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Current Status of In-Vivo Bioanalysis of Nano Drug Delivery System: A Review

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ABSTRACT: The development of nano drug delivery systems (NDDSs) is a revolutionary field of micro manufacturing involving physical and chemical changes to produce nano-sized material. It gives us new approaches to fighting against diseases. The word "nano" is a Latin word meaning "dwarf". Mathematically a nanometer is equal to one thousand millionth of a meter. The NDDSs are specially designed to serve as carriers for the delivery of active pharmaceutical ingredients to their target sites, which would certainly extend the benefit of their unique physicochemical characteristics, such as prolonged circulation time, improved targeting and avoiding of drug resistance. The conversion of a particle to nano scale size changes the properties of the material such as increase in surface area, dominance of quantum effects often associated with minute sizes, higher surface area to volume ratio. and varies material's magnetic, thermal and electrical property. The advanced bioanalysis for tracing the in vivo fate of NDDSs is summarized, including liquid chromatography tandem mass spectrometry (LC MS/MS), Forster resonance energy transfer (FRET), aggregation-caused quenching (ACQ) fluorophore, aggregation-induced emission (AIE) fluorophores, enzyme-linked immunosorbent assay (ELISA), magnetic resonance imaging (MRI), radiolabeling, fluorescence spectroscopy, laser ablation inductively coupled plasma MS (LA-ICP-MS), and size-exclusion chromatography (SEC).Nanomaterials have wide applications in pharmaceutical sciences and technology. Few other predominant areas of use of nanotechnology are in drug delivery, and as diagnostic imaging and biosensor. These devices of nanoscale size are popularly known as nanomedicine Nanotechnology may be considered as one of the main propellants for technological, economical change as industrial competition.

KEYWORDS: Nano drug delivery systems (NDDSs),Nanotechnology, biosensor, pharmaceutical ingredients, prolonged, physiochemical.

I. BACKGROUND:

In the last 30 years, development of nanotechnology has been productive and a large number of novel technologies have been applied to disease diagnosis, pharmaceutical discovery and tissue engineering. NDDS is a most rapidly developing nanomedicine Technique. IN 1995, Doxia®, liposomal doxorubicin (DOX), was the first approved NDDS which was used for the treatment of AIDS-related Kaposi's and ovarian cancer which had reduced side effects and unresisting tumor targeting effect.

In NDDSs, small molecular drugs are chemically bonded on the nanoparticles. NDDS exhibit material physio-chemical characteristics which are related to the drug delivering properties after administration, which is different from traditional pharmaceuticals enhances the pharmacological and the pharmaceutical properties of parent drugs by extending the duration of circulation time,hence improving the efficacy overcoming drug resistance, thus reducing immunogenicity and toxicity.

The supremacy of NDDS fascinated the global investment, the search funding of the nanomedicine in US at National Institutes of Health (NIH) from 2011 to 2019 is around 623 million Dollars. Although, only 51 nanomedical products have been approved by the Food and Drug Administration (FDA) till recent time. The low clinical transition ratio was comparatively due to the insufficient awareness of the pharmacokinetic properties of NDDS. The biological fate of NDDS was difficult to achieve. The conventional pharmacokinetic studying methods, such as fluorescence labeling, could not track or distinguish in vivo nanocarriers and payloads simultaneously.

Herein, we review the recent advances of the bioanalytical techniques for pharmacokinetic research on NDDSs for the first time. The measurement strategies and results for the released and encapsulated drug as to the carrier polymer of NDDSs and their biodistribution are enumerated, and obstacles and perspectives of these technologies are discussed.

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II. CLASSIFICATION:

Classification of nanocarriers

Types of nanocarriers

Liposome

Liposomes were the first type of nanocarriers, and are around 80−300 nm in size. They are spherical and consist of phospholipids and steroids. They can be prepared spontaneously by dispersing lipids in aqueous media. A drug can be encapsulated inside the liposome, and it can be subsequently released from the drug by changing parameters such as pH, osmotic gradient, and surrounding environment.

