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AN OVERVIEW ON NOVEL DRUG DELIVERY SYSTEMS

Surendra Kumar M*, Hameed Moosa S, Kavin K, Parkavi V.S., PradeepShankar U, Sivaranjani G, Astalakshmi N

Senghundhar College of Pharmacy, Kumaramangalam, Tiruchengode, Namakkal District, Tamilnadu, India.

Email: skshravansk@gmail.com

ABSTRACT

The higher demand for enhancing therapeutic efficacy and to reduce adverse effect in the pharmaceutical domain initiate to develop the NDDS in research of pharmacy field. Over past few decades there was greater advancement noted on development of novel drug delivery system. The concept of targeted drug delivery is designed for attempting to compactness drug in the tissues of interest while lowering the relative compactness of the medication in the remaining tissues. Conventional drug delivery system often suffers from limitations of poor bioavailability, rapid clearance and leading to lower the curative success, and increased the side effects. Conventional dosage form also release drug immediately and it causes fluctuation of drug level in blood depending on dosage form. So now new technique novel drug delivery system is applied to overcome the problems by targeted action. Evolution of an existing drug molecule from a conventional form to novel drug delivery can be significantly improve in its performance in term of patient acceptance, safety and efficacy.

KEYWORDS: Novel Drug Delivery System, Targeted Action, conventional drug delivery system, therapeutic efficacy, safety.

NOVEL DRUG DELIVERY SYSTEM

Introduction

Novel drug delivery system is an advanced techniques with wide application and also a new dosage form with far better active than other dosage form [1]. Certain medicament has slow progress in severe disease, for this case new strategies often called as novel drug delivery system is introduced in modern medicine field. this technique used to achieve control drugs delivery by incorporating the drug with carrier or changing the structure of the drug at molecular level These will control pharmacokinetics, pharmacodynamics toxicity, immunogenicity and efficacy of drug Novel drug delivery system was only a dream but now is a reality [2-4]. The development of new drugs with safe and effective therapy has been the common practice, however, it involved a long gestation period, efforts, and huge cost. Later on, it was realized that the system is efficacy and safety are largely influenced by the distribution of the drug within the biological system, as there is appropriate action at Target sites [5-6]. The NDDS should ideally fulfill

two prerequisites. Firstly, deliver the drug at a rate directed by the needs of the body, over the Period of treatment. Secondly, drug act on targeted sites [7].During the last decade DDS having successful development and growth in their research [8]. Newer developments in the formulation Approaches have raised hopes in making higher activity, more useful and acceptable [9].

CLASSIFICATION OF DRUG DELIVERY SYSTEM

LIPOSOMES

Structure

Liposomes are spherical in shape [10] A liposome is a tiny bubble (vesicle), with a membrane composed of a phospholipid bilayer. These bilayer membranes are made up of phospholipids like phosphatidyl ethanolamine and Phosphatidyl choline. The Structural Components are Phospholipids, and Cholesterol. .

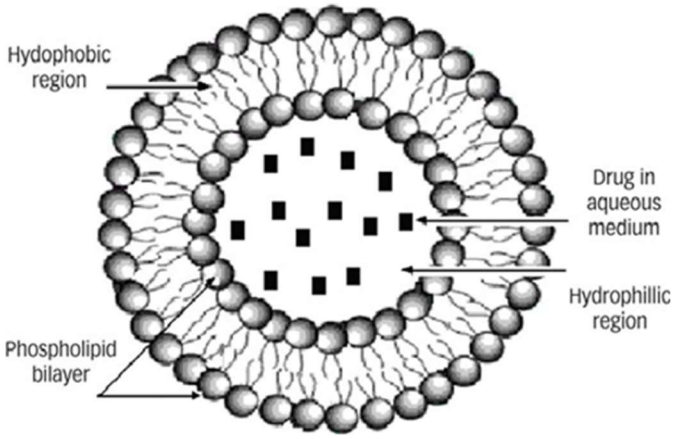

Figure 1: structure of liposome [11]

MATERIALS USED

- Diethyl ether or ether/methanol mixture [11]

METHOD OF PREPARATIONS

Drying lipids from organic solvents and then lipid is Dispersed in aqueous medium. Purified the resultant Liposome and analysis the final product.

