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A Comprehensive Review on Novasomes As Lipid-Based Drug Carriers

Rana E. Elnady[1], Yasmin Mortagi[1,]*

[1]Department of Pharmaceutics, Faculty of Pharmacy, Sinai University, Arish Branch, North Sinai 45511, Egypt

**Corresponding author*

Correspondence:

Yasmin Mortagi
Email: yasmin.mohamed@su.edu.eg

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ABSTRACT

Background: Novasomes (Novs) are a novel lipid-based drug delivery system (LBDDS) for enhanced drug delivery. Those systems are composed of surface active agents (SAA) and free fatty acids (FFA) that self-assemble into spherical bilayer structures to encapsulate a variety of therapeutic drugs. Novs have been extensively studied as drug carriers, including antifungals, antibiotics, anti-inflammatory, and anticancer drugs. They approved better solubility and permeability, greater therapeutic efficacy, and diminished side effects when compared to free drug formulations.

Aims of this review: This review provides a thorough outlook, including novasomal constituents, development techniques, advantages and disadvantages, variant characterizations, routes of administration, pharmacological applications, and future prospects in the field of novasomal research.

KEYWORDS: Novs, lipid-based nanocarrier, non-ionic surfactants, permeability.

1. INTRODUCTION

Many of the current pharmaceuticals face challenges of low solubility, low permeability, and reduced bioavailability. To overcome these limitations, nanotechnology offered a suitable methodology for carrying drugs into nanovesicles, enhancing their solubility, penetration, and stability. Lipid-based drug delivery systems exhibit the ability to deliver a wide range of diverse drugs, effectively directing them to specific sites while minimizing their potential adverse effects. Lipid-based drug delivery systems (LBDDSs) offer many advantages, such as improved solubility and bioavailability of poorly soluble drugs, especially class II and IV, according to the biopharmaceutical classification system [1]. LBDDSs have the potential for penetration through cells and drug targeting [2]. Liposomes are the first generation of LBDDSs that can encapsulate both hydrophilic and lipophilic pharmaceuticals with low toxicity and high biocompatibility [3, 4].

Due to the drawbacks of liposomes, new generations are developed to overcome leakage, low stability at different pHs, lipid rancidity, and high cost [5]. Novasomal nanotechnology is a patented method for encapsulating pharmaceuticals, improving their efficacy and efficiency. Novs, constructed from cholesterol, SAA, FFA and polyoxyethylene fatty acid, consist of a large central core. They are utilized to load vaccines [6, 7]. NOVAVAX, an American biotechnology company, developed Novasome technology, a patented encapsulation approach, to improve drug delivery performance over traditional techniques [8]. This review provides comprehensive knowledge on Novs, along with their preface, formulation, categories, preparation methods, characterization, advantages, applications, routes of administration, and previous research instances.

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2. STRUCTURE OF Novs

Novs is a modified generation of liposomes and niosomes, as it resembles liposomes in the bilayer structure, which contains cholesterol and which can hold both lipophilic and hydrophilic drug compounds [9]. Moreover, it is similar to niosomes in containing non-ionic surfactants. Novs are also called unsaturated fatty acid liposomes [10], or non-phospholipid liposomes [11]. The composition of Novs can differ according to the concentration of the components used [12]. The structure of Novs builds on FFA with non-ionic SAA-containing cholesterol embedded in between. They can load hydrophilic drugs in their core and lipophilic drugs in the bilayer. Fig. 1 describes the structure of Novs and their components.

