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SPANLASTICS AS VERSATILE ELASTIC NANOCARRIERS: ADVANCES IN DESIGN, CHARACTERIZATION, AND DRUG DELIVERY APPLICATIONS

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ABSTRACT

Spanlastics are a novel and adaptable class of elastic nanocarriers that have gained considerable attention in the field of drug delivery. They are made using non-ionic surfactants such as Span and edge activators like Tween. These vesicles are designed to be flexible enough to cross biological membranes, enhancing drug absorption and therapeutic effectiveness. They can be formulated through several methods including thin-film hydration, ethanol injection, and sonication, with each method influencing the final properties of the vesicles. To ensure their quality and performance, spanlastics undergo a variety of characterization tests. The vesicle size and polydispersity index (PDI) help assess the uniformity and distribution of the particles. Zeta potential is measured to evaluate the surface charge, which plays a key role in predicting stability during storage. Morphology analysis, often performed using microscopic techniques, reveals the shape and structural integrity of the vesicles. Elasticity or deformability studies are crucial, as they determine the vesicle's ability to adapt to tight junctions and penetrate deep tissue layers. Other important parameters include drug entrapment efficiency, release behaviour, and compatibility under different pH conditions. Spanlastics have shown promising results across various delivery routes. Orally, they help improve the solubility and absorption of poorly water-soluble drugs. In ocular formulations, they increase corneal retention and drug penetration. Their flexibility makes them effective in transdermal and intranasal applications,

offering enhanced bioavailability and targeted delivery. Additionally, they are being explored for gene therapy and vaccine delivery due to their safety, versatility, and ability to carry sensitive biomolecules.

KEYWORDS: Spanlastics, Elastic nanovesicles, Novel vesicular approach, Bilayered vesicles.

INTRODUCTION

Novel drug delivery system

The advent of innovative drug delivery systems (NDDS), which seek to increase therapeutic efficacy, decrease adverse effects, and boost patient compliance, has significantly changed the area of pharmaceutical science. In contrast to traditional dose forms, NDDS are made to distribute medications in a precise, efficient, and controlled way. The capacity of vesicular systems, including liposomes, niosomes, ethosomes, and transferosomes, to encapsulate hydrophilic and lipophilic medicines and to get beyond biological barriers has drawn a lot of attention.[1] However, many classic vesicular carriers still face issues like low permeability through strong membranes like the blood-brain barrier or stratum corneum, poor stability, and expensive production costs.[2] A more recent class of elastic or deformable vesicles.

Spanlastics

Spanlastics are seen as a possible substitute in the field of NDDS, in terms of structure, spanlastics are made up of edge activators (like sodium cholate or Tween 80) and non-ionic surfactants (like Span 60), which give the vesicle membrane flexibility. They can squeeze through small intercellular gaps. Thanks to this special mixture, which improves drug penetration through biological membranes like the skin, mucosa, or tissues of the eyes.[3]

Advantages of spanlastics

- One of the main benefits of spanlastics is their better deformability[4].
- It enhanced drug entrapment effectiveness.
- It also enhanced affordability and capacity to administer medications through a variety of routes like topical, transdermal, nasal, and ocular.
- Especially spanlastics are appealing for administering medications that are poorly soluble or poorly absorbed because of their stability over time and capacity to improve bioavailability.[5]

Disadvantages of spanlastics

However, despite their potential, spanlastics have some limitations.

- It includes the necessity for additional in vivo and clinical validation.[6]
- possibility of drug leakage during storage.
- Scalability problems in industrial production.

In pharmaceutical research, spanlastics are becoming more and more acknowledged as a novel and creative drug delivery approach deserving of more investigation and improvement because of their adaptable structure, multi-route administration, and capacity to get past delivery obstacles.[7]

Spanlastics

Spanlastics are a sophisticated type of vesicular drug delivery system that is perfect for ophthalmic, oral, topical, nasal, and transungual applications because of their site-specific targeting capabilities. These carrier's distinctive elasticity comes from their structural flexibility and composition, which is mostly made up of non-ionic surfactants like Span and edge activators like Tween. Because of their flexibility, spanlastics may change shape and pass across biological membranes, greatly improving medication penetration—particularly through difficult barriers like the ocular membrane. One of their main benefits is the regulated release of the medication, which is made possible by their bilayer structure and helps sustain therapeutic drug levels for an extended period of time.[8] Because spanlastics are chemically stable, biodegradable, and non-immunogenic, they provide a safer option than many other vesicular systems. By transporting medications straight to the intended location and reducing degradation or removal from the systemic circulation, they increase bioavailability. Additionally, because non-ionic surfactants are used, they are non-irritating, which makes them appropriate for sensitive applications, especially ocular administration. Their practical benefits are further enhanced by their affordability, convenience of use, and compatibility with many delivery routes (topical, parenteral, and oral).

