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Current Approaches to Surface Modification and Target Tactics for Oral Administration of Liposomes: An Overview

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ABSTRACT

Background: The future researcher will be able to improve on present platform and address the current translational and it is aware of liposomal technology advancement to obstacle that still need to resolve. Liposomes imitate natural cell membranes and have long been analyze as drug delivery carriers due to magnificent entrapment capacity, bio-compatibility and safety. Oral drug delivery via the gastrointestinal tract is the dominant route for drug administration. Liposomes carriers can increase the drug bioavailability, solubility and protect the encapsulated therapeutic agents from the extreme condition found in Gastrointestinal tract. Orally delivered liposomal carriers can enhance drug solubility and protect the encapsulated therapeutic agents from the extreme conditions found in GI tract. Liposomes, with their fluid lipid bilayer membranes and their nanoscale size, can significantly improve oral absorption. Unfortunately, the clinical application of conventional liposomes has been hindered due to their poor stability and availability under the harsh conditions typically presented in the GI tract.

Purpose: The purpose of this study is know the surface modification and target tactics for oral medication administration using liposomes. Despite the success of parenteral the liposomes oral delivery is blocked by various barriers such as instability in gastrointestinal tract difficulties in across. Perhaps substantially enhanced oral medication delivery by rectification of liposome bilayers and addition of polymers or ligands while accounting for liposome stability and permeability. To overcome this problem, the surface modification of liposomes has been investigated. Although liposomes surface modification has been extensively studied for oral drug delivery, so far no correction has been adequately integument in that topic.

Conclusion: The conclusion of overall study to overcome this problem, the surface modification of liposomes has been extensively studied for oral drug delivery.

1. Introduction

Even since the invention by Bangham in 1966, liposomes has been evolving steadily not only as nice tool to study the function of cell membranes but also as a unique drug carrier with enhanced efficacy and reduced toxicity (Fan & Zhang, 2013; TorchilinV.P, 2005). At present liposomes are available in an instant form and act as one of the best drug delivery system, solely owning to their capacity to encapsulate various drug entities excellent biocompatibility and easy interaction with bio membranes. The oral route is by far the most common route of drug administration in GI tract and can be used for both systemic drug deliveries for treating GI disease. It is most preferred route by patients' liposomes as drug carrier system for oral delivery resurged in recent year to modern modification technologies to enhance liposomal stability and permeation. By addition of polymer coating and modulating liposomal compositions both the stability of liposomes in the Gastrointestinal tract and trans epithelial absorption of active component have been significant improved. Oral delivery of liposomes has a long archive as well and can be discover to as early as the late 1970' (Patel & Ryman, 1976; Hashimoto & Kawada, 1979). Oral administration is the controlling route for drug delivery. It preferred above parenteral delivery due to its considerable clarity and convenience as well as increased patient consent as well as increased patient consent rates, all of which lead to magnify therapeutic well beings of patients. Liposome has been used as oral delivery aim for pharmaceutical, nutritional and nutraceutical substance. They can distribute to encapsulate both unstable hydrophilic and lipophilic compounds incorporate drugs, antimicrobial, vaccines and antioxidants, to shield and release them in a composed manner. (TorchillinV.P., 2005). In this review,

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the repute circumstances will be condensed on liposomes challenges and current approaches in surface modification functionalization and targeting strategies for oral drug delivery.

2. Classification of Liposome

Liposome dimension can vary via extremely small (0.025) up to large (2.5) vesicles. Besides, liposomes can have one or bilayer membranes. The vesicles dimension is an intense parameter in regulating the dissemination half-life of liposomes, and both dimension and number of bilayers influence the quantity of drug encapsulation within the liposomes. According to their dimension and number of bilayers, liposomes can further classify towards one of two section. (Shaheen *et al.,* 2006).

2.1. Based on Structural Parameters

2.1.1. Multilamellar vesicles (>0.5)	*MLV*
2.1.2. Oligolamellar vesicles (0.1-1)	*OLV*
2.1.3. Unilamellar vesicles (all size range)	*UV*
2.1.4. Small unilamellar vesicles (20-100nm	*SUV*
2.1.5. Medium sized unilamellar	*MUV*
2.1.6. Large unilamellar vesicles (>100)	*LUV*
2.1.7. Giant unilamellar vesicles (>1)	*GUV*
2.1.8. Multi vesicular vesicles (>1)	*MVV*

2.2. Based on Liposomes Preparation

2.2.1. Vesicles prepared by reverse phase evaporation method	*REV*
2.2.2. Multi lamellar vesicles by REV	*MLV-REV*
2.2.3. Stable plurilamellar vesicles	*SPLV*
2.2.4. Frozen and thawed MLV	*FATMLV*
2.2.5. Vesicles prepared by extrusion	*VET technique*
2.2.6. Fried reconstituted vesicles	*DRV (Siler-Marinkovic, 2006; Niu et al., 2012)*

3. Contrivance of Surface Modification in Oral Absorption of Liposome

To inaugurate this topic, it is major to outline the common circumstance of liposomes also the implanted drug contents subsequent oral administration. Orally executed liposomes are comparatively defeated consequently risk to gastric acid. Even with some of the substance drug is accomplished, substitute liposomes and its cargo recover. The vesicles and the constituent, generic bio macromolecules are encased in the oral bioavailability of liposomes at low intestinal permeability. Concentration of absorption raises beyond simultaneously polymer coating must be evidenced to successfully increase permeation through enteric epithelia. (Gauan *et al.,* 2015; Han *et al.,* 1997).

3.1. Enhanced Gastrointestinal Stability

Liposomes are susceptible to degeneration in respond to the associated consequence about gastric acids, bile salts and pancreatic lipases. Degeneration of liposomes conduct to the exposure of the payloads, thus more undergo to reactivation or degeneration of obligated drugs like protein and peptides. Exposure still induces precipitation of lipophilic component, thus decreasing the total fraction of oral absorption. Many studies show that enhancing the stability of liposomes or their payloads significantly improves oral bioavailability. In a sense, improving the stability means to enhance the surviving rate of liposomes and thereby enhance the opportunities to be taken up by intestinal epithelia. Several strategies have been applied to enhance the stability of liposomes, as the underlying mechanisms have been partly elucidated. (Wagner *et al.,* 2006)

3.2. Mucoadhesion

It relevant to suppose a certain mucoadhesive of liposomes to intestinal epithelia extends the liability of the vesicles in small intestine and upgrade chances for oral absorption. Polymers including polysaccharides. Further studies illustrate increased oral absorption to constancy of the polymers to the mucus layers and extended retention available in, expediting penetration of liposomes and contents through intestinal epithelial cells. (Huang *et al.,* 2011).