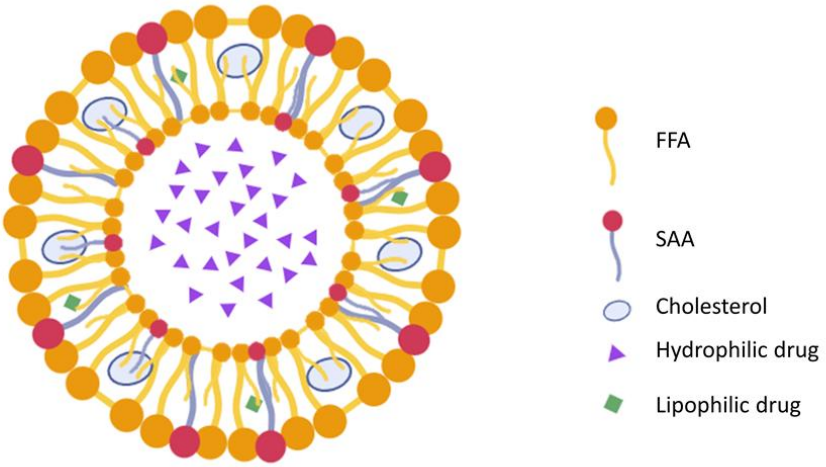

Fig. 1: Description of novasomal structure

3. ADVANTAGES OF Novs

Novs, as fatty acid-fortified vesicles, are predicted to possess higher penetration across the nasal membrane, increasing the drug's nose-to-brain targeting capability [13]. Novasome is a superior drug delivery system compared to niosome and ufasome. Niosomes are vesicular systems that are predominantly composed of nonionic surfactants and cholesterol bilayers. Niosomes can be used for controlling and targeting drug delivery for parenteral and oral routes with enhanced therapeutic performance of the drug [12]. Still, they suffer from the leakage of entrapped drugs, aggregation, and physical instability. Ufasomes are unsaturated fatty acid vesicles that resemble closed lipid bilayered suspensions made of unsaturated fats and their ionized groups (soaps). FFA in ufasomes figures is enhancing the penetration of bioactive materials through the stratum corneum. Ufasomes can efficiently carry different enzymes and drugs as they penetrate the hydrophilic layers of skin, but they are easily subjected to oxidation, permeation, and low stability. This inadequacy instability can be solved by merging FFA with amphiphilic compounds or another surfactant [14]. Novs are offering higher deformability, better drug deposition, and better stability [6]. Its stability is maintained even after 90 days of storage at 25°C and 4°C, while ufasome shows lowered drug content and entrapment efficiency at room temperature [15]. The Novs can sustain the drug's release and can thus be utilized efficiently to treat fungal infections of the skin [16]. The ability to make multilayering provides extra space for more drug-loading [6]. The combination of the lipophilic structure and the

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presence of non-ionic surfactant enhances the permeability through the skin and corneal barrier, offering good antibacterial management [7, 8].

4. STRUCTURAL COMPONENTS OF Novs

Novs are composed of the following main components:

4.1. Free Fatty Acids

Inclusion of FFA into nanocarriers enhances intestinal absorption, as they are considered permeation enhancers [17]. Different types of FFA are used in fabricating Novs, such as stearic acid, linolic acid and oleic acid. Stearic acid-containing vesicles showed considerably greater EE (%) than those with oleic acid, such as FFA. This could be the reason for the alkyl chain saturation in FFA [13]. The same alkyl chain length (C_{18}) was found in stearic and oleic acid. Nevertheless, the un-saturated double bond in the alkyl chain of oleic acid lowers its transition temperature than that of strearic acid, a thing that results in leaky vesicles and reduced entrappment [18]. On the other hand, oleic acid provides particles with a smaller sizes and lower polydispersity index [6]. However, using stearic acid can result in lower zeta-potential and higher drug release than oleic acid [18]

4.2. Surfactants

Designing lipid nanovesicles (LN) for drug administration requires a thorough understanding of how the combination of SAA and lipids affects particle size and colloidal stability [19]. Various types and ratios of non-ionic SAA are utilized, such as span 20, 60 and 80, tween 20, 40, 60, and 80, Brij 93 and Brij 58.

4.3. Cholesterol

Cholesterol is one of the most important components in the fabrication of Novs. According to recent studies, the stiff and hydrophobic lipid cholesterol can potentially alter the stiffness and integrity of the vesicle membrane by filling in the gaps left by other lipids, boosting the stability of the particles [20]. However, a marked reduction in the Entrapment efficiency (EE%) of the drug was observed with a gradual elevation of cholesterol content as shown in Fig. 2 [21].