Different surface modifications also improve the half-life of the liposomes. For example, addition of polyethylene glycol (PEG) increases the half-life of liposomes by preventing recognition by phagosomes.

Similarly, polyethylene glycol-phosphatidylethanolamine (PEG-PE) conjugates have also been added. PEG-PE conjugates are non-toxic and can be used to specifically target the nanocarrier to the mitochondria.

Nanoparticles based on solid lipids

Lipid based nanoparticles include solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), and lipid drug conjugates (LDC).

The SLN are based on solid lipids and provide good physical stability and tolerability. NLC and LDC are combinations of solid and liquid lipids with increased load capacity and reduced drug expulsion properties.

Polymeric nanoparticles

They are derived from synthetic polymers and range from 10−100 nm. They can be further sub-divided in to biodegradable and non-biodegradable. Drugs can be conjugated on the surface of these nanocarriers by polymerization and they can be released by desorption or diffusion in the target tissue.

Biodegradable nanocarriers can undergo hydrolysis inside the body to give lactic and glycolic acid. They are also stable in blood, non-toxic, and non-thrombogenic.

Dendrimer nanocarriers

Dendrimer nanocarriers consist of following features: core, dendrons (dendrimers), and surface-active groups. The dendrons are attached to the core and properties of the nanocarriers are determined by the type of surface-active groups.

Several ligands can attach to the surface of dendrimers, such as folic acid, antibodies, peptides, PEG, or antimicrobial agents. These additions modify the physical and chemical properties of dendrimers.

Silica materials

Silica materials used as nanocarriers include xerogels and mesoporous silica nanoparticles. MCM-41 is a well-known silica nanomaterial. The drug loading in these materials occurs via adsorption and the drug release is governed by diffusion.

However, recent studies have also shown certain hazardous effects where silica nanoparticles trigger oxidative stress and the production of reactive oxygen species in cells. Thus, there is a need for further investigation into the effects of these silica nanocarriers.

Carbon nanomaterials

Carbon nanomaterials include nanotubes and nano horns. They can be formed of single nanotubes rolled in to a sheet or multiple nanotubes arranged concentrically.

Surface modifications can be added to these to improve their biocompatibility. They have high mechanical strength and thus have also been used to as a support for other nanocarriers.

Drugs can be added to carbon nanotubes by encapsulation, adsorption, or attaching active agents to the nanotubes. The drug can be released by physical or chemical modification.

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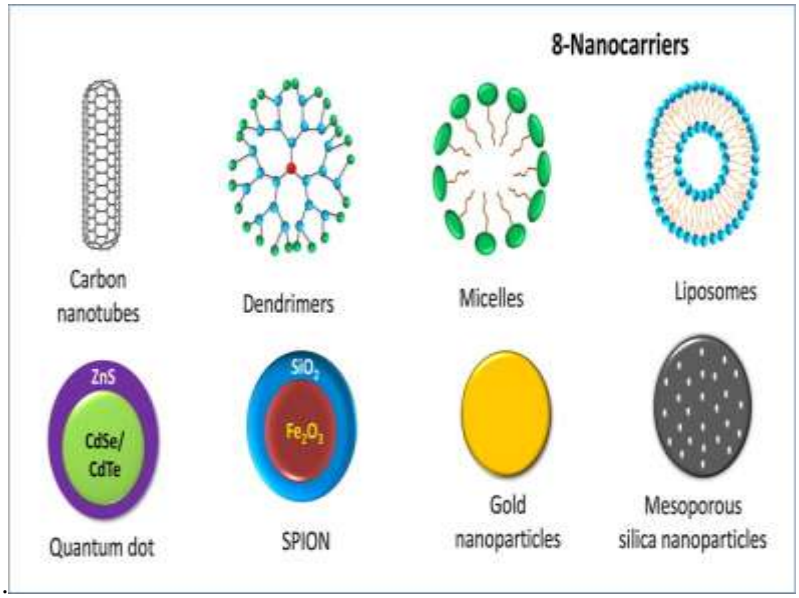