Passive loading technique

a) mechanical dispersion methods

- Lipid hydration method

  Lipid solution was dried so that a thin film was formed at the bottom of round bottom flask.Then film was hydrated by adding aqueous buffer. The hydration step is done at a temperature. Aqueous buffer or organic solvent used to encapsulate the compound.
- Micro emulsification

Micro emulsification used for preparing SLV. Microemulsifying lipid compositions using high shearing stress generated from high pressure homogenizer.

- Dried reconstituted vesicles

  Dehydration of mixture, Liposomes are added to an aqueous solution containing drug or mixed with lyophilized protein.
- Freeze thaw method

  this method SUVs were frozen rapidly. The formation of unilamellar products.

b) Solvent Dispersion

- Ethanol injection

  A lipid solution of ethanol was added to an aqueous buffer which immediately forms MLV.
- Ether infusion;Lipids dissolved in diethylether and is slowly injected to a solution of the material to be encapsulated at temperature 55-60◦ C29.

c) Detergent

Lipids were solubilized by detergent. As detergent is removed, miscelles become richer in phospholipids and finally combine to form LUV Eg;n-Alkyl -glucosides [12].

Active loading techniques

a) pro liposomes

In this method lipid and drug were coated onto a soluble carrier to form free flowing granular material in pro-liposome which forms an isotonic liposomal suspension on hydration.

b) **Lyophillization**

The removal of water from products in a frozen state at a reduced pressure is called Lyophilization. This method is generally used to dry the products that are thermo-liable [13].

NIOSOMES

STRUCTURE

Niosomes vesicle consists of a vesicle forming amphiphile i.e. a nonionic surfactant such as Span860, which is usually stabilized by the addition of cholesterol and a small amount of anionic surfactant such as diacetyl phosphate [14].

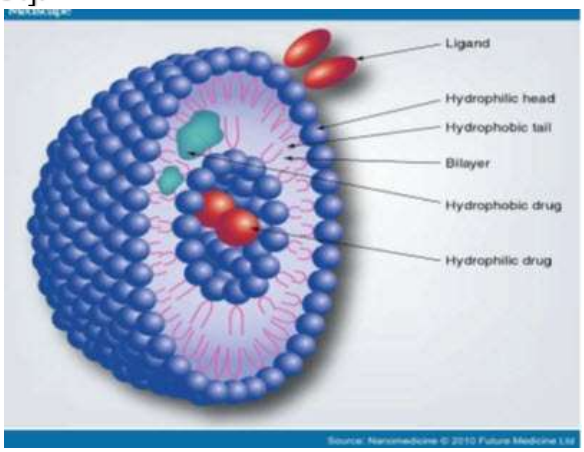

Fig 2: Structure Of Niosome [15]

MATERIAL USED

- Cholesterol
- Non-ionic surfactant and
- Other biodegradable lipids [16].

METHOD OF PREPARATION

a) Ether Injection method:

Surfactant is dissolved in diethyl ether Then the substance was injected into warm water maintained at 60°C through a 14gauze needle. Then Ether is vaporized to form single layered Niosomes.

b) Hand shaking method:

Dissolved surfactant and cholesterol in the volatile organic solvent in a RB flask. The organic solvent is evaporated at room temperature (20°C) using rotary evaporator. Then dried surfactant film can be rehydrated with aqueous phase.

c) Sonication method

Drug solution in buffer is added to the surfactant/cholesterol mixture. Then the mixture is probe sonicated at 60°C using a sonicator for 3 min to yield niosomes.

d) Micro fluidization method:

In this method two fluidized streams interact at ultrahigh velocities in micro channels within the interaction chamber. The impingement of thin liquid sheet along a common front is arranged such that the energy supplied to the system remains within the area of niosomes formation.

e) Multiple membrane extrusion method:

Evaporation of mixture of surfactant, cholesterol and dicetyl phosphate in chloroform is made into thin film. The film is hydrated with aqueous drug polycarbonate membranes, solution and the resultant suspension extruded.

f) Reverse phase evaporation technique:

Cholesterol and surfactant (1:1) are dissolved in a mixture of ether and chloroform. Adding aqueous phase containing drug and the resulting two phases are sonicated at 4-5°C. A clear gel is formed by addition of phosphate buffered saline (PBS). The organic phase is removed at low pressure. The noisome suspension is diluted with PBS and heated on a water bath at 60°C for 10 min to yield niosomes.

