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Novel Drug Delivery System & It's Future: An Overview

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Abstract

Now day's Recent advances in the understanding of pharmacokinetic & pharmacodynamic behaviour of drug have offer a more rational approach to the development of optimal drug delivery system. Now it's appreciable that future success in Drug delivery research will largely be result of multidisplinary efforts. If any therapeutic agent that can be the more efficacious and safe using and improved drug delivery system represent both lucrative marketing opportunities for pharmaceutical company and advancement in the treatment of diseases of mindkind. An ideally design drug delivery system delivers a specified amount of drug to target particular site at an appropriate time and rate as dictated or desired by the etiological and physiological needs of the body. Conventional Pharmaceutical Dosage forms are incapable ofcontrolling the rate of drug delivery to target site. As a result the distribution of drug in non- target tissue and body fluids necessitate therapeutic doses that could far exceed the amount required in target cells, the higher doses often lead to serious adverse during treatment thus, the novel drug delivery systems (NDDS) are carriers which maintain the drug concentration in therapeutic range for longer period of time and also, in addition, may deliver the content to the site of action if so desired as per requirements.

Keywards: Pharmacodynamic, drug delivery systems, therapeutic agent, target site, non-targeting tissues.

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Introduction

The method by which a drug is delivered can have a significant effect on its efficacy. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all[1]. On the other hand, the very slow progress in the efficacy of the treatment of severe diseases, has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues.

From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, biorecognition, and efficacy of drugs were generated. These new strategies, often called drug delivery systems (DDS), which are based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry, and molecular biology. To minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone, various drug delivery and drug targeting systems are currently under development.[1] Controlled and Novel Drug Delivery which was only a dream or at best a possibility is now a reality. During the last decade and half pharmaceutical and other scientists have carried out extensive and intensive investigations in this field of drug research.

Among drug carriers one can name soluble polymers, microparticles made of insoluble or biodegradable, natural and synthetic polymers, microcapsules, cells, cell ghosts, lipoproteins, liposomes, and micelles. The carriers can be made slowly degradable, stimuli-reactive (e.g., pH- or temperature-sensitive), and even targeted (e.g., by conjugating them with specific antibodies against certain characteristic components of the area of interest). Targeting is the ability to direct the drug-loaded system to the site of interest. Two major mechanisms can be distinguished for addressing the desired sites for drug release: (i) Passive and (ii) Active targeting.[1]

An example of passive targeting is the preferential accumulation of chemotherapeutic agents in solid tumors as a result of the enhanced vascular permeability of tumor tissues compared with healthy tissue. A strategy that could allow active targeting involves the surface functionalization of drug carriers with ligands that are selectively recognized by receptors on the surface of the cells of interest. Since ligand–receptor interactions can be highly selective, this could allow a more precise targeting of the site of interest (**see fig. 1**).

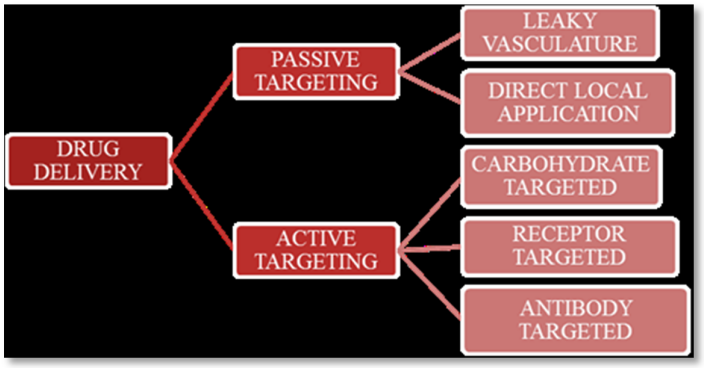

Figure 1: Drug Delivery System

Any drug delivery system may be defined as a system comprising of:

a) Drug formulation

b) Medical device or dosage form/technology to carry the drug inside the body

c) Mechanism for the release

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. These dosage forms have been found to have serious limitations in terms of higher dosage required, lower effectiveness, toxicity and adverse side effects. New drug delivery systems have been developed or are being developed to overcome the limitation of the conventional drug delivery systems to meet the need of the healthcare profession. These systems can be characterised as controlled drug release systems and targeted drug delivery systems. The therapeutic benefits of these new systems include:

- Increased efficacy of the drug
- Site specific delivery
- Decreased toxicity/side effects
- Increased convenience
- Viable treatments for previously incurable diseases
- Potential for prophylactic applications
- Better patient compliance.

There is no uniform and established definition of drug delivery systems. It is assumed to be based on two basic parameters: Route of entry (A) and Dosage form (B). Any member of the cartesian product of (A X B) is defined as a drug delivery system.

