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Short Communication

A Concise Review on Microspheres for Targeted Drug Delivery

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Abstract

Most of the recent dosage forms have poor pharmacokinetic and biopharmaceutical properties. Hence there is need to develop a suitable delivery system that distributes the active drug molecule only to the site of action, without affecting other tissue or organs. Targeted drug delivery is a method of delivering drugs to the patients at the targeted site or the site of action. This improves efficacy of treatment by reducing side effects of the drug administered. The inherent advantages of this techniques lead to reduction in dose of drug as well as reduced side effects. Various drug carriers which can be used in this advanced delivery system are Lipoproteins, Liposomes, Microspheres. The present review deals with the targeted drug delivery system, its advantages, disadvantages, need of Targeted drug delivery system and research update on Targeted drug delivery system.

Keywords: Targeted drug delivery system, Microspheres, Research update.

1. Introduction

Targeted drug delivery is a method of delivering medication to a patient in a manner that increases the concentration of the medication in some parts of the body relative to others. Targeted drug delivery seeks to concentrate the medication in the tissues of interest while reducing the relative concentration of the medication in the remaining tissues. This improves efficacy while reducing side effects. Drug targeting is the delivery of drugs to receptors or organs or any other specific part of the body to which one wishes to deliver the drugs exclusively. The desired differential distribution of drug by targeted delivery would spare the rest of the body and thus significantly reduce the overall toxicity while maintaining its therapeutic benefits. The drug's therapeutic index, as measured by its pharmacological response and safety, depends upon access of drug to and binding with its candidate receptor, whilst minimizing its interaction with non–target tissue. Thus targeted or site- specific delivery of drugs is a very attractive goal because this provides one of the most potential ways to improve the therapeutic index of the drugs. [1,4,7]

Properties of Targeted Drug Delivery System [7,8,10,11,12]

- It should be nontoxic, biodegradable, biocompatible and physicochemical stable invivo and invitro.
- Confine drug delivery to target cells or tissue or organ or should have uniform capillary distribution.
- Predictable and Controllable and rate of drug release.
- Drug release should not influence the drug delivery.
- Therapeutic amount of drug release.
- Minimal drug leakage during transit
- Carrier used should be biodegradable or readily eliminated from the body without any problem and no carrier should induce modulation of diseased state.

Components of Targeted Drug Delivery System [8,9,12]

Target: Target means specific organ or a cell or group of cells, which in chronic or acute condition need treatment.

Carrier or marker: Carrier is a special molecule or system essentially required for effective transportation of loaded drug up to the pre selected sites. They are engineered vectors, which retain drug inside or onto them either via encapsulation and/ or via spacer moiety and transport or deliver it into vicinity of target cell.

Novel Targeted Drug Delivery System[13]

- ✓ Liposomes
- ✓ Monoclonal antibodies and fragments
- ✓ Modified (plasma) proteins
- ✓ Nanoparticles
- ✓ Lipoproteins
- ✓ Dendrimers
- ✓ Microspheres

Microspheres AS A Targeted Drug Delivery System[2,3]

Microspheres are sometimes referred to as microparticles. Microspheres can be prepared from various natural and synthetic materials. Polymer microspheres, Glass microspheres and ceramic microspheres are commercially available. Polyethylene and polystyrene microspheres are two most common types of polymer microspheres.

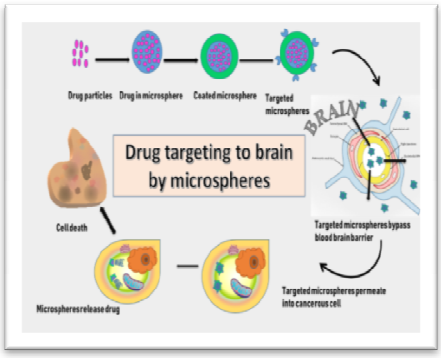

Fig:1 Mechanism of drug targeting to brain by microsphere

A relatively new direction in anti-tumor therapy, which comprises the application of particles, e.g. microspheres capable of releasing drugs is the so-called chemoembolization. This innovative technology focuses on achieving higher drug concentrations in the tumor and lower plasma levels compared to conventional cancer chemotherapy. For this purpose, drug carriers need to possess some essential features such as accurate delivery and controlled/prolonged release, ability to maintain high intra-tumor concentration for a long time without causing damage to surrounding tissues. They may contain non-degradable polymers such as polyvinyl alcohol (PVA) or biodegradable materials such as PLGA.