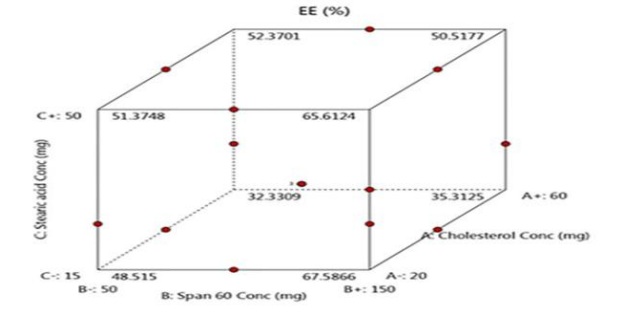

Fig. 2: Cube plot for the effect of cholesterol concentrations on EE% [21].

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5. TYPES OF Novs

5.1. ProNovs

ProNovs are dry, free-flowing particles with a dispersion structure that, when exposed to water, rapidly turns into novasomal suspension. ProNovs outperform regular Novs in terms of drug absorption. Because of their solid features, their physical stability can be enhanced while retaining their intrinsic properties. ProNovs are lyophilized pro-Novs that are used to provide physical stability to such an outstanding system [6].

5.2. Plated Novs

Plated Novs with elements like selenium or gold could be beneficial in pharmacokinetics and tumor targeting. Selenium-plated nanovesicles have been intensively explored because of their immense bioactivity, great bioavailability, reduced toxicity, and capacity to give a far larger margin between positive and harmful effects than inorganic and organic selenocompounds [22, 23]. Selenium-plated novasomes are a nanoparticle system developed to improve the pharmacokinetics and tumor targeting efficiency of quercetin. The QRC-NOVs, initially developed using oleic acid, Brij 35, and cholesterol, showed an entrapment efficiency of 67.21%. Coating them with selenium improved their cytotoxicity against human rhabdomyosarcoma cells. In vivo studies showed that 99mTc-labeled QRC-SeNOVs had higher tumor uptake than uncoated novasomes and the free drug [24]. Significant sustained-release could be noticed from selenium plating quercetin-loaded Novs, which caused thickening of the quercetin novasomal shell and structural reinforcement [24]. Furthermore, selenium plating can limit the external diffusion of drugs from lipid bilayers [25].

6. PREPARATION METHODS

Novs, like any vesicular system, could be fabricated by different methods similar to liposomes. The thin film hydration technique, ethanol injection method, micro-fluidization method, membrane extrusion method, reverse phase evaporation technique, and sonication method are the common methods for the fabrication of Novs [26]. The most frequently used methods are the thin film hydration technique, ethanol injection method, and vortex-sonication method (See Fig .3).

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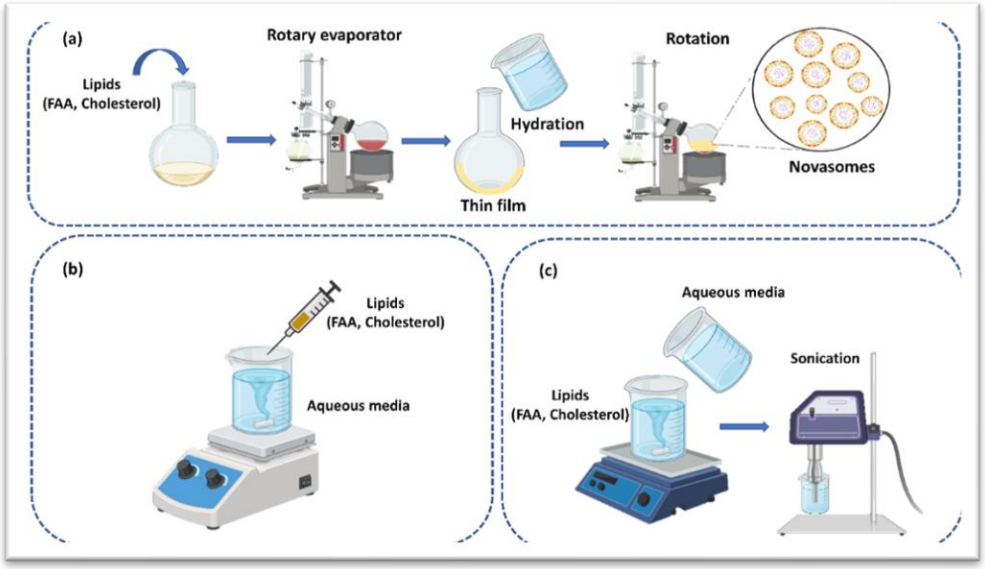