Structure of Spanlastics

Spanlastics are elastic nanovesicles made mostly of edge activators like sodium cholate or Tween 80 mixed with non-ionic surfactants like Span 60. This combination enables the trapping of both hydrophilic and lipophilic medicines by creating a flexible bilayer membrane around an aqueous core. The main structural characteristic of spanlastics is their great deformability, which is made possible by edge activators that improve membrane flexibility

by slightly disrupting the bilayer. Compared to conventional vesicular systems, spanlastics are able to pass through biological barriers more successfully because of their special structure. Furthermore, stability, low toxicity, and compatibility for a range of drug administration methods are offered by their non-ionic and biocompatible components.[9]

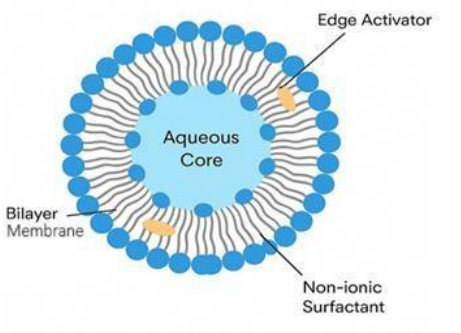

Fig. No. 1: Structure of Spanlastics.

Classification of Spanlastics

Spanlastics can be categorized based on the number of lipid bilayers they contain. The primary types include

1. Multi-lamellar Vesicles (MLVs)
2. Large Unilamellar Vesicles (LUVs)
1. 3.Small Unilamellar Vesicles (SUVs)

1. Multi-lamellar Vesicles (MLVs)

MLVs are composed of multiple concentric lipid bilayers, resembling an onion-like structure. These vesicles typically range in size from 0.5 to 1.0 microns. Due to their ease of preparation and long-term structural stability, they are frequently utilized in drug delivery applications.[10]

2. Large Unilamellar Vesicles (LUVs)

LUVs consist of a single lipid bilayer that encloses a relatively large aqueous core, making them suitable for encapsulating high volumes of hydrophilic substances. Their size generally falls between 100 nanometres and 1 micron.

3. Small Unilamellar Vesicles (SUVs)

SUVs are much smaller, typically ranging from 20 nanometres up to 50 nanometres. These vesicles are usually produced by sonication of larger multilamellar structures and are characterized by their high surface area-to-volume ratio.[11]

Composition of Spanlastics

Spanlastics are advanced vesicular drug delivery systems primarily composed of two main components

1. Non-ionic surfactants (e.g., Span series)
2. Edge activators (e.g., Tween series or bile salts)

These components work together to form flexible and deformable nanovesicles that enhance drug delivery, particularly for poorly soluble or sensitive molecules. The term "spanlastics" derives from the use of Span surfactants as the central bilayer-forming agents, which give these vesicles structural integrity and stability.

1. Non-Ionic Surfactants

Non-ionic surfactants are essential in constructing spanlastics due to their ability to form stable bilayered vesicles. Compared to ionic surfactants, non-ionic ones are less toxic, more biocompatible, and better suited for pharmaceutical applications. The most commonly used non-ionic surfactants are Span 20, 40, 60, and 80, which differ in their hydrophilic-lipophilic balance (HLB) and the length of their alkyl chains. These characteristics influence vesicle size, rigidity, drug entrapment efficiency, and release profile. It is applied for enhancing oral drug bioavailability and delivering sensitive drugs like peptides, steroids, and anti-inflammatory agents in transdermal systems where deeper tissue penetration is needed.[12]

Table No. 01: Different types of non-ionic surfactant used in spanlastics.

