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SPANLASTICS-FUTURE OF DRUG DELIVERY AND TARGETING

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ABSTRACT

Delivery of drugs to the targeted tissues is restricted by various barriers. Conventional drug delivery systems like solutions, suspensions, emulsions, tablets, capsules etc. have been devised for treatment of diseases. However, these regimens remained unsuccessful due to poor bioavailability and patient incompliance. Thus, novel drug delivery system (NDDS) such as nanoparticles, nano emulsions, liposomes, dendrimers etc. have been devised to achieve better drug delivery action. As an evolution in drug delivery systems, a new system has been introduced in 2011 named as Spanlastics®. These are highly elastic and deformable, non-ionic surfactant-based vesicles in which an aqueous solution of solute is entirely enclosed by a membrane resulting from the organization of surfactant macromolecules as bilayer. The current review summarizes the structure, advantages, composition, mechanism of drug penetration, method of preparation, evaluation and applications of Spanlastics in drug delivery and targeting. The work focuses on the utility of spanlastics® as drug carriers for site specific action.

KEYWORDS: Nanoparticles, Drug delivery, Spanlastics®, Non-ionic surfactant, Drug carriers.

INTRODUCTION

There are many issues in drug release via conventional as well as novel drug delivery systems such as: (1) Undesirable side effects arising as a result of unfavorable pharmacokinetics and biodistribution (2) Drug degradation and (3) Low drug efficacy due to inefficient uptake at the target site. Colloidal vesicular systems play an essential part in this segment. These nano

ranged carriers incorporate drugs into their vesicular structures and selectively bind to target cells. The main aim of nano drug delivery system is to produce therapeutically and useful formulations for treatment of site specific diseases.[1] Nanotechnology has played a significant role in overcoming the challenges associated with conventional systems for drug delivery. Introduction of elastic vesicular carriers have further added value to this segment. Elastic vesicular nano carriers aids in carrying drug across biological membranes such as skin, gastrointestinal mucosa, corneal membrane etc.[2] The first generation of elastic vesicles were developed in 1992 and referred to as Transfersomes. The carrier system could easily penetrate through the stratum corneum of skin and reach systemic circulation. In 1997 ethanol based soft vesicular carrier systems were developed for penetration through the skin. Second generation of elastic vesicles mainly consisting of non-ionic surfactants were introduced in 1999. Ganciclovir based elastic liposomes for enhanced trans ocular absorption were developed in 2007. It was proposed that Nano sized elastic vesicles can cross corneal structure having structural analogy with stratum corneum.[3,4]

Spanlastics

Spanlastic® are a special class of vesicular carriers for targeting drugs to specific sites including but not limited to ocular, oral, topical, nasal, otopical and trans-ungual application.

Structure and Composition

Spanlastics are composed of two integral parts, a nonionic surfactant and an Edge activator.[3,4]

Non-ionic Surfactant: Span-80 and Span-40 based vesicles show high degree of disruption, aggregation and instability in contrast to more sustainability with Span-60 based vesicles. It is the lipophilic nature of Span-60 that permits the formation of lamellar matrix vesicles[4-6].

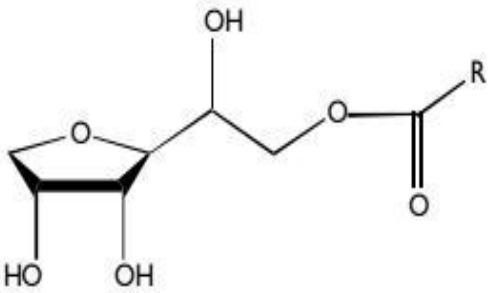

Figure 1: Chemical Structure of Span-60 (R=Saturated alkyl chain).