Advantages Of Novel Drug Delivery System

1. Protection from physical and chemical degradation.

2. Sustained delivery.

3. Improved tissue macrophages distribution.

4. Enhancement of stability.

5. Enhancement of pharmacological activity.

6. Protection from toxicity.

7. Increased bioavailability.

8. Enhancement of solubility.[2]

RecentDevelopments In NovelDrug Delivery System

Phytosomes

Phytosomes are lipid compatible molecular complex which are composed of “phyto” which means plant and “some” meaning cell-like.[3]

Complexing the polyphenolic phytoconstituents in the molar ratio with phosphatidyl choline results in a new herbal drug delivery system, known as “Phytosome”. Phytosomes are advanced forms of herbal products that are better absorbed, utilized to produce better results than those produced by conventional herbal extracts. Phytosomes show better pharmacokinetic and therapeutic profiles than conventional herbal extracts.[4]

Advantages of phytosome

1. Phytosome increases the absorption of active constituents, so its dose size required is small.

2. There is appreciable drug entrapment and improvement in the solubility of bile to herbal constituents, and it can target the liver.

3. In Phytosome, chemical bonds are formed between phosphatidylcholine molecules, so it shows good stability.[5]

4. Phytosome improves the percutaneous absorption of herbal phytoconstituents.[6]

Liposomes

Tiny pouches made of lipids, or fat molecules surrounding a water core widely used for clinical cancer treatment. Several different kinds of liposomes are widely employed against infectious diseases and can deliver certain vaccines. During cancer treatment they encapsule drugs, shielding healthy cells from their toxicity, and prevent their concentration in vulnerable tissues such as those of patient kidneys and liver. Liposomes can also reduce or eliminate certain common side effects of cancer treatment such as nausea and hair loss.

They are form of vesicles that consist either of many, few or just one phospholipid bi-layers. The polar character of liposomal core enables polar drug molecules to be

encapsulated. Amphiphilic and lipophilic molecules are solubilized within phospholipid bilayer according to their affinity towards phospholipids.[7]

Advantages of liposomes

1. The high biocompatibility.

2. The easiness of preparation.

3. The chemical versatility that allows the loading of hydrophilic, amphiphilic, and lipophilic compounds.

4. The simple modulation of their pharmacokinetic properties by changing the chemical composition of the bilayer components.[8]

Use of Liposomes

Another major and important advancement in the novel drug delivery systems is the use of liposomes for carrying the drugs to the site of action.

Liposomes in both modified and unmodified forms are able to change the course of pharmacokinetic parameters of the drugs. These are widely used in delivering the cytotoxic agents to the tumour tissue and preventing side effects like myelosuppression. These are also used in targeting through receptor-mediated endocytosis. Modified liposomes also have huge applications in targeting various drugs to the organs like heart, liver, kidney, lungs and bones.[9]

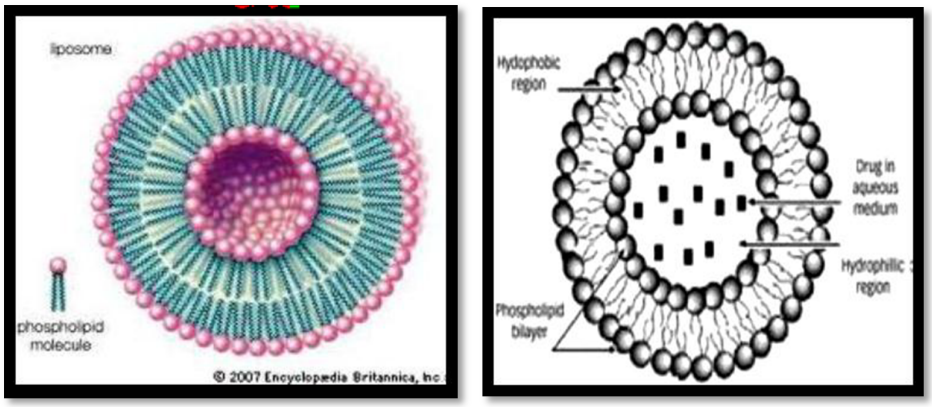

Figure 2: Structure Of Liposomes

Patent No.	Assignee/Inventors	Filed On	Title
US20100209492	SDG, Inc, Cleveland,OH	January 14,2010	Targeted Liposomal Drug Delivery System

US20070286898	Astellas Pharma Inc., Tokyo, JP	August 30,2005	Intracellular Drug Delivery Improving Liposome
US20070104777	Lau; John R; et al.	December 21, 2006	Targeted Liposomal Drug Delivery System
US20070014845	Zhang; Yuanpeng; et al.	June 30, 2006	Liposomal Delivery Vehicle For Hydrophobic Drugs
US20020182248	Daiichi Pharmaceuticals Co. Ltd.	August 29, 2001	Liposomes And Liposomal Dispersions

Table 1: Examples Of Patients For Liposomes

Table 2: Marketed Liposomal Based Products

Trade Name	Trade Name	Manufacturer	Indication
AmBisome	Amphotericin B	NeXstar Pharmaceuticals	Systemic fungal infections
Abelcet	Amphotericin B	The Liposome Company	Systemic fungal infections
Amphotec	Amphotericin B	Sequus Pharmaceuticals	Systemic fungal infections
Doxil	Doxorubicin	Sequus Pharmaceuticals	Kaposi's sarcoma
DaunoXome	Daunorubicin	NeXstar Pharmaceuticals	Kaposi's sarcoma