Sl. No	Non-Ionic Surfactant	Chemical Name	Characteristics	HLB Value	Reference
1	Span 20	Sorbitan monolaurate	Forms larger vesicles; lower membrane rigidity	8.6	Abdelbari et al., 2021.
2	Span 40	Sorbitan monopalmitate	Provides semi-flexible vesicles with moderate stability	6.7	Abdelbari et al., 2021.
3	Span 60	Sorbitan monostearate	Offers highly stable bilayers and enhanced drug entrapment	4.7	Bukhary et al., 2024.
4	Span 80	Sorbitan monooleate	Generate flexible vesicles suitable for deformable delivery system	4.3	El-Menshawe et al., 2019

2. Edge Activators (EAs)

Edge activators are surface-active agents added to spanlastics to enhance their flexibility and deformability. These molecules disrupt the tight packing of bilayers, making the vesicles capable of penetrating biological barriers more effectively. Typically, EAs are either non-ionic surfactants or anionic agents with a high HLB value, which improves hydrophilicity and vesicle permeability.[13]

Table No. 02: Different types of edge activator used in spanlastics.

Sl. No	Edge Activators	HLB Value	Category	Functionality	Reference
1	Sodium cholate	18	Anionic	Enhances membrane fluidity and drug permeability	Sallam et al., 2021.
2	Cremophor RH 40	15.65	Non-ionic surfactant	Improves solubilisation and vesicle deformability	Shamma et al., 2019.
3	Polyvinyl Alcohol	18	Polymer-based agent	Acts as stabilizer and edge activator	Elhabak et al., 2021.
4	Tween 20	16.7	Non-ionic surfactant	Increases vesicle flexibility and enhances absorption	Abdelrahman et al., 2017.
5	Brij 97	12.4	Non-ionic surfactant	Stabilizes vesicles and promotes membrane elasticity	Al-Mahallawiet al., 2017.
6	Tween 60	14.9	Non-ionic surfactant	Commonly used to increase hydrophilicity	Badria et al., 2020.
7	Tween 80	14.5	Non-ionic surfactant	Promotes vesicle deformability for transdermal and mucosal delivery	Gupta et al., 2023.
8	Brij 35	16.9	Non-ionic surfactant	Enhances flexibility and drug permeability	Sallam et al., 2021.

3. Ethanol

Ethanol is often included in spanlastic formulations as a membrane fluidizer and enhancer of drug entrapment. It aids in reducing membrane thickness, making it easier for the drug to partition into the vesicles. Ethanol also helps condense vesicular membranes, which improves the stability and loading capacity of the system. Moreover, ethanol contributes to drug solubility and enhances the permeation of vesicles through biological barriers.[14]

Methods of preparation of Spanlastics

Spanlastics vesicles can be prepared by different types of techniques, like forming the bilayer membrane using non-ionic surfactant where the drug is placed and the edge activators

(formed outside) for improving elasticity of the vesicles to enhance permeability and solubility of the drugs. Some techniques are given below.

1. Ethanol Injection Method

The ethanol injection method is a widely used and straightforward technique for preparing spanlastics. It begins with dissolving the drug in ethanol along with a specific non-ionic surfactant (typically a span such as Span 60). This lipid-ethanol mixture is then sonicated briefly to ensure uniformity. Meanwhile, an aqueous phase containing an edge activator (like Tween 80) is preheated to a temperature between 70–80°C. The ethanolic lipid solution is then slowly injected into the heated aqueous phase under constant stirring at speeds ranging from 800 to 1600 rpm. The mixing of ethanol with the hot aqueous phase facilitates spontaneous vesicle formation due to differences in polarity and solubility. Ethanol acts as a membrane softener and improves drug solubility, especially for hydrophobic drugs. After 30 minutes of stirring, distilled water is added to adjust the volume. The ethanol forms an azeotrope with water, which aids in efficient removal and enhances vesicle uniformity. This method is beneficial for producing spanlastics with small, uniform sizes and high encapsulation efficiency.[15]

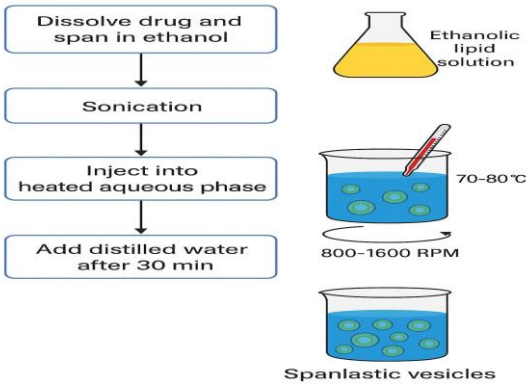

Fig. No. 2: Ethanol injection method.

