LIPOSOME TECHNOLOGY pdf

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The glutathione delivered through liposome technology is stable enough to penetrate mucous membranes. This permits rapid release of the products into your bloodstream. If you take glutathione orally without liposome technology, part of it is usually destroyed by your stomach acids.

Discovery[edit] The word liposome derives from two Greek words: Liposomes were first described by British haematologist Alec D Bangham [6] [7] [8] in published , at the Babraham Institute, in Cambridge. They were discovered when Bangham and R. The resemblance to the plasmalemma was obvious, and the microscope pictures served as the first evidence for the cell membrane being a bilayer lipid structure. Their integrity as a closed, bilayer structure, that could release its contents after detergent treatment structure-linked latency was established by Bangham, Standish and Weissmann in the next year. Around this time he was joined at Babraham by Gerald Weissmann , an American physician with an interest in lysosomes. Now an emeritus professor at New York University School of Medicine, Weissmann recalls the two of them sitting in a Cambridge pub and reflecting on the role of lipid sheets in separating the interior of the cell from the exterior milieu. This insight, they felt, was to cell function what the discovery of the double helix had been to genetics. It was Weissmann who proposed the more user-friendly term liposome. Hydrophobic chemicals associate with the bilayer. To deliver the molecules to a site of action, the lipid bilayer can fuse with other bilayers such as the cell membrane , thus delivering the liposome contents; this is a complex and non-spontaneous event, however. Liposomes can also be designed to deliver drugs in other ways. Liposomes that contain low or high pH can be constructed such that dissolved aqueous drugs will be charged in solution i. As the pH naturally neutralizes within the liposome protons can pass through some membranes , the drug will also be neutralized, allowing it to freely pass through a membrane. These liposomes work to deliver drug by diffusion rather than by direct cell fusion. A similar approach can be exploited in the biodetoxification of drugs by injecting empty liposomes with a transmembrane pH gradient. In this case the vesicles act as sinks to scavenge the drug in the blood circulation and prevent its toxic effect. Liposomes can be made in a particular size range that makes them viable targets for natural macrophage phagocytosis. Liposomes can also be decorated with opsonins and ligands to activate endocytosis in other cell types. The use of liposomes for transformation or transfection of DNA into a host cell is known as lipofection. In addition to gene and drug delivery applications, liposomes can be used as carriers for the delivery of dyes to textiles, [17] pesticides to plants, enzymes and nutritional supplements to foods, and cosmetics to the skin. Dietary and nutritional supplements[edit] Regarding the use of liposomes as a carrier of dietary and nutritional supplements; until very recently the use of liposomes were primarily directed at targeted drug delivery. However, the versatile abilities of liposomes are now being discovered in other settings. Liposomes are presently being implemented for the specific oral delivery of certain dietary and nutritional supplements. This new direction and employment of liposome science is in part due to the low absorption and bioavailability rates of traditional oral dietary and nutritional tablets and capsules. The low oral bioavailability and absorption of many nutrients is clinically well documented. These are very crucial elements which lead to the long term stability of the liposomes. These complex yet significant factors are the following: These primary and key elements comprise the foundation of an effective liposome carrier for use in increasing the bioavailability of oral dosages of dietary and nutritional supplements. They typically form after supplying enough energy to a dispersion of phospho lipids in a polar solvent, such as water, to break down multilamellar aggregates into oligo- or unilamellar bilayer vesicles. The original aggregates, which have many layers like an onion, thereby form progressively smaller and finally unilamellar liposomes which are often unstable, owing to their small size and the sonication-created defects. Sonication is generally considered a "gross" method of preparation as it can damage the structure of the drug to be encapsulated. Newer methods such as extrusion and Mozafari method [26] are employed to produce materials for human use. Using lipids other than phosphatidylcholine can greatly facilitate liposome preparation. These liposomes are known as " stealth liposomes ". They were first proposed by G. Blume [27] and, independently and soon thereafter, the groups of L. Torchilin [28] and are constructed with PEG Polyethylene Glycol

studding the outside of the membrane. The PEG coating, which is inert in the body, allows for longer circulatory life for the drug delivery mechanism. However, research currently seeks to investigate at what amount of PEG coating the PEG actually hinders binding of the liposome to the delivery site. In addition to a PEG coating, most stealth liposomes also have some sort of biological species attached as a ligand to the liposome, to enable binding via a specific expression on the targeted drug delivery site. These targeting ligands could be monoclonal antibodies making an immunoliposome , vitamins , or specific antigens , but must be accessible. Naturally toxic drugs can be much less systemically toxic if delivered only to diseased tissues. Polymersomes , morphologically related to liposomes, can also be used this way. Also morphologically related to liposomes are highly deformable vesicles, designed for non-invasive transdermal material delivery, known as Transfersomes. Liposomal cisplatin has received orphan drug designation for pancreatic cancer from EMEA. Results showed that these synthetic particles "soak into plant leaves more easily than naked nutrients," further validating the utilization of nanotechnology to increase crop yields.

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2: Liposome Technology - CRC Press Book

A liposome is a spherical vesicle having at least one lipid bilayer. The liposome can be used as a vehicle for administration of nutrients and pharmaceutical drugs. [2] Liposomes can be prepared by disrupting biological membranes (such as by sonication).