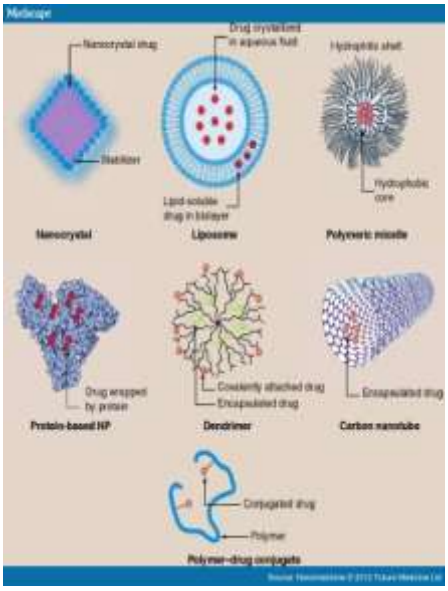

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III. FUTURE GLIMPSE:

Advancement of nano size drug delivery systems establishes a new paradigm in pharmaceutical field. Convergence of science and engineering leads a new era of hope where medicines will act with increase efficacy, high bioavailability and less toxicity in the recent past solid lipid nanoparticles (SLN) are escalating at a faster rate. Solid lipid nanoparticles introduced in 1991, signify an alternative carrier system to traditional colloidal carriers, such as emulsions, liposomes and polymeric microband nanoparticles Particulate drug carriers investigated for many years include oil-in-water (O/W) emulsions, liposomes, microparticles and nanoparticles based on synthetic polymers or natural macromolecules. Solid lipid nanoparticles are one of the novel potential colloidal carrier systems as alternative materials to polymers which is identical to oil in water emulsion for parenteral nutrition, but the liquid lipid of the emulsion has been replaced by a solid lipid. The biocompatibility of nanomaterials is of utmost importance because of the effect of the nanomaterials in the body ranging from cytotoxicity to hypersensitivity. With the advancement of nanotechnology, the biological phenomenon such as host response to a specific nanomaterial should also be clinically transparent. Therefore, it is quite essential to introduce cost effective, better and safer nano biomaterials which will provide efficient drug loading and controlled drug release of some challenging drug moieties for which there is no other suitable delivery available yet.

IV. CONCLUSION:

The ideal NDDS should provide APIs with the properties of sustained release, constant circulation time, improved stability, solubility and targeting. Annually, a great deal of pharmacokinetic information about drug-loaded NDDS has been reported. Nevertheless, the

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approved nanotechnology-based products are limited. The low drug pass-through rate may moderately attribute to the incomplete understanding of their pharmacokinetic properties.

Good examples have been encapsulated such as, the oleic acid-coated iron oxide nanoparticles for diagnostic applications through the near-infrared; photodynamic detection of the colorectal cancer using alginate and folic acid based chitosan nanoparticles; utilization of cathepsin B as metastatic processes fluorogenic peptide probes conjugated to the glycol chitosan nanoparticles; iron oxide coated hyaluronic acid as a biopolymeric material in the cancer therapy and dextran among the others.

The present review discusses recent advances in bioanalysis of the NDDS including technological progress in the analysis of released and encapsulated drug respectively. Apart from identifying their pharmacokinetics activities, bioanalysis of the polymer material of NDDSs is also discussed. Among the calculated analytical methods, LC-MS/MS is the most diversified approach for either profiling the pharmacokinetic [5].

behavior of NDDS in the clinical trial or for polymer quantitation in vivo. Because of the huge gap between the released active ingredients and NPs in their pharmacokinetics, a comprehensive understanding of in vivo fate of the NDDS is necessary to ensure their safe clinical applications. There has been a continued demand for developing efficient bioanalytical methods toward this goal. We hope this review will contribute to critical implications in the evaluation of NDDS in vivo.

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