Fig. 3: Preparation Method.

A. Thin Film Hydration Method (TFH)

Lipophilic components and SAAs are dissolved into organic solvents in a round bottom flask and then rotated in a rotary evaporator under vacuum at 40°C till the solvent evaporation leaves a thin film. The aqueous media is added to hydrate the formed film and rotated again without vacuum till a turbid solution of Novs is formed [18, 21, 27].

B. Ethanol Injection Method

All lipids (FFA and cholesterol) and SAA are dissolved into ethanol in a water bath, then the lipophilic mixture is subjected to the aqueous media by injection dropwise followed by magnetic stirring till the formation of a turbid solution of Novs [16].

C. Vortex-Sonication Method

Dissolving lipids and SAA in organic solvent is done first, then an aqueous medium is poured into the lipidic mixture and vortexed till turbidity. Then, this cloudy suspension is subjected to sonication for 15 minutes [10].

7. CHARACTERIZATION OF Novs

7.1. Entrapment Efficiency

Entrapment efficiency (EE%) is a crucial parameter in determining how well the drug succeeded in being embedded into novasomal formulations. Two methods can compute the EE% of the drug. The first one is the direct method for the entrapped drug in the Novs. It can be determined by a complete vesicular interruption. The EE% can be determined by utilizing the formula [8].

$$\mathbf{EE\%} = (\mathbf{entrapped\ drug\ /\ total\ amount\ of\ drug}) \times \mathbf{100} \quad (1)$$

The second method is the indirect method of detecting the free drug by exposing the novasomal suspension to a cooling centrifuge. A specified amount of the formula is introduced

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to centrifugation for 1h at 4°C and 20000 rpm [6, 8]. The free drug concentration is then spectrophotometrically investigated. The following equation can be utilized to estimate EE% [7].

$$\mathbf{EE\%} = [(\mathbf{Total\ amount\ of\ drug} - \mathbf{Free\ drug\ amount})/\mathbf{Total\ amount\ of\ drug}] \times \mathbf{100} \quad (2)$$

7.2. Determination of Particle Size (PS) & Polydispersity Index (PDI)

The embraced technology for assessing the average particle size and PDI values of drug-loaded Novs was Dynamic Light Scattering DLS adapting zetasizer Nano ZS. To attain convenient scattering intensity, the novasomal dispersions should be diluted. Low PDI values affirm uniform particle size distribution (below 0.3). Evaluation of vesicle zeta potential (ζ) by averaging their electrophoretic mobility by a laser Doppler anemometer is coupled with the same equipment at a distributing 90°angle [28]. Transmission Electron Microscope (TEM) and Scanning Electron Microscope (SEM) are utilized for direct investigation of the morphology of nanovesicles (Fig. 4). A scanning electron microscope (SEM) is a type of electron microscope that provides detailed images of a sample by scanning its surface with a focused beam of electrons. The electrons interact with atoms in the sample, generating various signals that provide information about the surface topography and composition. By scanning novasomes, a creamy appearance was found. This appearance id due to the utilization of cholesterol and oleic acid in the production. The drug-loaded novasomes also had a creamy look, but their surface appearance was different [29]. TEM revealed that the particles were nearly spherical, a confined size with a smooth surface, and non-aggregated [7, 21]. Novs range in size from 235 to 964 nm, but the accepted PS is below 500 nm [8].