Excellent batch to batch consistency Mild procedure for long-term stability Polymun has also established a broad spectrum of analytical methods that enable development of liposomal formulations for a wide range of pharmaceutically active ingredients such as oligonucleotides, small molecules and proteins as well as vaccine antigens. Liposomal Formulation of Drugs Liposomes can play a key role in protecting and transporting drug to the right place and releasing it at the best rate. This enables better efficacy with reduced dose and helps to avoid side effects by enabling non-invasive application. Thus liposomal formulation can measurably improve the therapeutic index of a drug. Advantages of liposomal formulations Liposomal formulations offer the following specific benefits: Liposomes can protect drugs from degradation, prolonging biological half-life in the human metabolism. Liposomes can enhance solubility within the lipid membrane and aqueous core. Depending on their lipid composition, liposomes are able to localize, to target and to interact specifically with the affected tissue. Liposomes can target mucosa to encourage fast uptake of formulations and other targets to reach the skin and supporting tissue. Alternatively, liposome inhalers can target the lung. Liposomes constitute a depot of the drug resulting in sustained release. Thereby, undesired peak concentrations are avoided and availability is prolonged. This results in a lower frequency of application and the reduction of side effects. Liposomal formulations are used in cancer treatment for reducing the toxic side effects of the drug. Crossflow injection is a very mild procedure that allows processing of sensitive drugs. High quality raw materials and precisely controllable process parameters guarantee high batch-to-batch consistency â€” essential for pharmaceutical products. Polymun technology can achieve long term stability of liposomes, even at room temperature. Polymun Liposome Technology Polymun has transformed liposomes from a promising scientific idea into a sound industrial solution. The production technology is suitable for a broad range of substances formulated by passive entrapment, active loading or membrane incorporation. Main Characteristics Polymun liposome technologies possess a number of key attributes that make them particularly useful in drug development. Full Scalability The injection module is the heart of the liposome production. The process parameters determine the size of the liposomes regardless of scale. For example, lab scale formulations can be prepared in a few seconds with liters of liposome produced in just 90 minutes. Large scale also can be achieved by using several injection modules in parallel. Aseptic Process A closed system is used for production. All components can be added via sterile filtration, with subsequent concentration by crossflow filtration where required. Homogeneous, Uniform Vesicles All process parameters are controlled precisely. This results in a very narrow size distribution, necessary for reliable targeting and transport characteristics. Single Step Process Liposome size is adjusted by modulating the process parameters during vesicle formation. No additional downsizing is required. Excellent Batch-to-Batch Consistency Use of high quality raw materials and precisely controlled process parameters guarantee the excellent reproducibility that is essential for pharmaceutical products. Mild Procedure â€” Stability The crossflow injection technique is a very mild procedure that allows the processing of sensitive drugs. Together with the high quality of raw materials and narrow size distribution, Polymun liposomes exhibit long-term stability, even at room temperature. Polymun uses a range of different encapsulation techniques, depending on the nature of the drug, ranging from passive trapping of hydrophilic substances, active loading of amphiphilic substances and incorporating hydrophobic drugs or membrane proteins into the membrane of the liposomes. Polymun is also able to implement third party technologies and existing customer processes at client request.

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3: Liposome: classification, preparation, and applications

Technology We specialize in a range of formulation and drug delivery technologies from solubility enhancement using liposomes, lipospheres and micellar systems to more sophisticated nano-enabled systems like PEGylated liposomes, PEGylated lipospheres and polymer-based nanoparticles for controlled/sustained delivery of various type of compounds.

