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Review Article

NANOPARTICLES AS A NOVEL DRUG DELIVERY SYSTEM: A Review

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Abstract

Nanotechnology is showing a significant impact on the drug-delivery system over a past few years. This technology is playing a distinct role in remodeling the future of novel drug delivery system (NDDS). Nanoparticles (NPs) are one of the NDDS which exhibit vast applications in the field of clinical medicine and research. The encapsulation of therapeutic drugs in the form of nanoparticles shows advantageous effects, such as increasing drug efficacy, safety, bio-degradability, bioavailability and therapeutic index, over conventional dosage forms of these therapeutic drugs. The current review article mainly focuses on different types of nanoparticulate drug delivery systems including nanotubes, solid lipid nanoparticles, superparamagnetic nanoparticles, liposomes, quantum dots, dendrimers, ceramic nanoparticles and nanoerythrosomes as well as their applications in different field.

Keywords: Phenylephrine HCl, chlorpheniramine maleate, dextromethorphan HBr, gradient separation, method validation, RP-HPLC

INTRODUCTION:

In the novel drug delivery systems (NDDS), there are various novel carriers which have advantage over conventional dosage forms. Conventional dosage forms show high dose and low availability, in-stability, first pass effect, plasma drug level fluctuations and rapid release of the drug (Buzea *et al.*, 2007). NDDS is one of the important tool expanding drug markets in pharmaceutical industry. NDDS can minimize problems by enhancing efficacy, safety, patient compliance and product shelf life (Roco and Bainbridge 2005).

Nanoparticles: Nanoparticles are the solid colloidal particles ranging in size from about 10 nm to 1,000 nm (Babaei *et al.,* 2008).Polymeric materials have been extensively used for the preparation of nanoparticles(Soppimath *et al.,* 2001).These polymeric materials are considered important due to their known biodegradability and biocompatibility (Kumari *et al.,* 2010). Several synthetic and natural origin polymers have been used for the preparation of nanoparticles.

The formulation of nanoparticles as targeted drug delivery system has been extensively studied (Moghimi *et al.,* 2001). Targeted drug delivery can be achieved either by active targeting or passive targeting. Active targeting of drugs can be attained either by conjugating drug molecule with tissue specific or cell specific ligand (Lamprecht *et al.,* 2001).Whereas, passive targeting of drugs can be attained either by incorporating drug molecule into a microparticles or nanoparticles.

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Nanoparticles (NP) are colloidal drug delivery system which are formulated by natural, synthetic, and semi synthetic polymers. Particle size of NP ranges from 10 nm to 1,000 nm in diameter (Shivakumar *et al.,* 2005). This colloidal drug delivery system shows different inner structure.

- Nanospheres in matrix type system
- Nanocapsules in reservoir type system

Advantages of nanoparticles:

NPs show number of advantages, which include

- Ease of preparation,
- Increased bio-availability,
- Increased residence time in the body,
- Site specific drug targeting (Jain and Singh 2012).

Types of nanoparticles:

The current review focuses on different types and applications of nanoparticles, as potential drug delivery system, in imaging, diagnostics and therapeutics.

Polymeric Nanoparticles:

Biodegradable nanoparticles, as effective drug delivery system, are being applied extensively over a past few decades (Brigger *et al.,* 2002). Nanoparticles formulated from various natural and synthetic polymers have gained importance (Herrero-Vanrell *et al.,* 2005).

This drug delivery system provides targeted drug delivery, increased bio-availability, and sustained release of drugs and protects drugs from enzymatic degradation (Kim and Lee 2001).

Fullerenes:

A fullerene is a molecule made up of carbon in different shapes such as tubes, hollow-sphere, and ellipsoid as mentioned in fig.1. Fullerene is similar to graphite in structure (Dresselhaus *et al.,* 1996).