Microspheres of sodium acrylate polyvinyl (SAP) have been developed, which have been applied for several years for embolization of hepatocellular carcinoma. They have been approved under the name HepaSphere® (EMA) and QuadraSphere® (FDA) for the treatment of primary and metastatic liver tumors. SAP microspheres are spherical embolization agents derived from a polyvinyl alcohol-sodium acrylate copolymer.[12,13]

Advantages

- ✓ Constant and sustained therapeutic effect.
- ✓ Improved drug utilization through bioavailability and reduction in the incidence or intensity of adverse effects.
- ✓ Controllable variability in deprivation and drug release.
- ✓ Dosing frequency is reduced and improves patient compliance.
- ✓ Due to its spherical shape and smaller size they can be injected.[14]

Limitations

- ✓ The release rate of the controlled release dosage form may vary due to variety of factors like food and the rate of transit though gut.
- ✓ Differences in the release rate from one dose to another.
- ✓ Controlled release formulations generally contain a higher drug load and thus any loss of integrity of the release characteristics of the dosage form may lead to potential toxicity.[6,9]
- ✓ Specialized delivery system adds to the cost of the formulation.

TYPES OF MICROSPHERES[7.8,13]

1. Bioadhesive microspheres:

Adhesion of drug delivery device to the mucosal membrane such as ocular, buccal, nasal, rectal etc., can be defined as bio adhesion. Bioadhesive microspheres exhibit a prolonged residence time at the site of application and cause intimate contact with the absorption site and produce better therapeutic action.

2. Magnetic microspheres:

This kind of delivery system localizes the drug to the disease site by the use of magnetic force. In

this type of delivery system, magnetite is generally incorporated. Once the delivery system reaches the target site, external magnetic force is applied. This retains the microspheres at site for longer time during which drug is released and acts on the target.

3. Floating microspheres:
In floating type, the bulk density is less than the gastric fluid and so remains buoyant in stomach without affecting gastric emptying rate. The drug is released slowly at the desired rate. It also reduces chances of striking and dose dumping. It produces prolonged therapeutic effect and therefore reduces dosing frequency.

4. Radioactive microspheres:
Radioactive microspheres deliver high radiation dose to the targeted areas without damaging the normal surrounding tissues. Here, radionuclide is enclosed within the microsphere and releases radiation in the form of α emitters, β emitters or γ emitters over a radioisotope typical distance. Such radioactive microspheres have therapeutic as well as diagnostic applications.

5. Polymeric microspheres:
Polymeric microspheres can be classified into biodegradable polymeric microspheres and synthetic polymeric microspheres.

- Biodegradable polymeric microspheres:
Biodegradable polymers prolongs the residence time when contact with mucous membrane due to its high degree of swelling and gel formation. The rate and extent of drug release is controlled by concentration of polymer and the release pattern.

- **Synthetic polymeric microspheres**: Synthetic polymeric microspheres are widely used in clinical application and are used as fillers, bulking agent, drug delivery vehicles, embolic particles etc.

PREPARATION OF MICROSPHERES [12]
Selection of method for preparation of microspheres depends on desired particle size, route of administration, duration of drug release, degree of cross linking, evaporation time, co-precipitation etc.

The various methods of preparations are
1. Solvent evaporation method,
a) Single emulsion technique.
b) Double emulsion technique.
2. Coacervation phase separation method.
3. Spray drying and spray congealing method.
4. Polymerization method.
I. Normal polymerization
II. Interfacial polymerization.

PHARMACEUTICAL APPLICATIONS [12]

- Cancer research
- Controlled-Release Vaccines
- DNA Encapsulation
- Ophthalmic Drug Delivery
- Gene delivery
- Intra tumoral and local drug delivery
- Oral drug delivery
- Nasal drug delivery
- Buccal drug delivery
- Gastrointestinal drug delivery
- Per oral drug delivery
- Transdermal drug delivery
- Colonic drug delivery

Diagnostic uses of radioactive microspheres: Thrombus imaging in deep vein thrombosis,

Blood flow measurements, Liver and spleen imaging, Bone marrow imaging, Tumour imaging.

OTHER APPLICATIONS [10,12,14]

- Assay - Coated microspheres provide measuring tool in biology and drug research
- Buoyancy - Hollow microspheres are used to decrease material density in plastics
- (Glass and polymer).
- Spacers - Used in LCD screens to provide a precision spacing between glass panels (Glass).
- Standards – mono disperse microspheres are used to calibrate particle sieves, and particle counting apparatus.
- Retro reflective - added on top of paint used on roads and signs to increase night
- visibility of road stripes and signs (glass)
- Thickening Agent - Added to paints and epoxies to modify viscosity and buoyancy

CONCLUSION
It is very difficult for a drug molecule to reach its destination (site of action) in the complex cellular network of an organism. Targeted delivery of drug is becoming one of the brightest stars in the medical sciences. The inherent advantage of this

technique has been reduction in the dose and the side effect of drug. This biological approach is more specific but it also has some limitations which may be overcome soon, keeping in mind the giant leaps taken by research scientists in the recent past. Amongst the various options in targeted drug delivery, microspheres are better choice because of target specificity and better patient compliance. Its applications are enormous as it is not only used for delivering drugs but also for imaging tumours, detecting bio molecular interaction etc. So in future microspheres will have an important role to play in the advancement of medicinal field.

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