Flexibility to couple with site-specific ligands to achieve active targeting Open in a separate window It has been displayed that phospholipids impulsively form closed structures when they are hydrated in aqueous solutions. Such vesicles which have one or more phospholipid bilayer membranes can transport aqueous or lipid drugs, depending on the nature of those drugs. Because lipids are amphipathic both hydrophobic and hydrophilic in aqueous media, their thermodynamic phase properties and self assembling characteristics influence entropically focused confiscation of their hydrophobic sections into spherical bilayers. Those layers are referred to as lamellae [4]. Generally, liposomes are definite as spherical vesicles with particle sizes ranging from 30 nm to several micrometers. They consist of one or more lipid bilayers surrounding aqueous units, where the polar head groups are oriented in the pathway of the interior and exterior aqueous phases. On the other hand, self-aggregation of polar lipids is not limited to conventional bilayer structures which rely on molecular shape, temperature, and environmental and preparation conditions but may self-assemble into various types of colloidal particles [5]. Liposomes are extensively used as carriers for numerous molecules in cosmetic and pharmaceutical industries. Additionally, food and farming industries have extensively studied the use of liposome encapsulation to grow delivery systems that can entrap unstable compounds for example, antimicrobials, antioxidants, flavors and bioactive elements and shield their functionality. Liposomes can trap both hydrophobic and hydrophilic compounds, avoid decomposition of the entrapped combinations, and release the entrapped at designated targets [6 - 8]. Because of their biocompatibility, biodegradability, low toxicity, and aptitude to trap both hydrophilic and lipophilic drugs [9] and simplify site-specific drug delivery to tumor tissues [10], liposomes have increased rate both as an investigational system and commercially as a drug-delivery system. Liposomal encapsulation technology LET is the newest delivery technique used by medical investigators to transmit drugs that act as curative promoters to the assured body organs. This form of delivery system proposal targeted the delivery of vital combinations to the body. LET is a method of generating sub-microscopic foams called liposomes, which encapsulate numerous materials. The contents of the liposomes are, therefore, protected from oxidation and degradation. This protective phospholipid shield or barrier remains undamaged until the contents of the liposome are delivered to the exact target gland, organ, or system where the contents will be utilized [14]. Clinical medication keeps an enormously broad range of drug molecules at this time in use, and new drugs are added to the list every year. One of the main aims of any cure employing drug is to increase the therapeutic index of the drug while minimizing its side effects. The clinical usefulness of most conservative chemotherapeutics is restricted either by the incapability to deliver therapeutic drug concentrations to the target soft tissue or by Spartan and harmful toxic side effects on normal organs and tissues. Selected carriers, for instance colloidal particulates and molecular conjugates, can be appropriate for this determination. Colloidal particulates result from the physical incorporation of the drug into a particulate colloidal system, for instance reverse micelles, noisome, micro- and nano-spheres, erythrocytes, and polymers and liposomes. Among these carriers, liposomes have been most studied. Their attractiveness lies in their composition, which makes them biodegradable and biocompatible. Liposome involves an aqueous core entrapped by one or more bilayers composed of natural or synthetic lipids. They are composed of natural phospholipids that are biologically inert and feebly immunogenic, and they have low inherent toxicity. Furthermore, drugs with different lipophilicities can be encapsulated into liposomes: The present review will briefly explain the characteristics of liposomes and explore the related problems and solutions proposed, with a focus on liposome preparation, characterizations, affecting factors, advantages, and disadvantages. In particular, we return to the literature relating to high-stability, long-circulating liposomes stealth liposomes , and their field of application. Classification of liposomes The liposome size can vary from very small 0. Moreover, liposomes may have one or bilayer membranes. The vesicle size is an acute parameter in

determining the circulation half-life of liposomes, and both size and number of bilayers affect the amount of drug encapsulation in the liposomes. On the basis of their size and number of bilayers, liposomes can also be classified into one of two categories: Unilamellar vesicles can also be classified into two categories: In unilamellar liposomes, the vesicle has a single phospholipid bilayer sphere enclosing the aqueous solution. In multilamellar liposomes, vesicles have an onion structure. Classically, several unilamellar vesicles will form on the inside of the other with smaller size, making a multilamellar structure of concentric phospholipid spheres separated by layers of water [17]. Methods of liposome preparation All the methods of preparing the liposomes involve four basic stages: Drying down lipids from organic solvent. Dispersing the lipid in aqueous media. Purifying the resultant liposome. Analyzing the final product. Method of liposome preparation and drug loading The following methods are used for the preparation of liposome: Passive loading techniques Passive loading techniques include three different methods: Detergent removal method removal of non-encapsulated material [18 , 19]. Mechanical dispersion method The following are types of mechanical dispersion methods: Lipid film hydration by hand shaking, non-hand. Dried reconstituted vesicles [18 , 19]. Sonication Sonication is perhaps the most extensively used method for the preparation of SUV. Here, MLVs are sonicated either with a bath type sonicator or a probe sonicator under a passive atmosphere. There are two sonication techniques: The tip of a sonicator is directly engrossed into the liposome dispersion. The energy input into lipid dispersion is very high in this method. Also, with the probe sonicator, titanium will slough off and pollute the solution. The liposome dispersion in a cylinder is placed into a bath sonicator. Controlling the temperature of the lipid dispersion is usually easier in this method, in contrast to sonication by dispersal directly using the tip. The material being sonicated can be protected in a sterile vessel, dissimilar the probe units, or under an inert atmosphere [20]. An important feature of the French press vesicle method is that the proteins do not seem to be significantly pretentious during the procedure as they are in sonication [21]. An interesting comment is that French press vesicle appears to recall entrapped solutes significantly longer than SUVs do, produced by sonication or detergent removal [22 - 24]. The method involves gentle handling of unstable materials. The method has several advantages over sonication method [25]. The resulting liposomes are rather larger than sonicated SUVs. The drawbacks of the method are that the high temperature is difficult to attain, and the working volumes are comparatively small about 50 mL as the maximum [18 , 19]. Freeze-thawed liposomes SUVs are rapidly frozen and thawed slowly. The short-lived sonication disperses aggregated materials to LUV. The creation of unilamellar vesicles is as a result of the fusion of SUV throughout the processes of freezing and thawing [26 - 28]. This type of synthesis is strongly inhibited by increasing the phospholipid concentration and by increasing the ionic strength of the medium. The consequent removal of ether under vacuum leads to the creation of liposomes. The main disadvantages of the technique are that the population is heterogeneous 70 to nm and the exposure of compounds to be encapsulated to organic solvents at high temperature [29 , 30]. Ethanol injection A lipid solution of ethanol is rapidly injected to a huge excess of buffer. The MLVs are at once formed. The disadvantages of the method are that the population is heterogeneous 30 to nm , liposomes are very dilute, the removal all ethanol is difficult because it forms into azeotrope with water, and the probability of the various biologically active macromolecules to inactivate in the presence of even low amounts of ethanol is high [31]. Reverse phase evaporation method This method provided a progress in liposome technology, since it allowed for the first time the preparation of liposomes with a high aqueous space-to-lipid ratio and a capability to entrap a large percentage of the aqueous material presented. Reverse-phase evaporation is based on the creation of inverted micelles. These inverted micelles are shaped upon sonication of a mixture of a buffered aqueous phase, which contains the water-soluble molecules to be encapsulated into the liposomes and an organic phase in which the amphiphilic molecules are solubilized. The slow elimination of the organic solvent leads to the conversion of these inverted micelles into viscous state and gel form. At a critical point in this process, the gel state collapses, and some of the inverted micelles were disturbed. The excess of phospholipids in the environment donates to the formation of a complete bilayer around the residual micelles, which results in the creation of liposomes. Liposomes made by reverse phase evaporation method can be made from numerous lipid formulations and have aqueous volume-to-lipid ratios that are four times higher than hand-shaken liposomes or multilamellar