Nanotubes:

Nanotubes (NTs) are cylindrical fullerenes. NTs have a closed end as well as open end as shown in fig.2. Fullerenes show various therapeutic

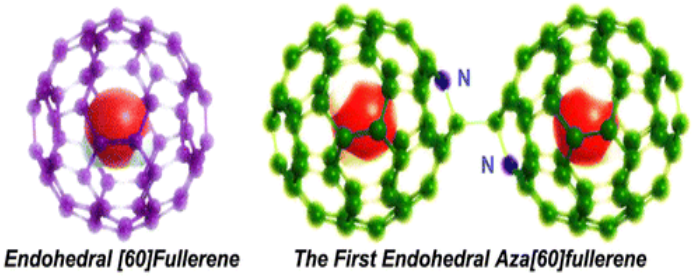

Figure No. 1: Endohedral Aza[60]fullerenes (Hashikawa et al., 2016)

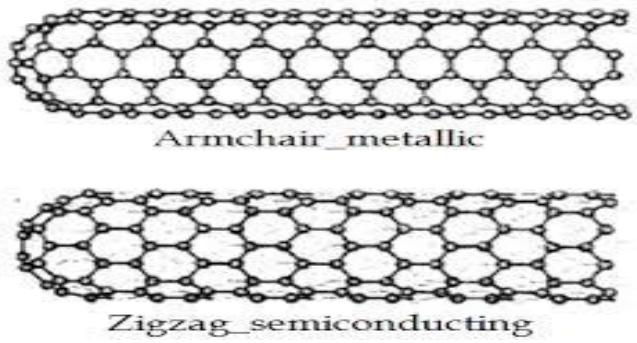

Figure No.2: Carbon Nanotubes (Xia and Li, 2014)

properties such as targeting cancerous cells, binding specific antibiotic to the specific structure of bacteria etc. (Tegos *et al.,* 2005)

Solid lipid nanoparticles (SLNs):

SLNs are lipids in nature which remain in solid phase at normal room temperature. The particle size of SLNs ranges from 50 nm to 1,000 nm. SLNs are composed of solid hydrophobic core and a single coating layer of phospholipids. SLNs are stabilized by different surfactants for emulsification and also show many properties such as increased bio-degradability , increased bio-availability and drug targeting in the brain (Yang *et al.,* 1999; Cavalli *et al.,* 2002).as shown in fig.3.

Different forms of lipids are used for formulating SLNs. These include a) fatty acids such as palmitic acid, decanoic acid, and behenic acid, b) triglycerides such as tri-laurin, tri-myristin, and tri-

palmitin, c) cholesterol, d) partial glycerides such as glyceryl mono-stearate and gylceryl be-henate and e) waxes such as cetyl palmitate. Different types of surfactants are also used for stabilizing lipid dispersions. These include lecithin, phosphatidyl choline, poloxamer 188, sodium-cholate, and sodium glycol-cholate (Yang et al. 1999; Mudshinge *et al.*, 2011; Gao *et al.,* 2014). SLNs have vast applications in cancer. SLNs have ability to accumulate tumor, and also increase allow anticancer drugs delivery to the brain (Zara *et al.,* 2002).

Super Paramagnetic Nanoparticles:

These are attracted towards a specific magnetic field. When the magnetic field is removed, these cannot retain their residual magnetism. Particles range in the size of 5 nm to 100nm and used for selective magnetic bio-separations and can be visualized in magnetic resonance imaging (MRI). These work on the principle of magnetic field and heated to trigger the drug release (Jain and Singh 2012).These have also shown major role in cancer therapy and diagnosis (Zhang *et al.,* 2002). Superconducting quantum interference device (SQUID) is a device with super paramagnetic nanoparticles and a microscope. This device is highly sensitive, specific, quantitative and used in the detection of biological targets (Chemla *et al.,* 2000).as shown in fig.4.

