A MEDICINE OF PRESENT ERA- Vesicular Novel Drug Delivery System

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Abstract : During last few decades world is facing with many disasters so better therapeutic action is to provided,which can be possible with Novel Drug Delivery System. In the present scenario we are progressing remarkably in NDDS focusing mainly on at Research and Development activities using particulate vesicle systems as such drug carriers for small and large molecules. Nanoparticles, Liposomes, Microspheres, Niosomes, Pronisomes, Ethosomes, Proliposomes, Enzymosomes SLN, NLC have been used as drug carrier in vesicle drug delivery system. In this review, we will throw a light on all about the vesicles which are used in NDDS.

Keywords: Dendrimer, Microparticle, Phytosomes, Microbubble, Liposomes.

INTRODUCTION

Any drug delivery system may be defined as a system comprising of drug formulation, medical device or dosage forms/technology to carry the drug inside the body, mechanism for the release[1]. In the novel drug delivery systems (NDDS), there are various novel carriers which have advantage over conventional dosage forms. Conventional drug delivery involves the formulation of the drug into a suitable form such as a compressed tablet for oral administration or a solution for intravenous administration Conventional dosage forms show high dose and low availability, in-stability, first pass effect, plasma drug level fluctuations and rapid release of the drug.

NOVEL DRUG DELIVERY SYSTEM

Novel Drug Delivery System (NDDS) refers to the approaches, formulations, technologies, & system for transporting in the body as needed to safely achieve its desired therapeutic effects. NDDS is a combination of advance technique and new dosage forms which are far better than conventional forms. Controlled drug release and subsequent biodegradation are important for developing successful formulations. Potential release mechanisms involve: (i) desorption of surface-bound /adsorbed drugs; (ii) diffusion through the

carrier matrix; (iii) diffusion (in the case of nano-capsules) through the carrier wall; (iv) carrier matrix erosion; and (v) a combined erosion /diffusion process. The mode of delivery can be the difference between a drug's success and failure, as the choice of a drug is often influenced by the way the medicine is administered[2,3].

DRUG DELIVERY CARRIER

Drug delivery carrier includes Dendrimer, Microparticle, Phytosomes, Microbubble, Liposomes, Nanosphere, Nano-capsule, Micelles, Hydrogels, Exosome.

Fig 1: Drug Delivery Carrier

DENDRIMER

Dendrimers are a novel class of structurally controlled macromolecules which have the structure like a tree or star shape, with a central core, interior branches and terminal groups decorate the surface and from the cavity inside the core[3,4]. Dendrimers have well defined size, shape, molecular weight and monodispersity and reactivity are determined by generation (shells) and chemical composition of the core, interior branching, and surface functionalities Dendrimers are being considered as additives in several routes of administration, including intravenous, oral, transdermal, pulmonary and ocular

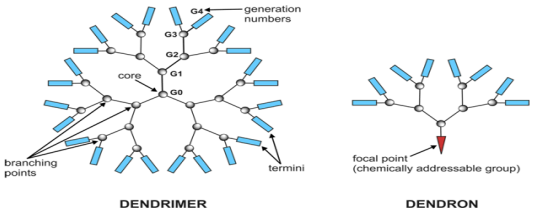

Fig 2: Dendrimer

Structure of Dendrimer Dendrimers are built from a starting atom, such as nitrogen, to which carbon and other elements are added by a repeating series of chemical reactions for the production of a spherical branching structure. The performance of these dendrimers are dependent upon its size, generation and surface functional groups with increase in dendrimer generation the dendrimer, the dendrimer increase linearly while the number of surface group increases exponentially[3].

Types of dendrimers

1. PAMAM Dendrimer monodisperse
2. PPI Dendrimer polymers
3. PAMAMOS Dendrimers
4. Chiral Dendrimer
5. Hybrid Dendrimer
6. Amphiphilic Dendrimer
7. Multilingual Dendrimer
8. Tecto Dendrimer
9. Frechet-Type Dendrimer
10. Peptide Dendrimer[4]

Synthesis of dendrimers:Dendrimers are generally prepared using either a divergent or a convergent method. There is a fundamental difference between these two construction methods.

Chracterization of dendrimers

- Spectroscopy technique
- Microscopy
- Size exclusion chromatography (SEC)
- Electrical techniques[5]
- Rheology, physical properties
- Microspheres

MICROSPHERES

Microspheres are solid spherical particles ranging in size from 1-1000µm. Microspheres can be manufactured from various natural and synthetic materials. Glass microspheres, polymer microspheres and ceramic microspheres are commercially available. They are spherical free flowing particles consisting of proteins or synthetic

polymers which are biodegradable in nature. Micromatrices are those in which entrapped substance is dispersed throughout the microspheres matrix[8].