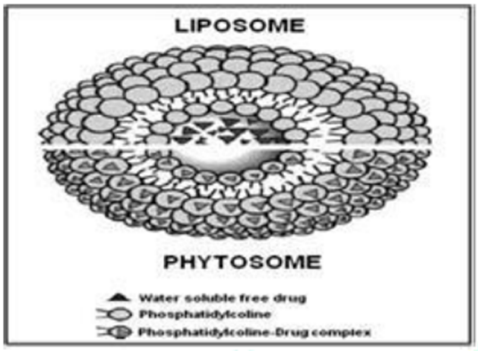

Figure 3: Structure Of Liposome & Phytosome

Nanoparticles

Nanoparticles (including nanospheres and nanocapsules of size 10-200 nm) are in the solid state and are either amorphous or crystalline. They are able to adsorb and/or encapsulate a drug, thus protecting it against chemical and enzymatic degradation. In recent years, biodegradable polymeric nanoparticles have attracted considerable attention as potential drug delivery devices in view of their applications in the controlled release of drugs, in targeting particular organs / tissues, as carriers of DNA in gene therapy, and in their ability to deliver proteins, peptides and genes through the peroralroute.[10]

Classification of nanomaterials

a) **Nanotubes:** They are hollow cylinders made of carbon atoms. They can also be filled and sealed, forming test tubes or potential drug delivery devices.

b) Nano wires: Glowing silica nano wire is wrapped around a single strand of human hair. It looks delicate. It is about five times smaller than virus applications for nano wires include the early sensing of breast and ovarian malignancies.

c) Nanocantilever: The honey comb mesh behind this tiny carbon cantilever is surface of fly's eye. Cantilevers are beams anchored at only one end. In nano world, they function as sensors ideal for detecting the presence of extremely small molecules in biological fluids.

d) Nanoshells: Nanoshells are hollow silica spheres covered with gold. Scientists can attach antibodies to their surfaces, enabling the shells to target certain shells such as cancer cells. Nano shells one day also are filled with drug containing polymers.

e) Quantum dots: Quantum dots are miniscule semiconductor particles that can serve as sign posts of certain types of cells or molecules in the body. They can do this because they emit different wavelengths of radiations depending upon the type of cadmium used in their cores. Cadmium sulfide for ultra violet to blue, cadmium selinide for most of the visible spectrum and cadmium telluride for far -infra red and near infra red.

f) Nano pores: Nano pores have cancer research and treatment applications. Engineered into particles, they are holes that are so tiny that DNA molecules can pass through them one strand at a time, allowing for highly precise and efficient DNA sequencing. By engineering nanopores into surface of drug capsule that are only slightly larger than medicines molecular structure, drug manufacturers can also use nanopores to control rate of drug's diffusion in body.

g) Gold Nanoparticles: These nanoparticles, seen in transmission electron micrograph image, they have solid core. Researchers at north western university are using gold particles to develop ultra sensitive detection systems for DNA and protein markers associated with many forms of cancer, including breast prostrate cancer.

h) Bucky balls: Bucky ball is common name for a molecule called buckminsterfullerene, which is made of 60 carbon atoms formed in shape of hollow ball, discovered in 1985. Bucky balls and other fullerenes because of their chemistry and their unusual hollow, cage like shape extremely stable and can withstand high temperatures.

Advantages of herbal nanoparticle delivery system

1. Nanoparticulate system delivers the herbal formulation directly to the site of action.

2. Increased efficacy and therapeutic index.

3. Increased stability via encapsulation.

4. Improved pharmacokinetic effect.

5. Producible with various sizes, compound surface properties.

Emulsions

Emulsion is a biphasic system in which one phase is intimately disperses in the other phase in the form of minute droplets in ranging in diameter from 0.1μm to 100 μm. In emulsion, one phase is always water or aqueous phase, and the other phase is oily liquid, i.e. non aqueous. Among them, the microemulsion is also called nanoemulsion, and the sub-micro-emulsion is called liquid emulsion. Microemulsion is a clear, thermodyanamically stable, frequently in combination with a co-surfactant.

Advantages of emulsion-based formulations

1. It can release the drug for a long time because it is packed in the inner phase and makes direct.

2. Contact with the body and other tissues.

3. As a result of the lipophilic drugs being made into o/w/o emulsion, the droplets of oil are phagocytosised by macrophages and increase its concentration in liver, spleen and kidney.

4. As the emulsion contains herbal formulation, it will increase the stability of hydrolyzed formulated material and improve the penetrability of drug into skin and mucous.

