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Spanlastics: An Innovative Nanovesicular Platform for Advanced Drug Delivery

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Abstract:

In recent years, researchers have increasingly focused on novel drug delivery systems to address limitations of conventional dosage forms, particularly for drugs with low solubility, poor bioavailability, and limited permeability. Traditional formulations such as liposomes, niosomes, and nanoparticles have been developed to improve drug delivery; however, they often face challenges related to flexibility, stability, and deformability. To overcome these drawbacks, spanlastics were introduced as an advanced vesicular system. Spanlastics are elastic, non-toxic vesicles capable of entrapping drugs within their core, offering controlled and targeted delivery. Their nanosized vesicles, referred to as nanospanlastics, enhance the bioavailability of poorly soluble drugs and provide improved stability compared to liposomes, niosomes, and conventional nanoparticles. These systems are particularly effective in delivering both hydrophilic and lipophilic drugs to specific sites, reducing side effects and improving therapeutic outcomes. This review highlights the classification, preparation methods, mechanisms, evaluation techniques, and diverse applications of spanlastics in modern drug delivery.

Keywords: Nanoparticles, Spanlastic, Method of Preparation, Applications

Introduction

Nanoparticles (NPs) have emerged as versatile carriers exploited by researchers for the development of targeted drug delivery systems due to their elasticity and surface modification properties. [1] Among the various NPs, lipidic nanoparticles are the preferred carriers for solubilizing poorly water-soluble drugs due to their rapid uptake, biodegradability, and low toxicity. [2] The development of targeted drug delivery was initiated in the 1990s by Paul Enrilch; when he found out a drug delivery mechanism that would target directly to diseased cells. [3] Spanlastics are a novel drug delivery system, which entraps the drug in the core cavity in the form of the bilayer. The term Spanlastic (Span+ Elastic) was coined for the first time in 2011. These are highly deformable and elastic carriers similar to transfersomes. [4] These deformable vesicular carrier systems show improved permeability in contrast to drug solution.

These are amphiphilic in nature, in which the medication is encapsulated in a vesicle which is made by non-ionic surfactant. The size of spanlastics is very small and microscopic. These are the special class of nanovesicles which overcome the disadvantages associated with liposomes such as chemical instability. [5] Chemical instability in liposomes is due to their

predisposition to oxidative degradation and variable purity of phospholipids. The elastic nature of these vesicles is attributed to the presence of edge activators in their structure. [6] Spanlastic is a special class of vesicular carriers that act as site-specific drug delivery systems for targeting drugs to the target sites including ocular, oral, topical, and nasal application. [7] The article represents some salient features along with an overview of the preparation technique and the current application.

Nano-Spanlastics

Nano-spanlastics are elastic, nanoscale vesicular systems composed primarily of non-ionic surfactants (spans) combined with an edge activator that imparts flexibility to the vesicle membrane, enabling them to withstand mechanical stress and penetrate biological barriers effectively. Their structure consists of a hydrophobic bilayer formed by spans, surrounding an aqueous core capable of encapsulating hydrophilic drugs, while lipophilic drugs can be incorporated within the bilayer itself. [8, 9] The addition of edge activators such as Tween or sodium cholate reduces membrane rigidity and enhances deformability, resulting in improved drug loading, stability, and permeability.

