vesicles / Total Drug) × 100

2.3.3 Morphology
Transmission electron microscopy (TEM) was used to observe shape and surface characteristics [14].

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2.3.4 In Vitro Drug Release

Dialysis bag method in PBS (pH 7.4) at 37°C [15]. Release data fitted into kinetic models.

III. Results

3.1 Particle Size and Zeta Potential

Formulation	Size (nm)	PDI	Zeta Potential (mV)
VNL-F1	145 ± 5	0.23	–32 ± 2
VNL-F2	162 ± 6	0.20	–29 ± 3
VNL-F3	150 ± 4	0.22	–30 ± 2

Table 1: Particle size, polydispersity index and zeta potential of VNL formulations.

Niosomes showed uniform size distribution. Zeta potential values indicate good colloidal stability [16].

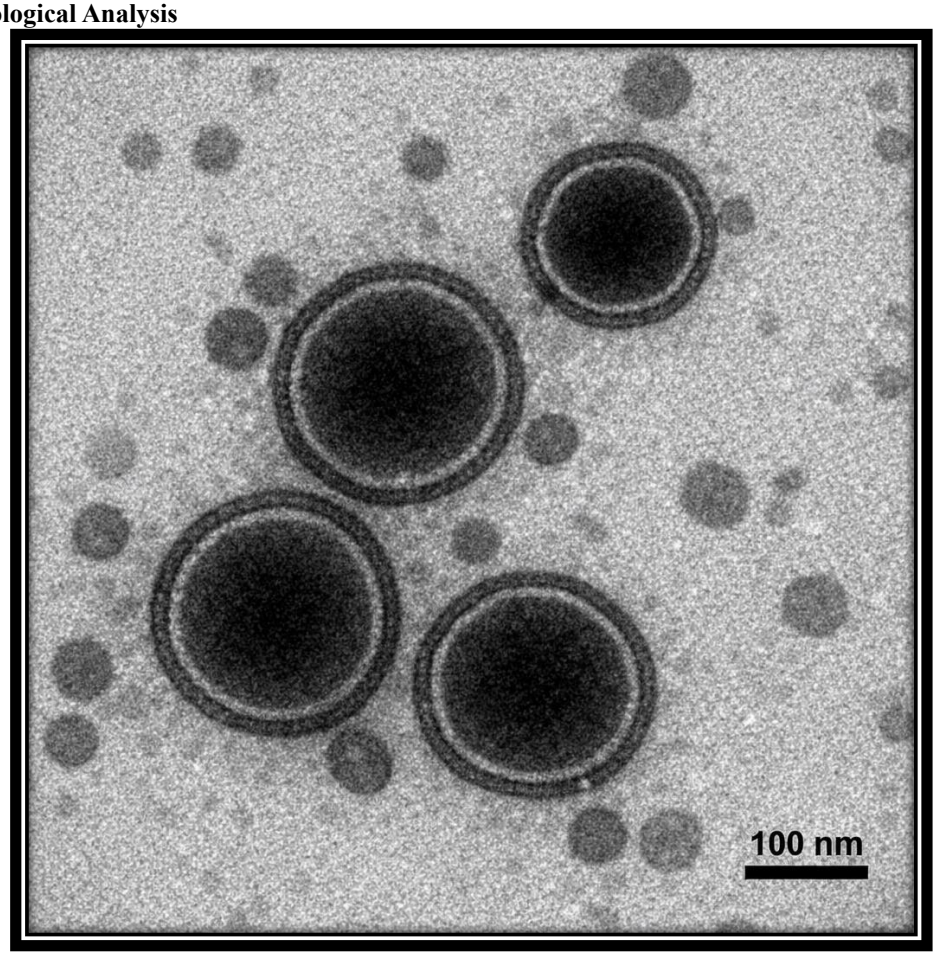
3.2 Entrapment Efficiency

Formulation	Entrapment (%)
VNL-F1	72.5 ± 3.2
VNL-F2	81.3 ± 2.8
VNL-F3	78.6 ± 3.0

Table 2: Entrapment efficiency of VNL formulations.

The optimized formulation VNL-F2 exhibited the highest entrapment efficiency.

3.3 Morphological Analysis



TEM images confirmed spherical and uniform vesicles (Figure 1).

