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A REVIEW ON DRUG TARGETING AND DRUG CARRIERS

Sravan Kumar. Pudota[*1], V. Shirisha[1], Raghavarapu Hemanth Kumar[1]

[1*]Department of Pharmaceutics, Narasaraopet Institute of Pharmaceutical Sciences, Narasaraopet, Guntur, Andhra Pradesh, India.

ABSTRACT

Targeted drug delivery system is different from conventional dosage in terms of its site specific treatment. This targeting can be used in the treatment of cancer like diseases. We can also target body part like liver, kidneys etc. Where the treatment is somewhat difficult through conventional treatment. This targeting can be achieved by using drug carrier particle like liposomes, Niosomes, microspheres and Nanoparticles etc. In this review, some basic concepts of this system has been discussed, also a brief of the type of drug carrier used in formulating such a dosage form is mentioned.

KEYWORDS

Targeting drug Delivery system, Drug carriers, Liposomes, Niosomes, Nanoparticles and Microspheres.

Author for correspondence:

Sravan Kumar. Pudota,

Department of Pharmaceutics,

Narasaraopet Institute of Pharmaceutical Sciences,

Narasaraopet, Guntur, Andhra Pradesh, India.

Email: sra1.pudota@gmail.com

INTRODUCTION[1,2]

Target drug delivery system may also be referred to as smart drug delivery system1is the currently used form of drug delivery system where the pharmacologically active drug (or pro-drug in some cases) is targeted or is delivered specifically to the site of action. Targeted drug delivery extensively used for selective and effective localization of pharmacologically active moiety at pre-determined target in therapeutic concentration, while restricting its access to non-target normal cellular linings, thus minimizing toxic effects and maximizing therapeutic index. Targeting of drugs also help us to bypass first pass metabolism so a drug can be administered in a form such that it reaches the receptor sites in

sufficient concentration without disturbing in extraneous tissue cells. Products based on such a delivery system are being prepared by considering the Specific properties of target cells, Nature of markers or transport carriers or vehicles, which convey drug to specific receptors and Ligands and physically modulated components. Ideally targeted drug delivery system should have following characteristics:

1. Should be biochemically inert (non-toxic).
2. Should be non-immunogenic.
3. Should be physically and chemically stable in vivo and in vitro conditions.
4. Target cells or tissues or organs and should have uniform capillary distribution.
5. Should have Controllable and predictable.
6. Rate of drug release and also Drug release should not affect the drug action.
7. Should have therapeutic amount of drug release.
8. Should have minimal drug leakage during transit.
9. Carriers used should be bio-degradable or readily eliminated from the body without any problem.
10. The preparation of the delivery system should be easy or reasonably simple, reproductive and cost effective.

Different types of drug targeting[3-5]

Three different types of targeting systems are there. They are

1. Passive Targeting
2. Inverse Targeting
3. Active targeting

Passive targeting

It refers to the accumulation of drug or drug-carrier system at a particular (like in case of anti-cancerous drug) site whose explanation may be attributed to physicochemical or pharmacological factors of the disease. Hence in case of cancer treatment the size and surface properties of drug delivery nano-particles must be controlled specifically to avoid uptake by the reticuloendothelial system (RES), to maximize circulation times and targeting ability.

Active targeting

Active targeting includes specific modification of a drug/drug carrier nano systems with active agents having selective affinity for recognizing and interacting with a specific cell, tissue or organ in the body .in case of cancer, it is achieved by conjugating the nanoparticle to a targeting component that provides preferential accumulation of nanoparticles in the tumor-bearing organ, totumor, individual cancer cells, intracellular organelles, or specific molecules in cancer cells. Such an approach is based on specific interactions such as lectin-carbohydrate, ligand-receptor, and antibodyantigen[3].

Inverse Targeting

In this type of targeting attempts are made to avoid passive uptake of colloidal carrier by RES and hence the process is referred to as inverse targeting. To achieve inverse targeting, RES normal function is suppressed by preinjecting large amount of blank colloidal carriers or macromolecules like dextran sulphate[6]. This approach leads to saturation of RES and suppression of defense mechanism. This type of targeting is a effective approach to target drug(s) to non-RES organs.