g) Remote loading technique:

Surfactant and cholesterol are dissolved in chloroform. The solvent evaporated under reduced pressure to get a thin film and hydrated with citric acid. The resulting multilamellar vesicles are frozen. In this niosomal suspension add aqueous solution of drug .PH raised to 7.0-7.2 with 1M disodium phosphate. The mixture is heated at 60°c for 10 minutes to give niosomes.

h) The Bubble Method

Water-cooled reflux and thermometer is positioned in the first and second neck and nitrogen supply through the third neck. Cholesterol and surfactant are mixed together in this buffer with high shear homogenizer. Immediately afterwards "bubbled" at 70°C using nitrogen gas to yield niosomes.

ETHOSOMES

STRUCTURE OF ETHOSOMES

Ethosomes includes multiple layers of flexible phospholipid bilayers, with a relatively high concentration of ethanol, glycols, and water [17-19].The high concentration of ethanol in Ethosomes gives them a unique ability to penetrate the stratum corneum, as ethanol disrupts skin lipid bilayer organization [20-21].

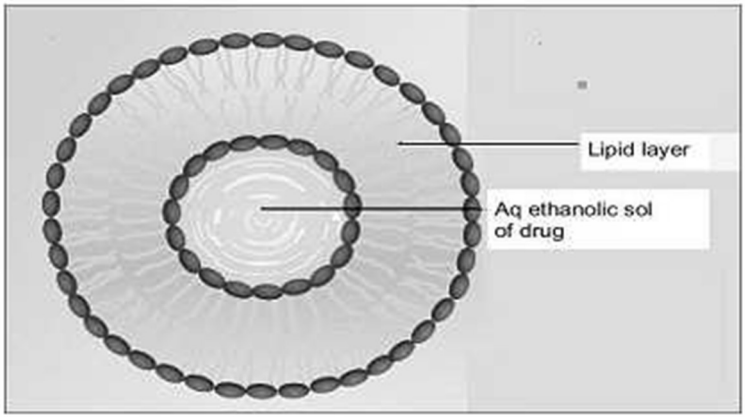

Fig 3: Structure of Ethosomes [16].

MATERIAL USED

Soft and malleable vesicles, known as ethosomes, are composed of phospholipids, water, and a high concentration of ethanol, offering a novel approach to enhanced skin delivery [22].

METHOD OF PREPARING ETHOSOMES

Ethosomes can be prepared using four simple and convenient methods, without requiring complex processes or sophisticated instruments. The four methods are,

- Cold method
- Hot method

a) Hot Method.

Dissolve phospholipid drug and other lipid material in ethanol, add propylene glycol and heat at 30°C.Add double distilled water while stirring, homogenize using a hand extruder.

b) Cold Method.

Disperse phospholipid in water (or) ethanol with propylene glycol at 40°C. Add drug solution with organic phase These methods produce ethosomes with varying properties, allowing for flexibility in formulation design [23].

MICROSPHERE

Microspheres are characteristically free flowing powders consisting of proteins or synthetic polymers, which are biodegradable in nature and ideally having a particle size less than 800nm [24]. This is the important approach in delivering therapeutic substance to the target site in sustained and controlled release fashion [25-26].

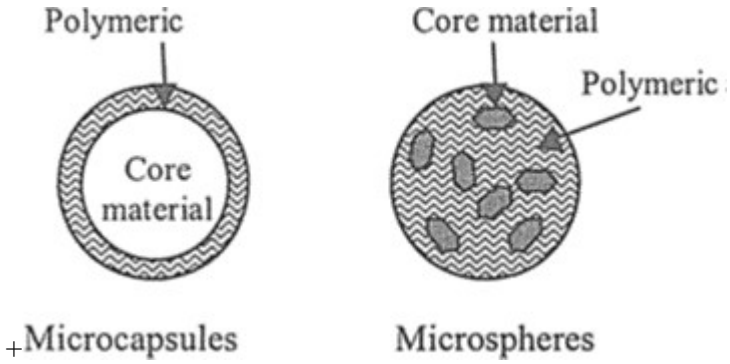

Fig 4: Structure of microsphere [24].

