Review Article

Nanocarriers and their Types for Targeted Drug Delivery

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ABSTRACT

Nanocarriers are relatively new but rapidly developing nowadays for targeted delivery of drugs at the infected site without infecting the normal cells thereby reducing the dose frequency and side effects. Different types of nanocarriers like liposomes, polymeric micelles, dendrimers, polymeric nanoparticles delivery the drug in a controllable manner. Inorganic nanoparticles like gold and silver nanoparticles, magnetic nanoparticles are used as diagnostic tools for the detection of disease and drug delivery. Detailed knowledge on disease pathophysiology is essential for selecting and designing a suitable carrier system that can deliver therapeutic doses of medicine to the target tissue and cure the disease. Site specificity is the major therapeutic benefit since it prevents drugs from being delivered to the wrong places. Nanocarriers show promise for use in chemotherapy because they can help decrease the adverse, broader scale toxicity of chemotherapy on healthy, fast-growing cells around the body. The present review mainly focuses on the types and significance of nanocarriers that deliver the drug to their target tissue for controlled drug delivery.

Keywords: Nanocarriers, Targeted drug delivery, Controlled drug delivery, Targeted tissue, site-specificity.

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INTRODUCTION

Nano-carriers ranges from size of diameter 1-1000nm.[1] The main goal of developing nano-sized drug carriers are to enhance the therapeutic potential by making them safer and more effective. Nano delivery systems have been found to improve administrative routes and biodistribution of drugs with low immunogenicity and side effects.[2] Nanocarriers deliver drugs to the ailment site either actively or passively.[3] Nanocarriers can deliver medications to target areas with reduced doses and in a more controlled manner, minimizing the adverse effects of medical therapy. They enable the resolution of the primary significant challenges associated with traditional pharmacological therapies, including non-specific distribution, fast clearance, unpredictable drug release, poor bioavailability. [4-6]

TYPES OF NANOCARRIERS

Solid Lipid Nanocarriers

SLN can be made from solid lipids and is stabilized by surfactants, highly purified triglycerides, complex glyceride mixtures, or even waxes. These have several advantages over liposomes such as tolerability and being biocompatible.[7]

SLN has been used in a wide range of drug delivery applications such as

- To improve ocular bioavailability of drugs [8]
- For targeting of drugs to the brain [9]
- For drug delivery via parenteral [10,11]
- Pulmonary and dermal routes [12,13]

Stealth SLN has been found to promote antineoplastic agent accumulation in tumors and to carry medication to the brain.[14] The drug can be dissolved or dispersed in the solid hydrophobic core matrix, which is coated by a phospholipid monolayer.[15] Smaller size, higher stability, the ability to include both hydrophilic and hydrophobic medicines with a variety of ligands for targeted delivery.[16] Different medications such as cotrimoxazole, camptothecin, and vinpocetine have been used to create SLN with improved targeted brain drug delivery.[17,18] These problems are basically due to the formation of a perfect crystalline structure when only solid lipids are used. [19] SLN can also be modified for size and surface charges in order to achieve site-specific drug delivery designed for immediate or prolonged release. The schematic representation of solid lipid nanoparticles was specified in Fig.1

Advantages:

- Good physical stability
- Improves bioavailability of drugs
- Increases drug loading ability
- Reduced cytotoxicity of drugs

Disadvantages:

- Easy clearance by the reticuloendothelial system
- Low loading capacity [20-22]