3.3. Facilitated Translocation Across the Mucus Layers

The intestinal absorbency of liposomes is known to be confined by the entrapping and speedy output of the mucus layers. The output juncture of the mucus layers are assumed to be a restricting circumstance that decides the transport juncture of mucoadhesive liposomes. The mucus -penetrating capacity is still to be assignation to the PEG chains of Pluronic F127 on the surface of liposomes such response hydrophobic and electrostatic interconnection of liposomes with mucins. (Thirawong *et al.,* 2008).

3.4. Enhanced Permeation Across the Enteric Epithelia

The oral bioavailability of liposomes is restricted by poor intestinal absorbency of each the vesicles and the contents, mostly bio macromolecules. Integration of absorption increases besides with polymer coatings has been displayed to successfully increases passing through across epithelia. (Gradauer *et al.,* 2013).Towards compact molecular weight drugs, the consequences and technique of absorption of augments are clear. It is merit neglecting that several absorptions increase such as bile salts act via multiple relative than a single technique.

3.5. Ligands-mediation Endocytosis

Encourage by the reality that a few nutrients are absorption, liposomes may be altered with nutritional ligands to attain active targeting to certain receptors in the enteric epithelial. Aggregation of liposomes at the position of absorption and sustained release of contents earlier to absorption supply to enhanced oral absorption also. (Parmentier *et al.,* 2014)

3.6. Uptake by M cells

M cells are differentiated epithelial cells detecting in the FAE of Payer's patches. They are capable of transfer a wide variety of particles, such as bacteria, viruses, and antigens, from the intestinal lumen to the ultimate lymphoid tissues. Accordingly, M cells are readily available for liposomes along procedure of adsorptive endocytosis, fluid phase endocytosis and phagocytosis. To further increases oral absorption, ligands as lectins, has been utilized to alter liposomes to target M cells channel bygone shown designate an appreciable route for the oral absorption of liposomes. (Parmentier *et al.,* 2010)

4. Challenges Confronting Liposomes as Oral Drug Delivery Systems

4.1. Poor Permeability

Conventional liposomes obtain poor permeability beyond intestinal epithelia considering of the adequately wide size of molecules and the occurrence of several epithelial barriers. There are frequently two recommended routes for enhancement of oral drug delivery determined liposomes. The vital is done drug release in the gastrointestinal lumen or ahead modification of vesicles across amalgamated micelles, and thus, alteration of drug molecule travel through the intestinal epithelia. (Hu *et al.,* 2013). Although inclusion concluded, the evidently path is superficially not empirical for susceptive bio macromolecules e.g. insulin. The enhanced penetration of bio macromolecules is evidently onward the second pathway; that is onward absorption of intact liposomes by M cells regulate in the follicle -associated epithelia of Peyer's patches. In dissimilar occurrence, the rapidly elimination and defending of gastrointestinal mucus therefore prohibit the oral absorption of liposomes also (Tian *et al.,* 2016), that are feasible captured in the mucus layer via hydrophobic coordination. Here is earlier no blunt indication substantiate the transit of entire liposomes through intestinal enterocytes.

4.2. Instability

Ordinary liposomes, are liable to connected deleterious consequence of gastric acid, bile salts and pancreatic lipases in the GIT, any one of which inculcate to convention absorption of intact liposomes and filling leakage. Developing formation by representing intestinal fluid for 120 min, a dimension of liposomes representation erratic shapes and obviously inappropriate membranes, whereas appropriate a compressed apportionment of liposomes regulate whole configuration. (He *et al.,* 2019). Pancreatic fluid such associate lipolytic enzyme such as lipases, phospholipase A2 and cholesterol esterase's, hydrolyses liposomal phospholipids with discompose liposomal configuration. whereas, the occurrence diverges for poorly water soluble drugs;attendantposition, the residual of liposomes can design recent disparate micelles, to that the envelop drugs are transferred to the prevalent vesicles and bring to intestinal epithelia determinant absorption. (Niu *et al.,* 2012).

4.3. Formulation Challenges

Although diverse liposomal methodology extinct strong marketed, the accomplish of liposomes is occasionally behind objection. Genuinely, the mass manufacture of liposomes is mostly unacceptable being batch-to-batch deviation. Despite it can have accommodated the necessity for parenteral preparation, the vast batch intensity still is not huge adequate for oral need, that generally desire higher doses and prolonged plan of treatment. Due to the uncertainty of liposomes in aqueous dispersion, there is every time a use to prepare liposomes into solid dosage conformation. (Chen *et al.,* 2010). Generally freeze-drying is engaged to outcome solid liposomal preparation with fine reestablish accommodations. Though, the freeze-drying technology is less potent and depletes much time and money, more potent technologies are desiderating for mass production of solid liposomal compound. (Kannan *et al.,* 2015).

5. Preparation of Liposome

Methods of liposome preparation

5.1. All the Methods of Preparing the Liposomes Associate Four Fundamental Divisions

5.1.1.Drying down lipids from organic solvent.

5.1.2.Dispersing the lipid in aqueous media.

5.1.3.Purifying the resultant liposome.

5.1.4.Analyzing the final product.

5.2. Method of Liposome Preparation and Drug Loading

The following methods are given for the preparation of liposome:

5.2.1. Passive loading techniques

5.2.2. Active loading technique.

5.2.1 Passive loading techniques include three different methods:

5.2.1.1 Mechanical dispersion method.

5.2.1.2 Solvent dispersion method.

5.2.1.3. Detergent removal method(removal of non-encapsulated material). (Hillaireau & Couvreur, 2009; Des *et al.,* 2006)

5.2.1.1. Mechanical dispersion method

The following are types of mechanical dispersion methods:

A. **Sonication**

Sonication is maybe the indisputable by and large use strategy as the assembling of SUV. These days, MLV is sonicated during a shower interaction sonicator or a test sonicator encompassed through a detached envelope. The fundamental impediments of such technique achieve outright under natural volume/epitome intensity, advantageous debasement of phospholipids and combined to be exemplified, the ruination of the monster molecule, metal contamination of test tip, and continuation of MLV created of SUV. (Agrawal *et al.,* 2014).

There are two sonication procedures:

a) Probe sonication. The point connected with a sonicator is totally consumed against the lysosome scattering. The intensity ingestion into lipid scattering is totally high in this strategy. The coupling of energy along the point end in neighborhood hotness; In this manner, the compartment likewise is invested in a water/ice shower. At the point when the sonication is responsible 1 h, also 5% with regard to the lipids may be esterified. Too, along the test sonicator, titanium will dispose of off and pollute the compound.

b) Bath sonication:The liposome scattering by means of a chamber is settled inside a shower sonicator. Taking advantage of the temperature of the lipid scattering is generally accessible in such technique, in variety of sonication over dispersal right away utilize the point. The material real sonicated perhaps moderated in a sterile vessel, particularly the test units, or embellishment an idle air. (Kastner *et al.,* 2014).