MATERIAL

Microspheres used usually are polymers. They are classified into two types

- Synthetic polymers.
- Natural polymers [33].

METHOD OF PREPARATION

a) Double emulsion fashion

The protein dispersed in a lipophilic organic continuous phase. The protein result may contain the active substances. Continuous phase is a polymer affect that eventually encapsulates of the protein. The primary emulsion is subjected to the homogenization or the sonication before addition to the polyvinyl alcohol. The double emulsion is formed. The emulsion is then subjected to removal either by solvent evaporation or by solvent extraction method. This results in the conformation of a double emulsion. The emulsion is also vanquished to removal either by solvent evaporation or by solvent birth system.

c) Single emulsion fashion

The natural polymer are dissolved in aqueous medium and then dispensed in non-aqueous medium. the cross linkage of the dispersed globule is carried out by heating (or) chemical cross linkers.

The chemical crosslinking agents used are as followings:

- Glutaraldehyde,
- Formaldehyde
- Di-acetyl acid chloride etc. [33]

d) Polymerization technique

- **normal polymerization**

In bulk, a monomer or a composition of monomers along with the creator or catalyst is generally toast to initiate polymerization. Polymer so attained may be molded as microspheres. during the polymerization process the drug can be loaded. Suspension polymerization also appertained pearl polymerization. It's carried out by toast the monomer or composition of monomers as droplets dispersion in a continuous arid phase. Droplets may also contain a creator and other accretive.

- **interfacial polymerization**
  This involves the response of various monomers at the interface between the two immiscible liquids to form a film of polymer that principally envelops the dispersed phase [44].

e) Spray drying and spray congealing

Polymer dissolved in suitable volatile organic solvent and then solid drug dispensed in polymer with high homogenization speed. Formation of droplets and evaporates the solvent. Then microsphere is yield, separated by cyclone separator.

f) Phase separation coacervation technique

The drug particles are dispersed in polymer and an incompatible polymer is then added ,the first polymer to separate and engulfment of the drug particles. Organic solvent results added for solidification of polymer. Poly lactic acid (PLA) microspheres is prepared. The agglomeration of the formed particles must be avoided by continuous stirring because as the process of microspheres formation starts the formed polymerize globules start to stick and form the agglomerates.

g) **Solvent extraction**

Manufacturing of microparticles, involves removal of the organic phase by extraction. Organic phase can be removed by extraction with water. The process involves direct incorporation of the drug to polymer organic solution. Rate of solvent removal by extraction method depends on the temperature of water, ratio of emulsion volume to the water and solubility profile of polymer.

h) **Quassi emulsion solvent diffusion**

Microsponges can be manufactured by the method of solvent diffusion using an external phase containing distilled water and polyvinyl alcohol. The internal phase is consisting of drug, ethanol and polymer. In emulsification process the internal phase is manufactured at 60ºC and then added to the external phase at room temperature and continuously stirred for 2 hours. Then filtered to separate the microsponges. The product is then washed and dried by vacuum oven. [26]

PHYTOSOMES

Encapsulates phytochemicals within a phospholipid complex. These complex mimics the natural structure of membrane and making the phytochemicals more compatible with the lipid environment of biological membranes. [27-29]

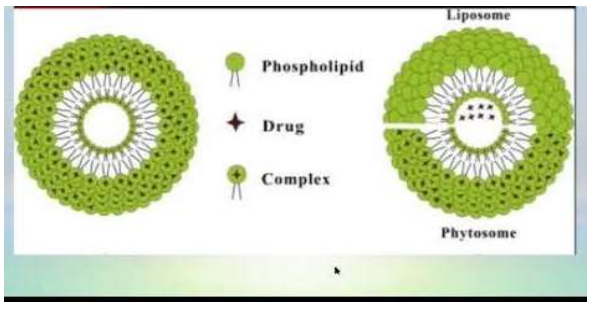

Fig 5: structure of phytosomes [27].

MATERIAL USED

The material used are phospholipids, acetone and phytoconstituents [30].