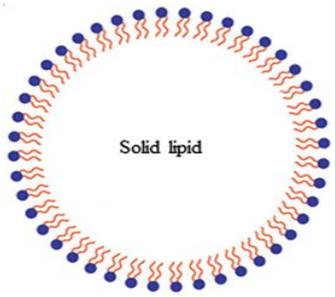

Figure 1: Solid lipid Nano-carrier

Liposomes

These are Nanocarriers that form spontaneously when certain lipids are suspended to the aqueous medium.[23] These have two major components an inner core and a surrounding phosphor lipids bilayer membrane.[24] They may contain a single lipid bilayer or multi lipid bilayers around the inner aqueous core.[25] The hydrophilic drugs are enclosed in the inner core while the hydrophobic drugs prefer the surrounding bilayer membranes hydrophobic environment.[26] Instability, insufficient drug loading, faster drug release, shorter blood circulation times are the problems associated with traditional liposomes.[27] Like other Nanocarriers liposomes also need to overcome the challenge presented by the RES, PEGylation helps liposomes escape the RES. Therefore PEGylated liposomes have a longer blood circulation time.[28] Monoclonal antibodies, antigen fragments, proteins, peptides, vitamins, carbohydrates and glycoproteins are usually grafted on the liposome to actively target the cancer site.[29-32] Smart liposomes are responsive to various external and internal stimulation including pH change, enzyme transformation, redox reaction, light, ultrasound, and microwaves.[33-35] Liposomes are often utilized as model cells for medicines, vaccines, cosmetics and nutraceuticals. [36] Liposomes can also be conjugated to antibodies or ligands in order to enhance target specificity. [37] The schematic representation of solid lipid nanoparticles was specified in Fig.2

Advantages:

- Good biocompatibility
- Non-toxic
- Encapsulate both hydrophilic and lipophilic drugs
- Increase the solubility of drugs
- Improve pharmacokinetic properties and protect the drugs from enzymatic degradation

Disadvantages:

- Low drug transport rate
- Poor stability [38-42]

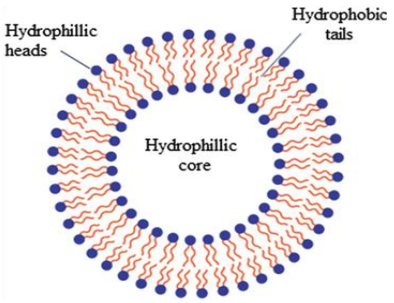

Figure 2: Liposomes

Dendrimers

Dendrimers are frequently branched macromolecules with various arms originating from the central core. Usually they are produced by using the natural or synthetic components which includes the sugars, nucleotides and aminoacids.[43] Due to their different molecular weight, the higher number of branching, spherical morphologies and monodispersed macromolecules with an average diameter of 1.4 -1.45 nm these characteristics are most suitable for drug delivery methods. [44] Recently dendrimers have been extensively used in fields of biomedicine including gene delivery The schematic representation of solid lipid nanoparticles was specified in Fig.3, immunology, magnetic resonance imaging, vaccines and antiviral, antibacterial, and anticancer drug delivery. [45] Dendrimers can enhance the solubility and bioavailability of hydrophobic medicines by trapping them in their intramolecular cavity and delivering them to their surface functional groups.[46] These are largely comprised of smaller units called dendrons. Dendrons are generated when core units are removed and can be differentiated into three sections the core, the interior, and the periphery. The dendrons vacant space can be used to entrap medication molecules for solubilization, controlled release, targeting from surrounding degrading environment. Dendrimers have a number of advantages including a uniform particle size, the capacity to bind a wide range of targeting agents to their high density peripheral functional groups, and the polyvalency of the end groups which helps in binding to a variety of receptors.[47]The schematic representation of solid lipid nanoparticles was specified in Fig.3

Advantages:

- Water soluble and biocompatible
- Good pharmacokinetic behaviour
- Ability to encapsulate and deliver various types of bioactive agents

Disadvantages:

- Poor drug release profile
- Rapid clearance
- Potential toxicity [48-49]

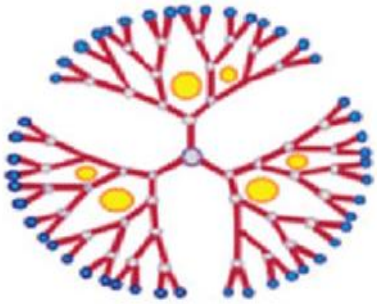

Figure 3: Dendrimers

Polymeric Micelles

Polymeric micelles are smaller than 100nm in size and have a narrow distribution to prevent rapid renal excretion. As a result of the EPR effect, they can accumulate in tumour tissues. These nanostructures have a promising future for hydrophobic drug delivery because their internal core structure allows for drug assimilation, which improves bioavailability and stability. [50,51] Drug targeting with diverse polymeric micelles based on several mechanism of action, such as greater permeability and holding effect stimulus; complexing of a specific targeting ligand molecule to the micelle surface. [52] The schematic representation of solid lipid nanoparticles was specified in Fig.4