B. French Pressure Cell: Extrusion

French strain cell involves the launch of MLV over a little orifice(Himanshu *et al.,* 2011), A broad trait of the French press vesicle methodology is such the proteins don't recommend being thus impacted until the strategy as that are in sonication. A hypnotizing audit is in which French press vesicle appears to recall trickery solutes thus drawn out than SUVs execute, shaped by sonication or cleanser evacuation. (Kataria *et al.,* 2011).

C. Freeze-thawed liposomes

SUVs are expediently frozen and defrosted slowly. The momentary sonication broke down gathered materials to LUV. The creation of unilamellar vesicles is the point at which a result of the combination of SUV during the activity of freezing and defrosting. This type of union is effectively prevented through rising the phospholipid fixation and through rising the ionic solidness of the medium. The exemplification potencies from 20% to 30% were accomplished. (Mayer *et al.,* 1986)

5.2.1.2. Solvent dispersion method

a) Ether injection (solvent vaporization)

An answer of lipids diffused in diethyl ether or ether-methanol combination is continually infused toward a watery arrangement containing the material to be epitomized at 55°C to 65°C or above decline pressure. The ensuing freedom of ether above vacuum head towards the arrangement of liposomes. The crucial downsides of the technique are such the populace is heterogeneous (70 to 200 nm) and the vulnerability of arrangement proceeds dense to natural solvents concerning to huge temperature.

Ethanol injection: A lipid arrangement of ethanol is rapidly infused to a gigantic over-burden in view of the cushion. The MLVs persevere at prior creation. The downside of the strategy is such the populace is heterogeneous (30 to 110 nm), liposomes are amazingly weakened, the disposal of all ethanol is trying since it structures toward azeotrope by water, and the shot at the various naturally dynamic macromolecules till latent in the presence of even low measure of ethanol is high. (Song *et al.,* 2011;Pick, 1981).

Reverse phase evaporation method

This methodology added to liposome innovation by taking into account the initial time the blend of liposomes with a high watery space-to-lipid proportion and the capacity to capture a huge piece of the fluid material. On the planning of upset micelles, turn-around stage vanishing is set up. These rearranged micelles are shaped by sonicating a combination of a cradled watery stage that contains the water-solvent particles to be typified into the liposomes and a natural stage that solubilizes the amphipathic compounds. The upset micelles are changed over to a gooey state and gel structure as the natural dissolvable is gradually eliminated. The gel state implodes at a basic stage simultaneously, disturbing a portion of the upset micellar. Because of a wealth of phospholipids in the climate, a full bilayer structures around the leftover micelles, bringing about the improvement of liposomes. Invert stage dissipation liposomes can be produced from an assortment of lipid details and have a four-overlay higher watery volume-to-lipid proportion than hand-shaken liposomes or multilamellar liposome. (Ohsawa *et al*., 1985; Deamer & Bangham, 1976).

5.2.1.3 Detergent removal method (removal of non-encapsulated material)

a) Dialysis

To solubilize lipids, cleansers were utilized at their basic micelle fixations (CMC). As the cleanser is eliminated, the micelles develop more phospholipid-rich and in the long run join to make LUVs. Dialysis was utilized to take out the cleansers. Lipo Preparation is a financially accessible gear (Diachema AG, Switzerland), It is feasible to wipe out cleansers utilizing a dialysis framework, which is a kind of dialysis framework. Dialysis should be possible in colossal cleanser free cushions encased in dialysis sacks (balance dialysis). (Schieren *et al.,* 1978; Batzri & Gardner, 1973).

b) Detergent (cholate, alkyl glycoside, Triton X-100) removal of mixed micelles (absorption)

Shaking a blended micelle arrangement with beaded natural polystyrene adsorbers such XAD-2 dots and Bio-globules SM2 accomplishes cleanser ingestion. Cleanser adsorbers enjoy the benefit of having the option to dispose of cleansers with a low CMC that aren't totally drained.

c) Gel-permeation chromatography

The cleanser is drained involving size exceptional chromatography in this methodology. For gel filtration, Sephadex G-50, Sephadex G-l 00, Sepharose 2B-6B, and Sephacryl S200-S1000 can be used. Liposomes can't pervade the pores of the dabs in a section. They permeate through the cleft between the globules. Liposomes and cleanser monomers can be isolated very well at low stream rates. Since the expanded polysaccharide globules assimilate a lot of amphiphilic lipids, pre-treatment is required. Void liposome suspensions are utilized to pre-soak the gel filtration section with lipids for pre-treatment.

d. Dilution

The micellar size and polydispersity basically rise when a fluid blended micellar arrangement of cleanser and phospholipids is weakened with cushion, and as the framework is weakened past the blended micellar stage limit, an unconstrained change from polydisperse micelles to vesicles happens.

6. Evaluation parameter of Liposomes

6.1. Optical Microscopy

The vesicle generation and discreteness of dispersed vesicles were seen under the created liposomes. A slide was made by putting a drop of liposome scattering on a glass slide, covering it with a cover slip, and review it under a 40X amplification optical magnifying lens. Photos were taken utilizing an advanced camera and moved to arranged slides. [Himanshu *et al*., 2011).

6.2. Scanning Electron Microscopy (SEM)

The surface morphology of the created vesicles was concentrated on utilizing filtering electron microscopy. A drop of liposomal scattering was stored on a straightforward glass stub, air-dried, covered with a Polaron E 5100 falter coater, and seen under a checking electron magnifying lens. (Kataria *et al*., 2011).

6.3. Particle Size Determination

The molecule size is resolved utilizing a Horibunano molecule analyzer, with the Powerful Light Dissipating procedure being applied for this situation. Since it grants molecule size down to 1 nm width, Dynamic Light Dispersing (DLS, otherwise called Photon Connection Spectroscopy or Semi Flexible Light Dissipating) is one of the most utilized light dispersing techniques. (Handa *et al.,* 2006). The essential standard is clear: a laser pillar enlightens the example, and a quick photon identifier distinguishes varieties of the dissipated light at a predefined dispersing point. Optical magnifying instrument was utilized to decide the molecule size of liposomes. Direct perception under a magnifying lens is utilized to decide molecule size as mean distance across. There are two stages to the method.

6.3.1. Measurement of eye-piece micrometer

There are 100 divisions in the eye piece micrometer. Adjustment is the most common way of deciding the genuine length of every division. This is estimated against a common stage micrometer. It was noticed that the quantity of divisions in the eye piece micrometer (x) matched the quantity of divisions in th**e** stage micrometer (y). (Daemen *et al.,* 1995) Each stage micrometer division approaches 0.01 mm or 10 micrometers. Number of divisions of stage micrometer (y) separated by number of divisions of eye piece micrometer rises to one division of eye piece micrometer.

6.3.2. Measurement of globule size

The normal molecule size was determined after a bead of liposome plan was saved on a glass slide and set on the mechanical phase of a magnifying lens. The globule breadth was estimated and recorded for 100 globules.