2. Thin-Film Hydration Method

The thin-film hydration method is one of the most frequently used techniques in nanovesicle and liposomal drug delivery systems, including spanlastics. It involves dissolving the non-ionic surfactant (typically Span 60) in a volatile organic solvent like chloroform within a round- bottom flask. This solution is then subjected to evaporation under vacuum at around 55°C using a rotary evaporator. As the solvent evaporates, it leaves behind a thin lipid film on the interior surface of the flask. An aqueous solution containing the drug and an edge

activator (e.g., Tween 80 or sodium cholate) is prepared separately. Once the organic solvent has fully evaporated, the aqueous phase is added to hydrate the film. The flask is reconnected to the evaporator and rotated at 60°C for an additional 30 minutes to aid detachment and dispersion of the film into the aqueous medium. Afterward, the system is allowed to stand at room temperature for two hours and then stored at 4°C overnight for stabilization. This method enables high encapsulation efficiency and is compatible with both hydrophilic and lipophilic drugs, depending on which phase they are introduced into.[16]

Fig. No. 3: Thin film hydration method.

3. Hand Shaking Method

The hand-shaking method is one of the earliest and simplest approaches to vesicle formation, often used in laboratory-scale experiments. In this process, a non-ionic surfactant such as Span is dissolved in an organic solvent like chloroform, benzene, or diethyl ether. The mixture is placed in a round-bottom flask and evaporated under reduced pressure using a rotary vacuum evaporator. This leads to the formation of a thin surfactant film on the inner wall of the flask. An aqueous drug solution is then added to rehydrate the lipid film, followed by gentle agitation. During hydration, the amphiphilic molecules absorb water and swell. This swelling eventually results in the self-assembly of bilayered vesicles, the structural core of spanlastics. This method is particularly suitable for drugs that are stable in organic solvents and can be encapsulated efficiently during the hydration phase. Though simple, it may yield vesicles with varied size distribution unless further size reduction techniques like sonication or extrusion are applied.[17]

4. Microfluidization Method

The Microfluidization method is an advanced, high-shear technique designed for producing highly uniform, small-sized spanlastic vesicles with excellent reproducibility. In this method,

two fluid streams, one containing the surfactant and the other the drug, are pumped at very high velocities through narrow microchannels within a micro fluidization chamber. These streams collide under high pressure, typically using the submerged jet principle, which generates intense shear forces and turbulence. This high-energy interaction results in the breakdown of larger lipid aggregates into uniformly sized nanovesicles. Microfluidization not only ensures batch-to-batch consistency but also significantly enhances drug encapsulation and vesicle stability. It is especially useful for scaling up formulations for industrial production and for drugs that require precise control over particle size and distribution. However, it may not be suitable for heat-sensitive compounds due to localized temperature increases during processing.[18]

5. Ether Injection Method

In the ether injection method, the surfactant (e.g., Span 60) is first dissolved in diethyl ether. The resulting solution is then injected slowly into a hot aqueous phase maintained at approximately 60°C, typically using a syringe with a 14-gauge needle at a controlled rate (e.g., 25 mL/min). Upon contact with the hot aqueous environment, the ether rapidly evaporates due to its low boiling point. This quick vaporization induces the self-assembly of surfactant molecules into vesicles. The remaining organic solvent is then removed completely using a rotary evaporator to prevent any residual toxicity. The vesicles formed are usually uniflagellar and can be optimized by adjusting the injection rate and temperature. This method is effective for producing small, stable vesicles, but it requires careful handling of volatile solvents and may not be ideal for thermosensitive drugs due to the high temperature involved.[19]

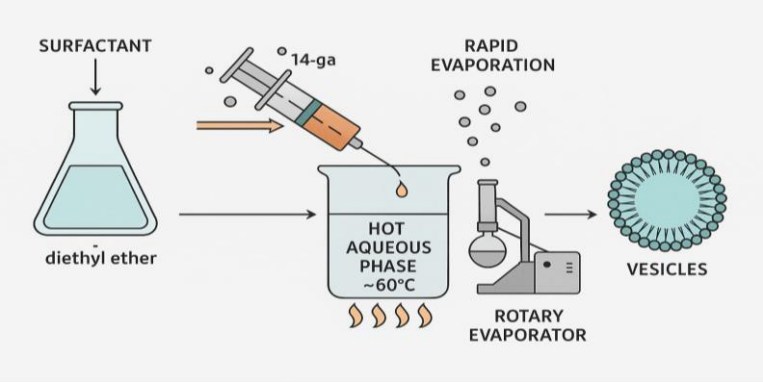

Fig. No. 4: Ether injection method.