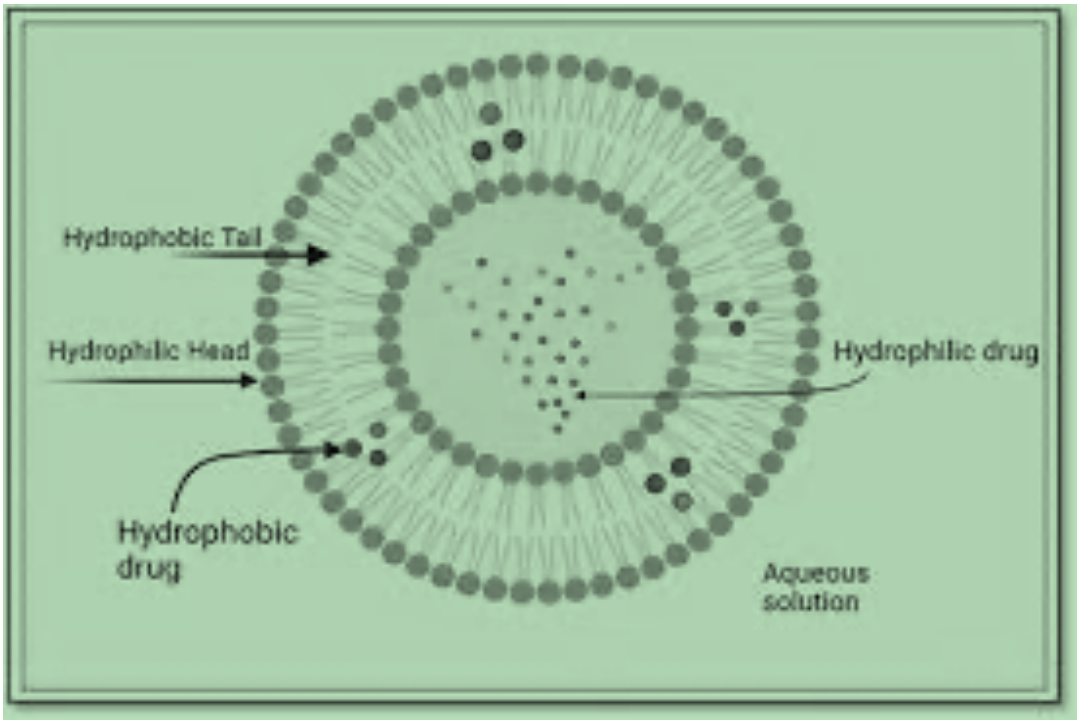

Figure 1: Structure of spanlastic

Fig. 1 illustrates that spanlastics consist of concentric bilayers, which may be either unilamellar or multilamellar depending on the number of bilayer membranes surrounding the core. Based on vesicle size, they are further categorized into small unilamellar vesicles (SUVs), typically ranging from 10-100 nm, and large unilamellar vesicles (LUVs), generally falling within the 100–300 nm range. [9]

Classification of Spanlastics

They can be classified based on the numbers of layer it composes of; which is illustrated as table 1

Table 1: Types of Spanlastics Vesicles [9, 10]

Type of Vesicle	Description	Size	Key Features
Multi-Lamellar Vesicles (MLV)	Consist of multiple bilayers; most widely used type	~0.5–1.0 µm	Simple to prepare; mechanically stable during long-term storage
Large Unilamellar Vesicles (LUV)	Contain a single large bilayer	100–300 nm (typically)	High aqueous-to-lipid ratio; capable of entrapping larger volumes of bioactive materials
Small Unilamellar Vesicles (SUV)	Formed from MLVs using sonication, French press, or extrusion	10–100 nm	Small size; produced by size-reduction techniques

Salient Features of Spanlastics:

- Spanlastics are capable of entrapping solutes that are both osmotically active and stable.
- Their bilayer structure enables controlled and sustained release of the encapsulated drug.
- They exhibit structural flexibility, allowing their properties to be adjusted according to specific therapeutic requirements.
- Spanlastics enhance drug availability at the target site by protecting the active ingredient from degradation in the biological environment.
- Their versatile design supports improved drug loading, stability, and overall delivery efficiency. [11]

Advantages:

- Spanlastics are biodegradable, non-immunogenic, and exhibit high compatibility with biological systems due to their nonionic surfactant composition.
- They significantly improve bioavailability by protecting drugs from degradation and ensuring efficient delivery to the target site.
- Their design enables target-specific drug delivery, minimizing off-target effects and enhancing therapeutic performance.
- These vesicles are osmotically active, stable, and capable of increasing the stability of entrapped drugs.
- Spanlastics are easy to handle and store, as surfactants require no special storage conditions.
- They can be administered via oral, parenteral, and topical routes, offering versatile drug-delivery options.
- Their structure helps prolong the systemic circulation time of drugs, supporting sustained and controlled drug release.
- Spanlastics are highly elastic and deformable, providing superior corneal permeability compared to conventional niosomes.
- Their flexibility allows them to penetrate both anterior and posterior ocular segments, reaching tissues such as the corneal membrane, vitreous cavity, and retinal pigment epithelium.
- They offer advantages such as chemical stability over liposomes, minimal eye irritation, cost-effective preparation methods, and easy availability of raw materials. [12, 13]

Limitations of Spanlastics

- Limited Encapsulation Efficiency for Hydrophilic Drugs
- Possible Vesicle Instability
- Surfactant-Related Irritation
- Residual Solvent Issues

- Temperature Sensitivity
- Short Shelf Life [14]

Components of Spanlastics

Spanlastics have a structural analogy with conventional liposomes. These are similar to Transfersomes which are highly deformable and elastic liposomes. Spanlastics are composed of two integral parts, a nonionic surfactant and an edge activator. Since these vesicles are primarily composed of Spans (Surfactants); hence, they have been named as Spanlastics. [15, 16]