6.4. Drug Entrapment Efficiency

The general medication content of the liposome scattering and the unentrapped drug content of the scattering was utilized to figure the medication capture productivity. The scattering's absolute burrowed content is determined by assessing complete medication ensnared and unentrapped. A volumetric jar was loaded up with 5 mL of liposome scattering. 30 minutes, the scattering was sonicated in a shower sonicator. The mix was then sifted and surveyed utilizing a UV Noticeable Spectrophotometer at 280 nm frequencies after a fitting weakening (Alpes *et al.,* 1986) For the free unentrapped drug, 5 ml of the liposome scattering was centrifuged at 18000 rpm for 40 minutes toward 50 degrees Celsius utilizing a Remi axis. The unmistakable supernatant was gathered independently, and how much free medication in the supernatant was determined utilizing a UV Apparent Spectrophotometer after an adequate weakening at 255 nm frequency. The accompanying equation was utilized to work out the ensnarement proficiency of the relative multitude of definitions.

% Entrapment Efficiency = 1– Unentrapped drug content Total drug content × 100

6.5. In vitro Diffusion Studies

The Franz dispersion cell gadget was utilized to lead in vitro dissemination examinations. The receptor compartment had a limit of 20 mL, and the region of the benefactor compartment was presented to the receptor compartment. Offers a dialysis layer 50 with an atomic weight cutoff of 12000 to 14000 Da. (Srinivas *et al.,* 2015) The examination utilized a Ltd with a level width of 24.26 mm and a distance across of 14.3 mm with a limit of 1.61 mL/cm. The film was absorbed phosphate cushion pH 7.4 short-term prior to being loaded up with 10 mL of created liposomal scattering containing 10 mg of medicine and embedded in the giver cell. Between the benefactor cell and the receptor, the cell was embedded in a dialysis film. In the receptor cell, 20 ml of phosphate cradle (pH 7.4) was utilized to wet the base surface of the dialysis film. To keep the receptor stage uniform, the temperature and the receptor compartment were upset with an attractive stirrer. (Chandran & P.VP, 2016) At various time spans, 3 ml aliquots were separated. A new medium was used to supplant the example extricated with an equivalent volume of the new medium. In a UV-Noticeable spectrophotometer, the examples were assessed at 255 nm, and how much drug delivered at various time stretches was assessed.

6.6. Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectrophotometry was utilized to investigate any expected connections between the medication and the excipients under assessment. Infrared spectroscopy with KBr as a background. To decrease dissipating impacts from huge gems, a little amount of the example is coarsely ground with a cleaned salt, regularly potassium bromide. In a mechanical pass-on press, the powder blend was squashed to frame a clear pellet through which the spectrometer's shaft could move. After cautiously eliminating the squeezed test from the pass-on, it was put in the FTIR test holder. (Chinnala & Panigraphy, 2016)

6.7. Microbiological Assay

The cup plate strategy was utilized to play out the Itraconazole microbiological testing. At a temperature, the potato dextrose agar medium was ready, cleaned, and immunized with candida Albicans microorganism. The immunized medium was immediately poured into Petri plates to give a uniform profundity of (4 to 5) mm and put away for cementing. Utilizing a cleaned chamber molded drill, little cavities of 10 mm distance across were made on set agar Petri plates. Every cavity got 500 l of the pre-arranged norm and test arrangements (comparing to 1 g/ml and 5 g/ml drug fixations, separately. As pre-hatching dissemination, these Petri plates are set at room temperature for 1 to 4 hours to diminish the effect of worldly contrasts between various solutions. (Faizi *et al.,* 2012) The width of round inhibitory is not entirely set in stone following 48 hours of brooding at 27 0C on arranged Petri plates. Microbiological examinations utilize the T-test to check whether there is a critical distinction between traditional and Itraconazole liposomal definitions.

7. Recent Advances in Modulating Liposomes for Oral Drug Delivery

7.1. Stabilization

Since liposomes are unsound during assembling, stockpiling, and travel through the GIT, an assortment of ways of further developing liposome strength have been explored, including lipid content control, surface covering, and inward thickening.

7.2. Modulation of Lipid Compositions

Phospholipids and cholesterols are normal parts of customary liposomes, which repeat the physiological arrangements of bio layers. Liposomes are touchy to the unfriendly gastrointestinal climate, despite the fact that they show some sturdiness in vitro and in vivo. Bile salts thoroughly harm liposomes containing phospholipids with stage change temperatures (Tp) underneath, albeit this effect is less articulated for those with Tp higher. It is a basic choice to work on the actual steadiness of liposomes in the beginning phases of improvement by changing lipid compositions. (Moghimipour *et al.,* 2015). Liposomes with stearyl amine are emphatically charged and equipped for lessening insulin processing by trypsin68 and working on the hypoglycemic impact. Because of further developed dependability in the GIT, supplanting phospholipids or cholesterols with specific lipids or sterols builds the presentation of oral drug conveyance of liposomes. Insulin-stacked liposomes produced using dipalmitoylphosphatidylcholine (DPPC) and a soybean-inferred sterol blend have a preferable hypoglycemic effect over standard liposomes, which the creator's characteristic to further developed lipid bilayer inflexibility (Ramana *et al.,* 2007) Bile salts, a sort of surfactant created by hepatocytes, have been proposed as the essential driver of liposome interruption in the GIT. Shockingly, past incorporation of bile salts into liposomal bilayers was found to ensure layers against the harmful impacts of physiological bile salts. It is generally settled that physiological phospholipids and bile salts rapidly structure colloidal blended micelles, which is the essential component for aliphatic corrosive and glyceride retention in the mouth. (Wasankar *et al.,* 2012).

7.3. Surface Coating

One more practical choice for shielding liposomes from the threatening gastrointestinal climate is to cover them with layers of polymers like intestinal polymers, proteins, and chitosans. Intestinal coatings have for quite some time been known to keep liposomes from dissolving in the stomach, further developing retention by permitting more liposomes to make due and be uncovered in the small digestive system. When contrasted with business tablets50, liposomes covered with Eudragit L100 increment the oral bioavailability of alendronate sodium by 12-crease in rats. (Miller & Bartha, 1989; Richards & Gardner, 1978) Be that as it may, a layer of intestinal polymers, like Eudragit S100, doesn't consistently secure against bile salt harm. For this reason, liposomes-in-microspheres conveyance frameworks utilizing chitosan-covered liposomes inside Eudragit S100 microspheres have been shown to be especially fruitful in opposing bile salt assault. One more sort of utilitarian covering material used to settle liposomes in the GIT84-87 is polysaccharides. At pH, arabinoside-stacked liposomes covered with O-palmitoylpullutan (OPP), a polysaccharide-ide subsidiary, may endure the harm delivered by sodium cholate (SC) up to 16 mol/L. (Hashimoto & Kawada, 1979) Moreover, contrasted with uncoated liposomes, OPP-covered liposomes showed a lower discharge rate at pH 2.0 and 5.6 at 37 1C84. In contrast with stripped liposomes, polysaccharide-covered liposomes stacked with ox-like serum egg whites (BSA) produce more significant levels of serum IgA and IgG, inferring further developed solidness of the model medication.