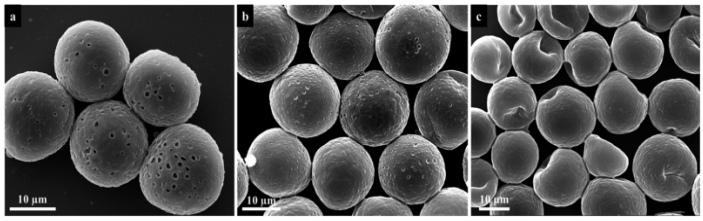

Fig 3: Microsheres

Types of microspheres

1. Bioadhesive microspheres
2. Magnetic microspheres
3. Floating microspheres
4. Radioactive microspheres
5. Mucoadhesive microspheres

Advantages: Studies on the macrophage uptake of microspheres have demonstrated their potential intargeting drugs to pathogens residing intracellularly.

- **Blood flow determination**: This study has been carried out using radio labelled microspheres.

- The size, surface charge and surface hydrophilicity of microspheres have been found to be important in determining the fate of particles in vivo

- Microspheres received much attention not only for prolonged release, but also for targeting of anticancer drugs to the tumour[6,7,8].

Ideal properties

- Longer duration of action
- Control of content release
- Increase of therapeutic efficiency
- Protection of drug
- Reduction of toxicity
- Biocompatibility, Sterilizability
- Relative stability
- Water solubility and dispersibility
- Bio resorbability, Target ability
- Polyvalent[8]

PHYTOSOMES

The term "Phyto" means plant and "some" means cell.Phytosomes means herbal drug loaded in vesicles, which is available in the Nano form. The phytosome provide an envelope, like coating around the active constituent of drug and due to this the chief constituent of herbal extract remains safe from degradation by digestive secretion and bacteria. Phytosome is effectively able to absorb from a water loving environment into lipid loving environment of the cell membrane and finally reaching to blood circulation. It is also mentioned as herbosomes. Standardized plant extracts mainly flavonoids are derived as phytosomes. Selection of flavonoids are done from the groups consisting of quercetin, kaemferol, quercretin-3, rhamnoglucoside, quercetin-3-rhamnoside, hyperoxide, vitexin, diosmine, 3-rhamnoside, (+) catechin, (-). The first phytosome generation was prepared by combining selected polyphenolic extract with phospholipids in nonpolar solvent, but recently the phytosome generations are developed by using hydro- ethanolic solvent, to comply with current food specifications[10].

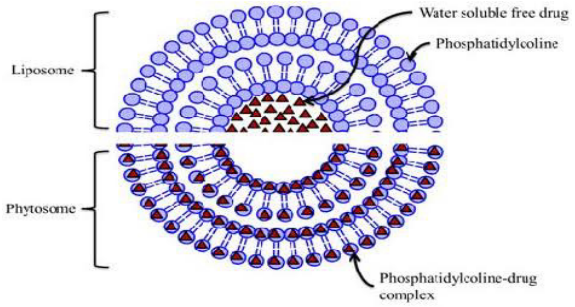

Fig 4: Phytosomes

Advantages: Small dose is required, as absorption is increased manifolds. Phytosomes possess better drug entrapment efficiency. Phosphatidylcholine is not merely a carrier; it is also having hepatoprotective activity and nutritional value. Due to formation of chemical bonds, phytosomes show

better stability profile. Phytosomes can be used for systemic targeting of herbal drugs, as phytosome can easily transit from hydrophilic environment into the lipid friendly environment of the enterocyte cell membrane and from there to into the cell. Cosmetic and other topical use of phytoconstituents can be done by phytosome formulations[10].

MICROBUBBLES

Micro bubbles are small spherical type of bubble which consists of a gas, they are separated from each other, so they cannot agglomerates. Actually, they have size range in micrometers usually 1-100 micrometer[11,12].

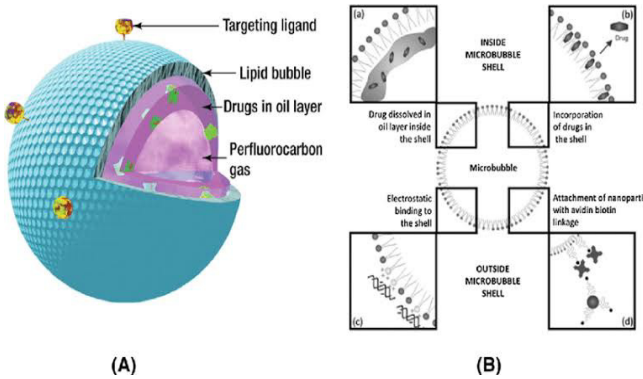

Fig 5: Microbubbles

They are capable of penetrating even into the smallest blood capillaries & releasing drugs or genes, incorporated on their surface, under the action of ultrasound. Microbubbles in general have a wide variety of applications. Gradually, the gas within the micro bubbles dissolves into the water and the bubbles disappear. Micro bubbles are applicable to a wide variety of field like medical field, Gene therapy etc[10,11].