5. The new type, viz., Elemenum emulsion, is used as an anti-cancer drug and causes no harm to the heart and liver.

Microspheres

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 200 μm. Materials used for preparing Microspheres are polymers. They are classified into two types:

1. Synthetic Polymers

2. Natural polymers

Synthetic polymers are divided into two types

a. Non-biodegradable polymers

- Poly methyl methacrylate (PMMA)
- Glycidyl methacrylate
- Epoxy polymers

b. Biodegradable polymers

- Lactides, Glycolides & their co polymers

- Poly alkyl cyano acrylates
- Poly anhydrides

Synthetic polymers

Poly alkyl cyano acrylates is a potential drug carrier for parenteral as well as other ophthalmic, oral preparations. Poly lactic acid is a suitable carrier for sustained release of narcotic antagonist, anti cancer agents such as cisplatin, cyclo phosphamide, and doxorubicin. Sustained release preparations for anti malarial drug as well as for many other drugs have been formulated by using of co-polymer of poly lactic acid and poly glycolic acid. Poly anhydride microspheres (40μ) have been investigated to extend the precorneal residence time for ocular delivery. Poly adipic anhydride is used to encapsulate timolol maleate for ocular delivery. Poly acrolein microspheres are functional type of microspheres. They do not require any activation step since the surfacial free CHO groups over the poly acrolein can react with NH2 group of protein to form Schiff's base. In case of non-biodegradable drug carriers, when administered parenterally, the carrier remaining in the body after the drug is completely released poses possibility of carrier toxicity over a long period of time. Biodegradable carriers which degrade in the body to non-toxic degradation products do not pose the problem of carrier toxicity and are more suited for parenteral applications.

Natural polymers obtained from different sources like proteins, carbohydrates and chemically modified carbohydrates.

Proteins: Albumin, Gelatin, and Collagen

Carbohydrates: Agarose, Carrageenan, Chitosan, Starch

Chemically modified carbohydrates: Polydextran, Poly starch.

Natural polymers

Albumin is a widely distributed natural protein. It is considered as a potential carrier of drug or protiens (for either their site specific localization or their local application into anatomical discrete sites). It is being widely used for the targeted drug for the targeted drug delivery to the tumour cells.

Gelatin microspheres can be used as efficient carrier system capable of delivering the drug or biological response modifiers such as interferon to phagocytes. Starch belongs to carbohydrate class. It consists of principle glucopyranose unit, which on hydrolysis yields D-glucose. It being a poly saccharide consists of a large number of free OH groups. By means of these free OH groups a large number of active ingredients can be incorporated within as well as active on surface of microspheres. Chitosan is a deacylated product of chitin. The effect of chitosan has been considered because of its charge. It is insoluble at neutral and alkaline pH values, but forms salts with inorganic and organic salts. Upon dissolution, the amino groups of chitosan get protonated, and the resultant polymer becomes positively charged.[11]

Ethosomes

Ethosomes are developed by mixture of phospholipids and high concentration of ethanol. This carrier can penetrate through the skin deeply lead to improve drug delivery into deeper

layer of skin and in blood circulation. These formulations are useful for topical delivery of alkaloids in form of gel and cream for patients comfort. They show increase in their permeability through the skin by fluidizing the lipid domain of the skin. Unstable nature and poor skin penetration are limits for Ethanosomes tropical delivery. The Ethosomes was developed and examined for their ability the topical absorption of Tetrandine through dermal delivery, and the relation of formulations to the pharmacological activity of Tetrandrine loaded in the formulation was also accessed. Result of the drug levels in rat plasma showed that when Tetrandrineloded Ethosomes were topically administered in rats the drug level was low to be detected in rat plasmaIn conclusion, Ethosomes were demonstrated to be promising carrier for improving topical delivery of Tentrandrine via skin.[12]

Advantages of ethosomal drug delivery

1. Ethosomes enhance transdermal permeation of drug through skin.

2. Ethosomes are a platform for the delivery of large amounts of diverse groups of drugs.

3. Ethosomal drug is administered in semisolid form resulting in improvement in patient's compliance.

Solid Lipid Nanoparticles

SLNsare a new pharmaceutical delivery system or pharmaceutical formulation. The conventional approaches such as use of permeation enhancers, surface modification, prodrug synthesis, complex formation and colloidal lipid carrier based strategies have been developed for the delivery of drugs to intestinal lymphatics. In addition, polymeric nanoparticles, self-emulsifying delivery systems, liposomes, microemulsions, micellar solutions and recently solid lipid nanoparticles (SLN) have been exploited as probable possibilities as carriers for oral intestinal lymphatic delivery.A solid lipid nanoparticle is typically spherical with an average diameter between 10 and 1000 nanometers. Solid lipid nanoparticles possess a solid lipid core matrix that can solubilize lipophilic molecules. The lipid core is stabilized by surfactants (emulsifiers). The term lipid is used here in a broader sense and includes triglycerides (e.g. tristearin), diglycerides (e.g.glycerolbahenate), mono-glycerides (e.g. glycerol monostearate), fatty acids (e.g. stearic acid), steroids (e.g. cholesterol), and waxes (e.g. cetylpalmitate). All classes of emulsifiers (with respect to charge and molecular weight) have been used to stabilize the lipid dispersion. It has been found that the combination of emulsifiers might prevent particle agglomeration more efficiently.[13]

Niosomes

Niosomes are multilamellar vesicles formed from non-ionic surfactants of the alkyl or dialkylpolyglycerol ether class and cholesterol. Earlier studies, in association with L'Oreal have shown that, in general, niosomes have properties as potential drug carriers similar to liposomes. Niosomes are different from liposomes in that they offer certain advantages over liposomes.