7.4. Interior Thickening

Thickening the inside fluid periods of liposomes can likewise further develop their actual steadiness. Inside thickening is typically set off by expanding the consistency of the inside watery stages, or by reconstituting lipid bilayers to encompass hydrogel dabs after blending them in with liposomes. The alleged Very sub-atomic Bio vector (SMBVTM), which consists of charged, cross-connected polysaccharide centers encompassed by lipid layers, has been found to be a decent protein transporter. One more gathering portrayed lipo beads made by self-collecting lipid bilayers encompassing hydrogel globules, which were set off by acrylamide-functionalized lipids appended to the outer layer of the beads. (Lwanaga *et al.,* 1997;Hosny *et al.,* 2013) Even at temperatures underneath Tp, in vitro testing uncovered further developed lipid bilayer strength. In situ gelling after the development of liposomes because of actual improvements can likewise bring about inside thickening. Lipo beads with higher mechanical strength and steadiness have been made utilizing UV-actuated polymerization inside liposomes. At the point when liposomes were warmed to a temperature over the gelling temperature (T gel), inward thickening was accomplished by embedding reverse-stage thermosensitive in situ gel into the watery period of the liposomes. (Barea *et al.,* 2012).

7.5. Other Strategies

Different strategies have been utilized to work on the security of liposomes notwithstanding the ones laid out above. For example, inventive twofold liposomes made by sifting preformed internal liposomes through a glass channel covered with lipid bilayers show stunningly better solidness. The external bilayers go about as defensive covers against gastrointestinal compound corruption, bringing about significantly better hypoglycemic (insulin) or hypocalcemia (salmon calcitonin) effects. (Kazakor & Levon, 2006) Liposomes were set in gelatin grids to settle the lipid bilayers and give controlled vesicle discharge in another review, notwithstanding the way that now in vivo information was provided.

8. Absorption Enhancement

8.1. Mucoadhesion-initiated Expanded Ingestion

Mucoadhesion gives liposomes a more drawn-out GIT home, permitting liposomes and additionally payloads to keep in touch with digestive epithelia for longer, expanding the odds of oral assimilation of either liposomal vesicles or payloads. Surface charges can be regulated or polymer coatings can be utilized to further develop mucoadhesionEmphatically charged liposomes work on oral bioavailability by acquiring mucoadhesion as well as protection from catalyst eradication. (Miguel *et al.,* 1995) One of the most encouraging procedures to accomplish mucoadhesion has all the earmarks of being covering liposomes with mucoadhesive polymers like polysaccharide. Gelatins are a kind of polysaccharide that is widely utilized. With high-methoxylated gelatin-covered liposomes playing out the insulin, gelatin-covered liposomes exhibit adherence to mucin.

8.2. Enhancer-facilitated Absorption

Various assimilation enhancers were utilized to test the oral retention of liposome payloads. At the point when TPGS 400, cetylpyridinium chloride, and cholylsarcosine were combined with stearylamine, the oral assimilation of liposomal fluorescein isothiocyanate (FITC)- dextran, a hydrophilic macromolecule1, was confirmed. (Katayama *et al.,* 2003) When Tween-80, a surfactant commonly utilized as a dissolvable, is added into liposomes at centralization of 1%, it further develops insulin's oral bioactivity. In an examination study, cetylpyridinium chloride beat a couple of other ingestion enhancers, for example, D-TPGS 400, phenylpiperazine, and sodium caprate octadacanehiol1 in working on the oral bioavailability of human development chemicals. Bile salts are a kind of physiological surfactant that aids in lipid retention. By joining bile salts into the lipid bilayers of liposomes, the oral bioavailability of an assortment of hydrophilic and lipophilic medications has been extensively expanded. There are people in total. (Ebato *et al.,* 2003; Takeuchi *et al.,* 2003) In light of the fact that medication discharge from liposomes is somewhat sluggish, the improvement is in all probability due to further developed SDC assimilation rather than expanded delivery. Non-ionic surfactants are additionally utilized as retention enhancers. Unreinforced liposomes were demonstrated to be essentially less viable than Tween 80-supported liposomes containing SPC and cholesterol. In contrast with the arrangement control 129, a higher region under the bend (AUC) and longer mean home time (MRT) improved ()-catechin retention following oral dosing. To help the retention of liposomal biomacromolecules, chemical inhibitors are constantly utilized related to enhancers. (Hashimoto & Kawada, 1979).

8.3. Polymer-facilitated Absorption

In addition to liposomal stability and mucoadhesion, polymers promote intestinal permeability. N-trimethyl chitosan has emerged as a popular polymer for coating liposomes for oral delivery of a variety of substances. Due to its capacity to open tight junctions. Another chitosan derivative, methylated N-(4-N, N-dimethylaminobenzyl) chitosan, was utilized to wrap FITC-tagged liposomes in Caco-2 cell monolayers to increase the permeability of a model protein, BSA. (Parmentier *et al.,* 2010). The efficiency of chitosans was increased by adding a cell-penetrating peptide such oligoarginineThese drugs may have both favorable and negative effects on epithelial junctions, it should be noted. The latter could result in poisons and payload entering at the same time, posing a threat. The advantages and disadvantages of using chitosans are still being researched. Liposome permeability across the mucus layer is obstructed by mucus trapping capacity and rapid turnover, both of which are well-known properties. (Parmentier *et al.,* 2014; Chen *et al.,* 2016) Liposomes have recently been coated with mucus-penetrating polymers to increase penetration. Liposomes coated with chitosan-thioglycolic acid 6-mercaptonicotinamide-conjugate (an S-protected thiomer chitosan with mucus-penetrating properties) enhanced physiological bioavailability by 8.2 times (areas above curves). Calcitonin (blood calcium levels) in rats after oral treatment.