Liposomes:

Liposomes are made up of phospholipids and cholesterol. These are in the form of vesicles which consist of hydrophilic core surrounded by hydro-phobic lipid bi-layer as shown in fig.5. Liposomes show versatile applications in pharmaceutical and cosmoceutical formulations. Nano-liposomes are also vesicular in shape and their particle size is in the range of nanometers (Zhang and Granick 2006). Different factors influence the properties of liposomes such as composition of liposomes, particle size, charge on surface and formulation method. Nano-liposomes are mostly used as a carrier for anti-bacterials, anti-virals, insulin, anti-neoplastics and plasmid DNA (Cevc 1996).

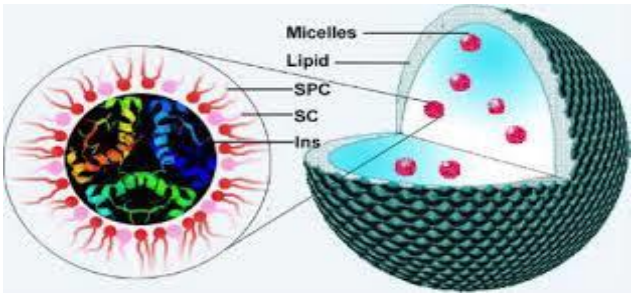

Figure No. 3: Solid Lipid Nanoparticles (Yadav et al., 2013)

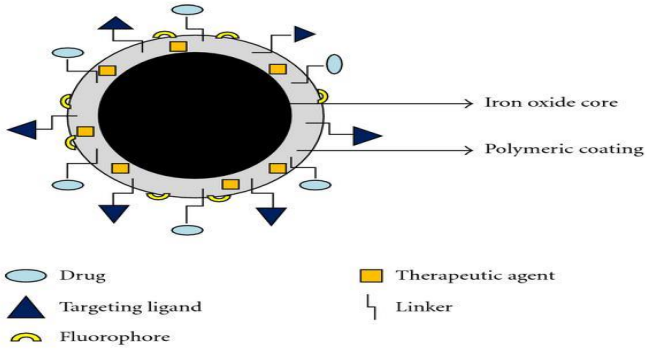

Figure No. 4: Super Paramagnetic Nanoparticle

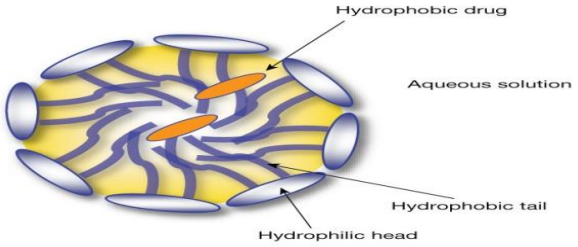

Figure No. 5: Structure of Liposome

Nanostructure lipid carriers (NLC):

NLC are prepared by using blend of solid lipids and liquid lipids. The particles remain in solid state at normal room temperature. Nanostructure lipid carriers (NLC) and the lipid drug conjugate (LDC)

nanoparticles are prepared in the form of matrices. These matrices increase drug loading capacity and bio-availability (Wissing *et al.,* 2004). These are used for drug delivery via different routes such as oral, topical and parenteral (subcutaneous, intramuscular, intravenous etc.). These also have applications in the fields of cosmetics, food and agricultural. These have been extensively used in the delivery of anti-inflammatory drugs, cosmetic preparation, and topical cortico- therapy (Müller *et al.,* 2002).

Nanoshells:

Nanoshells, also known as core-shells, are spherical cores of concentric particles which are surrounded by an outer coating of thin layer of another material as shown in fig.6(Jiang *et al.,* 1999; Xia *et al.,* 2000). Nanoshells have biomedical imaging and therapeutic applications. These exhibit distinct property such as reduced susceptibility to chemical/thermal denaturation (Loo *et al.,* 2004)

Quantum Dots (QD):

The QD are known as semiconductor nano-crystals and core-shell nano-crystals. These are 2 nm to 10 nm in size (Choi Hak *et al.,* 2007). These are used as drug delivery system for various hydrophilic drugs such as small interfering RNA (si-RNA) and anti-sense oligo-deoxy-nucleotide (ODN)) as well as targeting antibodies, peptides etc. QD have extensive applications in imaging contrast as shown in fig.7.