liposomes [19 , 20]. Briefly, first, the water-in-oil emulsion is shaped by brief sonication of a two-phase system, containing phospholipids in organic solvent such as isopropyl ether or diethyl ether or a mixture of isopropyl ether and chloroform with aqueous buffer. The organic solvents are detached under reduced pressure, resulting in the creation of a viscous gel. The liposomes are shaped when residual solvent is detached during continued rotary evaporation under reduced pressure. The method has been used to encapsulate small, large, and macromolecules. The main drawback of the technique is the contact of the materials to be encapsulated to organic solvents and to brief periods of sonication. These conditions may possibly result in the breakage of DNA strands or the denaturation of some proteins [32]. Modified reverse phase evaporation method was presented by Handa et al. Detergent removal method removal of non-encapsulated material Dialysis The detergents at their critical micelle concentrations CMC have been used to solubilize lipids. As the detergent is detached, the micelles become increasingly better-off in phospholipid and lastly combine to form LUVs. The detergents were removed by dialysis [34 - 36]. A commercial device called LipoPrep Diachema AG, Switzerland , which is a version of dialysis system, is obtainable for the elimination of detergents. The dialysis can be performed in dialysis bags engrossed in large detergent free buffers equilibrium dialysis [17]. The great benefit of using detergent adsorbers is that they can eliminate detergents with a very low CMC, which are not entirely depleted. Gel-permeation chromatography In this method, the detergent is depleted by size special chromatography. The liposomes do not penetrate into the pores of the beads packed in a column. They percolate through the inter-bead spaces. At slow flow rates, the separation of liposomes from detergent monomers is very good. The swollen polysaccharide beads adsorb substantial amounts of amphiphilic lipids; therefore, pre-treatment is necessary. The pre-treatment is done by pre-saturation of the gel filtration column by lipids using empty liposome suspensions. Dilution Upon dilution of aqueous mixed micellar solution of detergent and phospholipids with buffer, the micellar size and the polydispersity increase fundamentally, and as the system is diluted beyond the mixed micellar phase boundary, a spontaneous transition from polydispersed micelles to vesicles occurs. Stealth liposomes and conventional liposomes Although liposomes are like biomembranes, they are still foreign objects of the body.

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4: Liposome Technology: Liposome Preparation and Related Techniques - Google Books

Polymun technology can achieve long term stability of liposomes, even at room temperature. Polymun Liposome Technology Polymun has transformed liposomes from a promising scientific idea into a sound industrial solution.

Table of Contents Summary Liposome Technology, Second Edition, is an updated, expanded new edition of a classic volume in the field. It covers all aspects of liposome technology, including liposome preparation and analysis, drug entrapment, and techniques used for in vivo and in vitro evaluation of liposomes. Leading authorities have contributed 70 chapters to create what is destined to be the standard liposome technology book for the s. Liposome Technology, Second Edition will be an essential reference volume for academic and industrial researchers in pharmacology, pharmacy, medicine, biochemistry, and immunology. The 2nd Edition covers significant developments in liposome technology that have occurred since the publication of the 1st Edition in These developments include the following: From Serendipity to Targeting Demetrios Papahadjopoulos. Implications for Drug Delivery and for Biocompatibility R. Juliano and Michael Meyer. Pharmacodynamics of Liposomal Drug Carriers: Methodological Considerations Marcel B. Hope, and Rajiv Nayar. Moein Moghimi and Harish M. Sterically Stabilized Stealth Liposomes: Pharmacokinetic and Therapeutic Advantages T. Derksen, and Folkert Kuipers. Immunoliposome Targeting in a Mouse Model: Kar Kruijt, Halbe H. Spanjer, Herman Jan M. Kempen, and Gerrit L. Handly, and Bruce P. Richards, and Nabila M. Tolerability in Liposomes In Vivo G.

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5: Memproâ„¢ Liposome Technology - Creative Biostructure

Liposome Technology works by utilizing liposomal micro spheres to deliver the ingredient, meaning directly into the cells within the body. Liposomal micro spheres are completely sealed microscopic.