8.4. Ligand-mediated Targeting to Epithelial Cells

To make up for the low penetrability of customary liposomes, ligands have been contemplated to further develop digestive tract take-up by epithelial cells by means of receptor-

intervened endocytosis. Lectins have been generally used to change liposomes for oral sharpening or oral medicine conveyance since most cell proteins and lipids in GIT cell layers are glycosylated. This is conceivable on the grounds that lectins perceive and tie to glycans in a particular way. (Chen *et al.,* 1996) When contrasted with Ulexeuropaeus agglutinin 1 (UEA 1)- adjusted liposomes containing insulin, raw grain agglutinin (WGA)- changed liposomes with insulin gave more noteworthy blood glucose regulation. However, the discoveries go against those of another exploration, which asserted that UEA 1 beat WGA. Mannose subordinates were utilized to change liposomes to target mannosyl receptors communicated in antigen-introducing cells (APCs) by exploiting the cooperation among lectins and glucans. IgA-covered liposomes containing ferritin showed worked on resistant reactions in that case. (Li *et al.,* 2011) The researchers ascribed the improvement to upgraded retention by means of M cells, despite the fact that they didn't determine which receptors were included. Fc pieces were utilized as ligands to change liposomes for dynamic focusing to neonatal Fc receptors in a new report. Insul146's hypoglycemic impacts were enormously further developed utilizing these liposomes. non-peptide ligands, for example, folic corrosive (FA) and biotin are prescribed for liposomal surface 40 because of the flimsiness of peptide ligands in the GIT. (Patil & Jadhar, 2014).

9. Mass Production

The act of creating liposomes as oral prescription conveyance strategies has ignited examination towards modern scale liposome large scale manufacturing. Liposomes can be made in the lab using an assortment of methods, including flimsy film scattering, switched stage dissipation, cleanser dialysis, dissolvable infusion, and a couple of others. (Hashimoto & Kawada, 1979). Helpless size dispersion, helpless cluster to-group repeatability, physicochemical flimsiness, natural dissolvable buildups, and high assembling costs are the whole issues that emerge during amplification. In late many years, a ton of exertion has gone towards beating these issues. On a one-liter scale, a persistent high-pressure expulsion framework was made to make liposomes of uniform size. The deficiency of meds during expulsion is viewed as a burden of this method. (Chan *et al.,* 2016). Liposomes with great actual security and embodiment viability have been made utilizing a high-velocity scattering strategy. The making of more modest liposomes, going in size from 280 to 350 nm, could be a worry with this technique. Huge liposomes containing plasmid DNA were cut back utilizing financially accessible instruments and high-pressure homogenization/expulsion. Regardless of the way that this methodology is prepared to do huge scope constant creation (1-1000 L/h), drug spillage and the high creation expenses of this mind-boggling process limit its modern applicability. (Gauan *et al.,* 2015; Han *et al.,* 1997). The ethanol infusion strategy is as of now the best option for modern organizations because of its straightforwardness and security. An enormous scope creation, the size dissemination might be constrained by changing the watery stage temperature. As of late, a micro-engineered nickel layer was utilized to deliver a clever ethanol infusion technique.

Conclusions and Prospective

Although each growing measurement about examinations at liposome circulation in the mouth, significant improvements are however needed to create and showcase these items for clinical utilization. The absence of comprehension of assimilation components is a hindrance to the making of oral liposomes. Liposomes are step by step separated as they venture out from the stomach to the small digestive tract. The medication payloads can either be delivered straightforwardly into the gastrointestinal lumen or moved onto auxiliary transporters like blended micelles and conveyed to the digestive epithelia for ingestion. This is the main method of prescription assimilation. This outlined the main strategy for medication retention. Delivered bits of labile bio macromolecules break down quickly and are not ingested; just liposomes that endure the gastrointestinal climate and infiltrate the bodily fluid layers can arrive at the digestive epithelia and be retained close by the payloads. The principal issue in further developing liposome and payload oral retention is to keep up with liposome respectability and draw out gastrointestinal home, taking into account better infiltration of the bodily fluid layers. Late advances are centered around adjusting the syntheses of the lipid bilayers or altering the liposomal surfaces with polymers or ligands to balance the in vivo fate of liposomes after oral organization.

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Authorship Contribution

Printy Dadwal: Conceptualization, Writing-Original Draft.
Adeeba Zahoor: Methodology, investigation, Writing-Review & Editing.
Nirmala: Data curation, resources.
Gurfateh Singh: Supervision, administration.

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Conflict of Interests

The authors declare no conflict of interest.

Declaration

It is an original data and has neither been sent elsewhere nor published anywhere.

References

Agrawal, A. K., Harde, H., Thanki, K., & Jain, S. (2014). Improved stability and antidiabetic potential of insulin containing folic acid functionalized polymer stabilized multilayered liposomes following oral administration. *Biomacro Molecules*, *15*(1), 350–360. https://doi.org/10.1021/bm401580k

Alpes, H., Allmann, K., Plattner, H., Reichert, J., Rick, R. and Schulz, S., (1986). Formation of large unilamellar vesicles using alkyl maltoside detergents. *Biochimicaet Biophysica Acta (BBA)-Biomembranes*, 862(2), 294-302.

Barea, M. J., Jenkins, M. J. *et al.,* (2010). Evaluation of liposomes coated with a pH responsive polymer. *International Journal of Pharmaceutics*, *402*(1-2), 89–94. https://doi.org/10.1016/j.ijpharm.2010.09.028

Barea, M. J., Jenkins, *et al.,* (2012). Encapsulation of Liposomes within pH Responsive Microspheres for Oral Colonic Drug Delivery. *International Journal of Biomaterials*, 2012, 458712. https://doi.org/10.1155/2012/458712

Barea, M. J., Jenkins, M. J., Gaber, M. H., & Bridson, R. H. (2010). Evaluation of liposomes coated with a pH responsive polymer. *International Journal of Pharmaceutics*, *402*(1-2), 89–94. https://doi.org/10.1016/j.ijpharm.2010.09.028

Batzri, S., & Korn, E. D. (1973). Single bilayer liposomes prepared without sonication. *Biochimica et Biophysica Acta*, *298*(4), 1015–1019. https://doi.org/10.1016/0005-2736(73)90408-2

Chandran, M. P. S., and Pandey, V. P. (2016). Formulation and Evaluation of Glimepiride-Loaded Liposomes by Ethanol-Injection Method. *Asian Journal of Pharmaceutical and Clinical Research*, *9*(4), 192-195.

Chen, C., Han, D., Cai, C. and Tang, X. (2009). An overview of liposome lyophilization and its future potential. *Journal of Controlled Society*, *142*(3), 299–311.

Chen, H., Wu, J., *et al.,* (2012). N-trimethyl chitosan chloride-coated liposomes for the oral delivery of curcumin. *Journal of Liposome Research*, *22*(2), 100–109. https://doi.org/10.3109/08982104.2011.621127

Chen, H., Torchilin, V., & Langer, R. (1996). Lectin-bearing polymerized liposomes as potential oral vaccine carriers. *Pharmaceutical Research*, *13*(9), 1378–1383. https://doi.org/10.1023/a:1016030202104

Chen, W. L., Yuan, Z. Q., *et al.,*(2016). Liposomes coated with N-trimethyl chitosan to improve the absorption of harmine in vivo and in vitro. *International Journal of Nanomedicine*, *11*, 325–336. https://doi.org/10.2147/IJN.S95540

Chinnala, K. M. and Panigrahy, R., (2016). Formulation and Evaluation of Acyclovir Liposomes. *International Research Journal of Pharmaceutical and Biosciences*, *4*(1).