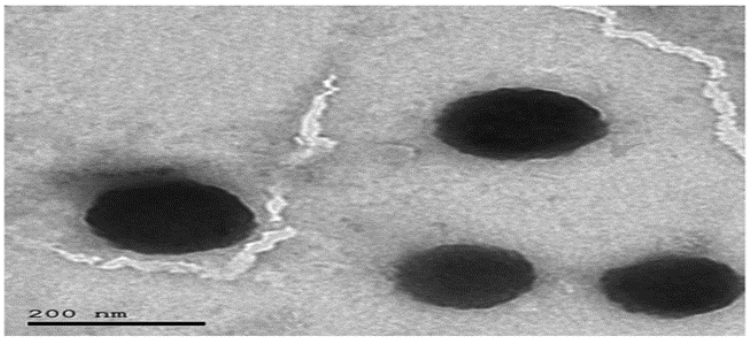

Fig. 4. Transmission electron micrograph of novasomes [21].

7.3. Zeta Potential (ζ)

The magnitude and type of the surface charge conclude the interaction of nanovesicles with their biological surroundings and their electrostatic interaction with bioactive compounds. The colloidal stability of the nanovesicles can be figured out by zeta potential (ζ). The reference value is between -30 mV and +30 mV. The zeta potential (ζ) is a tortuous measurement of the surface charge [30]. Colloidal vesicles stability is guaranteed by the evaluated value of zeta potential (ζ) even if they are positive or negative values. It also secures the absence of aggregations. The values of the zeta potential (ζ) can indicate the degree of surface hydrophobicity and also provide a clue on the nature of the embedded drug within the nano-vesicles or absorbed on the surface [31].

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7.4. In *vitro* Release Studies

Drug-loaded novasome discharge can be estimated by utilizing the USP dissolution tester. The dialysis method can be adopted using a cellulose membrane. A fixed volume of Novs should be inserted in a glass cylinder. A pre-soaked cellulose membrane in PBS should vigorously conceal each tube from one end while the other edge is moored to the shaft of the apparatus [8]. The beakers are replete with dissolution medium, phosphate buffer solution (PBS). A constant speed (50 or 100 rpm) at 37°C is acclimatized to allow the rotation of cylinders. To customize of the evaporation of the dissolution medium, it is better to cover the cylindrical vessels during the experiment. At scheduled time intervals (starting from 0.5 up to 24 h), aliquots should be pulled periodically and replaced with fresh medium to maintain sink conditions. After that, aliquots were assayed spectrophotometrically at a predetermined λ_{max}[32]. For an appraisal of the best release kinetics for the drug from Novs, the obtained data has to be introduced into different kinetic models such as zero-order, first-order, Higuchi, Hixson-Crowell, and Korsmeyer-Peppas models. The degree of determination coefficients (R^2) can scrutinize the convenient arithmetic order [18, 24].

8. ROUTE OF ADMINISTRATION

8.1. Transdermal Administration

Novs display improved skin permeability due to the existence of free fatty acids. They also have a good impact on stability because of an embodiment of non-ionic surfactants [18]. Novs have been recommended to improve drug bioavailability. They also accomplish a sustained release in comparison with the release achieved after oral admission of drug dispersion. The relevance of drug-loaded Novs transdermal system is increasing the drug bioavailability, which may be due to the collegial improvement effect of the constituents of Novs which are surfactants, cholesterol, and free fatty acids [18]**.** In addition, the occupation of a broad surface area of Novs could augment the close contact of drug-loaded nanovesicles with the aimed organ [33]. Tawfek *et al*. prepared Novs of Agomelatine for transdermal delivery [28]**.**