METHOD OF PREPARATION

1. Selection of Phytochemicals: Active phytochemical components, such as curcumin, quercetin, or silymarin, are chosen based on their therapeutic potential.
2. Formation of Phytosome Complex: The selected phytochemical is reacted with phospholipids, such as phosphatidylcholine, in an appropriate solvent system.
3. Purification: The resultant Phytosome complex is purified to remove any unreacted components.
4. Drying and Formulation: The purified Phytosome complex is dried and formulated into suitable dosage forms, such as capsules, tablets, or topical preparations [31-32]

MICRO ENCAPSULATION
INTRODUCTION

Microencapsulation is a process by which solids or liquids enclosed in bitsy patches conformation of thin coatings of wall material around the drug. Microencapsulation is the smallness of the coated patches and their posterior use and adaptation wide variety [33]

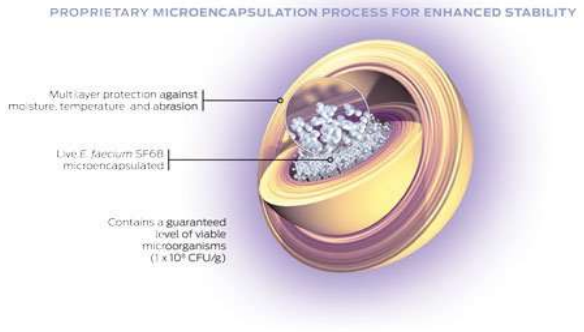

Fig 6: Structure of Microencapsulation [33]

METHODS MICROENCAPSULATION

- Air suspension
- Coacervation phase separation
- Multi-orifice-centrifugal process
- Spray drying and congealing
- Pan coating
- Solvent evaporation techniques

MONOCLONAL ANTIBODIES

INTRODUCTION

Monoclonal antibodies (mAbs) are among the most important remedial protein types used to treat a variety of conditions (e.g., oncology, inflammation and autoimmune conditions) [34-36]

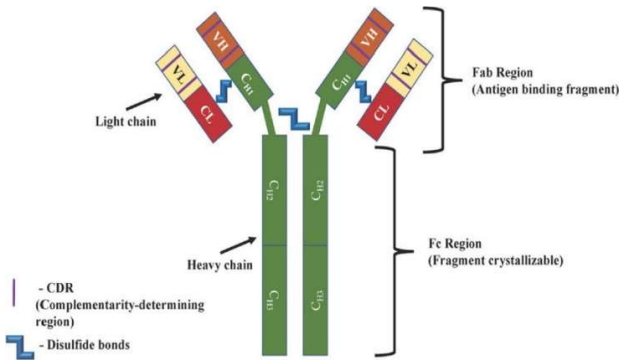

Fig 7: structure of monoclonal antibodies [34]

METHOD OF PREPARATION

Steps involved are-immunization of specific animal which generate hybridoma cell with spleen cell

1. ISOLATION OF MYELOMA CELLS
2. FUSION OF SPLEEN AND MYELOMA CELL

PEG (Polyethylene glycol) is required for fusion. It can also be done by electro-fusion .

- Fused plasma
- Fused myeloma
- Hybridoma
- Unfused plasma
- Unfused myeloma

3. SELECTION OF HOT MEDIUM
    - Salvage pathway
    - De-novo synthesis
4. ISOLATION OF HYBRIDOMA CELL
5. SCREENING OF HYBRIDOMA CELL **[34-37].**

CUBOSOMES

INTRODUCTION

Cubosomes are square rounded lyotropic liquid crystalline and thermodynamically stable nanoparticle having roughly 200 nm in periphery, correspond of amphiphilic lipids, stabilizers, and water in definite proportions [38-40].Cubosomes are two types. Liquid precursor cubosomes and Powdered precursor cubosomes [41]

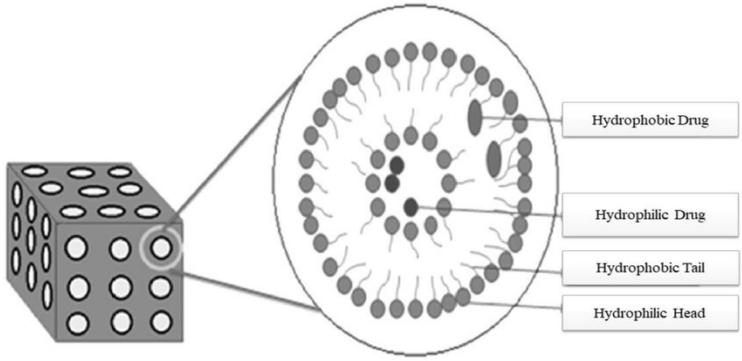

Fig 8: Structure of Cubosomes [38]