Daemen, T., Hofstede, G., *et al.,* (1995). Liposomal doxorubicin-induced toxicity: depletion and impairment of phagocytic activity of liver macrophages. *International Journal of Cancer*, *61*(5), 716–721. https://doi.org/10.1002/ijc.2910610520

DeMiguel, I., Ioualalena, K., Bonnefous, M., Peyrot, M., Nguyen, F., Cervilla, M., Soulet, N., Dirson, R., Rieumajou, V., Imbertie, L. and Solers, C., (1995). Synthesis and characterization of supramolecularbio vector (SMBV) specifically designed for the entrapment of ionic molecules. *Biochimica et Biophysica Acta (BBA)-Biomembranes*, *1237*(1), 49-58.

Deamer, D., & Bangham, A. D. (1976). Large volume liposomes by an ether vaporization method. *Biochimica et Biophysica Acta*, *443*(3), 629–634. https://doi.org/10.1016/0005-2736(76)90483-1

desRieux, A., Fievez, V., *et al.,* (2006). Nanoparticles as potential oral delivery systems of proteins and vaccines: a mechanistic approach. *Journal of Controlled Release Society*, *116*(1), 1–27. https://doi.org/10.1016/j.jconrel.2006.08.013

Fan, Y. and Zhang, Q., (2013). Development of liposomal formulations: From concept to clinical investigations. *Asian Journal of Pharmaceutical Sciences*, *8*(2), 81-87.

Gradauer, K., Barthelmes, J., *et al., (*2013). Liposomes coated with thiolated chitosan enhance oral peptide delivery to rats. *Journal of Controlled Release Society*, *172*(3), 872–878. https://doi.org/10.1016/j.jconrel.2013.10.011

Guan, P., Lu, Y., Qi, J., Niu, M., Lian, R., & Wu, W. (2015). Solidification of liposomes by freeze-drying: the importance of incorporating gelatin as interior support on enhanced physical stability. *International Journal of Pharmaceutics*, *478*(2), 655–664. https://doi.org/10.1016/j.ijpharm.2014.12.016

Han, M., Watarai, S., Kobayashi, K., & Yasuda, T. (1997). Application of liposomes for development of oral vaccines: study of in vitro stability of liposomes and antibody response to antigen associated with liposomes

after oral immunization. *The Journal of Veterinary Medical Science*, *59*(12), 1109–1114. https://doi.org/10.1292/jvms.59.1109.

Handa, T., Sakano, M., Naito, S., Hiramatsu, M. andTsuboi, M., (2006). Thermal sio and h13co+ lineobservations of the dense molecular cloud g0. 11–0.11in the galactic center region. *The Astrophysical Journal*, *636*(1), 261.

Hashimoto, A., & Kawada, J. (1979). Effects of oral administration of positively charged insulin liposomes on alloxan diabetic rats: preliminary study. *Endocrinologia Japonica*, *26*(3), 337–344. https://doi.org/10.1507/endocrj1954.26.33

He, H., Lu, Y., Qi, J., Zhu, Q., Chen, Z., & Wu, W. (2019). Adapting liposomes for oral drug delivery. *Acta Pharmaceutica Sinica B*, *9*(1), 36–48. https://doi.org/10.1016/j.apsb.2018.06.005

Hillaireau, H., & Couvreur, P. (2009). Nanocarriers' entry into the cell: relevance to drug delivery. *Cellular and Molecular Life Sciences: CMLS*, *66*(17), 2873–2896. https://doi.org/10.1007/s00018-009-0053-z

Himanshu, A., Sitasharan, P. and Singhai, A.K., (2011). Liposomesas drug carriers. *IJPLS*, *2*(7), 945-951.

Hosny, K. M., Ahmed, O. A., & Al-Abdali, R. T. (2013). Enteric-coated alendronate sodium nanoliposomes: a novel formula to overcome barriers for the treatment of osteoporosis. *Expert Opinion on Drug Delivery*, *10*(6), 741–746. https://doi.org/10.1517/17425247.2013.799136

Hu, S., Niu, M., Hu, F., *et al.,* (2013). Integrity and stability of oral liposomes containing bile salts studied in simulated and ex vivo gastrointestinal media. *International Journal of Pharmaceutics*, *441* (1-2), 693–700. https://doi.org/10.1016/j.ijpharm.2012.10.025

Iwanaga, K., Ono, S., *et al.,* (1999). Application of surface-coated liposomes for oral delivery of peptide: effects of coating the liposome's surface on the GI transit of insulin. *Journal of Pharmaceutical Sciences*, *88*(2), 248–252. https://doi.org/10.1021/js980235x

Kannan, V., Balabathula, P., Thoma, L. A., & Wood, G. C. (2015). Effect of sucrose as a lyoprotectant on the integrity of paclitaxel-loaded liposomes during lyophilization. *Journal of Liposome Research*, *25*(4), 270–278. https://doi.org/10.3109/08982104.2014.992023

Kastner, E., Kaur, R., Lowry, D., Moghaddam, B., Wilkinson, A., & Perrie, Y. (2014). High-throughput manufacturing of size-tuned liposomes by a new microfluidics method using enhanced statistical tools for characterization. *International Journal of Pharmaceutics*, *477*(1-2), 361–368. https://doi.org/10.1016/j.ijpharm.2014.10.030

Kataria, S., Sandhu, P., Bilandi, A., Akanksha, M. and Kapoor, B., (2011). Stealth Liposomes: A Review. *International Journal of Research in Ayurveda & Pharmacy*, *2*(5), 1534-1538.

Katayama, K., Kato, Y., Onishi, H., Nagai, T., & Machida, Y. (2003). Double liposomes: hypoglycemic effects of liposomal insulin on normal rats. *Drug Development and Industrial Pharmacy*, *29*(7), 725–731. https://doi.org/10.1081/ddc-120021771

Kazakov, S., & Levon, K. (2006). Liposome-nanogel structures for future pharmaceutical applications. *Current Pharmaceutical Design*, *12*(36), 4713–4728. https://doi.org/10.2174/138161206779026281

Li, K., Chen, D., Zhao, X., Hu, H., Yang, C., & Pang, D. (2011). Preparation and investigation of Ulexeuropaeus agglutinin I-conjugated liposomes as potential oral vaccine carriers. *Archives of Pharmacal Research*, *34*(11), 1899–1907. https://doi.org/10.1007/s12272-011-1110-3

Mayer, L. D., Bally, M. B., Hope, M. J., & Cullis, P. R. (1986). Techniques for encapsulating bioactive agents into liposomes. *Chemistry and Physics of Lipids*, *40*(2-4), 333–345. https://doi.org/10.1016/0009-3084(86)90077-0

Miller, R.M. and Bartha, R., (1989). Evidence from liposomeencapsulation for transport-limitedmicrobial metabolism of solid alkanes. *Applied and Environmental Microbiology*, *55*(2), 269-274.