Advantages of Drug Targeting

1. Drug administration protocols may be simplified
2. Drug quantity may be greatly reduced as well as the cost of therapy
3. Drug concentration in the required sites can be sharply increased without negative effects on non-target compartments.

Disadvantages

1. Rapid clearance of targeted systems.
2. Immune reactions against intravenous administered carrier systems.
3. Insufficient localization of targeted systems into tumour cells.
4. Diffusion and redistribution of released drugs.

Ideal Characteristics

1. Targeted drug delivery system should be-biochemically inert (non-toxic), non-immunogenic.
2. Both physically and chemically stable *in vivo* and *in vitro*.

3. Restrict drug distribution to target cells or tissues or organs and should have uniform capillary distribution.
4. Controllable and predictable rate of drug release.
5. Drug release should not affect the drug action.
6. Therapeutic amount of drug release.
7. Minimal drug leakage during transit.
8. Carriers used must be bio-degradable or readily eliminated from the body without any problem.
9. The preparation of the delivery system
10. Should be easy or reasonably simple, reproductive and cost effective.

Drug Carriers used in targeting system

Carriers used in the targeting system are as follows

1. Microspheres
2. Nanoparticles
3. Liposomes
4. Niosomes
5. Resealed erythrocytes

Microspheres

Microencapsulation is rapidly expanding technology. The process is applying relatively thin coatings to small particles of solids or droplets of liquid and dispersions.

In this two parts are there

1. Core material
2. Coating material

Core material

Core material is defined as the specific material to be coated, can be liquid or solid in nature.

Composition

Liquid core

1. Dispersed materials
2. Dissolved materials

Solid core

Mixture of active constituents.

Example of core material

Acetaminophen activated charcoal, aspirin, progesterone, and urease.

Coating material

The coating materials are selected against the background of the purpose of coating. The properties of following;

1. Strength
2. Flexibility
3. Impermeability
4. Optical properties
5. Stability
6. Cohesiveness
7. Permeability
8. Moisture absorption
9. Solubility
10. Clarity and Purity.

The commonly used for coating material

Acacia, gelatin, starch, silicones, paraffin wax, cetylalcohol, stearic acid, polyacrylate, etc.

APPLICATIONS OF MICROENCAPSULATION[7-10]

Microencapsulation is a promising field applied in various areas like

1. Pharmaceuticals
2. Scratch and sniff perfumes
3. Various food industries
4. Detergent industries, Some powder detergents contain protein reactive enzymes such as protease, used in removing blood stains.
5. Pesticide and herbicides industries. Etc
6. Carbonless copy paper
7. Flavors and essences
8. Textiles
9. Adhesives
10. Visual indicators
11. Thermo chromic dyes.

NANOPARTICLE

A **nanoparticle** is a microscopic particle whose size is measured in nanometres (nm). It is defined as a particle with at least one dimension <200nm. or nanoparticles are solid colloidal particles ranging in size from 10nm to 1000nm. They consist of macromolecular materials in which the active principle is dissolved, entrapped or encapsulated, and/or to which the active principle is absorbed or attached[1].

Ideal Properties

1. Natural or synthetic polymer
2. Inexpensive
3. Nontoxic
4. Biodegradable
5. Nonthrombogenic
6. Nonimmunogenic

7. Particle diameter <100nm

Preparation of Nanoparticles

Nanoparticles can be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. The selection of matrix materials is dependent on many factors including[7]:

(a) Size of Nanoparticles required;

(b) Inherent properties of the drug, e.g., aqueous solubility and stability;

(c) Surface characteristics such as charge and permeability;

(d) Degree of biodegradability, biocompatibility and toxicity;

(e) Drug release profile desired; and

(f) Antigenicity of the final product.

Applications

1. Targeted drug delivery
2. Alternative drug and vaccine delivery mechanisms (e.g. inhalation, oral in place of injection).
3. Bone growth promoters
4. Cancer treatments
5. Biocompatible coatings for implants
6. Sunscreens (e.g. using ZnO and TiO2) / cosmetics
7. Biolabeling and detection (e.g. using Au)
8. Carriers for drugs with low water solubility
9. Fungicides (e.g. using ZnO)
10. MRI contrast agents (e.g. using superpara magnetic iron oxide)
11. New dental composites
12. Biological binding agents (e.g. for high phosphate levels)
13. Antiviral, antibacterial (e.g. Ag), anti-spore non-chemical creams and
14. Powders (using surface tension energy on the nanoscale to destroy biological particles).