This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. This article has been cited by other articles in PMC. Abstract The combination of liposomes with polymeric scaffolds could revolutionize the current state of drug delivery technology. Although liposomes have been extensively studied as a promising drug delivery model for bioactive compounds, there still remain major drawbacks for widespread pharmaceutical application. Two approaches for overcoming the factors related to the suboptimal efficacy of liposomes in drug delivery have been suggested. The first entails modifying the liposome surface with functional moieties, while the second involves integration of pre-encapsulated drug-loaded liposomes within depot polymeric scaffolds. This attempts to provide ingenious solutions to the limitations of conventional liposomes such as short plasma half-lives, toxicity, stability, and poor control of drug release over prolonged periods. This review delineates the key advances in composite technologies that merge the concepts of depot polymeric scaffolds with liposome technology to overcome the limitations of conventional liposomes for pharmaceutical applications. Introduction Over the past few decades, liposomes have received widespread attention as a carrier system for therapeutically active compounds, due to their unique characteristics such as capability to incorporate hydrophilic and hydrophobic drugs, good biocompatibility, low toxicity, lack of immune system activation, and targeted delivery of bioactive compounds to the site of action [1 â€” 4]. Additionally, some achievements since the discovery of liposomes are controlled size from microscale to nanoscale and surface-engineered polymer conjugates functionalized with peptide, protein, and antibody [5 , 6]. Although liposomes have been extensively studied as promising carriers for therapeutically active compounds, some of the major drawback for liposomes used in pharmaceutics are the rapid degradation due to the reticuloendothelial system RES and inability to achieve sustained drug delivery over a prolonged period of time [7]. New approaches are needed to overcome these challenges. Two polymeric approaches have been suggested thus far. The first approach involves modification of the surface of liposomes with hydrophilic polymers such polyethylene glycol PEG while the second one is to integrate the pre-encapsulated drug-loaded liposomes within depot polymer-based systems [3]. A study conducted by Stenekes and coworkers [8] reported the success of using temporary depot of polymeric materials to control the release of the loaded liposomes for pharmaceutical applications. This achievement leads to new applications, which requires collaborative research among pharmaceuticals, biomaterials, chemistry, molecular, and cell biology. Numerous studies in this context have been reported in the literature dealing with temporary depot delivery system to control the release of pre-encapsulated drug-loaded liposomes [9 â€” 12]. This system was developed to integrate the advantages while avoid the disadvantages of both liposome-based and polymeric-based systems. The liposome-based systems are known to possess limitations such as instability, short half-life, and rapid clearance. However, they are more biocompatible than the polymer-based systems [13]. On other hand, the polymer-based systems are known to be more stable and provide improved sustained delivery compared to liposome-based systems. However, one of the major setbacks is poor biocompatibility which is associated with loss of the bioactive i. The benefits of a composite system, however, include improvement of liposome stability, the ability of the liposome to control drug release over a prolonged period of time, and preservation of the bioactiveness of the drugs in polymeric-based technology. In addition, increased efficacy may be achieved from this integrated delivery system when compared to that of purely polymeric-based or liposome-based systems. The aim of this article therefore, is to review the current liposome-based and polymeric-based technologies, as well as the integration of liposome-based technology within temporary depot polymeric-based technology for sustained drug release. The discussion will focus on different types of liposome-based technology and depot polymeric scaffold technologies, various methods for embedding drug-loaded liposomes within a depot, and various approaches

reported to control the rate of sustained drug release within depot systems over a prolonged period of time. Liposome-Based Technology A liposome is a tiny vesicle consisting of an aqueous core entrapped within one or more natural phospholipids forming closed bilayered structures Figure 1 [5]. Liposomes have been extensively used as potential delivery systems for a variety of compounds primarily due to their high degree of biocompatibility and the enormous diversity of structures and compositions [14 , 15]. The lipid components of liposomes are predominantly phosphatidylcholine derived from egg or soybean lecithins [15]. Liposomes are biphasic a feature that renders them the ability to act as carriers for both lipophilic and hydrophilic drugs. It has been observed that drug molecules are located differently in the liposomal environment and depending upon their solubility and partitioning characteristics, they exhibit different entrapment and release properties [15 , 16]. Lipophilic drugs are generally entrapped almost completely in the lipid bilayers of liposomes and since they are poorly water soluble, problems like loss of an entrapped drug on storage are rarely encountered. Hydrophilic drugs may either be entrapped inside the aqueous cores of liposomes or be located in the external water phase. Noteworthy is that the encapsulation percentage of hydrophilic drugs by liposomes depends on the bilayer composition and preparation procedure of the liposomes [17 , 18].

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6: NutriProtect Liposomal Technology - Nutrivitality

Liposome Technology, Third Edition, Three Volume Set is an ideal resource for pharmaceutical scientists, researchers, regulatory personnel, FDA personnel, and medicinal chemists working in this discipline.