Proniosomes

Proniosomes gel system is step forward to niosome, which can be utilized for various applications in delivery of actives at desire site. Proniosomal gels are the formulations, which on in situ hydration with water from the skin are converted into niosomes.[14]

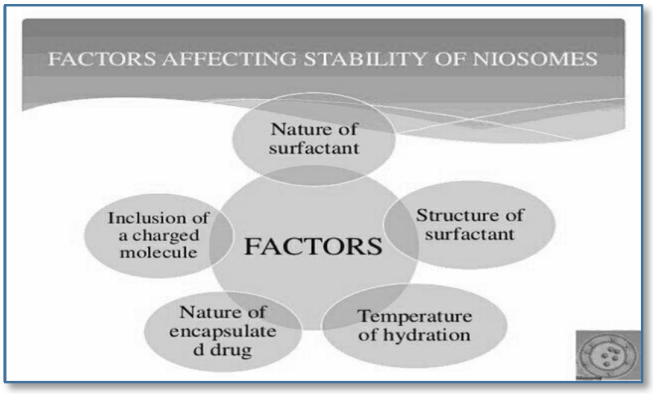

Figure 4: Factors Influencing Niosomes Physical Stability

Dendrimers

Dendrimers are precisely defined, synthetic nanoparticles that are approximately 5–10 nm in diameter. They are made up of layers of polymer surrounding a control core. The dendrimers surface contains many different sites to which drugs may be attach and also attachment sites for materials such as PEG which can be used to modified the way of dendrimer which interacts with body. PEG can be attached to dendrimer to 'disguise' it and prevent the body's defense mechanism for detecting it, there by slowing the process of break down. This fascinating particle holds significant promise for cancer treatment. Its many branches allow other molecules to easily attach to its surface. Researchers have fashioned dendrimers into sophisticated anticancer machines carrying five chemical tools – a molecule designed to bind to cancer cells, a second that fluorescence upon locating genetic mutations, a third to assist in imaging tumor shape using x–rays, a fourth carrying drugs released on demand, and a fifth that would send a signal when cancerous cells are finally dead. The creators of these dendrimers hadsuccessful tests with cancer cells in culture and plan to try them in living animals soon.[15]

Hydrogels

Hydrogels are three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water or biological fluids. The networks are composed of homopolymers or copolymers, and are insoluble due to the presence of chemical crosslinks (tie-points, junctions), or physical crosslinks, such as entanglements or crystallites. Hydrogels exhibit a thermodynamic compatibility with water, which allows them to swell in aqueous media. They are used to regulate drug release in reservoir-based, controlled release systems or as carriers in swellable and swelling-controlled release devices. On the forefront of controlled drug delivery, hydrogels as enviro-intelligent and stimuli-sensitive gel systems modulate release in response to pH, temperature, ionic strength, electric field, or specific analyte concentration differences. In these systems, release can be designed to occur within specific areas of the body (e.g., within a certain pH of the digestive tract) or also via specific sites (adhesive or cell-receptor specific gels via tethered chains from the hydrogel surface). Hydrogels as drug delivery systems can be very promising materials if combined with the technique of molecular imprinting.

Classification of hydrogels

- Based on the methods of preparation- Homo-polymeric Hydrogel, Co-polymeric hydrogel, Inter Penetrating Network,
- Stimuli-sensitive hydrogels- Temperature-sensitive hydrogels, pH-sensitive hydrogels, Dual pH-thermal sensitive systems
- Based on mechanism of release-Diffusion controlled, swelling controlled.

Advantages of Hydrogels

1) Biocompatible, biodegradable and can be injected

2) Hydrogels possess wide degree of flexibility similar to natural tissue.

3) Have good transport properties and easy to modify.[16]

Released Erythrocytes As Drug Carriers

Erythrocytes, the most abundant cells in the human body, have potential carrier capabilities for the delivery of drugs. Erythrocytes are biocompatible, biodegradable, possess very long circulation half lives and can be loaded with a variety of chemically and biologically active compounds using various chemical and physical methods. erythro = red and cytes = cell, Erythrocyte is red cell. Erythrocyte is biconcave discs, anucleate Filled with hemoglobin (Hb), a protein that functions in gas transport. It contains the plasma protein spectrin. Healthy adult male=4.5millions/µml Healthy adult female=4.8million/ µml Immature RBC are called "RETICULOCYTES."[17]

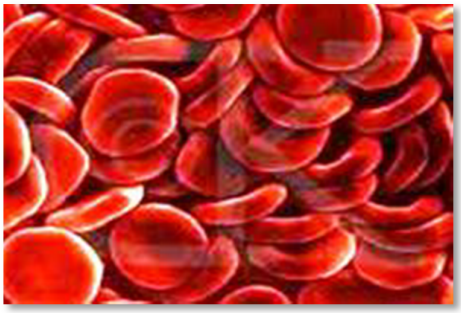

Figure 5: Erythrocytes

Properties of resealed erythrocyte of novel drug delivery carriers

1) The drug should be released at target site in a controlled manner.