LIPOSOMES

Liposomes are a form of vesicles that consist either of many, few or just one phospholipid bilayers.
Liposomes are colloidal spheres of cholesterol non-toxic surfactants, sphingolipids, glycolipids, long chain fatty acids and even membrane proteins and drug molecules or it is also called vesicular system. It differs in size, composition and charge and drug carrier loaded with variety of molecules such as small drug molecules, proteins, nucleotides or plasmids etc. Few drugs are formulated as liposomes to improve their therapeutic index. Hence a number of vesicular drug delivery systems such as liposomes, niosomes, transfersomes and pharmacosomes are developed. The focus of this article is to study various method of preparation, characterization of liposomes, advantages and applications, etc[12].

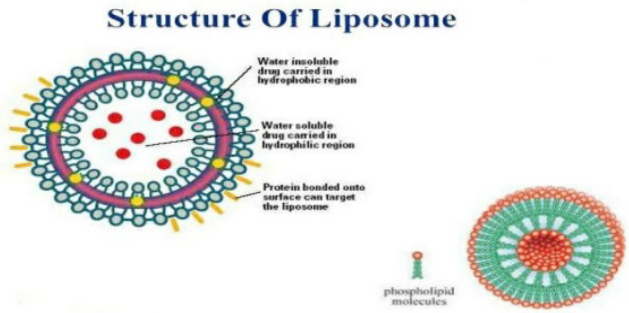

Fig 6: Liposomes

Designing of liposomes is done to achieve the following optimized properties[12]

1. Drug loading and control of drug release rate
2. Overcoming the rapid clearance of liposomes
3. Intracellular delivery of drugs
4. Receptor-mediated endocytosis of ligand-targeted liposomes
5. Triggered release
6. Delivery of nucleic acids and DNA

Mechanism of Action of Liposomes

A liposome consists of a region of aqueous solution inside a hydrophobic membrane. Hydrophobic chemicals can be easily dissolved into the lipid membranes; in this way liposomes are able to carry both hydrophilic and hydrophobic molecules. While the extent of location of the drug will depend upon its physiochemical characteristics and composition of lipid. For the deliverance of necessary drug molecules to the site of action, the lipid bilayers fuse with other bilayers of the cell (cell membrane) to release the liposomal content[11,12]

NANOSPHERES

Nanospheres are the particles having the size range between 10-200 nm in diameter. Nanospheres can be amorphous or crystalline in nature and also they have the ability to protect the drug from enzymatic and chemical degradation. The tiny capsule of drug store house is called vesicles and the solid skeleton structure is called Nanospheres. Nanospheres are the spherical particles which have the size between 10-200 nm in diameter and that exhibit some new enhanced size dependent properties in comparison of larger spheres of the same material.

Benefits of Nanospheres drug delivery system: Nanospheres can easily pass through the smallest capillary vessels due to their ultra tiny volume14-15. They can avoid the rapid clearance by phagocytes so that duration in bloodstream can be prolonged. Nanospheres can easily penetrate the cells and tissue gap to arrive at target organs eg. Liver, spleen, lungs, spinal cord, and lymph's.It shows the controlled release property.Site specific targeting by attaching the ligands to the surface of the spheres. They can be easily administered by various routes including oral, nasal, parenteral, etc16 . Reduction of toxicity is also an important advantage of Nanospheres[10,11].

Method of preparation of Nanospheres: There are various types of method by which Nanospheres are prepared.

- •Polymerization(Emulsification polymerization)
- • Solvent Evaporation.
- • Solvent displacement technique.
- • Phase inversion temperature methods.

NANO-CAPSULES

Nanocapsules, as characteristic class of nanoparticles, are made up of one or more active materials (core) and a protective matrix (shell)[11]in which the therapeutic substance may be confined. Nanocapsules have been developed as drug delivery systems for several drugs by different routes of administrations such as oral and parental. Reduce the toxicity of drugs. Polymeric nanoparticles are named nanocapsules.

Nano capsules are prepared by different method those are a) Solvent evaporation b) Nano precipitation c) emulsification / Solvent diffusion d) Salting out e) Dialysis f) Super critical fluid technology[11,12].