Liposomes

Liposomes are defined as structure consisting of one or more concentric spheres of lipid bilayers separated by water or aqueous buffer compartments. (OR) Liposomes are simple microscopic vesicles in which an aqueous volume is entirely enclosed by a membrane composed of lipid bilayers. The liposomal structure follows as in Figure No.1.

Advantages

1. It provides controlled drug delivery.
2. It should be biodegradable, biocompatible, and flexible.
3. It should be non-ionic.
4. It can carry both water and lipid soluble drugs.
5. The drugs can be stabilized from oxidation.
6. It should be improve the protein stabilization.
7. It provides controlled hydration.
8. It provides sustained release.

Applications of Liposomes

Liposomes are used to Target drugs to the tumors.

a. The liposomal Ara -C inhibit DNA synthesis in the lungs

b. For targeted drug delivery for blood born Neoplasms

c. By active targeting using monoclonal antibodies, by magnetosomes or by temperature sensitive liposomes

d. By passive targeting to liver, spleen, R.E.S cancers.

Niosomes

A niosome is a non-ionic surfactant-based liposome. Niosomes are formed mostly by cholesterol incorporation as an excipient. Other excipients can also be used. Niosomes have more penetrating capability than the previous preparations of emulsions. They are structurally similar to liposomes in having a bilayer, however, the materials used to prepare niosomes make them more stable and thus niosomes offer many more advantages over liposomes[1].

The sizes of niosomes are microscopic and lie in nanometric scale. The particle size ranges from 10nm-100nm.

Structure of niosomes

A typical niosome vesicle would consist of a vesicle forming amphiphile i.e. a non-ionic surfactant such as Span-60, which is usually stabilized by the addition of cholesterol and a small amount of anionic surfactant such as dicetyl phosphate, which also helps in stabilizing the vesicle[3, 7, 9]. The structure of Niosomes as of Figure No.2.

Advantages of niosomes

Use of niosomes in cosmetics was first done by L'Oreal as they offered the following advantages[1, 2 - 7].

1. The vesicle suspension being water based offers greater patient compliance over oil based systems.
2. Since the structure of the niosome offers place to accommodate hydrophilic, lipophilic as well as amphiphilic drug moieties, they can be used for a variety of drugs.
3. The characteristics such as size, lamellarity etc. of the vesicle can be varied depending on the requirement.
4. The vesicles can act as a depot to release the drug slowly and offer a controlled release.

Applications of niosomes

The application of niosomes technology is widely varied and can be used to treat a number of diseases. The following are a few uses of niosomes which are either proven or under research.

1. It is used as Drug Targeting.
2. It is used as Anti-neoplastic Treatment i.e. Cancer Disease.
3. It is used as Leishmaniasis i.e. Dermal and Mucocutaneous infections e.g. Sodium stibogluconate.
4. It is used act as Delivery of Peptide Drugs.
5. It is used in Studying Immune Response.
6. Niosomes as Carriers for Hemoglobin.
7. Transdermal Drug Delivery Systems Utilizing Niosomes
8. It is used in Ophthalmic drug delivery
9. Other Applications.

Resealed Erythrocytes

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. Application of erythrocytes as promising slow drug release or site-targeted delivery systems for a variety of bioactive agents from different fields of therapy has gained a remarkable degree of interest in recent years. Figure No.3 shows the structure of RSE.

Advantages

1. A remarkable degree of biocompatibility, particularly when the autologous cells are used for drug loading.
2. Complete biodegradability and the lack of toxic product(s) resulting from the carrier biodegradation.
3. Avoidance of any undesired immune responses against the encapsulated drug.
4. Considerable protection of the organism against the toxic effects of the encapsulated drug, e.g. antineoplasms.
5. Remarkably longer life-span of the carrier erythrocytes in circulation in comparison to the synthetic carriers. In the optimum condition of the loading procedure, the life-span of the resulting carrier cells may be comparable to that of the normal erythrocytes.
6. An easily controllable life-span within a wide range from minutes to months.