Advantages:

- Biocompatibility
- Possibility of solubilizing lipophilic drugs
- The surface groups can be conjugated with targeting ligands

Disadvantages:

- Low drug loading capacity
- Used only for lipophilic drugs [53]

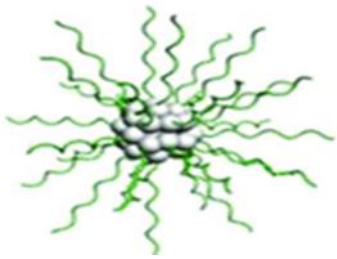

Figure 4: Polymeric micelles

Carbon Nanotubes

Iijima developed carbon nanotubes in 1991, [54] which are nanoscale, hollow, tube-like assemblages of carbon atoms. These are part of the fullerene family and are made by rolling graphene sheets into a tube-like shape .[55] Carbon nanotubes are divided into two types single graphene sheets and multi-walled carbon nanotubes, which are made by rolling many concentric graphene sheets into a tube-like structure. Carbon nanotubes have certain unique physiochemical and biological properties that make them a suitable drug delivery carrier.[56] These can be changed to allow for better circulation within the body. Covalent or noncovalent bonding can be used to make such modifications. Within the body, changes can increase or reduce circulation time. When carbon nanotubes are altered to be soluble in aqueous body fluids, they have no significant toxicity. They are easily absorbed by the cells. [57] One of the best nanocarriers for cancer therapy is carbon nanotubes. [58] Anticancer medications can be enclosed in the inner cavity of the carbon nanotubes or affixed to the carbon nanotubes surface either covalently or noncovalently.[59] Plasmid DNA, small interfering ribonucleic acid (SiRNA), antisense oligonucleotides and aptamers have all been carried by carbon nanotubes.[60] Carbon nanotubes can be employed as functionalized tools for early cancer diagnosis to gene transfer, and their great optical absorption in the near-infrared range makes them a promising tool for photo thermal ablation of a cancer location.[61] The schematic representation of solid lipid nanoparticles was specified in Fig.5

Advantages:

- Ease of synthesis and conjugation of multiple bioactive agents
- Ability to encapsulate and deliver various types of bioactive agents
- Protects entrapped drug and provides sustained release

Disadvantages:

- Poorly soluble in water
- Poor pharmacokinetics
- Non- biodegradable [62]

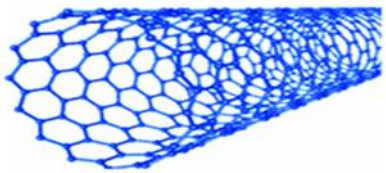

Figure 5: Carbon nanotubes

Polymeric Nanoparticles

Polymeric nanoparticles are solid, nanoscale colloidal particles composed of biodegradable polymer.[63] Nanocapsules and nanospheres are classified as two types of polymeric nanoparticles based on their structure. The medication can be dissolved, entrapped, adsorbed, encapsulated or conjugated to the matrix in nanospheres, which contain matrix like structures. A polymeric shell surrounds an inner core in nanocapsules. The medication is normally dissolved in the center of the cell, although it can also be adsorbed at the surface.[64,65] Low toxicity, pharmacotechnological stability, biodegradability, and the existence of surface functional groups that modulate the drug release rate are essential characteristics that make

