ISSN: 2582-8118 ***Volume 3, Issue 5; Sept 2023***

INTERNATIONAL JOURNAL OF RESEARCH AND ANALYSIS IN SCIENCE AND ENGINEERING

Web: https://www.iarj.in/index.php/ijrase/index

4. Nanoparticles in Drug Delivery

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ABSTRACT

Drug delivery is the study which deals with processes and methods of administering drugs and other pharmaceutical compounds to achieve the best therapeutic effect in humans or animals. Conventional administrations of drugs have several problems associated with it. The unaltered drug is given through the mouth (orally), nose (nasally) or through injection directly into the blood stream. Problems associated with these methods are poor distribution, large dosage requirements, side effects on other cells, drug degradation, cell rejection and other problems. Rather than administering the unaltered drug directly, we can change some of the drug's properties or administer it in some other ways. Nanoparticles (called nanocarriers) show great potential as drug delivery systems. The drug or compound is altered by combining or encapsulating it with nanoparticles. How the properties are altered depends on the type, shape and size of the nanoparticles used. Improving safety efficacy ratio of drugs has been attempted using different methods such as individualizing drug therapy, dose titration, and therapeutic drug monitoring. Delivering drug at controlled rate, slow delivery, targeted delivery are also very attractive methods. It can be specialized for anticancer treatments, brain targeting, lung targeting and so on. The types of nanoparticles used are: Liposomes, solid lipids nanoparticles, dendrimers, polymers, silicon or carbon materials, and magnetic nanoparticles. Magnetic Nanoparticles (MNPs) are metallic nanoparticles that are controlled by an external magnetic field after it is administered to the patient. Magnetic nanoparticles exhibit a wide variety of attributes, which make them highly promising carriers for drug delivery. They are divided into the categories of pure metals (Mn2+ etc), their alloys and oxides. Presently, only iron oxide nanoparticles (e.g.Fe2O3) are approved for use due to their favourable properties. MNPs There are many drawbacks and limitations to current nanoparticulate drug delivery. Despite all these problems, nanoparticle DDS which respond to slight changes in the local cellular environment have a potential to resolve many of the current drug delivery problems. Nanoparticles can be used in a multifunctional way to not only deliver drugs but also to mark abnormal cells for future therapy. But before nanoparticle drug delivery becomes possible, challenges which include developing toxicity testing protocols, improving biocompatibility, drug loading, targeting, transport and release, controlling interaction with biological barriers, detecting and monitoring exposure level and assessing the impact on the environment have to be met. Problems of the limitations of current technology and techniques also must be overcome. Most importantly, a generalized method

for creating nanoparticles must be developed with the aim of manufacturing biocompatible and non-toxic drug delivery systems. If these challenges are met and the problems overcome, the potential for nanoparticulate drug delivery is immense. Unique solutions can be used to cure cancers, HIV and many diseases. At the same time the treatments will be more cost effective and affordable to the general public. Not only can treatments be improved but also medical knowledge can be increased as nanoparticles are used for diagnostic applications. Also consider the magnetic targeted drug delivery system. It is one of the most attractive strategies in targeted therapy. Magnetic nanoparticles have their unique magnetic properties and they can be attracted by magnetic fields, thus, acting as drug carriers in a target therapy.

KEYWORDS:

Drug, magnetic field, nanoparticle, liposomes.

Introduction:

Nanocarriers must have two very important properties. They must be biocompatible and non- toxic. They must be able to affect the body without being rejected or causing immune responses. At the same time they must be non toxic to all the other cells in the body, except the target cells if needed. These properties are a result of multiple factors. These include the size, shape, chemistry, amount, immune reaction, residence time, target cells etc of the nanoparticles. Due to the number of variables, it is difficult to make generalizations about the particle behaviour in biological systems. New studies must be carried out for every new drug delivery compound and nanoparticle type. We can however establish that smaller nanoparticles are more reactive and more toxic. Larger nanoparticles are quickly filtered from the blood and removed from the body. A hydrodynamic diameter of 10-100 nm is generally considered to be optimum for nanocarriers (Wilczewska et al, 2012).

The construction of nanocarriers varies depending on the type of nanoparticles to be created.