Applications of Resealed Erythrocytes

1. It is used as slow drug release

Erythrocytes have been used as circulating depots for the sustained delivery of antineoplastics, antiparasitics, veterinary antiamoebics, vitamins, steroids, antibiotics and cardiovascular drugs.

1. It is used to Targeting the liver such as Enzyme deficiency/replacement therapy, Treatment of hepatic tumors, Treatment of parasitic diseases.
2. Removal of RES iron overload

Desferrioxamine-loaded erythrocytes have been used to treat excess iron accumulated because of multiple transfusions to thalassemic patients.

1. It is used to Removal of toxic agents.
2. It is used as Enzyme Replacement Therapy in Gaucher's Disease.
3. It is used to Delivery of antiviral agents such as azidothymidine derivatives, azathioprene, acyclovir, and fludarabine phosphate.

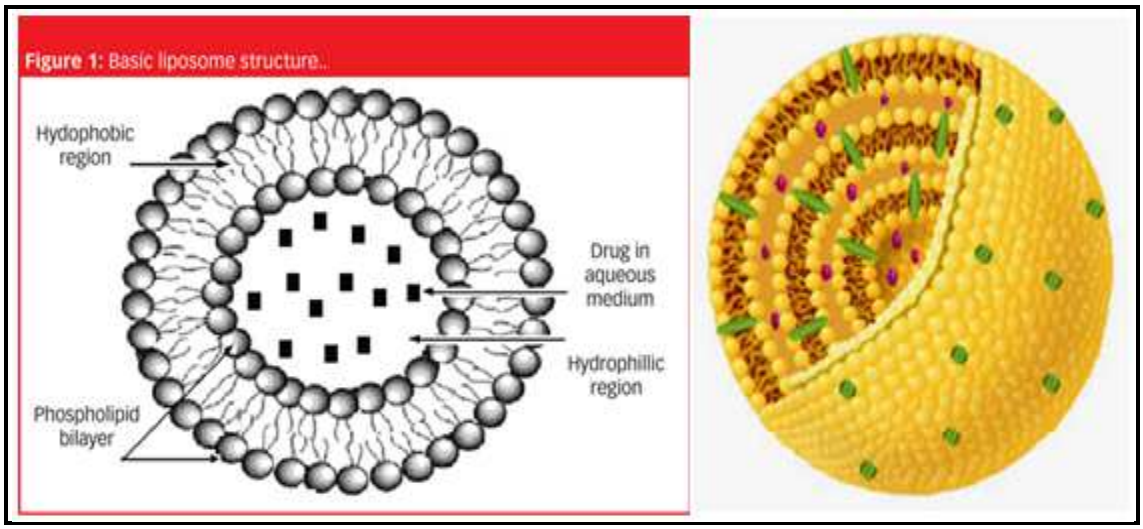

Figure No.1: Liposomal Structure

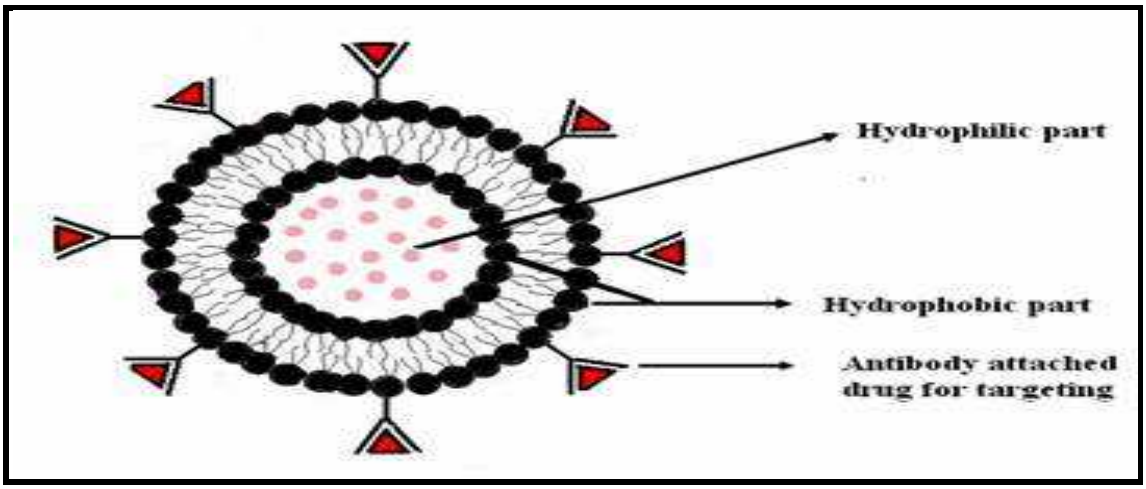

Figure No.2: Structure of Niosomes

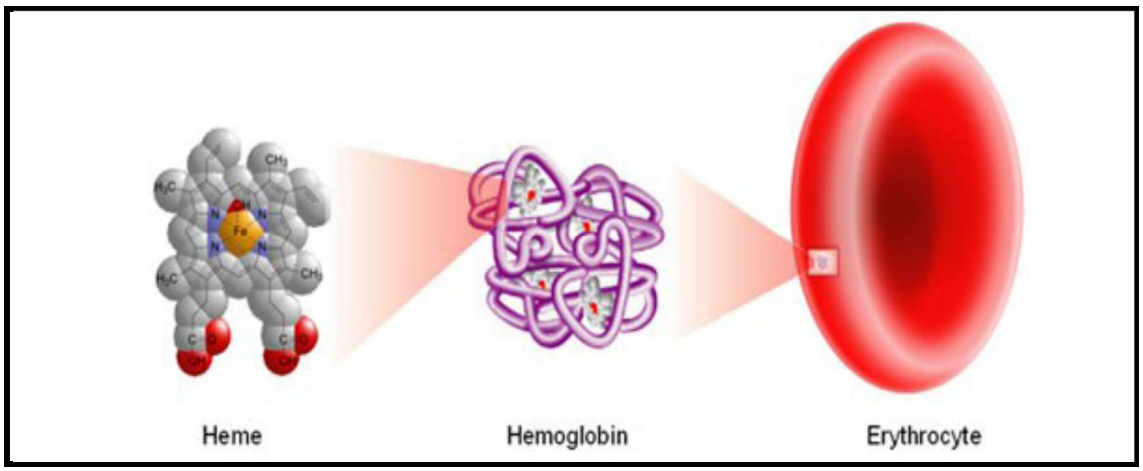

Figure No.3: Compositions of erythrocytes

CONCLUSION

It is very difficult for a drug molecule to reach its destination (site of action) in the complex cellular network of an organism. By using this targeting carrier system we can easily target the required site to treat the diseases like tumors etc. all the particulate carriers are efficient to carry the drug to the targeted site.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Gregoriadis G. Targeting of drugs: implications in medicine, *Lancet*, 2(8240), 1981, 241-246.