6. Sonication Method

The sonication method is a simple and effective approach to reduce vesicle size and enhance uniformity in spanlastic preparations. In this process, a drug solution is prepared using an appropriate aqueous buffer. This solution is then mixed with a surfactant blend (typically a combination of a Span and an edge activator) in a small vial or container. The mixture is then subjected to sonication using a probe sonicator, usually equipped with a titanium tip. The application of ultrasonic energy disrupts larger vesicles and breaks them down into nanosized particles, promoting uniform distribution of the drug within the vesicles. Sonication is particularly useful as a post-processing step after initial vesicle formation via methods like thin film hydration or hand shaking. It enhances drug entrapment, reduces polydispersity, and improves the bioavailability of encapsulated agents. However, excessive sonication can lead to vesicle destabilization or drug degradation, so optimization is essential.[20]

Characterization of Spanlastics

Understanding the physical and functional characteristics of spanlastics is essential for ensuring their effectiveness, stability, and safety in drug delivery. The following parameters are commonly assessed during spanlastic formulation studies:

1. Vesicle Size

The size of spanlastic vesicles is a critical parameter that influences drug release, stability, and cellular uptake. Dynamic Light Scattering (DLS) is typically used to measure vesicle size by analysing the scattering patterns of light as it interacts with the particles. This method is especially useful in detecting variations in vesicle behaviour caused by Brownian motion. Instruments like the Zetasizer are widely employed in this analysis.[21]

2. Polydispersity Index (PDI)

PDI is used to assess the uniformity of the vesicle population in a spanlastic formulation. A lower PDI value indicates a more homogeneous distribution of vesicle sizes, which is preferable for consistent drug delivery and predictable release profiles. Like vesicle size, PDI is also determined using the DLS technique with the help of a Zetasizer.[22]

3. Morphology Analysis

To visually examine the shape and structural characteristics of the vesicles, Transmission Electron Microscopy (TEM) is often used. TEM provides high-resolution images that help confirm the spherical nature and lamellarity (single or multilayered structure) of spanlastic

vesicles. This method is crucial for verifying that the vesicles are well-formed and suitable for drug encapsulation.[23]

4. Zeta Potential

Zeta potential measures the surface charge of the vesicles, which reflects their electrostatic stability in suspension. A higher magnitude of zeta potential—whether positive or negative—typically means the vesicles are less likely to aggregate over time. This parameter is measured using a Zetasizer, which operates based on the principle of electrophoretic mobility in an electric field.[24]

5. Elasticity Measurement

The flexibility or deformability of spanlastic vesicles is evaluated using the Deformability Index (DI). This test involves forcing the vesicles through a polycarbonate membrane with defined pore sizes under controlled pressure. The degree to which the vesicles deform and pass through the pores gives insight into their ability to navigate biological barriers like mucosal membranes. A higher deformability index suggests better penetration potential. The DI is calculated using the formula[25]

$$DI = J\left(\frac{rv}{rp}\right)^2$$

Where

- J = amount of vesicle suspension extruded in 10 minutes
- rv = size of spanlastic vesicles after extrusion
- rp = pore size of the membrane

6. Stability Assessment

To evaluate long-term stability, spanlastic formulations are typically stored at 4°C and 25°C for a period of up to three months. At defined intervals (such as 30, 60, and 90 days), samples are withdrawn to assess parameters like drug retention, vesicle size, and percentage entrapment efficiency (%EE). This helps in determining how well the formulation maintains its integrity and drug-holding capacity over time.[26]

7. Drug Content

Determining the total drug content involves disrupting the spanlastic vesicles to release the encapsulated drug. Isopropyl alcohol is commonly used to rupture the vesicles. The released

drug is then quantified using UV-visible spectrophotometry. This test ensures that the correct dosage has been incorporated into the system.[27]