METHOD OF PREPARATION OF CUBOSOMES

a) **Sonication and homogenization method.**
Dissolving lipids in a solvent, and evaporation of the solvent under nitrogen atmosphere. Excess water removal by lyophilizer for creating lipid films then hydrated. The mixture was sonicated or homogenized to form a dispersion. Low volume ultrasonicator operated for 2.5-10 minute was utilized.

b) **Dilution Method.**
The dilution method form cubosome through facilitated nucleation at low shear stress. This method was reported to produce a few vesicles with lower polydispersity in contrast to sonication
. **PROCESSING TECHNIQUES**

- **Top-down approach**
the polymeric stabilizing agent, drug solution, and amphiphiles are agitated by high energy techniques such as shearing or ultrasonication to form a homogenous dispersion. Pluronic F127 is used many times as a steric stabilizing agent in a multiple preparation methods.By using a high-pressure homogenization technique used to form cubosomes
- **Bottom-up approach**
- The hydrotrope is dissolved results in formation of liquid precursors. At high concentrations, less energy input is required to avoid liquid crystals formation. In water at 80°C, dispersing the inverse micellar phase droplets and then gradual cooling that leads to the formation of cubosomes [42].

TRANSFEROSOMES
INTRODUCTION

Transfersomes being an ultra-deformable vesicle and elastic in nature can squeeze itself through a severance which is numerous times lower than its size owing to its plainness. Hence among colorful vesicular systems, Transfersomes have gained enormous significance in the last decade for sustained and targeted medicine delivery[43,44].

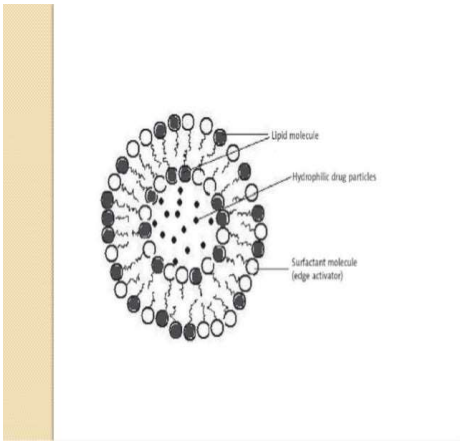

Fig 9: structure of transferosomes [44]

METHOD OF PREPARATION OF TRANSFEROSOMES

a) Rotary Film Evaporation Method

Dissolving phospholipids and surfactant in volatile organic solvent to form a thin film, then organic solvent evaporated. final traces of solvent removed under vacuum. then prepared film hydrated with buffer and vesicle sonicated at 40°C.The drug is added in solvent and incorporated.

b) Ethanol injection method

Aqueous drug solution is heated. phospholipids and activators dissolved in ethanol and injected in aqueous drug solution,Formation of bilayer drug.

c) Reverse phase evaporation method

Phospholipid dissolved in organic solvent in RBflask then add aqueous solution of surfactants under nitrogen purging. The drug incorporated into lipid and sonicated.excess organic solvent is evaporated to form viscous gel.

d) Vortexing sonication method.

Mixture of phospholipids and drug is added in phosphate buffer and vortexing process give milky suspension then suspension is sonicated for 30°C.

e) Freeze thaw method

The multilamellar vesicle exposed by alternated cycling of low temperature for freezing and the suspension dipped in a nitrogen bath and exposed at high temperature.

f) Multiple handshaking method

Drug, lithium, activator are dissolved in ethanol and chloroform and excess organic solvent are removed by evaporation. Formation of thin film and hydrated the film with phosphate buffer.[43,44].

CONCLUSIONS

Adopting novel drug delivery system, the dosage form of novel drug is a combination of advanced technology and also superior to traditional dosage form. A novel drug delivery system not only reduce the repeated administration to overcome non-compliance. It improves efficacy by reduce toxicity and increase

the bioavailability. Extensive research developing on incorporating the herbal drug in novel drug delivery system. This technique is used to release the drug in controlled manner.

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