2. Ghosh, Tapash K, Jasti Bhaskar R. Oral controlled release Solid Dosage Forms; in theory and practice of contemporary Pharmaceutics, *CRC Press*, 1(1), 2009, 335-337.
3. Vyas S P, Khar R K. Basis of targeted Drug Delivery, In Targeted and controlled Drug Delivery, *CBS Publishers and Distributors*, 1(1), 2008, 74.
4. Florence A T. Drug delivery: Advances and Commercial opportunities, *Connect Pharma, Oxford*, 49, 1994, 79-82.
5. Vyas S P, Khar R K. Basis targeted Drug Delivery, In Targeted and controlled Drug Delivery, *CBS Publishers and Distributors*, 1, 2008, 42-46.
6. Illium L, Wright J, Davis S S. Targeting of microspheres to sites of inflammation, *Int. J. Pharm*, 52(3), 1989, 221-224.
7. Yie W Chien. Concepts and System Design for Rate- Controlled Drug Delivery. Novel Drug Delivery System, *Marcel Dekker, Inc, New York*, 2nd Edition, 1992, l-42.
8. Yie W Chien. Rate-controlled Drug Delivery Systems, *Ind J Pharm Sci*, 2(3), 1988, 63-65.
9. Allen TM. Liposomal drug formulations: Rationale for development and what we can expect for the future, *Drugs*, 56(5), 1998, 747-756.
10. Handjani-vila RM. Dispersion of lamellar phases of nonionic lipids in cosmetic products, *Int J Cosmetic Sci*, 1(5), 1979, 303-314.

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