2) It should be appropriate size, shape and should permit the passage through capillaries. And Minimum leakage of drug should take place.

3) It should be biocompatible and should have minimum toxic effect.

4) It should possess the ability to carry a broad spectrum of drug.

5) It should possess specific physicochemical properties by which desired target size could be recognized.

6) The degradation product of the carriers system , after release of the drug at the selected site should be biocompatible. It should be physico-chemically compatible with drug.

7) The carrier system should have an appreciable stability during storage.

Advantage

1) They are natural part of body, so they are biodegradable in nature.

2) The entrapment of drug does not require the chemical modification of drugs

3) The entrapment of drug also does not require the chemical modification of the substance to be entrapped.

4) They are non immunogenic in action and can be targeted to disease tissue/organ..

5) They prolong the systemic activity of drug.

6) Isolation of erythrocyte is easy and larger amount of drug can be encapsulated in small volume of cells

7) They can target the drug within reticuloendothelial system.

8) They facilitate incorporation of protein and nucleic acid in eukaryotic cells by cell infusion with RBC.

Disadvantage

1) They have a limited potential as carrier to non-phagocyte target tissue.

2) Possibility of clumping of cells and dose dumping may be there.

Drug loaded Erythrocytes

This is one of the growing and potential systems for delivery of drugs and enzymes. Erythrocytes are biocompatible, bio-degradable, posses long circulation half life and can be loaded with variety of biologically active substances. Carrier erythrocytes are preapared by collecting blood sample from the organism of interest and separating erythrocytes from the plasma. By using various physical and chemical methods cells are broken and drug is entrapped into erythrocytes, finally they are resealed and resultant carriers are then called as “resealed erythrocytes”. Upon reinjection the drug loaded erythrocytes serve as slow circulation depots targets the drug to reticulo-endothelial system.

Transdermal Drug Delivery System

Transdermal drug delivery is defined as self contained, discrete dosage forms which, when applied to the intact skin, deliver the drug, through the skin at controlled rate to the systemic circulation. Transdermal drug delivery system (TDDS) established itself as an integral part of novel drug delivery systems. Delivery via the transdermal route is an interesting option because transdermal route is convenient and safe.

The positive features of delivery drugs across the skin to achieve systemic effects are:

- Avoidance of first pass metabolism
- Avoidance of gastro intestinal incompatibility
- Predictable and extended duration of activity

- □ Improving physiological and pharmacological response
- □ Termination of therapy is easy at any point of time
- □ Greater patient compliance due to elimination of multiple dosing profile
- □ Provide suitability for self administration
- □ Enhance therapeutic efficacy[18]

Mucoadhesive Drug Delivery System

Bioadhesion may be defined as the state in which two materials, at least one of which is biological in nature, are held together for extended period of time by interfacial forces. In pharmaceutical sciences, when the adhesive attachment is to mucus or a mucous membrane, the phenomenon is referred to as mucoadhesion.

The potential of mucoadhesive polymers was shown in ocular, nasal, vagina and buccal drug delivery systems leading to a significantly prolonged residence time of sustained release delivery systems on this mucosal membranes. In addition, the development of oral mucoadhesive delivery systems was always of great interest as delivery systems capable of adhering to certain gastrointestinal (GI) segments would offer various advantages.[19]