Dendrimers:

Dendrimer is derived from a Greek word Dendron which means a tree. Dendrimers are polymeric molecules made up of multiple perfectly branched monomers .Different polymers such as poly-amido-amine (PAMAM), melamine, poly-L-glutamic acid, poly-ethylene-imine (PEI), poly propylene-imine (PPI), and polyethylene glycol, and chitin are used in formulation of dendrimer (Li et al. 2004). These are extensively applied in magnetic resonance imaging and targeting cancerous cells (Um *et al.,* 2006).as shown in fig.8

Ceramic nanoparticles:

Ceramic nanoparticles are porous in nature and particle size is less than 50 nm. These possess distinct properties such as sol-gel process, work in ambient temperature condition and product produced of desired size, shape and porosity (Jain *et al.,* 1998) as well as effective in hiding the

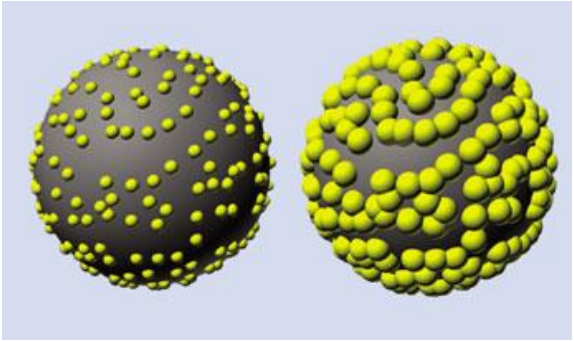

Figure No. 6: Nanoshells

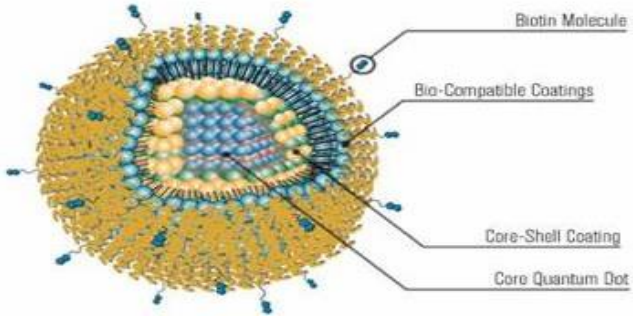

Figure No. 7: Quantum Dots with Coatings

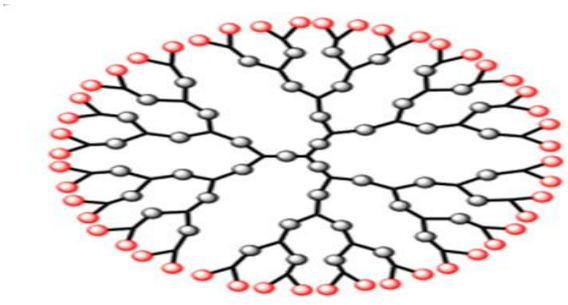

Figure No. 8: Basic Structure of Dendrimer

uptake by reticulo endothelial system (Gref *et al.,* 1994).

These are broad applications such as novel non-viral vector for genes delivery (Zhu *et al.,* 2002; Li *et al.,* 2005), photodynamic therapy (Konan *et* al., 2002; Roy *et al.,* 2003) , and in diabetic wounds healing (Mishra *et al.,* 2008). These also play major role in the field of orthopedic and used as orthopedic biomaterial because these provide support to natural bone (Liu and Webster 2010; Liu and Webster 2011).

XPclad® nanoparticles:

XPclad® nanoparticles are novel carriers for the poor hydrophilic drugs which face significant problem of bio-availability and absorption. These are prepared by novel method in which planetary ball milling and vibratory ball milling are used. This method results in particles of uniform size and maximum loading efficiency of drugs. These nanoparticles are used for systemic, cutaneous, and oral administration of anti-cancer drugs, vaccines, and therapeutic proteins (Koo *et al.,* 2005; Koo *et al.,* 2006). These are regarded as useful in tumor therapy because of lower toxicities and cause the destruction of prostate tumor cells (Tan *et al.,* 2011).