Moghimipour, E., Salami, A., & Monjezi, M. (2015). Formulation and Evaluation of Liposomes for Transdermal Delivery of Celecoxib. *Jundishapur Journal of Natural Pharmaceutical Products*, *10*(1), e17653. https://doi.org/10.17795/jjnpp-17653

Niu, M., Lu, Y., Hovgaard, *et al.,* (2012). Hypoglycemic activity and oral bioavailability of insulin-loaded liposomes containing bile salts in rats: the effect of cholate type, particle size and administered dose. *European Journal of Pharmaceutics and Biopharmaceutics*, *81*(2), 265–272. https://doi.org/10.1016/j.ejpb.2012.02.009

Ohsawa, T., Miura, H., & Harada, K. (1985). Improvement of encapsulation efficiency of water-soluble drugs in liposomes formed by the freeze-thawing method. *Chemical & Pharmaceutical Bulletin*, *33*(9), 3945–3952. https://doi.org/10.1248/cpb.33.3945

Parmentier, J., Hartmann, F. J., & Fricker, G. (2010). In vitro evaluation of liposomes containing bio-enhancers for the oral delivery of macromolecules. *European Journal of Pharmaceutics and Biopharmaceutics*, *76*(3), 394–403. https://doi.org/10.1016/j.ejpb.2010.09.002

Parmentier, J., Hofhaus, G. *et al.,* (2014). Improved oral bioavailability of human growth hormone by a combination of liposomes containing bio-enhancers and tetraether lipids and omeprazole. *Journal of Pharmaceutical Sciences*, *103*(12), 3985–3993. https://doi.org/10.1002/jps.24215

Patel, H. M. and Ryman, B. E., (1976). Oral administrationof insulin by encapsulation within liposomes. *FEBS Letters*, *62*(1), 60-63. https://doi.org/10.1016/0014-5793(76)80016-6

Patil, Y. P. and Jadhav, S., (2014). Novel methods for liposome preparation. *Chemistry and Physics of Lipids*, *177*, 8-18. https://doi.org/10.1016/j.chemphyslip.2013.10.011

Pick U. (1981). Liposomes with a large trapping capacity prepared by freezing and thawing of sonicated phospholipid mixtures. *Archives of Biochemistry and Biophysics*, *212*(1), 186–194. https://doi.org/10.1016/0003-9861(81)90358-1

Ramana, M.V., Chaudhari, A.D., Himaja, M., Satyanarayana, D. and Dua, K., (2007). An approach to minimize pseudomembranous colitis caused by clindamycin through liposomal formulation. *Indian Journal of Pharmaceutical Sciences*, *69*(3), 390. https://doi.org/10.4103/0250-474X.34548

Richards, M. H., & Gardner, C. R. (1978). Effects of bile salts on the structural integrity of liposomes. *Biochimica et Biophysica Acta*, *543*(4), 508–522. https://doi.org/10.1016/0304-4165(78)90305-7

S. R., Faizi, S. M. and Deshmuk, A. D. (2012). Formulation and development of liposomal gel for topical drug delivery system. *International Journal of Pharmaceutical Sciences and Research*, *3*(11), 4461.

Schieren, H., Rudolph, S., Finkelstein, M., Coleman, P., & Weissmann, G. (1978). Comparison of large unilamellar vesicles prepared by a petroleum ether vaporization method with multilamellar vesicles: ESR, diffusion and entrapment analyses. *Biochimica et Biophysica Acta*, *542*(1), 137–153. https://doi.org/10.1016/0304-4165(78)90240-4

Shaheen, S. M., Shakil Ahmed, F. R., Hossen, M. N., Ahmed, M., Amran, M. S. and Ul-Islam, M. A., (2006). Liposome as a carrier for advanced drug delivery. *PakJ Biol Sci*, *9*(6),1181-1191.

Siler-Marinkovic, S., (2016). Liposomes as drug delivery systems in dermal and transdermal drug delivery. *Percutaneous Penetration Enhancers Chemical Methods in Penetration Enhancement*, 15-38.

Song, H., Geng, H., *et al.,* (2011). Development of Polysorbate 80/Phospholipid mixed micellar formation for docetaxel and assessment of its in vivo distribution in animal models. *Nanoscale Research Letters*, *6*(1), 354. https://doi.org/10.1186/1556-276X-6-354

Srinivas, L., Tenneti, V. V. K. and Rajasri, A., (2015). Preparation and evaluation of liposome formulations for poorly soluble drug itraconazole by complexation. *Der Pharmacia Lettre*, *7*(8),1-17.

Takeuchi, H., Matsui, Y., Yamamoto, H., & Kawashima, Y. (2003). Mucoadhesive properties of carbopol or chitosan-coated liposomes and their effectiveness in the oral administration of calcitonin to rats. *Journal of Controlled Release Society*, *86*(2-3), 235–242. https://doi.org/10.1016/s0168-3659(02)00411-x

Thirawong, N., Thongborisute, J., Takeuchi, H., &Sriamornsak, P. (2008). Improved intestinal absorption of calcitonin by mucoadhesive delivery of novel pectin-liposome nanocomplexes. *Journal of Controlled Release Society*, *125*(3), 236–245. https://doi.org/10.1016/j.jconrel.2007.10.023.

Tian, J. N., Ge, B. Q., Shen, Y. F., He, Y. X., & Chen, Z. X. (2016). Thermodynamics and Structural Evolution during a Reversible Vesicle-Micelle Transition of a Vitamin-Derived Bolaamphiphile Induced by Sodium Cholate. *Journal of Agricultural and Food Chemistry*, *64*(9), 1977–1988. https://doi.org/10.1021/acs.jafc.5b05547

Torchilin V. P. (2005). Recent Advances with Liposomes as Pharmaceutical Carriers. *Nature Reviews Drug Discovery*, *4*(2), 145–160. https://doi.org/10.1038/nrd1632

Wagner, A., Platzgummer, M., Kreismayr, G., Quendler, H., Stiegler, G., Ferko, B., Vecera, G., Vorauer-Uhl, K., &Katinger, H. (2006). GMP production of liposomes--a new industrial approach. *Journal of Liposome Research*, *16*(3), 311–319. https://doi.org/10.1080/08982100600851086

Wasankar, S.R., Faizi, S.M. and Deshmuk, A.D., (2012). Formulation and development of liposomal gel fortopical drug delivery system. *International Journal of Pharmaceutical Sciences and Research*, *3*(11), 4461.

Yamabe, K., Kato, Y., Onishi, H., & Machida, Y. (2003). Potentiality of double liposomes containing salmon calcitonin as an oral dosage form. *Journal of Controlled Release*, *89*(3), 429–436. https://doi.org/10.1016/S0168-3659(03)00160-3

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