Table 2: Components of Spanlastics [16]

Component	Role / Function	Examples
Non-ionic Surfactant (Span)	Forms the primary vesicular bilayer; provides structural integrity	Span 20, Span 40, Span 60, Span 80
Edge Activator	Increases elasticity and deformability of vesicles; enhances penetration	Tween 20, Tween 60, Tween 80, Sodium cholate
Drug / Active Pharmaceutical Ingredient (API)	Therapeutic agent encapsulated within the vesicles	Hydrophilic or lipophilic drugs
Aqueous Phase	Hydrates surfactant mixture and forms vesicle core; aids in encapsulation	Distilled water, buffer solutions
Stabilizers / Additives (optional)	Improve stability, prevent vesicle aggregation, enhance shelf life	Cholesterol, antioxidants

Mechanism of Penetration of Spanlastics

Edge activators (EAs) destabilize the lipid bilayers, thereby enhancing the deformability of spanlastic vesicles. The surfactants incorporated into these systems induce pore formation within lipid structures and, at higher concentrations, can even promote solubilization or lysis. Owing to their elastic nature, these vesicles are able to squeeze through intercellular pathways under the influence of a water gradient, a process governed by membrane-bending energy that depends on vesicle composition. [17, 18] As illustrated in Fig. 2, drug penetration occurs through two principal mechanisms:

- Elastic vesicles interact with epithelial cell membranes, functioning as penetration enhancers by modifying the intercellular lipid lamellae.
- Elastic vesicles serve as drug-carrier systems, enabling intact vesicles to traverse intercellular spaces and deliver the drug across biological membranes.

Successful passage of these carriers is primarily influenced by two factors:

- The stress-dependent elasticity of the vesicle bilayers, and
- The presence of an osmotic gradient.

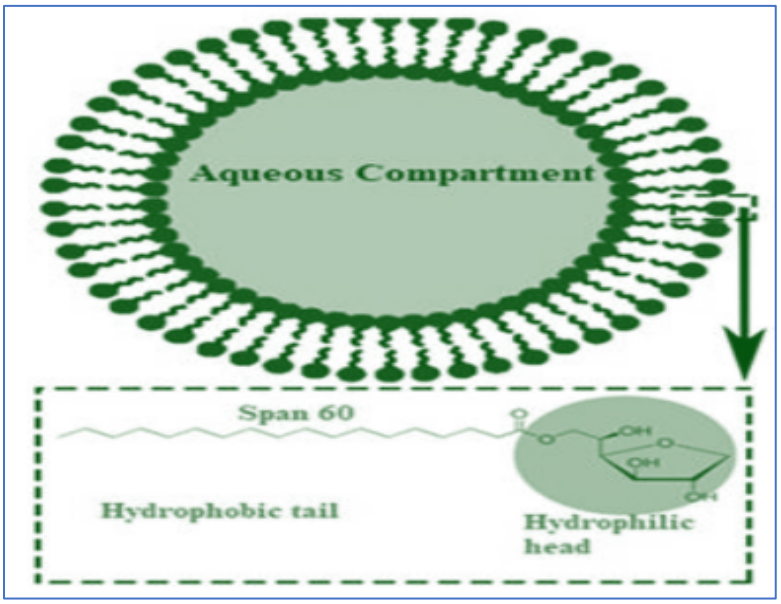

Fig. 2: Structure Of Surfactant Based Vesicular Carrier

Factors Affecting the Physico-Chemical Properties of Spanlastics:

Membrane Additives

The stability of spanlastics can be increased by the number of additives into the formulation along with the main surfactant and drug. The membrane stability, morphology, and permeability of vesicles are affected by numbers of additives e.g. tweens enhance the flexibility of the formed vesicles to easily enter into targeted area. [19]

Temperature of Hydration

Shape and size is also influenced by the hydration temperature. Assembly of the vesicles is affected by the temperature change of the system. The temperature change can also induce vesicle shape transformation.