Nanofibers:

Nanofibers are produced by electro spinning technique in which fabrication of polymers in a fine and dense mesh works directly from solution and requires an electric field. These have dimension less than 100 nm as mentioned in fig.9. Polymeric nanofibers are effective carriers for drug delivery and show advantages such as specific surface with small pore size, porosities, reduced toxicity (Yang *et al.,* 2007) and increased therapeutic level and bio-compatibility (Jia *et al.,* 2007). Different polymers such as polyvinyl alcohol (PVA), gelatin, collagen, chitosan and carboxymethylcellulose (CMC) are used. Nanofibers are considered ideal for the preparation of biosensors and biochips, as drug delivery systems, wound care and scaffold for tissue engineering. Nanofibers of indomethdacin for colonic drug drug delivery system found to be very effective (Akhgari *et al.,* 2013).

Gold Nanorods:

Gold nanorods were first time prepared in mid-1990 (Foss Jr *et al.,* 1994; Hornyak *et al.,* 1997). These exhibit distinct optical and electronic properties and depend on shape, size and aspect ratios (Vigderman *et al.,* 2012; Chen *et al.,* 2013). These can be easily stabilized, conjugated to antibodies and show distinctive biological applications (Liao and Hafner 2005; Niidome *et al.*, 2006).shown in fig .10.

Nanoerythrosomes:

Nanoerythrosomes are derived from a red blood cell membrane by the process of haemo-dialysis through filter. Nanovesicles are of defined pore

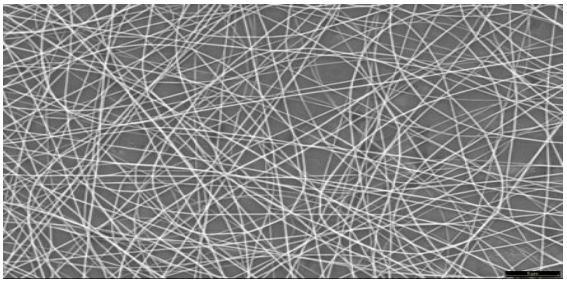

Figure No. 9: Nanofibers

Figure No. 10: Gold Nanorods

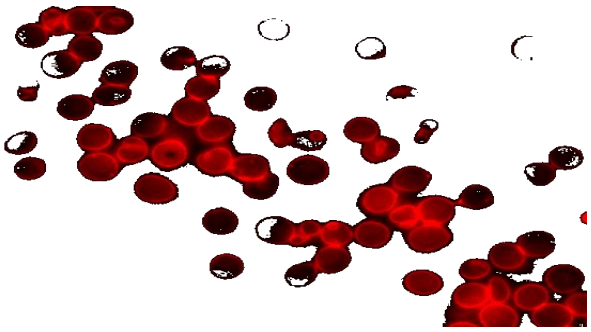

Figure No. 11: Nanoerhythrosomes

size and composed of proteins, phospholipids and cholesterol. These can load a variety of biologically active agents such proteins. Nanoerthroysomes composed of a natural membrane which allows the insertion of recombinant ligands along with better stability. The membrane allows the conjugation by using simple and well known molecule such as monoclonal antibodies (Lejeune *et al.,* 1996). As shown in fig.11.

CONCLUSION: Different targeted and novel drug delivery system for improving dosage form, increasing bio-availability and patient compliance, and reducing side effects are being applied in current scenario. The most preferred and targeted delivery of drugs can be attained by nanoparticles. The nanoparticles have wide range of applications as drug carriers, and targeting specific site in the body. Importance of nano drug delivery systems is increasing day by day I pharmaceutical industry which will grow further in future. Various nano based products are available in the market and many of them are under clinical assessment.

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