8.2. Trans nasal Administration

An excellent permeability aspect of lipid nanovesicles has a good impact on improving nasal diffusion of numerous drugs via disturbing the mucosal membrane [34]. The transmittal of Zolmitriptan to the brain is embellished by intranasal Novs delivery over the olfactory pathway to reach brain tissue from the nasal cavity [35]. Embracing the Novs via the narrow gap in the olfactory neurons into the brain is due to the reduced particle size of Novs [36]**.** Zolmitriptan-loaded Novs conducted through the nasal way may resemble progress in the control of acute migraine attacks [18]**.** When compared to the reference commercially available Flumin® tablets, trans-nasal administration of novasomes resulted in an improved antidepressant effect as well as a fivefold increase in Fluvoxamine (FVM) bioavailability. The trans-nasal route similarly exhibited a longer half-life (25.63 h) than oral (11.46 h). The trans-nasal route can protect the drug-loaded novasomes from first-pass metabolism through the oral route, leading to a marked enhancement in bioavailability [37].

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8.3. Topical Administration

Colloidal nanocarrier Novs are appealing systems for skin application because of abundant and fascinating outcomes on the skin [38]. Albash *et al*. declared the capability of the fenticonazole Novs to show great antifungal action [8]**.** Fatima *et al*. evolved fluconazole loaded Novs that hand over the anti-fungal drug to the intended site for a protracted duration with favorable antifungal action [16]**.** Further, the novasome formulations are deliberated non-toxic and safe preparations as demonstrated from toxicity studies. The Novs can be dramatically utilized for controlling skin fungal infections as they can prolong the release of the drug. In conclusion, topically administered curcumin-loaded pro-novasomes lyophilized gel provides a regulated, non-invasive strategy for the targeted distribution of antitumorigenic drugs, with probable dose reduction, relieved side effects, and increased compliance [39]. In vivo studies against acute otitis media in rats, as well as histological research, confirmed therapeutic effectiveness, safety, and superiority over NA suspension. The findings primarily demonstrated the high efficacy of novasomes for trans-tympanic administration of NA in the treatment of middle ear inflammation [40].

8.4. Ocular Administration

The drug corneal diffusion was improved when the ophthalmic drug was prepared as Novs with enhancement of their efficacy, improved safety, and high bioavailability. Ahmed *et al*. assured the potency of fenticonazole nitrate-loaded Novs to promote corneal diffusion and anti-fungal action [7].

8.5. Respiratory Administration

The pulmonary route is auspicious expediency to support the therapeutic response of the drug, decreasing clearance, and augmenting delivery with minimum local and systemic toxicity. Anti-asthmatic drugs loaded with Novs were proved to be the most efficient ways in enhancing drug bioavailability and reducing the application rate because of nanosized drug with suitable aerodynamic properties. El komy *et al*. developed terbutaline sulfate-loaded Novs which facilitate sustained release of the drug with improved stability [21]. The pharmacokinetic investigations revealed that the optimal terbutaline sulfate Novs increases bioavailability by 3.88 times when compared to the oral solution [21].

8.6. Parenteral Use

Novs were introduced into animals by intravenous injection. The biodistribution and the pharmacokinetic study of Quercetin Selenium plate Novs aggravate collaborative cytotoxicity as opposed to carcinoma cells. Besides, higher AUC and prolonged $T_{1/2}$ in comparison with Quercetin solution [24]**.**

9. APPLICATION OF Novs

Novs are widely used in medical applications due to their ease of manufacture and adaptability. As Novs contain elements analogous to innate biological components, they can be classified as LBDDS. No problem is found with the oral administration of Novs, as they can collaborate with different cells and tissues. They are even non-toxic and biodegradable. Because of these features, they are ideal for antifungal delivery. An important application of

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Novs is their utilization in cancer therapy, with promising findings in clinical studies. Table 1, outlines all drugs placed into Novs, including their fabrications and outcomes.