This is an open access article distributed under the Creative Commons Attribution License , which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. Abstract Liposomes, spherical vesicles consisting of one or more phospholipid bilayers, were first described in the mid 60s by Bangham and coworkers. Since then, liposomes have made their way to the market. Today, numerous lab scale but only a few large-scale techniques are available. This paper summarizes exclusively scalable techniques and focuses on strengths, respectively, limitations in respect to industrial applicability. An additional point of view was taken to regulatory requirements concerning liposomal drug formulations based on FDA and EMEA documents. History, Definition, and Classification of Liposomes The story of success of liposomes was initiated by Bangham and his colleagues in the early s who observed that smears of egg lecithin reacted with water to form quite intricate structures. They were analyzed by electron microscopy showing that a multitude of vesicles were formed spontaneously. These more or less homogenous lipid vesicles were first called smectic mesophases [1]. Later on, a colleague of Bangham termed themâ€”more euphoniouslyâ€”liposomes [2]. In the following years, liposomes were primarily used as artificial membrane models mimicking simple cell systems for the investigation of transport functions and mechanisms, permeation properties, as well as adhesion and fusion kinetics. Liposomes were very soon recognized as promising candidates for drug delivery systems [3 , 4], and in this regard more and more tailor-made formulations were investigated for certain purposes such as medical applications, cosmetics but also in food and agricultural industry, whereby the main activities were focused on pharmaceutical and in particular biopharmaceutical applications. Both are indicated as anticancer drugs, which were successfully tested in clinical studies, followed by the US Food and Drug Administration FDA approval in the s. In general, liposomes are defined as spherical vesicles with particle sizes ranging from 30 nm to several micrometers. They consist of one or more lipid bilayers surrounding aqueous compartments, where the polar head groups are oriented towards the interior and exterior aqueous phases. However, self-aggregation of polar lipids is not restricted to conventional bilayer structures which depend on temperature, molecular shape, and environmental and preparation conditions but may self-assemble into various kinds of colloidal particles [5 , 6]. Due to this fact, the liposome family includes various kinds of colloidal particles and structures which hamper systematic classification. However, they can be classified by structure, composition, and preparation, as shown in Table 1. Technology and application are driven by two major facts. First, the transfer from academic bench to a highly regulated, high technology industry was difficult for liposome technology because of the lack of appropriate methods to produce large quantities in a controlled and reproducible manner. Although several methods are suitable for large-scale production, their development, implementation, and quality control needed a certain time. Second, early clinical trials were not as successful as expected because the stability of conventional liposomes was low, caused by inefficient preparation, physical properties, and unfavorable choice of lipids. Furthermore, they were to a great extent cleared by liver and spleen very rapidly so that neither a prolonged biological half-life nor specific targeting was achieved. More stable conventional liposomes and second-generation formulations, such as the stealth technology, gave new impulses to the industry as well as to clinicians with the development of industrial processes in the s. Currently, EMA has not yet published any summarizing document or guideline which is dealing exclusively with nanoparticular structures. In detail, recommendations concerning the submission of a new liposomal product are given regarding physiochemical properties, description of manufacturing process and process controls, and control of excipients and drug products. Control of excipients includes all parameters which are necessary to define lipid components, including description, characterization, manufacture, and stability. Control of drug products is dealing with the specifications. In particular, physicochemical parameters are critical for product quality for each batch. Furthermore, aspects are addressed such as assaying encapsulated and nonencapsulated drug

substance, lipid components, and degradation products, as well as in vitro tests for drug release from liposomes. The second part of this document is dealing with human pharmacokinetics and bioavailability. In particular, requirements concerning the quality and potency of bioanalytical methods are discussed. Therefore, the recommendations are focused on the validation of these methods and the capability to distinguish between encapsulated and nonencapsulated drug substances. Similar recommendations are given for in vivo integrity and stability considerations, respectively. In an additional chapter, studies for pharmacokinetics and bioavailability are recommended, such as mass balance studies and pharmacokinetic studies. Finally, general recommendations concerning the labeling requirements are given. Unfortunately, during the intensive discussion process no conclusion regarding the appropriate approaches to access pharmacokinetics and bioavailability was achieved. Hence, this document has only draft status to this date. In , a reflection paper was published on nanotechnology-based medicinal products for human use reflecting the current thinking and the initiatives by EMA in view of recent developments in relation to this scope. As mentioned in this document, medicinal products containing nanoparticles, including liposomes, have already been authorized both in EU and US under the existing regulatory frameworks. Nevertheless, the European Commission has developed a number of initiatives with emphasis on safety and ethical considerations but also to evaluate the appropriateness of existing methodologies to assess the potential risks associated with nanotechnology. In this context, it is mentioned that there is still insufficient knowledge and data concerning nanoparticles characterization, their detection and measurement, the persistence of nanoparticles in humans and the environment, and all aspects of toxicology related to these particles to allow satisfactory risk assessments. In order to deal with this issue, the EMEA has created the Innovative Task Force for the coordination of scientific and regulatory competence. Because novel applications of nanotechnology will span the regulatory boundaries between medicinal products and medical devices, the mechanism of action will be the key to decide whether a product should be regulated as a medical product or a medical device. Furthermore, evaluation of the quality, safety, efficacy, and risk management must be discussed in more detail. In conclusion, it is likely that the evaluation of such new products will require special considerations. Therefore, EMA will promote this process either to develop specific guidelines or for the update of existing once. General Introduction into Techniques Lipid molecules have to be introduced into an aqueous environment for the preparation of liposomes independent of liposome size and structure. A general overview representing the correlation of the way of lipid hydration, respectively, the way of primary liposome formation with the resulting liposome structure, was originally developed by Lasic [38]. Several ways of treating the lipids are known to support the hydration of these molecules, as lipid molecules themselves are poorly soluble in aqueous compartments. These procedures can be categorized as shown in Table 2. Methods of liposome preparation and the resulting product. Partly from Lasic and Barenholz [39]. Additional methods have been developed such as freeze thawing, freeze drying, and extrusion. However, they are all based on preformed vesicles. In addition, the advantages and disadvantages of each technique are pointed out. Furthermore, focus is given on discussing the techniques with respect to their applicability regarding large-scale production for clinical purposes and good manufacturing practice GMP relevant issues. Preparation by Film Methods Properties of lipid formulations can vary depending on the composition cationic, anionic, and neutral lipid species. However, the same preparation method can be used for all lipid vesicles regardless of composition. The general steps of the procedure are preparation of the lipids for hydration, hydration with agitation, and sizing to a homogeneous distribution of vesicles [40]. Since then, many different variations of this method have been developed differing in the organic solvents used for lipid solubilization, the way of lipid drying, and the way of film rehydration. Despite the various modifications, all these methods have in common that heterogeneous populations of multilamellar liposomes are produced. However, vesicle size is influenced by the lipid charge. Charged lipids form smaller liposomes with less lamellae. Other influencing parameters are the nature of the aqueous phase as well as energy and power input of agitation. The film method has several advantages. It can be used for all different kinds of lipid mixtures. In addition, the method is easy to perform, and high encapsulation rates of lipid as well as aqueous soluble substances can be achieved because high lipid concentrations can be used. One major drawback of this method is the difficulty of scaling up to several tens