8. Entrapment Efficiency (%EE)

Entrapment efficiency refers to the percentage of drug successfully encapsulated within the vesicles compared to the total drug used. After centrifuging the formulation to separate unencapsulated drug, the supernatant is analysed. The amount of drug retained in the vesicles is then calculated using the formula.

$$\%EE = \frac{Entrapped\ drug}{Total\ drug\ added} \times 100$$

This parameter is crucial for optimizing drug loading and therapeutic efficacy.[28]

9. In Vitro Drug Release

To study how the drug is released over time, in vitro release tests are conducted using Franz diffusion cells. The spanlastic formulation is placed in a donor compartment, separated from a receptor compartment by a semi-permeable membrane. The receptor chamber contains a buffer solution and is maintained at body temperature (around 37°C). Samples are collected at specific time intervals and analysed spectrophotometrically to determine drug release kinetics.[29]

Factors influencing the physiochemical properties of spanlastics

The structural and functional integrity of spanlastics is influenced by multiple formulation and processing variables. These factors determine the vesicles' morphology, stability, entrapment efficiency, and overall therapeutic performance. Below are the major contributors.

1. Membrane Additives

The inclusion of additives such as surfactants (e.g., Tweens) alongside the main ingredients can enhance vesicle flexibility, allowing better passage through biological membranes. These supplements affect the vesicle's shape, size, and membrane permeability, thereby supporting the stability and bioavailability of spanlastic formulation.[30]

2. Drug Properties

The nature of the drug being encapsulated plays a crucial role in vesicle formation and behaviour. Parameters like molecular weight, solubility (hydrophilic/lipophilic balance), and

the chemical structure influence drug entrapment efficiency. Higher drug interaction with surfactants often leads to larger vesicles due to repulsive forces between bilayers.[31]

3. Hydration Temperature

Temperature during the hydration phase directly impacts vesicle size and shape. Elevated temperatures can promote the formation of spherical vesicles, whereas moderate hydration results in more elongated or varied structures. Cooling spherical vesicles post-hydration often leads to the development of smaller, clustered vesicles with different morphologies.[32]

4. Surfactant Type and Concentration

The hydrophilic-lipophilic balance (HLB) of surfactants governs vesicle size and drug loading capacity. Surfactants with lower HLB (e.g., Span 85 with HLB 1.8) tend to form smaller vesicles, while those with higher HLB (e.g., Span 20 with HLB 8.6) result in larger, more hydrophilic structures. An optimal HLB value (\~8.6) has been observed to offer better drug entrapment, while excessively high or low values compromise vesicle formation.[33]

5. Surfactant Packing Structure

The spatial arrangement of surfactant molecules affects vesicle geometry. This is measured using the Critical Packing Parameter (CPP), calculated as[34]

$$CPP = V / (lc \times a_0)$$

Where

- V is the volume of the hydrophobic tail,
- lc is the length of the tail at the critical point, and
- a_0 is the area of the hydrophilic head.

A well-balanced CPP ensures predictable and efficient vesicle formation.

6. Edge Activators

Edge activators, typically surfactants with low surface tension (e.g., Tween 80), increase membrane fluidity and flexibility. Those with a low HLB promote small, deformable vesicles, improving drug delivery. However, overly hydrophilic activators may destabilize the vesicles, while highly lipophilic ones can hinder encapsulation.[35]

7. Entrapment Efficiency

Entrapment efficiency (%EE) indicates the formulation's ability to retain the drug within the vesicles. It is affected by surfactant composition, preparation method, drug properties, and edge activators. Higher %EE is associated with an optimal balance between vesicle stability and membrane fluidity.

8. Sonication Time

The duration of sonication influences particle size and entrapment. Prolonged sonication reduces vesicle size due to increased energy input but may also decrease %EE. An optimized sonication protocol ensures vesicle uniformity without compromising drug loading.[36]

Applications of spanlastics

Nanovesicles, initially popular in cosmetics, are now widely explored for drug delivery due to their ability to encapsulate both hydrophilic and hydrophobic drugs. Spanlastics, a type of nanovesicle, offer advantages like low toxicity, affordability, biocompatibility, and stability. They can co-deliver multiple drugs, making them effective for achieving targeted therapeutic outcomes. Their small size enhances penetration and retention in tumor tissues, showing promise for cancer treatment applications.