them a suitable choice for brain targeted drug delivery. [66] Polymeric nanoparticles were created using a variety of biocompatible and biodegradable natural and synthetic polymers. These polymers are biodegradable they are broken down into individual monomers inside the body and eliminated by regular metabolic processes.[67] Albumin, alginate, chitosan, collagen, heparin, and dextran are the most often utilized natural polymers. Polylactic acid, polyglycolic acid, and polyglutamic acid are examples of synthetic polymers.[68] In comparison to polymeric micelles and liposomes, polymeric nanoparticles have greater storage stability, and increased drug payload, a more homogeneous particle size distribution, better and controllable physicochemical characteristics and greater drug circulation times, and more controlled drug delivery. [69] In the context of cancer treatment, all of these features are extremely desirable. Surface modification with PEG or Poly (ethylene oxide) containing copolymers, can increase plasma circulation times and facilitate passive transport.[70] In response to certain environmental signals, the polymers can change their physicochemical features, resulting in more targeted delivery of drugs in cancer treatment.[71] The schematic representation of solid lipid nanoparticles was specified in Fig.6

Advantages:

- Biocompatibility and biodegradability
- Good stability
- Low cost
- Less toxicity
- Ease in production
- Low immunogenic response
- Controlled drug release

Disadvantages:

- Uncertain potential toxicity
- Slow degradability [72-77]

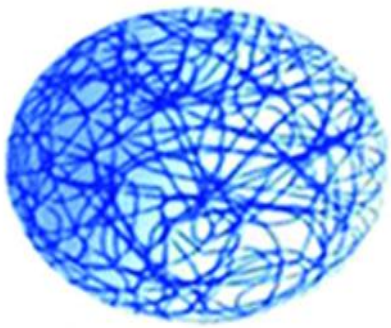

Figure 6: Polymeric nanoparticles

Magnetic Nanoparticles

Magnetic nanoparticles have been studied and used to diagnose and treat a variety of malignancies. [78] When synthesized with polymers, these nanoparticles can carry therapeutic substances on their surface or in their bulk, which can subsequently be pushed to the target organ under an external field and then released at target site. [79] Nanoparticles made up of the three major ferromagnetic elements (Fe, Ni, and Co) can be used as targeted carriers to deliver drug to achieve intra tumoral levels or to mediate a hyperthermic action that causes tumor necrosis.[78] Magnetic particle size, charge, and surface chemistry are particularly essential since these variables have a significant impact on both their blood circulation time and their bioavailability with in the body.[79] Furthermore, the size of magnetic particles has a major impact on their magnetic characteristics and internalization in target tissue. [80] For example, the spleen frequently eliminates systemic delivery of magnetic nanoparticles of larger particles with a diameter more than 200 nm, resulting in reduced blood circulation times. Smaller particles having a diameter of less than 10 nm are quickly eliminated through extravasation and renal clearance. For intravenous injection and the longest blood circulation time of particles with a diameter of 10 to 100 nm are suitable. The ideal size range of magnetic nanoparticles is small enough to avoid the body's RES and penetrate microscopic capillaries within body tissues, allowing for successful distribution in particular tissues.[81] A new water dispersible oleic acid pluronic coated iron oxide magnetic nanoparticle formulation that can be readily loaded with high doses of water-insoluble anticancer drugs was recently developed. After drug loading the magnetic property of core iron oxide stays constant. In breast and prostate cancer cell lines, these nanoparticles exhibit persistent intracellular drug retention as well as a dose dependent antiproliferative activity. This formulation can be employed as a carrier system for water insoluble medicines in systemic administration.[82]The schematic representation of solid lipid nanoparticles was specified in Fig.7

Advantages:

- Excellent biodegradability
- Low cytotoxicity to biomass cell
- Ease of synthesis
- Ability to bind multiple targeted compounds
- Maintain stability after physical, mechanical, chemical modification.

Disadvantages:

- High cost of synthesis material
- Poor dispersion abilities
- Mobility dependent on environmental compatibilities [83]