Edge Activators: Elastic nature of the vesicles is attributed to the incorporation of an edge activator like Tween-80. These hydrophilic surfactants can destabilize the vesicular membranes thus, increase their deformability.[8]

Ethanol: The membrane condensing ability of ethanol causes a decrease in thickness of vesicular membrane, thus, reducing vesicular size and resulting in some degree of steric stabilization.[9-12]

Morphology

Spanlastics® are spheroid structures consisting of amphiphilic molecules acting as suitable matrices for bio encapsulation.[13]

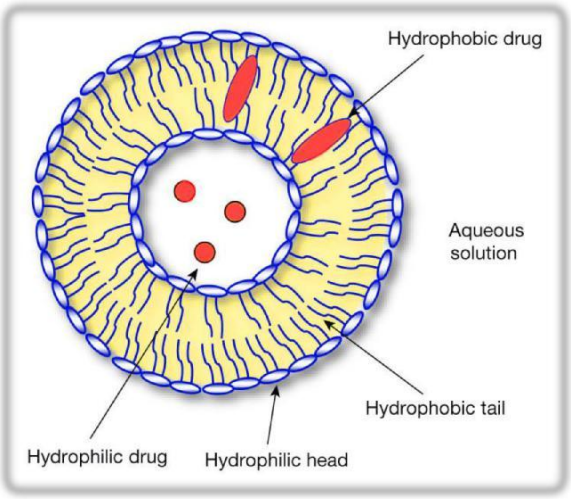

Figure 2: Structure of Spanlastic® Vesicle.

Mechanism of Action

There are two mechanisms for drug penetration.[4,14]

The elastic vesicles interact with the epithelial cell membrane and act as penetration enhancers, and subsequently modify the intercellular lipid lamellae.

The elastic vesicles can act as drug-carrier systems, whereby intact vesicles carrying the drug pass through the intercellular spaces and reach across the biological membrane. Following factors contribute towards successful passage of these carriers:

The highly stress-dependent elasticity of the vesicle bilayers

The existence of an osmotic gradient.

The surfactant provokes a solubilization (lysis) in the higher concentration range.