Spanlastics in Site-Specific Drug Delivery

1. Ocular Drug Delivery

Spanlastics have shown great potential in delivering drugs directly to ocular tissues, overcoming barriers such as the corneal epithelium and aqueous humor. Their elasticity allows them to carry both hydrophilic and lipophilic drugs efficiently, improving retention and therapeutic efficacy compared to traditional eye drops. For instance, ketoconazole-loaded spanlastics prepared with Span 60 and Tween 80 achieved prolonged ocular retention and effective antifungal activity.[37]

2. Oral Drug Delivery

Although oral delivery is common, it presents challenges like low solubility, poor permeability, and first-pass metabolism. Spanlastics help overcome these by enhancing drug solubility and stability. For example, pravastatin-loaded spanlastics with Tween 80 showed significant improvement in bioavailability and sustained drug release when coated with an enteric polymer like Eudragit.[38]

3. Transdermal Drug Delivery

Spanlastics are ideal for delivering drugs through the skin, especially those with poor water solubility. Their deformable nature allows them to penetrate the stratum corneum and release active ingredients like NSAIDs and vitamins directly at the site. Studies have shown that spanlastic formulations can enhance skin permeation and provide long-lasting therapeutic effects.

4. Intranasal Drug Delivery

Spanlastics have also been developed for intranasal applications, targeting the central nervous system. Their ability to cross the blood–brain barrier via the olfactory route makes them useful for neurological conditions like epilepsy and Parkinson's disease. For example, piperine-loaded spanlastics demonstrated improved brain delivery and therapeutic efficiency via nose-to-brain transport.[44]

General Pharmaceutical Applications of Spanlastics

5. Gene Therapy

Gene therapies often face limitations due to delivery issues. Spanlastics, due to their nano-vesicular form, are being explored as non-viral carriers to safely deliver genetic material such as DNA. Their biocompatibility and flexibility make them promising tools for future gene delivery approaches.[39]

6. Protein and Peptide Delivery

Proteins and peptides like insulin and bacitracin suffer from degradation and low bioavailability. Nano-vesicular systems like spanlastics offer a solution by protecting these biomolecules and facilitating their transport across biological barriers. DGAVP (desglycinamide arginine vasopressin) is one example of a successful peptide delivered via such a system.[40]

7. Vaccine Delivery

Vaccines are sensitive to degradation and require stable carriers. Spanlastics made from non-ionic surfactants protect vaccine components and enhance their delivery. These systems help avoid degradation and maintain vaccine efficacy during administration.[43]

8. Chemical Drug Delivery

Spanlastics can encapsulate both hydrophilic and lipophilic chemical drugs, offering a versatile and cost-effective option for drug delivery. Their biocompatibility, biodegradability, and stability make them ideal for co-delivery of multiple drugs. A good example is carvedilol; a cardiovascular drug successfully loaded in spanlastics for enhanced therapeutic benefits.[42]

9. Miscellaneous Applications

Spanlastics have also been tested in parasitic diseases. Sodium stibogluconate-loaded nano-vesicles demonstrated better accumulation in the liver and bone marrow compared to conventional formulations, improving the treatment of parasitic infections.[45]

Applications of Spanlastics in Drug Delivery

Tabel No. 3: Adapted and rewritten from Lakshmi *et al.*, J. Adv. Med. Pharm. Sci. 2025; 27(5): 33–52.