HYDROGEL

A hydrogel can be described as a three dimensional network formed by hydrophilic polymers which can expand in water. These polymers can hold copious amounts of water without disrupting the structure. . Hydrogels are novel drug deliverers that can aid in the delivery of several kinds of drug molecules either therapeutic or diagnostic nature. They are also suitable carriers for immunological products such as vaccines and other biological products like plasmas and seras and valvular intestinal cells[7,8].

Properties of Hydrogels

Hydrogels are finding many applications in domestic and industrial areas due to its properties. Hydrogels have: a) Both solid and liquid-like properties b) High biocompatibility c) Maximum absorption capacity d) Preferred particle size and desired porosity. e) Shrink on drying f) Responsive to stimuli.

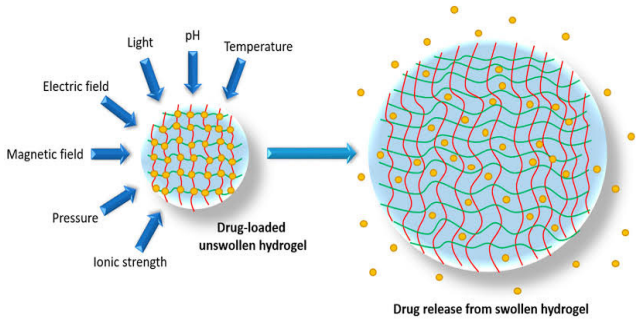

Fig 7: Hydrogel

Methods of Preparation of Hydrogels : They consist of cross-linked water interacting network of polymer that gives it an elastic structure. To produce a hydrogel such techniques are used that

can form a cross-linked polymer. A standard method to produce cross-linkage is the free-radical polymerization. Some ways to cross-link water-soluble linear polymers include: a) Linking the polymer chains via a chemical reaction b) Use of ionizing radiation for the generation of main-chain free radicals that can recombine as cross-link junctions c) Physical interactions, i.e., electrostatics.

EXOSOMES

Exosomes are small endosome derived lipid nanoparticles (50-120 nm in diameter) secreted into extracellular space by most types of cells. Exosomal vesicles content includes lipids, genomic DNA, RNA, proteins. Many studies have shown cumulative evidence that exosomes have performed may biological functions particularly in cell-cell communication by providing means for intercellular exchange of proteins, lipids, mRNA, miRNA, and DNA. Its associated proteins and microRNAs that are closely related to the pathogenesis of most human diseases are invaluable biomarkers for disease diagnosis, prognosis, and therapy. Therefore, exosome isolation and characterization becomes crucial to understand its biological function and therapeutic application[8,9].

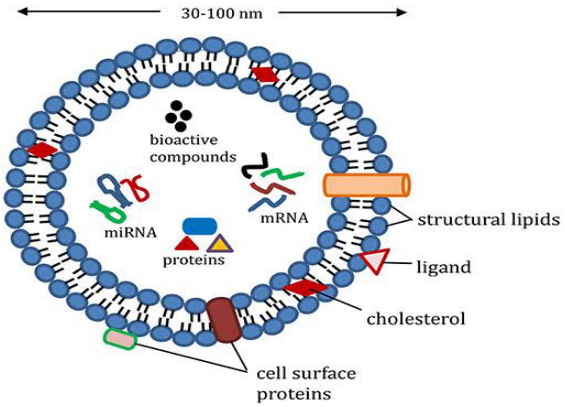

Fig8: Exosomes

CONCLUSION

Liposomes	Liposomes are good candidates for increasing the solubility of poorly soluble drugs. But the stability issue of liposomes remains same ie formation of ice crystals in liposomes, the subsequent instability of bilayers leads to the leakage of entrapped material. The oxidation of cholesterol and phospholipids also leads to the formulation instability. Chemical instability primarily indicates hydrolysis and oxidation of lipids. Liposomes in plasma are prone to aggregation and exhibit leakage. The destabilization of liposomes is due to the lipid exchange between the liposomes and hdls[13].
Dendrimers	Dendrimers are highly ordered, branched polymeric molecules.Typically, dendrimers are symmetric about the core, and often adopt a spherical three-dimensional morphology[14,15].
Phytosomes	Phytosome is one of the lipid-based vesicular delivery systems which can be used for encapsulation of drugs and plant-derived nutraceuticals such as polyphenolic compounds. They are newly introduced food-grade delivery system, can potentially decrease problems associated with the solubility and bioavailability of polyphenolic compounds, making them applicable in development of the new drug and food formulations[16].
Exosomes	Exosomes are small intracellular membrane-based vesicles with different compositions that are involved in several biological and pathological processes[17].

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