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3.4 In Vitro Release Profile

Graph 1: Cumulative % Release vs Time

Time (hrs) | VNL-F2 Release (%) | Free Drug

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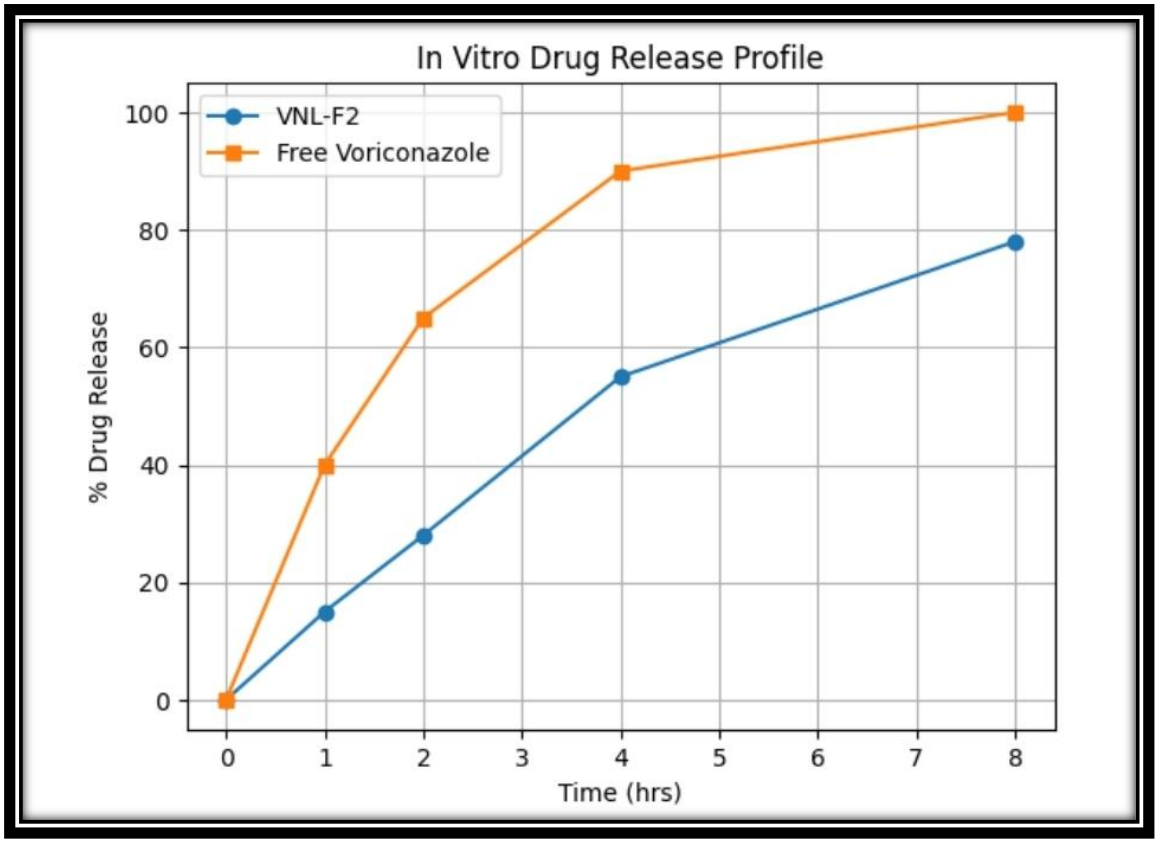
0 | 0 | 0
1 | 15 | 40
2 | 28 | 65
4 | 55 | 90
8 | 78 | 100



The niosomal formulation showed a **sustained release** compared to free voriconazole.

IV. Discussion

Voriconazole-loaded niosomes were successfully prepared with controlled size, high entrapment efficiency, and sustained release. The formulation stability is attributed to optimal surfactant:cholesterol ratios, enhancing bilayer rigidity and drug retention [17–19]. Compared to free voriconazole, niosomal systems demonstrated prolonged drug release and potential reduction in dosing frequency.

Niosomes also present advantages in targeted delivery, as their size enables passage through fungal biofilms and infected tissues [20–22]. Previous studies support enhanced antifungal activity of vesicular systems [23–25].

V. Conclusion

This study achieved a **stable and effective niosomal formulation of voriconazole**. The optimized vesicular system provides controlled release and enhanced physicochemical properties. Future work should involve in vivo evaluation to establish clinical potential.

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