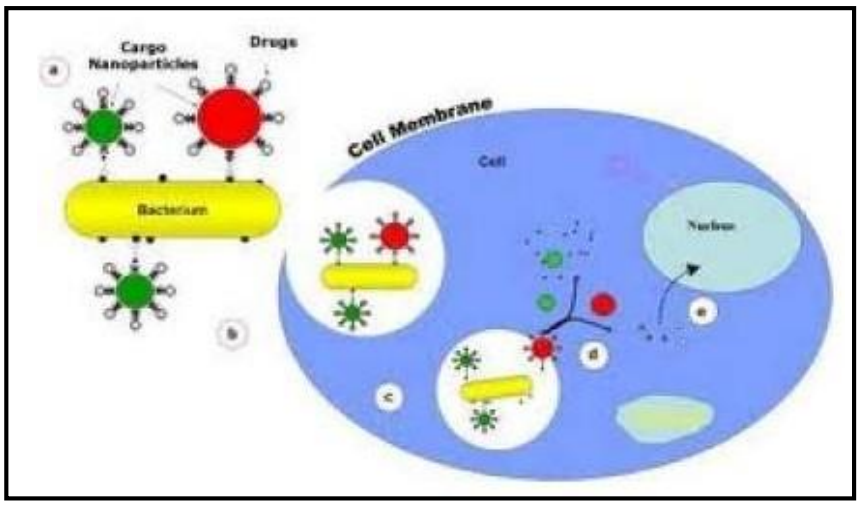

Fig.1 Action of nanoparticles

Methods:

Liposomes are the first type of nanoparticle to be investigated for its possible ability to deliver drugs. These particles are rather easy to create. They are formed spontaneously when certain lipids are dispensed in an aqueous solution e.g. with sonication etc. The result is 10- 400 nm spherical vesicles composed of phospholipids, steroids (like cholesterol), bi layers or other surfactants (Wilczewska et al, 2012). The drug is usually present in the solution at the time of formation. They consist of macromolecular materials in which the active agent (drug or biologically active material) is dissolved, entrapped, and/or encapsulated, or to which the active agent is adsorbed or attached (Kozako et al, 2012)

The effects of liposomes on drug activity are as follows: Decreased drug amounts, minimized side effects, increase in uptake and speed of observable effects, better solubility and better drug activity especially in anticancer drugs. It was observed in experiments that the residence time was increased and the drugs were better protected against degradation. The release of the drugs could be controlled by conditions such as pH, liposome content, surrounding chemical conditions and osmotic gradient. In particular, liposomes are well recognized as pharmaceutical carriers because of their biocompatibility, biodegradability, and low toxicity and can be clinically used for efficacy enhancement and toxicity reduction. Liposomes have good longevity in the blood that allows their accumulation in pathological areas. Furthermore they can be modified to have a long shelf life. These nanocarriers are easier to scale up and inexpensive as compared to other nanoparticles. Cell-specific targeting by modified liposomes (containing specific proteins, lipids etc) increases the advantages (Wei-Kuo Chang et al, 2011). There are some limitations to be overcome. Liposomes may accumulate in the cells outside their targets causing some rejection. Unpredictable effects on other cells have also been observed in animal tests.

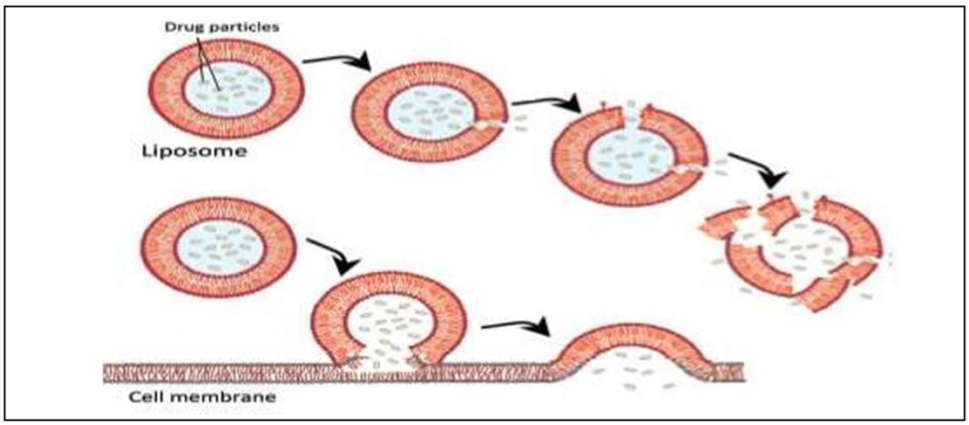

Fig 2. Drug delivery by liposomes

Construction of Magnetic Nanoparticles

There are two methods for nanoparticle creation: coprecipitation and microemulsion. Preparation of nanoparticles utilizing the coprecipitation method involves two approaches, i.e., partial oxidation of ferrous hydroxide suspension by different oxidizing agents such as nitrates, and addition of base to an aqueous solution containing a mixture of ferrous