Delivery Route	Drug	Purpose	Reference
Ocular	Ketoconazole	Enhances drug permeation through cornea	Kakkar & Kaur, 2011
Transdermal	Simvastatin	Improves skin permeability	Badr-Eldin *et al.*, 2022
Ocular	Clotrimazole	Increases ocular bioavailability	Abdelbari *et al.*, 2021
Intranasal	Lercanidipine HCl	Enhances absorption and nasal mucosal diffusion	Bukhary *et al.*, 2024
Transdermal	Fluvastatin sodium	Increases oral availability via skin absorption	El Menshawe *et al.*, 2019
Buccal (Mucoadhesive)	Carvedilol	Avoids hepatic metabolism, improving effect and uptake	Sallam *et al.*, 2021
Topical	Retinoic acid	Promotes skin penetration for better topical effect	Shamma *et al.*, 2019
Topical	L-Ascorbic acid	Enhances stability and potency	Elhabak *et al.*, 2021
Nasal (Brain Targeting)	Risperidone	Improves brain uptake and systemic absorption	Abdelrahman *et al.*, 2017
Trans-tympanic	Ciprofloxacin	Provides localized ear treatment for acute infections	Al-Mahallawi *et al.*, 2017
Transdermal	Sodium valproate	Boosts transdermal drug delivery	Badria *et al.*, 2020
Nose-to-Brain	Piperine	Enhances brain permeability and mucosal solubility	Gupta *et al.*, 2023
Buccal	Lacidipine	Improves absorption by bypassing liver metabolism	Mary D'Cruz *et al.*, 2021
Transdermal	Haloperidol	Facilitates skin-mediated drug penetration	Fahmy *et al.*, 2018

Ocular	Levofloxacin	Enhances corneal drug absorption	Agha *et al*., 2023
Transdermal	Thymoquinone	Improves drug stability and skin permeability	Alaaeldin *et al*., 2021
Nose-to-Brain	Flibanserin	Avoids hepatic metabolism; targets central nervous system	Alharbi *et al*., 2022
Transdermal	Fenoprofen calcium	Reduces GI side effects by dermal administration	Farghaly *et al*., 2017
Transdermal	Dapagliflozin	Improves skin absorption and drug stability	Barakat *et al*., 2024
Nose-to-Brain	Rasagiline mesylate	Boosts brain bioavailability	Ali *et al*., 2023
Topical	Benzalkonium chloride	Increases dermal penetration of antiseptics	Wagdi *et al*., 2023
Oral	Epigallocatechin Gallate	Enhances gastrointestinal absorption	Mazyed *et al*., 2021
Ocular	Itraconazole	Improves corneal delivery of antifungal drugs	ElMeshad & Mohsen, 2016
Ocular	Cyclosporine A	Enhances drug solubility for eye applications	Liu *et al*., 2019
Oral (Liver Targeted)	Ledipasvir	Improves liver-specific absorption	Fatouh *et al*., 2022
Topical	Luliconazole	Enhances transdermal penetration of antifungal agents	Marques *et al*., 2023
Nose-to-Brain	Zolmitriptan	Bypasses liver metabolism and targets the brain	Saleh *et al*., 2021
Intranasal	Cefdinir	Enhances solubility and nasal delivery	Chettupalli *et al*., 2024
Trans-ungual	Efinaconazole	Boosts nail bed penetration	Almuqbil *et al*., 2022
Transdermal	Raloxifene	Improves systemic bioavailability	Ansari *et al*., 2022
Ocular	Fluconazole	Provides prolonged drug effect for eye infections	Kaur *et al*., 2012
Transdermal	Letrozole & Quercetin	Increases efficacy, bioavailability, and reduces side effects	Mekkawy *et al*., 2022
Transdermal	Tacrolimus	Improves skin penetration for immunosuppressive therapy	Zaki *et al*., 2022
Buccal	Felodipine	Avoids hepatic metabolism and improves oral uptake	Natekar *et al*., 2023
Ocular	Ketotifen fumarate	Enhances bioavailability for allergic eye treatment	Elhabal *et al*., 2025

CONCLUSION

Spanlastics have emerged as a highly promising platform in the landscape of modern drug delivery, offering multiple advantages over conventional systems. Their unique structure,

composed of flexible surfactants and edge activators, allows them to deform and pass through biological barriers with greater efficiency. This adaptability enables improved drug absorption, sustained release, and enhanced therapeutic action across a range of delivery routes including oral, ocular, transdermal, intranasal, and even in advanced fields such as gene therapy and vaccine delivery. Comprehensive characterization such as evaluating vesicle size, surface charge, elasticity, and morphology is essential for ensuring the stability, functionality, and reproducibility of spanlastics formulations. These tests help optimize formulation parameters and predict their behavior in biological environments. Despite their many strengths, spanlastics still face challenges related to large-scale production, long-term stability, and drug leakage. However, continuous research and technological advancements are addressing these issues, bringing spanlastics closer to clinical application. As the demand for safer, more efficient, and patient-friendly drug delivery options grows, spanlastics stand out as a versatile and forward-looking solution in pharmaceutical innovation.

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