of liters. Furthermore, the process becomes more time and cost intensive because additional processing is recommended for a defined liposome suspension, whereby product losses are generated. Several downsizing techniques have been established in order to make the heterogeneous vesicles more uniform. The first published downsizing method was sonication [41]. A very high energy input based on cavitation is applied to the liposomal dispersion either directly with a tip or indirectly in a bath sonicator. Other methods also aiming at breaking down the large MLVs are homogenization techniques, either by shear or pressure forces. In this group, methods are included such as microfluidization, high-pressure homogenization, and shear force-induced homogenization techniques. The most defined method for downsizing is the extrusion technique whereby liposomes are forced through filters with well defined pores. Homogenization Techniques Similar to the ultrasound methods, homogenization techniques have been used in biology and microbiology for breaking up the cells. Therefore, many scientists have used them for reducing the size and number of lamellae of multilamellar liposomes. The French press [42] originally was established for breaking up cells under milder and more appropriate conditions compared to the ultrasound techniques, because lipids as well as proteins or other sensitive compounds might be degraded during the sonication procedure. This system is normally used in the volume of 1 to 40 mL and therefore is not suitable for large-scale production. However, a scale-up-based strategy on this technique was established as the microfluidization. This continuous and scaleable variation of the French press technique enforces downsizing of Liposomes by collision of larger vesicles at high pressure in the interaction chamber of the microfluidizer. Starting volumes from 50 mL upwards are applicable, and again high pressures are used for disruption of multilamellar systems. The system works in a pressure range of 0â€” bar and is equipped with heating and cooling systems to control sample temperature during processing [43]. The liposome suspension passes the exchangeable orifices several times up to thousands of passes. Liposomes are formed in the size range from 50 to nm by this process. This technique is suitable for large-scale production and sterile liposome preparation. In contrast to the microfluidizer, where the fluid stream is split and mixed by collision in a mixing chamber, homogenizers work on a different principle. In a homogenizer, the fluid beam is pressed with high pressure through an orifice, and this beam collides with a stainless steel wall. The liposome suspension is continuously pumped through the homogenizer system, where high pressures are generated to downsize lipid vesicles [44]. The most prominent scalable downsizing method is the extrusion. Size reduction is managed under mild and more reproducible conditions compared to those discussed above. In this method, preformed vesicles are forced through defined membranes by a much lower pressure as described in the French press method. Extrusion through polycarbonate filters was first published by Olson et al. Depending on the apparatus and scale, the diameters of these membranes range from 25 to mm. As suggested for all downsizing methods, liposomes should be extruded above the Tc of the lipid composition; this system can be tempered. The Lipex extruder system is available in a jacketed mode to allow extrusion at higher temperatures. An alternative is the Maximator device, established by Schneider et al. It is a continuous extrusion device working with a pumping system.

LIPOSOME TECHNOLOGY pdf

7: Liposome Technology, Second Edition, Volume III - CRC Press Book

Liposome Technology, Volume I: Liposome Preparation and Related Techniques, Third Edition, is a thoroughly updated and expanded new edition of a classic text in the field. Including step-by-step technical details, Volume I illustrates numerous methods for liposome preparation and auxiliary techniques necessary for the stabilization and.