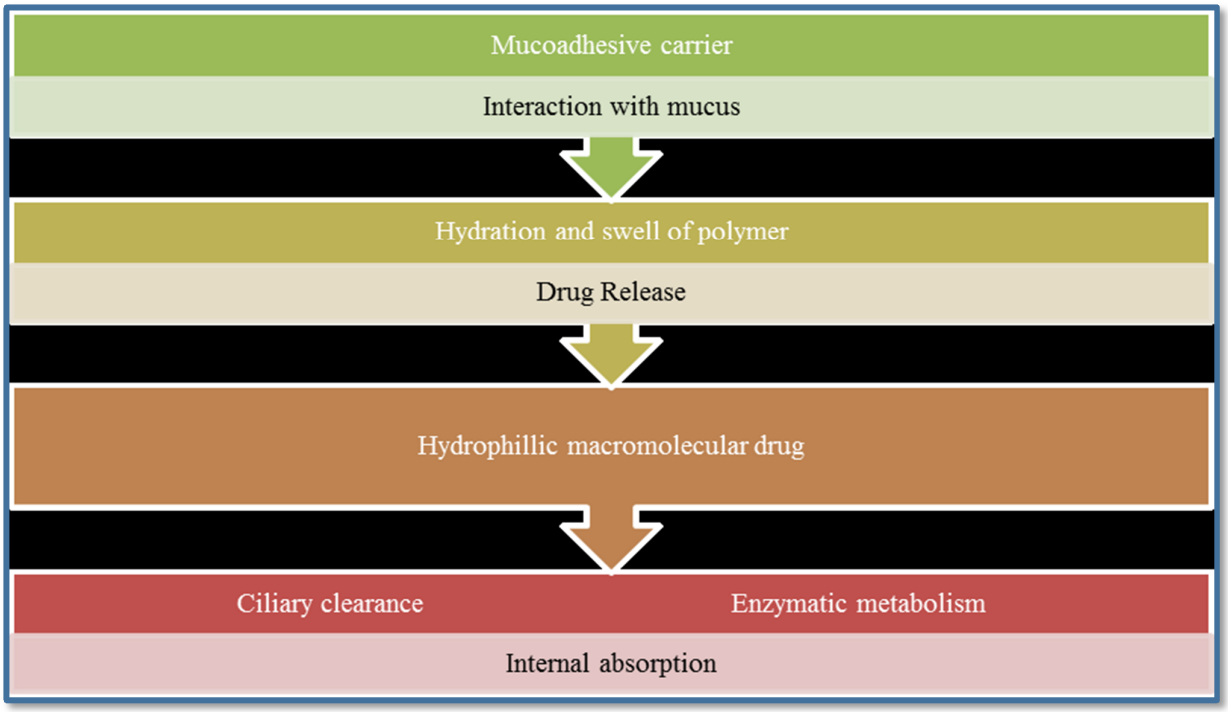

Figure 7: Encapsulation

Microencapsulation

Microencapsulation is the process in which small droplets or particles of liquid or solid material are surrounded or coated by a continuous film of polymeric materials. Firstly the microencapsulation procedure was discovered by Bungen burg de Jon and Kan in 1931 and which were deal with the preparation of gelatin spheres and use of a gelatin coacervation process.

The controlled drug delivery system has used to reduce the problems associated with conventional therapy and to improve the therapeutic efficacy of a given drug. The maximum therapeutic efficacy can be achieved by delivering of the active agent in the optimal rate to the target tissue, then causing little toxicity and minimum side effects. Microencapsulation process helps for converting the liquids to solids, changing the colloidal and surface properties, providing environmental protection and controlling the release characteristics of different coated materials. Some of these properties can be achieved by macropakaging techniques but in microencapsulation the small coated particles are used to make a wide variety of dosage forms and has not been feasible.

Novel drug delivery systems which were initiate with the course of optimizing the bioavailability by the modification of the bioavailability of the drug concentration in blood. With the sustained and controlled release products, drug therapy can be improved that is the common goal achieved over with their non sustained and controlled release with the same drug. Microencapsulated products (micro particles) are the small entities that have an active agent know as the core material surrounded by a shell known as the coating material or embedded into a matrix structure. Most Microparticle shells are of organic polymers, but waxes and lipids are also used. Generally the size of the microencapsulated products (microparticles) is considered as larger than 1 micrometer and up to 1000 micrometers in diameter. Commercially available microparticles contained 10- 90% w/w core. A number of core materials can be encapsulated like that live cells, adhesives, flavors, agrochemicals, enzymes, pharmaceuticals. The more recent result of pharmaceutical research is that the absorption rate of a drug can be controlled by controlling its rate of release from the dosage form .The controlled released dosage forms are so designed and formulated as having the sustained action, sustained release, prolonged action, delayed action and timed release medication. This has been done by developing the new drug entities, discovering of new polymeric materials that are suitable for prolonging the drug release, safety, improvement in therapeutic efficacy.[20]

Future Prospects And Opportunities In India

India is one of the most strategic regions for the pharmaceutical market. Therefore many multinational giants have been keen to invest and grow preferentially in this sector. Developments in the new and advanced techniques in the field of NDDS will create huge demand for variety of excipients usage and development. India is well known for its quick adaptability to new excipients and associated technologies. So market for excipients in India will grow on two aspects; one is in the form of exporting new organic excipients and the second one in the form of employing new excipients in various advanced delivery technologies. Majority of the pharmaceutical companies in the country have been applying and receiving new patents in the field of the Novel drug delivery systems. This eventually, in the near future derives huge demand for the products and services offered by pharmaceutical and allied businesses. Nanotechnology offers various modern applications in novel drug delivery systems that potentially improve the diagnosis, treatment and help monitoring of post-administration transformation of drug composition within the body systems. Another important milestone to be mentioned here is Computer aided Drug Design, which offers a lot of scope for the development of this kind of novel and advanced systems. Computer aided Drug Design helps in designing and developing the drugs and

delivery systems consuming less time and resources with more accuracy and quality compared to traditional methods.[21]