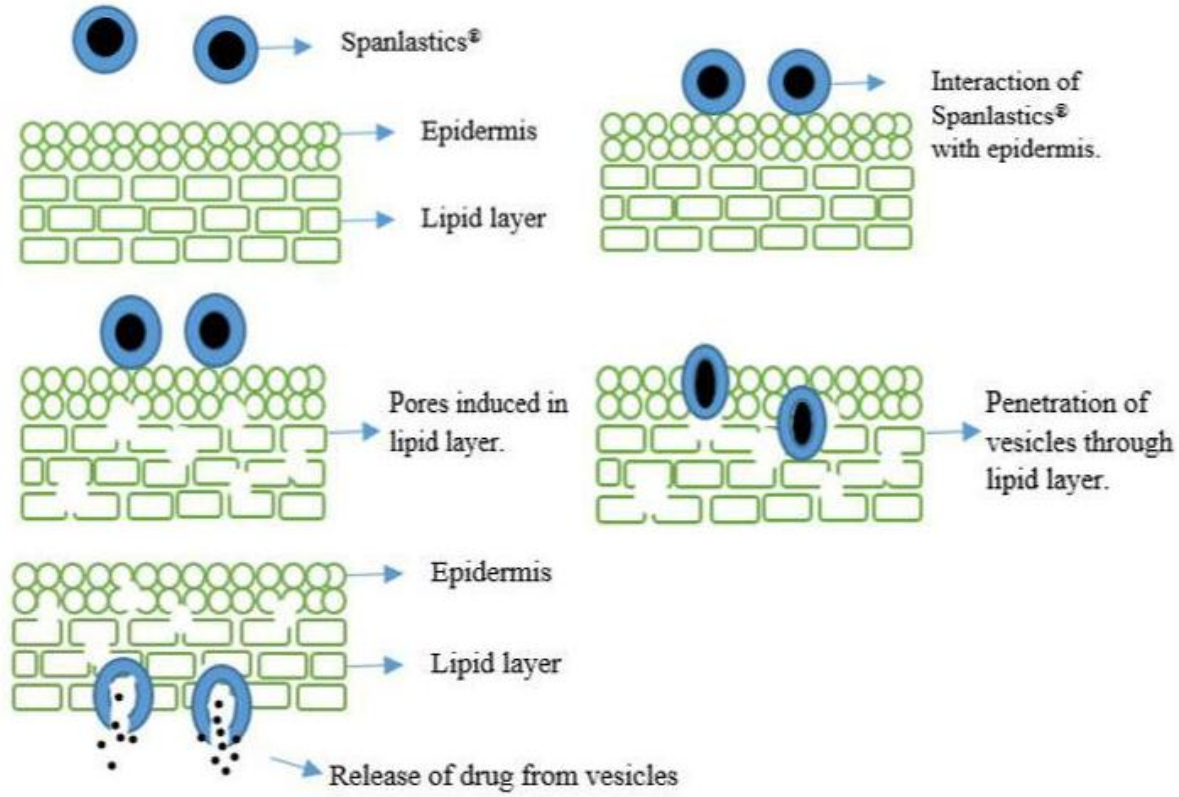

Figure 3: Schematic representation of mechanism of penetration of Spanlastics.

Advantages

Spanlastics are biodegradable and non-immunogenic in nature.

They protect the drug from biological environment by entrapping the drug within the lipid bilayer structure.[15,16]

Both hydrophilic as well as lipophilic drugs can penetrate through biological membranes like cornea via Spanlastics system.

They enable delaying the clearance of drug molecules from systemic circulation and exhibit low toxicity character.[6,17]

They are designed to achieve site specific action. The elastic nature of these vesicles enables them to squeeze through the corneal membrane, thus, they can reach the anterior segment of eye as well as to the posterior segment of eye to target the retinal pigment epithelium, vitreous cavity, choroid.[18,19]

They are chemically stable as compared to liposomes.

Handling of surfactants requires no special precautions and conditions.

The irritation power of surfactants decreases in the following order: cationic > anionic > ampholytic > nonionic so the nonionic surfactant based spanlastics® are non-irritant to the eyes.[20]

Economic method of preparation: Ethanol Injection Method. Access to raw materials is convenient.

METHOD OF PREPARATION

Ethanol injection method: Spanlastics containing nonionic surfactant and edge activator in a fixed ratio can be prepared by ethanol injection method. Span along with the drug to be encapsulated are dissolved in ethanol. The lipid solution is sonicated for 5 minutes. This solution is now injected at a constant rate into a preheated aqueous phase containing an edge activator (E.g. Tween-80) which is continuously stirred on a magnetic stirrer at 800-1600 rpm and 70-80°C for 30 minutes. The formulation is continued to stir for another 30 minutes at cold temperature. The final formulation is adjusted to 10 ml with distilled water. A drawback with this method is the difficulty in removing residual ethanol because it forms azeotrope with water and the possibility of various biologically active macromolecules to get inactivated in the presence of even low amounts of ethanol.[16,21]

Characterization of Spanlastics

Precise and reproducible quality control tests are required for accessing the in vitro and in vivo behavior of Spanlastics® formulation.[21-32]

Morphological examination-Structural attributes like lamellarity, uniformity of size, shape and physical stability characteristics are evaluated using transmission electron microscope (TEM).

Vesicle Size & PDI-The size and polydispersity index (PDI) of formulation can be evaluated by dynamic light scattering technique.

Zeta potential-It helps in determining the causes of dispersion, aggregation or flocculation. A low value of zeta potential indicates aggregation within a short time.

No. of vesicles per cubic millimeter- The number of vesicles per cubic mm can be counted using hemocytometer.

Entrapment efficiency-The entrapment efficiency of the Spanlastics® can be determined by ultracentrifugation method.

Elasticity measurement- Elasticity of vesicle membrane can be expressed in terms of deformability index.

Differential scanning calorimetry -It is one of the reliable methods to predict the drug-excipient interactions with the aid of thermograms.

In vitro drug release- Drug release from prepared Spanlastics® can be evaluated by dialysis bag membrane diffusion technique.

Corneal permeability-The permeability of the vesicles through cornea can be evaluated via freshly excised goat cornea mounted on Franz diffusion cell apparatus.

Stability-The prepared formulation can be examined for stability by storing for a period of 2 months and evaluating the formulation for various parameters.

Safety Considerations- Spanlastics® formulation can be evaluated by a range of tests such as Dermal irritation test, Ocular irritancy test, Mutagenic activity (Ames test).

Table 1: Characterization parameters for Spanlastics.