Table 1. Potential of Novs in loading drug molecules with their applications

No.	Drug	Materials	Method	Outcomes	Ref.
1	Curcumin	Span 60, span 80 cholesterol, Oleic acid	TFH	• The optimized formula showed high EE%, small PS with good homogeneity, high ZP and controlled in-vitro release profile. • Topical therapy induced advanced apoptosis and necrosis, as well as a similar reduction in tumor area. • Superior skin penetration and bioavailability of topical treatment.	39
2	Fenticonazole nitrate (FTN)	Span 80, cholesterol, Stearic acid	Ethanol injection Method	• The optimized formula proved small PS with spherical morphology, high EE% confirmed by DSC and FTIR studies. • and accepted ZP. • Enhanced ex-vivo corneal permeation and high stability after gamma irradiation. • FTN-loaded Novs demonstrated effective antifungal activity through in vivo corneal tolerance, uptake, and susceptibility tests. •	7
3		Span 60, Brij 93, Brij 58, and cholesterol, Oleic acid		• Optimum formula exhibited favorable EE%, PS, charge, morphology, and stability. • Displayed high antifungal potential against Trichophyton mentagrophytes relative to FTN suspension. • Proved its magnitude in clinical cure of tinea corporis compared to MiconazVR cream.	8
4	Terbutaline sulfate (TBN)	Cholesterol, Span 60, chloroform, Stearic acid	TFH	• The TBN-NVS formulation enabled TBN release over an extended period of time in a sustained manner. • accentuated stability over the storage period. • The pharmacokinetics results manifested therapeutic TBN efficacy, minimize clearance, maximize delivery and diminish local and systemic toxicity. • Displayed a high clinical treatment potential nanovector for the pulmonary delivery of TBN.	21
5	Luteolin	Stearic acid, cholesterol, Brij 52	TFH	• The optimum formula showed improved antimicrobial activity with lower MIC against a group of MRSA	44

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				clinical isolates compared to LUT dispersion. • Exhibited higher anti-virulence activity by effective inhibition of biofilm formation and suppressing α-hemolysin activity in MRSA isolates.	
6	Quercetin	Quercetin, cholesterol, Brij 35, Tween 80	TFH	• The optimum QRC-SeNOVs exhibited high EE%, small PS, non-aggregating spherical structure, and prolonged in vitro release profile over 24 h. • QRC-SeNOVs provoked synergic cytotoxicity against RD cells. • The pharmacokinetic and biodistribution studies revealed higher AUC0, extended T1/2 and MRT besides reinforced tumor uptake of 99mTc-QRC-SeNOVs compared to 99mTc-QRC-NOVs and 99mTc-QRC solution.	24
7	Agomelatine (AGM)	Stearic acid, Span 60, cholesterol, and span 80, Oleic acid	TFH	• Novasomal gel systems combined the advantages of the active and passive permeation techniques, could enhance the bioavailability of AGM.	41
8	Zolmitriptan (ZT)	Cholesterol, Tween 20, 40, 60, 80 and 85, Span 60, 80 and 85, 20, Oleic acid, Stearic acid	TFH	• The optimized formula showed high percentage of a hydrophilic ZT in the nano-size. • 99mTc-ZT-loaded Novs showed enhanced nose to brain targeting compared with the I.V 99mTc-ZT solution.	18
9	Terconazole	Span 60, Span 80, Stearic acid, oleic acid, cholesterol	Ethanol injection Method	• The optimized formulat owed small PS, spherical morphology, and high EE%. • Microbiological assessment showed its successful potential against Candida albicans relative to TCZ suspension. • Augmented deposition in the skin as compared to traditional formulation and TCZ suspension. • Confirmed its dermatological safety. • Proved the superior activity compared to placebo against Candida albicans infections.	6
10	Oxiconazole	Oleic acid, tween, cholesterol	Vortex-sonication	• Optimum formula showed a higher drug release; flux and permeability coefficient compared to other formulations. • Tea tree oil based Novs gel formulation shown higher antifungal activity and stability up to 3 months as compared to other formulations.	10

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11	Fluvoxamine (FVM)	Span 60, cholesterol, arachidonic acid, carboxymethyl chitosan	Ethanol injection Method	• Optimum formula showed 99% and 90% FVM release and permeation, respectively. • The novasomal adherence time was 24 h. • Improved antidepressant effect along with five-fold increase in bioavailability of FVM was noticed • after trans-nasal administration compared to the commercial reference.	37