Molecular imprinting Technology

The molecular imprinting technology has an enormous potential for creating satisfactory drug dosage forms. Molecular imprinting involves forming a pre-polymerization complex between the template molecule and functional monomers or functional oligomers (or polymers) with specific chemical structures designed to interact with the template either by covalent, non-covalent chemistry (self-assembly) or both. Once the pre-polymerization complex is formed, the polymerization reaction occurs in the presence of a cross-linking monomer and an appropriate solvent, which controls the overall polymer morphology and macroporous structure. Once the template is removed, the product is a heteropolymer matrix with specific recognition elements for the template molecule. Examples of MIP-based drug delivery systems involve: (i) rate-programmed drug delivery, where drug diffusion from the system has to follow a specific rate profile, (ii) activation-modulated drug delivery, where the release is activated by some physical, chemical or biochemical processes and (iii) feedback-regulated drug delivery, where the rate of drug release is regulated by the concentration of a triggering agent, such as a biochemical Substance, the concentration of which is dependent on the drug concentration in the body. Despite the already developed interesting applications of MIPs, the incorporation of the molecular imprinting approach for the development of DDS is just at its incipient stage. Nevertheless, it can be foreseen that, in the next few years, significant progress will occur in this field, taking advantage of the improvements of this technology in other areas. Among the evolution lines that should contribute more to enhance the applicability of imprinting for drug delivery, the application of predictive tools for a rational design of imprinted systems and the development of molecular imprinting in water may be highlighted.[22]

Administration Routes

The choice of a delivery route is driven by patient acceptability, the properties of the drug (such as its solubility), access to a disease location, or effectiveness in dealing with the specific disease. The most important drug delivery route is the peroral route. An increasing number of drugs are protein and peptide based. They offer the greatest potential for more effective therapeutics, but they do not easily cross mucosal surfaces and biological membranes; they are easily denatured or degraded, prone to rapid clearance in the liver and other body tissues and require precise dosing. At present, protein drugs are usually administered by injection, but this route is less pleasant and also poses problems of oscillating blood drug concentrations. So, despite the barriers to successful drug delivery that exist in the gastrointestinal tract (i.e., acid-induced hydrolysis in the stomach, enzymatic degradation throughout the gastrointestinal tract by several proteolytic enzymes, bacterial fermentation in the colon), the peroral route is still the most intensively investigated as it offers advantages of convenience and cheapness of administration, and potential manufacturing cost savings.

Pulmonary delivery is also important and is effected in a variety of ways - via aerosols, metered dose inhaler systems (MDIs), powders (dry powder inhalers, DPIs) and solutions (nebulizers), all of which may contain nanostructures such as liposomes, micelles, nanoparticles and dendrimers. Aerosol products for pulmonary delivery comprise more than

30% of the global drug delivery market. Research into lung delivery is driven by the potential for successful protein and peptide drug delivery, and by thepromise of an effective delivery mechanism for gene therapy (for example, in the treatment of cystic fibrosis), as well as the need to replace chlorofluorocarbon propellants in MDIs. Pulmonary drug delivery offers both local targeting for the treatment of respiratory diseases and increasingly appears to be a viable option for the delivery of drugs systemically. However, the pulmonary delivery of proteins suffers by proteases in the lung, which reduce the overall bioavailability, and by the barrier between capillary blood and alveolar air (air-blood barrier). Transdermal drug delivery avoids problems such as gastrointestinal irritation, metabolism, variations in delivery rates and interference due to the presence of food. It is also suitable for unconscious patients. The technique is generally non-invasive and aesthetically acceptable, and can be used to provide local delivery over several days. Limitations include slow penetration rates, lack of dosage flexibility and / or precision, and a restriction to relatively low dosage drugs.[23]

Marketed Opportunities Of Sustained Released Dosage Forms

The global market for advanced drug delivery systems amounted to $134.3 billion in 2008, and was projected to increase to $139 billion in 2009. The estimate for 2014 is $196.4 billion, for a compound annual growth rate (CAGR) of 7.2% in the 5-year period. The largest segment of the market is targeted drug delivery, which reached $50.9 billion in 2009 and is expected to increase to $80.2 billion in 2014, for a CAGR of 9.5%.Sustained-release products have the second-largest market share, with estimated sales of $36.1 billion in 2009 and $45.8 billion in 2014, for a CAGR of 4.9%. Benefits for short half-life drugs, sustained release can mean less frequent dosing and thus better compliance reduce variations in plasma/blood levels for more consistent result.[24]

Conclusion

NDDS not only reduces the repeated administration to overcome noncompliance, but also helps to increase the therapeutic value by reducing toxicity and increasing the bioavailability, and so on. Extensive research is going on for herbal drugs to incorporate them in novel drug delivery systems. Application of these novel techniques to natural medicines will led to enhanced bioavailability, reduced toxicity, sustained release action, protection from GI degradation which cannot be obtained through conventional drug delivery system due to large molecular size, poor solubility, degradation of herbal medicines in Gastrointestinal media.

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