Parameter	Importance	Method
Morphology	Determine lamellarity	Optical microscopy, TEM
Size and PDI	Stability and size distribution	DLS measurements, Zetasizer
Zeta Potential	Stability of vesicles	DLS measurements, Zetasizer
No. of vesicles per cubic millimeter	Optimizing the composition and other process variables	Hemocytometer
Entrapment efficiency	Suitability of method, deciding the amount Important in of vesicle preparation to be used	Ultracentrifugation
Elasticity	Determine deformability of vesicles.	Extrusion method
Differential scanning calorimetry	Determine thermal properties of vesicular formulation.	Differential scanning calorimeter
In vitro drug	Determine the drug release rate	Diffusion bag method

release	from vesicle	
Corneal permeability	Determine penetration through corneal membrane.	Franz diffusion cell
Stability	To determine the shelf life of vesicle formulation	TEM, DLS, Ultracentrifugation
Safety	Determine safety for ophthalmic application.	Dermal irritation test, Ocular irritancy test and Ames test

Effect of Formulation Variables

Table 2: Effect of formulation variables.[34-36]

Formulation variables	% EE	Particle size & PDI	Drug release
Sonication time	Higher the sonication time of formulation, lower will be the % entrapment efficiency.	Higher the sonication time, lower will be the size of vesicles.	Drug release from vesicles decreases with an increase in sonication time.
Ratio of non-ionic surfactant and edge activator	% EE increases with increase in ratio of non-ionic surfactant and edge activator. Beyond a certain limit, any increase in this ratio will cause a reduction in % EE.	There is a significant decrease in particle size with an increase in concentration of edge activator.	High ratio leads to disruption of vesicular structure resulting in low drug release.
Stirring speed	Higher the stirring speed of the formulation, higher will be the drug entrapment in vesicles.	Higher speed of stirring will considerably reduce the particle size as well as cause a low value of PDI.	Stirring speed does not have a considerable effect on cumulative drug release from the vesicles.

Applications of Spanlastics® In Drug Delivery and Targeting

Nanotechnology has played a vital role in delivering drugs to target sites. Colloidal drug delivery systems such as nanoparticles, liposomes, niosomes, nano tubes etc. have achieved considerable attention in overcoming various barriers to drug delivery. However, some issues are still. Unaddressed. Existing systems need some modifications to successfully target drugs and other physiologic agents to the target site. Current literature provides evidence for establishing the usefulness of these elastic vesicular carriers in delivering drugs to target sites and overcoming barriers to drug delivery via various routes of administration. The applications of Spanlastics® in site specific drug delivery are described hereunder:

A. Ocular delivery
B. Oral delivery
C. Topical delivery
D. Nasal delivery

E. Otopical delivery

F. Ungual delivery

A. Ocular delivery

Ocular drug delivery system poses various challenges to researchers and pharmacologists. The limitations associated with ophthalmic drug delivery system are accounted to various pre-corneal and corneal barriers such as pre corneal drug loss due to lacrimation, reflex blinking, lower residence time of drug in cul-de-sac, complex structure of cornea acting as a barrier for penetration of drugs. The corneal tissues comprise three major layers of cells, i.e., a lipophilic outermost layer called the epithelium, a hydrophilic middle layer called the stroma, and an innermost layer of single cells called the endothelium. This complex structure of cornea act as a selective barrier to drugs. This leads to lower concentration of the drugs to targeted ocular tissues, thus, limiting ocular bioavailability. Nanotechnology has played a significant role in overcoming the challenges associated with conventional systems for ophthalmic drug delivery. Introduction of elastic vesicular carriers have further added value to this segment. Spanlastics® being a special class of vesicular carriers act as site specific drug delivery systems for targeting drugs to the anterior segment of eye that constitutes corneal membrane and aqueous humor as well as to the posterior eye segment that includes vitreous cavity, retinal pigment, epithelium and choroid. Spanlastics® can deliver both lipophilic as well as hydrophilic drug to ocular tissues.[4,33] Considerable research has been done for targeting different classes of drugs to specific ocular tissues for correcting various ophthalmic diseases. Some of them are described as follows.