Polyhydral vesicles of C16G2

solulan C24 (91: 9) is formed at 25 °C, but it is converted into spherical vesicles at 45 °C and on cooling from 55 to 49 °C, the vesicles produced a cluster of smaller spherical nano-vesicles. [20]

Characteristic of Drugs

Molecular weight, chemical structure, hydrophilicity, lipophilicity as well as the hydrophilic-lipophilic balance (HLB) value of the drug can affect the drug entrapment efficiency. Vesicle size may increase due to the entrapment of drugs. The surfactant head group does the interaction with drug particle, which probably leads to increase the charge on polymer and thus causes repulsion of the surfactant bilayer which further results in an increase in vesicle size. [21]

Content and Surfactant Type

The mean size of vesicles got increased proportionally as we increase the HLB value of surfactants like span 85 (HLB 1.8) to span 20 (HLB 8.6). It could be because of surface free energy that will decrease with the increment of hydrophilicity of surfactant. Alkyl chain is present in a well-ordered structure in a gel state, while in the liquid state the structure of the bilayer is more disordered. The gel–liquid phase transition temperature (TC) is used for the characterization of surfactant and lipids 30. Phase transition is also the reason for affecting Entrapment efficiency i.e. span 60

having higher TC, provide better entrapment efficiency. The entrapment efficiency of the spanlastics is affected by the HLB value for e.g. spanlastics have high entrapment efficiency at HLB value 8.6 but HLB value 14 to 17 is not suitable for their formulation. [22]

Method of Preparation

Preparation methods of spanlastics such as handshaking, ether injection or sonication hamper the final formulation characteristic an appreciable degree. For example, vesicles made up by ether injection are smaller when compared with the vesicles prepared by handshaking method. Therefore, hydrating the above mixture and then vortexing will help to reduce the vesicles made by hand-shaken method. [23]

In-vivo Behaviour of Spanlastics

In-vivo spanlastics have been found equiactive to nanovesicles and their distribution follows the same pattern as that of colloidal drug delivery system. The level of disposition of these constituents is appreciably high in life because of the natural vectoring process. Size variation also affects the pattern of drug disposal from blood; as larger sized vesicles get entrapped in the alveolar section of lungs due to retention or perhaps phagocytic action. While small-sized vesicles can easily pass through sinusoidal epithelium and will have better access to the spleen. [24]

Method of Preparation

There is different method of spanlastics preparation showed in table 3. [24, 25, 26, 27]

Table 3: Method of Preparation

Method	Procedure	Outcomes
Ether Injection Method	Slow injection of surfactant in 20 ml ether through a 14-gauge needle (25 ml/min) into preheated 4 ml aqueous drug phase at 60 °C. Ether is evaporated using a rotary evaporator.	Formation of single-layered vesicles after solvent evaporation.
Sonication Method	Drug solution in suitable buffer is added to surfactant mixture in a 10 ml vial. The mixture is sonicated using a titanium probe.	Produces small, uniform vesicles due to high-energy sonication.
Hand Shaking Method	Surfactants dissolved in organic solvent (ether/chloroform/benzene). Solvent is evaporated under reduced pressure. Dry surfactant film is rehydrated with aqueous drug solution under shaking.	Swelling of surfactant layer leads to vesicle formation with drug entrapped.
Extrusion Method	Surfactant and diacetyl phosphate film is prepared by solvent evaporation. Rehydrated with aqueous drug solution, then extruded through a 0.1 μm polycarbonate membrane for ~8 cycles.	Produces uniform-sized vesicles via repeated extrusion.
Microfluidization Method	Drug solution and surfactant solution are pumped at ultrahigh velocity through microchannels in an interaction chamber following the submerged jet	Provides high uniformity, reduced particle size, and reproducibility.

	principle.	

Spanlastics Characterization:

The in-vitro and in-vivo quality control test are needed for the nano spanlastics such as:

Spanlastics Morphology

The Transmission Electron Microscope (TEM) is a used to identify the morphological analysis such as size, shape, lamellarity, homogeneity and physical stability the samples were analysed at an accelerated voltage of 120Kv [28]

Vesicles Size and Poly Dispersity Index (PDI)

The size of vesicles and polydisperity index of the formulation is possible to measure by using dynamic light scattering [29].

Zeta Potential

Zeta potential (ZP) is indicating the stability of colloidal dispersion. When ZP value exists between 30 mv. The system is stable due to sufficient amount of repulsive force present between particles [30]. The zeta potential of the formulation can be measured by using zeta sizer equipment [31].