(Fe2+) and ferric (Fe3+) ions with 1:2 stoichiometries in an oxygen-free environment. Smaller and more uniform particles can be synthesized using the microemulsion approach. Water-in-oil (w/o) microemulsions (i.e., reverse micelle solutions) are transparent, isotropic, and thermodynamically stable liquids. In these systems, the aqueous phase is dispersed as microdroplets in the continuous oil phase, i.e., entrapped within the assembly of stabilizing surfactants. These microdroplets serve as nanoreactors in which the nanoparticles are formed. By controlling the size of the microdroplets, particles in the desired size range can be obtained. (Wahajuddin and Arora, 2011)

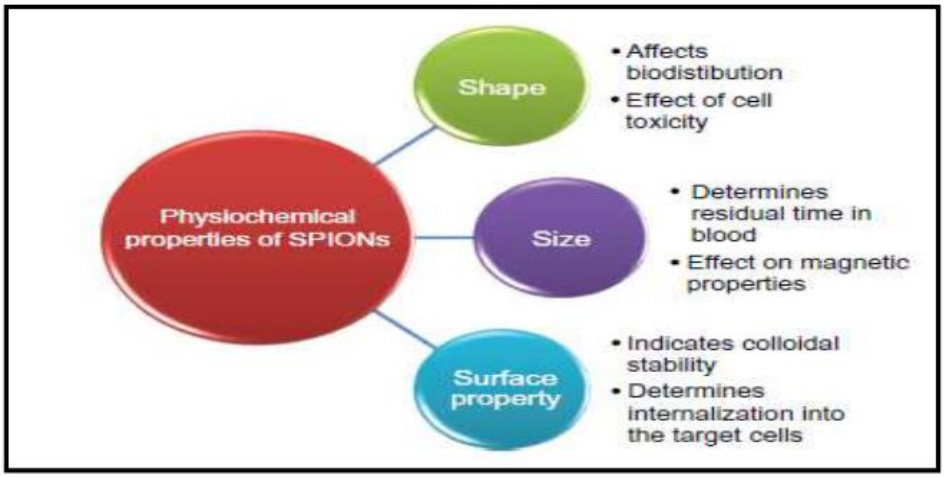

Fig 3. Physiochemical properties of super paramagnetic iron oxide nanoparticles (SPIONs)

There were observations that sometimes the particles could be opsonized and quickly removed from the body by macrophages. Liver and spleen therefore, showed the maximum accumulation of macrophages. Long chain polymers were shown to be less toxic than short chain polymers coated on the particle surface. Accumulation in the brain showed that the nanoparticles could cross the blood-brain-barrier. Some examples of drugs tested in iron oxide drug delivery systems are given below.

Table 1: Magnetic nanoparticles as drug delivery systems

Drug	Therapeutic activity	Nanocarrier (core @ shell)
Ciprofloxacin	**Anti-infective agents (antibiotic)**	**Fe3O4 @ poly (vinyl alcohol)-g-poly (methyl methacrylate)**
Gemcitabine	**Antimetabolites, cancer chemotherapy**	**Fe3O4 @ poly (ethylene glycol)**
Doxorubicin	**Antineoplastic agent**	**Fe3O4 @ gelatin**
5-Fluorouracil	**Antimetabolites, anticancer drug,**	**Fe3O4 @ ethyl cellulose**

As the table shows, iron oxide nanoparticles have been studied as nanocarriers for many drugs ranging from cancer treatment to antibiotics.

Conclusion:

There are many drawbacks and limitations to current nanoparticulate drug delivery. Despite all these problems, nanoparticle DDS which respond to slight changes in the local cellular environment have a potential to resolve many of the current drug delivery problems. Nanoparticles can be used in a multifunctional way to not only deliver drugs but also to mark abnormal cells for future therapy. But before nanoparticle drug delivery becomes possible, challenges which include developing toxicity testing protocols, improving biocompatibility, drug loading, targeting, transport and release, controlling interaction with biological barriers, detecting and monitoring exposure level and assessing the impact on the environment have to be met. Problems of the limitations of current technology and techniques also must be overcome. Most importantly, a generalized method for creating nanoparticles must be developed with the aim of manufacturing biocompatible and non-toxic drug delivery systems.

If these challenges are met and the problems overcome, the potential for nanoparticulate drug delivery is immense. Unique solutions can be used to cure cancers, HIV and many diseases. At the same time the treatments will be more cost effective and affordable to the general public. Not only can treatments be improved but also medical knowledge can be increased as nanoparticles are used for diagnostic applications.

Also consider the magnetic targeted drug delivery system. It is one of the most attractive strategies in targeted therapy. Magnetic nanoparticles have their unique magnetic properties and they can be attracted by magnetic fields, thus, acting as drug carriers in a target therapy.

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