A. 1. Imidazole antifungals

Disease targeted- Macular degeneration, Endophthalmitis, Chorioretinitis, Fungal Keratitis. Ketoconazole, a hydrophobic drug with large molecular weight and poor aqueous solubility shows a limiting ocular absorption. Incorporation of the drug in lipid bilayer of spanlastics® proved successful in improving corneal permeation and entry of drug to the posterior segment of eye. The preparation made use of non-ionic surfactant, Span-60 and edge activator, Tween-80. The drug loaded nano-vesicular formulation was prepared by ethanol injection method and showed better corneal permeability in contrast to conventional niosomal formulation. The formulation was evaluated for particle size, zeta potential, polydispersity index, elasticity, entrapment efficiency, in-vitro drug release, stability and safety. Spanlastics® loaded with carboxyfluorescein were prepared. The presence of fluorescence in

deep ocular tissues confirmed the penetration of drug loaded vesicles in the posterior segment of eye. The formulation was observed to be stable under various storage conditions and proved to be safe for topical application.

Studies lead to a conclusion that spanlastics® can be successfully employed to delivery different classes of drugs such as antivirals, antivascular endothelial growth factor, and oligonucleotides as well as antiangiogenic agents to target sites.[4]

Hydrophobic antifungal agent, clotrimazole, was successfully incorporated into surfactant based nano vesicle, Spanlastic®. The system constituted of Span-60 and edge activators Tween-80, sodium cholate or sodium deoxycholate. Formulations with varying types and concentrations of surfactant and edge activators were prepared and analyzed statistically. The optimized formulation was determined and comprised of sodium deoxycholate as edge activator and Span-60: edge activator ratio as 90:10. The drug loaded spanlastics® formulation showed remarkable entrapment efficiency % as 87.92% along with a zeta potential of -33.7 mV. Clotrimazole loaded spanlastics® showed sustained antifungal activity for a period of 12 hrs.[27]

A. 2. Bis-triazole antifungals

Disease targeted- Fungal Keratitis Elastic vesicular system containing Fluconazole for ocular delivery were successfully prepared and characterized. Fluconazole being hydrophilic with low molecular weight (306 Da) and having low protein binding was unable to reach in sufficient concentration to target ocular sites. To overcome this obstacle, non-ionic surfactant (Span-60) based nano vesicles were prepared that possessed elasticity and deformability due to various edge activators. Fluconazole loaded spanlastics® were prepared by ether injection method. The formulation showed better permeability across cornea in contrast to available market formulation Zocon® (0.3% w/v solution of fluconazole). The system was proved to be stable and safe in terms of genotoxicity, cytotoxicity and ocular irritation (as per OECD guidelines). The vesicular preparation showed good drug entrapment % (~66%) indicating the potential of spanlastics® as carriers for various classes of drugs to ocular regions.[5]

Spanlastics® containing span-60 and edge activators as Tween-20 or Tween-80 were examined to improve corneal permeability and anti-mycotic activity of Itraconazole. Poorly water soluble Itraconazole was loaded in lipid bilayer of spanlastics® that were prepared by modified ethanol injection method. Ex-vivo study using bovine cornea revealed that vesicles

were successful in achieving sustained drug release for 24 hrs. over conventional niosomal formulation. Anti-mycotic activity of experimental formulation was compared with existing marketed capsules Itrapex®. Placebo along with drug loaded spanlastics® was evaluated for antimycotic action using agar cup diffusion method. Highest diameter of the zone of inhibition was exhibited by Itrapex® followed by drug loaded spanlastics®. Placebo also showed a significant zone of inhibition that explains the anti-mycotic action of the vesicles alone that can be due to the presence of edge activators. Spanlastics showed entrapment efficiency of 88% and was safe in terms of ocular irritation and toxicity. Thus, it can be concluded that spanlastics can act as a promising vehicle for delivering Itraconazole as well as other anti-fungal agents across corneal membrane.[3]