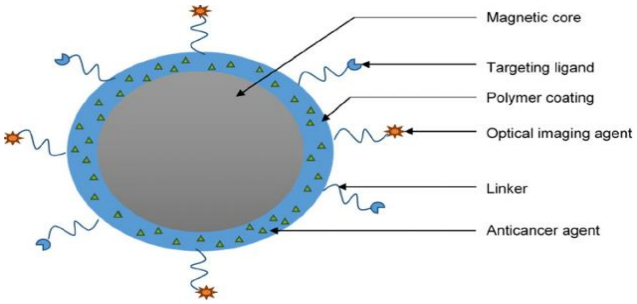

Figure 7: Magnetic nanoparticles

Inorganic Nanoparticles

Nanocarriers for targeted drug delivery have recently been discovered in inorganic nanostructured materials. [84] These are made up of two sections a core and a shell. Inorganic components such as gold, silica or iron oxide are found in the core which is surrounded by an organic polymer shell that serves as a suitable substrate for biomacromolecule conjugation or protects the core from unwanted physiochemical interactions with the external biological environment. [85,84.] Silver, gold, iron oxide, and silica nanoparticles are examples of inorganic nanoparticles, SPR (Surface Plasmon resonance) is a property of metal nanoparticles, silver, and gold that liposomes, dendrimers, and micelles do not have. They demonstrated various benefits, including strong biocompatibility and adaptability in surface functionalization. [86] Drugs can be conjugated to gold nanoparticles surfaces through ionic or covalent bonding and physical absorption, and they can transport and control drug release via biological stimuli or light activation.[87] When compared to organic materials these are non-toxic, hydrophilic, biocompatible and very stable. Due to their high cellular absorption capacity, non-immunogenic rection, and low toxicity, inorganic nanoparticles have received a lot of attention as medication or gene delivery vehicles. Size and shape are known to have a major influence on the electromagnetic, optical and catalytic properties of noble metal nanoparticles including gold, silver and platinum. Metal based nanoparticles are utilized in a variety of biomedical applications including electron microscopy probes to see biological components, drug delivery (vehicle for delivering medicines, proteins, peptides, plasmids, DNAs, etc), detection, diagnosis and treatment.[88] Recent advancements in nanotechnology, numerous additional inorganic nanoparticles, such as iron oxide nanoparticles and fullerences, have been explored as drug delivery vehicles due to their nanoscale size, which allows them to move readily inside the body. The drug might be injected or attached to the surface of the particle. It has been demonstrated that nanoparticles can be taken up by cells to transfer nucleic acids into living cells, increasing the value of these inorganic nanoparticles. Silica. Gold, iron oxide, manganese phosphate, and double hydroxides are some of the inorganic materials that have been examined for delivering DNA.[89] The schematic representation of solid lipid nanoparticles was specified in Fig.8

Advantages:

- Can easily penetrate cells because of their small size, high efficiency in cellular uptake
- Easy conjugation to biomolecules
- Can be easily functionalized by surface modification [90]

Disadvantages:

- Non-biodegradable
- High cost of largescale production
- Nanoparticle aggregation [91]

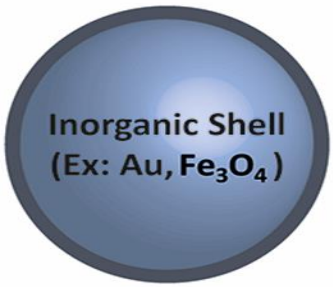

Figure 8: Inorganic nanoparticles

CONCLUSION

Nanocarriers are essential for the efficient transport of drug molecules to their target sites as well as the controllable release of therapeutic molecules. Nanocarriers reduce the amount of medicine required to produce certain therapeutic effects, lowering costs and reducing side effects. Nanocarriers have a number of advantages over standard drug delivery methods, including reduced side effects, enhanced drug half-life, delayed or controlled release, reduced drug dose, and the ability to improve drug crossing through the blood-brain barrier. Day by day a growing number of unique therapeutic agents are being discovered, paving the way for even more initiative advancements in nano-based targeted drug delivery. Nanocarriers are being employed to overcome the issues of traditional chemotherapy in the delivery of anticancer drugs. The development of nano-sized drug carriers needs a thorough understanding of the nanosized system's interactions with cell membranes, receptors and intracellular pathways, and sorting mechanisms. For drug targeting a better understanding of nanocarrier biodistribution and interactions with blood proteins and tissues is required. Several concerns have been raised regarding their negative consequences and the environment. As result toxicity and comprehensive studies for determining efficacy and safety in humans should be evaluated while producing a medicine.

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