This section is reserved for healthcare professionals. Glutathione is the most abundant cellular antioxidant in oxygen-using cells. Alterations, including deficiencies in glutathione levels, have been found in several neurological conditions. It binds with toxins to form a water-soluble complex that can be excreted through the liver. Diminished levels of glutathione can lead to decreased efficiency in a number of body systems, including the immune cells designed to kill invading organisms. A wide range of health conditions are associated with low levels of glutathione. Through a unique process we place reduced glutathione into liposomes, liquid bubbles made from essential phospholipids, to ensure bioavailability. Liposome Technology Our liposome technology is unique and received a patent in Liposomes have a fat-soluble exterior and an interior that is watery. They are made from the same type of material as our cell membranes, phospholipids. The phospholipids in our liposomes are derived from lecithin, which is an extraction taken from soy oil. There is no soy protein in the product. The unique structure of liposomes allows them to encapsulate biologically active ingredients. The liposomes in our products are very stable, which allows use in an oral drink or an oral spray. Liposomes penetrate mucosal tissues allowing for rapid release into the blood stream. Nutrients that are not in liposomes have to pass through the stomach to reach the liver where they are metabolized and released into the bloodstream. Some nutrients are destroyed or compromised by stomach acids. Liposomes avoid the digestive system. A paper published in Bangham, A. Since then they have been the subject of great interest and study. A liposomal delivery system of certain anti-cancer drugs has been used to target various malignancies, and other applications for liposomes range from gene therapy to skin care. Currently there are over 40, articles listed on the PubMed website www.

LIPOSOME TECHNOLOGY pdf

8: Liposome Technology - Return2Health

Liposome Technology works by utilizing liposomal micro spheres to deliver the ingredient, meaning directly into the cells within the body. Liposomal micro spheres are completely sealed microscopic bubbles that trap ingredient's molecules inside a protective envelope.

Certified Organic Why Liposomal Nutrients? Liposome Nutrients are the most effective efficient oral means to for the body to absorb vital nutrients into your body. Liposomes are microscopic sized spherical sac or sphere of phospholipid molecules enclosing a nutrient, such as our Aurora Vitamin C or Glutathione. Enclosing the vitamin in a liposome allows the Vitamin to pass through the stomach acids and bile salts in the digestive GI tract and into the bloodstream without causing stomach or intestinal distress. It also is proven technology that efficiently delivers the nutrient to the bloodstream. Liposomal supplements are typically 4. Reduced Gastric Discomfort Liposomal supplements avoid the nausea side effects common to traditional oral form supplements. Nutrients enclosed in a liposome pass through the digestive tract and into the bloodstream without stomach or intestinal distress. Improved Health Benefits Your ultimate goal in taking supplements is to achieve tangible health benefits. Liposomes deliver much higher doses of vitamins to your body, leading to improved health benefits. You can buy with confidence knowing the very real and tangible benefits of Liposomal technology. We have seen a tremendous decrease in missed school days. My husband and I feel like any virus we do catch is much less severe and shorter than what others have experienced this year as well. I had elective surgery over a year ago. My recovery and healing was much faster than normal. These products give me more energy all around. Easy to use, inexpensive, easy on the stomach and good tasting to boot. Great company that actually cares about its clients. About a week after my first order I received a surprise phone call from them as they wanted to be sure everything was fine with my order! If you call them, they actually answer the phone and your questions. I give them a 5 star rating. Began taking the glutathione for initial 3 days, I could barely keep from doing cartwheels, due to the fact that I felt so much better so much energy. The Liposomal Vitamin C video tutorials inform that vitamin C as an antioxidant is so dominating, that it will overcome all other antioxidants, if taken at the same time.

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9: Liposomal technology helps to improve your health | NaturalHealth

Summary Liposome Technology, Second Edition, is an updated, expanded new edition of a classic volume in the field. It covers all aspects of liposome technology, including liposome preparation and analysis, drug entrapment, and techniques used for in vivo and in vitro evaluation of liposomes.

Table of Contents Summary Offering step-by-step technical details, Liposome Technology, Third Edition, Three Volume Set provides comprehensive coverage of all aspects of liposome technology, including liposome preparation and analysis, entrapment of drugs and other materials into liposomes, and liposome interaction with the biological environment to be applied in the detection, therapy, or prevention of disease. The text offers critical discussions of the methodologies of each technology discussed so that readers can examine the benefits and limitations and compare it to other methods. This Third Edition features 55 chapters written by leading international experts. Because of the considerable progress in liposome related techniques and their application in therapy since the publication of the Second Edition in , over half of the chapters are new to the edition, and the other chapters have been extensively updated. Liposome Technology, Third Edition, Three Volume Set is an ideal resource for pharmaceutical scientists, researchers, regulatory personnel, FDA personnel, and medicinal chemists working in this discipline. Formation of Large Unilamellar Vesicles by Extrusion. Immunopotentiating Reconstituted Influenza Virosomes. Mixed Vesicles and Mixed Micelles: Formation, Thermodynamic Stability and Pharmaceutical Aspects. Stabilization of Liposomes by Freeze-Drying: Coupling of Peptides to the Surface of Liposomes: Application to Liposome-Based Synthetic Vaccines. Encapsulation of Nucleic Acid-Based Therapeutics. Radiolabeling of Liposomes for Scintigraphic Imaging. Liposomal Bisphophonates for the Treatment of Restenosis. Influenza Virosomes as Adjuvants in Cancer Immunotherapy. Lipid Peptide Vectors for Gene Therapy. Uptake and Intracellular Fate of Liposomes. Effect of Lipid Dose and Dosing Frequency. Targeting Tumor Angiogenesis Using Liposomes. Targeting of Cationic Liposomes to Endothelial Tissue. Folate Receptor Targeted Liposomes. Targeting of Liposomes to Lymph Nodes. Liposomes for Intracavitary and Intratumoral Drug Delivery. Liposomes in Cancer Immunotherapy. From Animal to Man.

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