A. 3. Carbonic anhydrase inhibitor

Disease targeted- Glaucoma Another discovery in ocular therapeutics was the preparation of mucoadhessive gellan gum in-situ gels of methazolamide nanovesicles. In order to avoid side effects due to oral administration of methazolamide and to prolong the retention time of drug in eye so as to reduce intraocular pressure, methazolamide was incorporated in spanlastics® and the system was formulated into in-situ gels. Different formulations consisting of a mixture of span-60 and various edge activators (Brij-35, Brij-58, Tween-60 and Tween-80) were prepared and evaluated for corneal permeability, residence time, intra ocular pressure reduction. Results revealed that in-situ gel containing Span-60 and Tween-60 (90:10) had better corneal permeability, highest residence time and considerable reduction in intra ocular pressure. Thus, spanlastics® can be employed in delivering anti-glaucoma agents to eye.[18]

B. Oral delivery

The most preferred route for drug administration is the oral route due to the advantages offered such as patient compliance and ease of administration. However, majority of the existing and newly discovered drugs administered by oral route undergo bioavailability problems due to various reasons such as poor solubility, frequent dosing, drug interactions, unpredictable absorption, first pass metabolism and systemic adverse effects. Several strategies have been introduced to improve drug bioavailability via oral administration. One such approach is the development of a novel surfactant based vesicular system. This requires the encapsulation of the drug in the spanlastics® system to overcome the barriers associated with oral drug delivery.

B. 1. Anti-neoplastic agent

Disease targeted-Multiple myeloma, Advanced ovarian adenocarcinoma, Breast cancer, Childhood neuroblastoma. Research was carried out with the aim of achieving sustained delivery of Melphalan for oral administration using spanlastics® carrier. Melphalan spanlastics® were prepared by ethanol injection method using non-ionic surfactants (Span-40 & Span-60) and Tween-20, Tween-60, Tween-80, Sodium taurocholate and Sodium deoxycholate as edge activators in varying ratios. The formulations were analyzed statistically by Design-Expert® software to determine the optimized formulation. The formula containing Span-60 and Sodium taurocholate (STC)/ Sodium deoxycholate (SDC) in ratio of 80:20 w/w was considered as optimized formulation. Characterization of this formulation revealed spherical vesicles with high entrapment efficiency of 78% and percentage drug release of 80%. It was observed that the particle size and zeta potential depended on the HLB (Hydrophilic Lipophilic Balance) value of the surfactant used. The vesicular size of optimized spanlastics formulation was 234 nm. The study revealed that melphalan loaded spanlastics® can be a good approach to provide sustained drug delivery for 8 hours by oral route.[36]

C. 2. Hypolipidaemic agent- HMG-CoA reductase inhibitor (Statins)

Disease targeted- Dyslipidemia, Cardiovascular disorders Research was envisaged for the encapsulation of Pravastatin sodium in enteric coated spanlastics® dispersions in order to achieve controlled release and targeted delivery at the duodenum. Drug loaded spanlastics® dispersions were prepared by ethanol injection method using non-ionic surfactant span-60 and edge activators in appropriate ratios. Prior to and post enteric coating of spanlastics® dispersions, the system was evaluated for various formulation variables. The optimized formulation showed nano sized vesicles (645 nm) with spherical shape and negative zeta potential. System exhibited high entrapment efficiency (~64%), higher Cmax, delayed Tmax, longer elimination half-life and improved oral bioavailability. Thus, the experiment revealed the utilization of spanlastics® in targeting lipid lowering drugs like pravastatin sodium to duodenum in controlled manner. It also contributed in improvement of oral bioavailability of the drug as compared to aqueous drug solution.[10]

C. Topical delivery

Administration of drugs via oral and parenteral routes are often associated with several adverse effects such as gastrointestinal intolerance, frequent dosing, first pass metabolism,

patient incompliance etc. Dermal application of therapeutic agents can overcome these barriers. Dermal drug delivery is superior than conventional oral and parenteral systems in several ways such as, it is a non-invasive therapy, improves patient compliance, avoids first pass metabolism, improves bioavailability, targets drug to the affected skin portion, prevents drug interaction as well as does not require frequent dosing of drugs. Stratum corneum acts as selective barrier to the permeation of drugs via skin. Hence, only limited preparations can be delivered via dermal route. Conventional topical formulations like topical gel does not allow the drug to penetrate deep into the skin. It is therefore, of utmost importance to overcome the permeability barrier of stratum corneum and achieve optimum drug concentration in the skin layers. This can be achieved by encapsulating the drug in a deformable elastic vesicular system i.e. Spanlastics® that can easily penetrate through the skin independent of concentration.