Entrapment Efficiency

The entrapment efficiency of the formulation such as spanlastics can be determined by using centrifugal method. The samples which are filled in 10 ml vial and kept in centrifuge for 30 minutes at 17,000 rpm. Then take 1ml of the supernatant liquid the volume is made up of suitable solvent. Using UV spectrophotometry, the amount of drugs present in the samples can be calculated. [32]

Spanlastics Elasticity

Elasticity is termed as deformability index the elasticity of nano spanlastics can be determined by using the extrusion process using a poly carbonate filter membrane consists of 200 nm pore width used to determine the elasticity extruded for 10 minutes at a constant pressure. [33]

Deformability index (DI)= J[rv/rp]2×100 (1)

In-vitro Studies

Using Franz diffusion cell the drug release can be determined in which consists of donor and receptor compartment which was separated by cellophane barrier In the receptor compartment the ph buffer solution 6.8 is placed and the samples were placed on the dialysis membrane Maintenance of temperature at 37°c and magnetically stirred at 500rpm.at different time interval the samples which are withdrawn and analysed through uv spectroscopy to determine the % release of drugs after proper dilution. [34]

Stability [45]

The non spanlastics formulation was under tested for stability by being kept in a glass vial at 4°c for 3 months. At different days interval such as 30,60&90 days of storage withdrawn and check the stability such as size, drug release was assessed. [35]

Application of Nano-Spanlastics

Originally developed for the cosmetics industry, nano-vesicles are now gaining popularity as an advanced drug delivery system due to their ability to encapsulate both hydrophilic and hydrophobic substances. Spanlastics, a type of nano-vesicle, are considered one of the most effective drug delivery mechanisms and have been developed for various therapeutics, including doxorubicin, vaccines, insulin, and siRNA. These vesicles can also serve as co-delivery systems, allowing simultaneous loading of two different drugs to achieve synergistic

therapeutic effects. From a formulation standpoint, spanlastics exhibit minimal toxicity, biodegradability, high stability, cost-effectiveness, and ease of storage. Their small size and enhanced permeability make them particularly useful for targeted cancer therapy, improving retention time in tumor tissue. Moreover, these nanovesicles can be conveniently administered via multiple routes, including transdermal, oral, and intravenous pathways, demonstrating versatile and efficient drug delivery capabilities. The various application of nanovesicles are given in table 4.

Table 4: Applications of Nano-Spanlastics [36-45]

Application	Description	Examples
Ocular Delivery	Spanlastics overcome pre-corneal and corneal barriers to improve ocular bioavailability. Can deliver site-specific drugs to both anterior (cornea, aqueous humor) and posterior (choroid, vitreous cavity, epithelium) segments. Can carry both lipophilic and hydrophilic drugs.	Enhances drug distribution and retention in ocular tissues.
Oral Delivery	Spanlastics improve oral bioavailability by overcoming poor solubility, frequent dosing, drug interactions, and systemic side effects. Enteric-coated spanlastic dispersions allow controlled release.	Example: Sodium pravastatin encapsulated in spanlastics showed improved oral bioavailability compared to aqueous solution.
Transdermal Delivery	Enables continuous drug release through the skin, avoids hepatic metabolism, and improves bioavailability and therapeutic efficiency.	Useful for sustained drug delivery and improved patient compliance.
Nasal Delivery	Spanlastics facilitate drug transport from the nasal cavity to the CNS via the trigeminal and olfactory pathways, bypassing the blood-brain barrier.	Effective for CNS-targeted drugs.
Topical Delivery	Provides localized therapy for skin disorders with improved penetration and efficacy.	Used for inflammatory conditions, fungal infections, and other dermatological ailments.
Peptides & Protein Delivery	Protects unstable proteins/peptides (e.g., insulin, bacitracin) from degradation, enhancing bioavailability during administration and storage. Supports oral delivery and vaccination.	Example: Insulin-loaded nanovesicles showed improved pharmacokinetics in diabetic rats and resistance to degradation in simulated gastric/intestinal fluids.
Vaccine Delivery	Non-ionic surfactant-based nanovesicles protect vaccines, improving stability and therapeutic efficacy.	Enhances safety and effectiveness of vaccines.
Gene Therapy	Nanovesicles help deliver DNA and other genetic materials, addressing challenges of clinical application due to delivery	Being explored to improve formulation and delivery efficiency.

	limitations.	
Miscellaneous Applications	Spanlastics have been used for specialized drug delivery against parasites and other conditions.	Example: Sodium stibogluconate-loaded nanovesicles effectively targeted spleen, liver, and bone marrow.

Conclusion

The development of novel surfactant-based vesicles, such as spanlastics, offers a noninvasive and efficient approach for delivering drugs directly to their target sites, reducing the need for frequent administration. These vesicles effectively address challenges like poor solubility, instability, low bioavailability, and rapid drug degradation. Consequently, spanlastics represent a significant advancement in nano-vesicular drug delivery systems. They can be utilized for site-specific delivery of both lipophilic and hydrophilic drugs and are currently being applied for drug administration via ocular, oral, topical, transungual, nasal routes, as well as delivery to the middle ear.

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