10. RESULTS

There are many factors influencing the characterization of Novs. According to results from previous studies, FFAs type could affect the EE% of the drug, stearic acid vesicles have a higher EE (%) than oleic acid FFAs due to their alkyl chain saturation. Moreover, unsaturated oleic acid has a lower T°C (13°C) and more leaky vesicles, resulting in lower entrapment [13]. Increasing the concentration of FFAs has a favorable and significant effect on lipophilic drug loading into Novs [7]. Eradication of the lipid matrix of Novs can occur due to a high level of oleic acid that leads to a reduction in the EE%. For the effect of different surfactant types, it was shown to have a significant negative effect on EE with span 60. On the other hand, higher efficiency with span 80. The reason for that can be referred to as the difference in the degree of unsaturation and phase transition temperature of both surfactants [6]. It was noticed that a reduction in the EE% at high levels of cholesterol was due to the incubation of cholesterol in spaces of the bilayer rather than the drug. Moreover, the lipophilicity of cholesterol provokes the expulsion of hydrophilic drugs [21]. Increasing the amount of lipids, such as FFAs and cholesterol, had a significant impact on increasing PS. However, increasing SAA levels would have a synergistic effect in decreasing PS [41]. Increasing the cholesterol amount provides more stability to novasomal vesicles, making them less leaky and more rigid [21]. Increased HLB value of surfactant monomers leads to larger vesicles, with Span 60 having a higher HLB than Span 80. Larger particle size Novs have a higher drug EE% [27]. PDI of vesicles containing span 80 or oleic acid have lower PDIs due to forming smaller vesicles [27]. No significant impact on the ZP when changing Span 60 and oleic acid amounts. Alteration between different types of Brij had an impact on Novs characters. Brij 58 had a low negative charge due to Brij 58's hydrophilic nature, which shields the negative charge, but Brij 93 had a great negative ZP [8].

11. CONCLUSION

Lipid-based drug delivery systems, such as Novs are promising carriers and attractive ways to manage infected barriers such as skin or cornea. Furthermore, Novs proved their ability in controlling tumors owing to excellent permeability and targeting characteristics. The prospects for Novs as LBDDS for topical preparations appear more promising. The ease of preparing Novs makes it one of the most important drug nanocarriers. Novs, as FFA-enriched vesicles, are projected to have higher penetration across the nasal membrane, increasing the drug's nose-to-brain targeting capability. Currently, Novs has established their performance in different fields in the market through cosmetic products, food supplements, vaccines and skin care.

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12. Future Prospective

Novs are a promising development for vesicular drug delivery systems with the potential to overcome many of the limitations of conventional liposomes. Novs can be designed to have a larger drug loading capacity than liposomes, allowing for more efficient delivery of medicinal drugs [16, 26]. The unique structure and composition of Novs make them more stable than liposomes, with better shelf life and resistance to leakage of encapsulated drugs [26]. Novs can be designed to provide controlled and prolonged release of drug, improving therapeutic efficacy and reducing dosing frequency [41, 42]. The surface of Novs can be modified with targeting ligands to achieve site-specific delivery of drugs to diseased tissues or cells [26, 27]. Novs can be used to deliver a wide range of drugs including small molecules, peptides, proteins, and nucleic acids, via various routes such as topical, transdermal, parenteral, and mucosal [37, 26]. Novs can enhance the solubility and permeability of drugs, leading to improved oral bioavailability and therapeutic outcomes [37, 42]. By encapsulating drugs in Novs, it is possible to reduce drug-related toxicity and side effects while maintaining efficacy [26]. In conclusion, the unique structure of Novs makes them a desirable foundation for developing next-generation drug delivery systems with increased therapeutic potential. We suppose enhanced drug delivery of Novs to the brain through the trans-nasal route, which is beneficial in treating brain diseases such as Alzheimer's disease, Parkinsonism and neurodegenerative diseases. More research is needed to fully realize its potential and to convert it into therapeutic applications.

CONFLICT OF INTEREST

There is no conflict of interest.

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None is declared

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