C.1. Non-steroidal anti-inflammatory agent

Disease targeted- Mild to moderate pain, rheumatoid arthritis and osteoarthritis Recently, a non-steroidal anti-inflammatory drug (NSAID) Fenoprofen calcium (FPCa) was encapsulated in Spanlastics® nanovesicular system by thin film hydration technique. The formulation was optimized by Design-Expert® software. Optimized formulation was evaluated for entrapment efficiency, particle size, and in vitro drug release. The optimized formula comprised of Span-60 and Tween-60 in the ratio of 8: 2 (w/w) in presence of Transcutol P as a cosolvent. The system exhibited the highest % entrapment efficiency (49.91 ± 2.60%), particle size of 536.1 ± 17.14 nm, deformability of 5.07 ± 0.06 g, and sustained drug release for 24 hrs. The in-vivo efficacy and anti-inflammatory effect of the developed spanlastics® gel via carrageenan-induced rat paw edema method revealed that the experimental formulation was three times better than the conventional FPCa gel. Thus, spanlastics® gel could be a potential approach for improving topical delivery of NSAIDs such as fenoprofen calcium as well as provide sustained anti-inflammatory and improved action.[35]

D. Nasal delivery

Intranasal drug delivery provides an alternative approach in delivering drugs to the target tissues without producing any systemic side effects that are often seen with oral and parenteral formulations. Nasal application offers several advantages over conventional oral an IV preparations such as, eliminates first pass metabolism, non-invasive technique, reduce the risk of drug degradation by gastric fluids and eliminates the need of frequent dosing.

Highly permeable structure of nasal membrane and presence of rich vasculature permits the rapid absorption of drugs that ultimately leads to rapid onset of action in contrast to IV and Oral preparations.

However, nasal delivery includes some setbacks such as, low permeability of nasal membrane for large molecules, mucociliary clearance, tissue irritation and presence of proteolytic enzymes. Strategies to overcome these drawbacks include: use of bioadhesive polymer and incorporation of enzyme stabilizers in nasal formulations as a means to prevent drug degradation. In addition, intranasal route also provides an effective transport to centrally acting drugs. Delivery of therapeutic agents to central nervous system is impaired due to blood brain barrier surrounding the brain. Incorporation of such therapeutic agents in a suitable nasal drug delivery system van overcomes this obstacle.

D. 1. Antiemetic agent

Disease targeted- Nausea and vomiting

Recently, a research has been done to develop Granisetron hydrochloride spanlastics® in the form of a nasal delivery system (nasal gels and nasal inserts) to target central nervous system and to improve bioavailability. Drug loaded spanlastic® dispersions were prepared by ethanol injection method and were evaluated for % entrapment efficiency, in-vitro drug release, particle size, zeta potential and polydispersity index. Evaluation results showed that the spanlastic® systems were of nano size with negative zeta potential that indicated stability of formulation. Granisetron loaded spanlastics® were effective in releasing drug for 6 hrs. and offered high entrapment efficiency. Study showed that granisetron spanlastics® in the form of nasal inserts resulted in higher % entrapment efficiency in comparison to nasal gel. This indicated the efficiency and potential of drug loaded spanlastics® based nasal insert in delivering therapeutic agents to brain.[37]

E. Otopical delivery

Middle ear infections are treated so far with conventional dosage forms like solutions, suspensions, tablets and capsules. But, these dosage regimens have been intended for systemic action. However, localized action is important for treating ailments affecting middle ear like acute otitis media. The local delivery of drugs at the infected site in middle ear can be attained via otopical delivery of antibacterial agents across tympanic membrane. This will help in elimination of pathogens and also prevents antibiotic resistance. One of the barriers to trans-tympanic delivery of antibiotics to middle ear is the impermeability of stratum corneum

of tympanic membrane. This highlights the need of developing an elastic nano vesicular system that could target drugs through the tympanic membrane to treat middle ear infections.

E.1. Quinolone antibiotics

Disease targeted- Acute otitis media

A similar research involved the encapsulation of ciprofloxacin into spanlastics® for otopical treatment of acute otitis media. Drug loaded spanlastics® were prepared by thin film hydration technique. The formulation was optimized statistically. Results revealed that optimal spanlastics® formulation comprising of Brij-35 (20 %) were of nano size (287.55 nm) with a high entrapment efficiency (51.81%) and good stability upon storage. Comparison of optimized formulation with commercial Ciprocin® drops revealed the superiority of spanlastics® in successfully targeting drugs to middle ear. Thus, spanlastics® can be promising approach for enhancing trans-tympanic delivery of ciprofloxacin.[38]

F. Ungual delivery

Human Nail apparatus (finger/toe) is vulnerable to attacks by fungal species (mostly *Trichophyton rubrum*) leading to a type of infection called as onchomycosis. Various treatment options have been deduced for onchomycosis. Oral administration of antifungal agents is the most common way, but, is accompanied with several unwanted effects such as, gastrointestinal side effects, drug interactions, lactose intolerance, relapse probability of infection etc.

Nail acts as a barrier to the entry of any foreign material. It therefore, forbids the permeation of antifungal agents via topical formulation. The delivery of antimicrobial agents via nail plate to achieve desired therapeutic action is quite a challenging task for research scientists and pharmacologists. In order to achieve the desired action, the antifungal agent should reach the target site. This highlights the need of developing a novel topical formulation for effectively delivering the drug via trans-ungual route to eliminate the infection.

E. 1. Allylamine antifungals

Disease targeted- Onchomycosis Terbinafine hydrochloride is the most potent antifungal agent for treatment of onchomycosis. Commercially it is available as Lamisil® 1% cream and Lamisil® oral tablets. Oral formulation is accompanied by various side effects as discussed above. Impermeability of the nail also forbids the delivery of drug via topical preparation. This necessitates the need to develop a novel topical system for targeting terbinafine to the

site of infection without causing any side effects. Terbinafine hydrochloride was loaded in Spanlastics® vesicular carrier system to enhance drug delivery via nails. The formulation comprised of Span-60 or Span-65 along with edge activators Tween-80 or Sodium deoxycholate. The drug loaded spanlastics® were prepared by ethanol injection method. Formulation was optimized by a full factorial design via design expert software.

The optimized formulation was evaluated for various parameters like particle size, polydispersity index, morphology, entrapment efficiency, drug release etc. Optimization of the formulation enabled the researchers to understand the effect of process and formulation variables on the vesicular preparation. It was observed that the sonication time had a profound effect on entrapment efficiency and particle size of terbinafine loaded spanlastic® system. Increased sonication time resultant in reduced particle size that caused a reduction in drug entrapment. Edge activators also had a considerable effect. Nanovesicles containing sodium deoxycholate resulted in greater entrapment efficiency in contrast to Tween-80. A similar effect was seen with the type of span used. Span-65 produced a higher drug release over span-60. Observations revealed that formula containing span-65 and sodium deoxycholate exhibited smaller particle size, high entrapment efficiency (62.35%), spherical shape and sustained drug release for 8 hrs.

Thus, spanlastics system hold a great potential in delivering antimicrobial agents via trans-ungual route for the treatment of onchomycosis.[34]

CONCLUSION

Spanlastics act as a breakthrough in ophthalmic drug delivery system. These vesicular systems can be exploited to achieve site specific action for both lipophilic and hydrophilic drugs. These elastic carrier systems have found applications in delivering drugs to ocular, oral, topical, trans-ungual, and nasal and to the middle ear. Spanlastics act as a vesicular system with the advantage of drug to be administered in the form of a drop, which increases patient compliance.

Future Prospects

This review summarizes the usefulness and potential of spanlastics in delivering dugs to the target site. These elastic nano vesicles hold a very bright future in site specific drug delivery. Spanlastics can be further investigated to explore the hidden advantages in targeting therapeutic agents to site of infection via ocular, oral, nasal, otopical, ungula and topical.

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