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Drug Delivery Systems: A New Frontier in Nano-technology

Chamindri Witharana[1]* and Janith Wanigasekara[2]

[1]Senior Lecturer, Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Colombo, Sri Lanka

[2]Post Graduate Student, Department of Biochemistry and Molecular Biology, Faculty of Medicine, University of Colombo, Sri Lanka

**Corresponding e-mail: chamindri@bmb.cmb.ac.lk*

ABSTRACT

Nano-technology is a recent advancement in science, defined as "Science, engineering, and technology conducted at the Nano scale" (National nanotechnology initiatives in USA). Applications of Nano-technology cover a vast range from basic material science, personal care applications, agriculture, and medicine. Nano-technology is used in field of medicine for treatment, diagnostic, monitoring, genetic engineering, and drug delivery. There are two main types of Nano Particles (NPs) used in drug delivery; organic NPs and inorganic NPs. In drug delivery, the drug-Nano-Particle (NP) conjugate should be able to deliver drugs to the target site without degradation in gastrointestinal track and without reducing drug activity. Further, it should attack to target cells without causing any adverse effects. The ultimate goal of NP drug delivery is to improve proper treatment, effectiveness, less side effects with safety and patient adherence as well as reduction in the cost.

Keywords: Nano particles, DDS, Cancer treatment, Therapeutics

INTRODUCTION

More than 150 years ago, Michael Faraday who prepared gold particles in nanometer scale made the first breakthrough that would pave the way for major change in how medicine will be practiced in the future. Later researchers conjugated these colloidal gold particles with antibodies for target specific staining known as immune-gold staining. This can be considered as the precursor of recent application for drug delivery in nanotechnology. In 1960s, liposomes and polymer micelles were first prepared, however they were not referred as Nano-particles (NP) until 2000. In 1970s, NPs and dendrimers were first introduced. The successful development of micelles as drug delivery system (DDS) was reported in 1980. In 1990s, block co-polymers of polyethylene glycol (PEG), PEG-Polylysine were invented. The modern use of Nano-technology in drug delivery began when United States launched the national Nano-technology initiative [1]. The ideal NP drug delivery should achieve targeted delivery and thereby improve effectiveness, reduce side effects, ensure patient adherence, and lead to overall reduction of the cost.

Role of Nano-technology in drug delivery

DDS is defined by national institute of health in USA as, "Formulation of a device that enables the introduction of therapeutic substances in to the body and improves efficiency and safety by controlling the rate, time and place of release of drug in the body" [2,3]. Conventional DDSs has many drawbacks including poor bioavailability, side effects, low drug loading capacity, plasma fluctuation of the drug levels, low therapeutic effectiveness, and lack of target delivery. Traditional DDS circulate drugs to the cells in body non-selectively, which can lead to serious consequences such as side effects, multiple drug resistance (MDR) and reduced drug concentration at target location. For example, in cancer treatment the conventional drug delivery to the tumour cells can affect normal tissues causing nephrotoxicity, neurotoxicity, cardiotoxicity. These drawbacks have motivated on scientists to investigate more about new DDS [4].

How Nano-technology can overcome these drawbacks can be understood by discussing the mechanism of drug

delivery using Nano-particles (NP). The process of drug delivery can be mainly divided as; the administration of the drug or therapeutic product; release of the active part of the drug and transport active ingredients across the biological membrane to the target site to perform action.

Use of Nano-technology in DDS includes delivery and targeting of pharmaceutical, therapeutic, and diagnostic agents by the help of NPs to the cells. The drug-NP conjugate should be able to deliver drugs to the target site without degradation in gastrointestinal track and without reducing drug activity. Secondly it should attack to target cells without causing harm to other cells and reduces side effects [5,6].

How NPS improve drug delivery?

The chemical and physical properties of NPs make then efficient DDSs that have the potential to improve the bioavailability, drug carrying capacity, stability for the drugs within the body, controlled release, and targeted delivery [7].

Nano-technology increases bioavailability of drugs as a result of their special uptake mechanisms such as absorptive endocytosis and the ability to avoid degradation in the gastrointestinal track. The drug incorporated in to the NP is easily diffused through biological membranes. Drug-polymer attachment changes the drug solubility, hydrophobicity, and permeability. The drug loading capacity can be increased by minimizing solubility, increasing ionic interactions between drug and matrix and by maximizing the absorption of drug load [1,6].

The NPs are also able to remain in the blood for long period. The drugs attached NP can avoid being attacked by the immune system by having a particle surface decorated with biodegradable, hydrophilic copolymers. Poly- glycolic acid (PGA), poly-lactic acid (PLA) and their co-polymers are widely used for decorating the surface [3].

The self-controlling system of drug release helps to reduce the plasma fluctuation and minimize the side effects. Controlled drug releasing in particular sites can be controlled by different ways, 1) polymers are biodegradable and it is degraded in controllable manner to release drugs to the site 2) pores within the polymer can be altered so that drug diffusion occurs more readily or slowly, 3) the distance of fusion and surface area of the NP can be altered by changing size. Smaller size means larger surface area and drug release and dissolving becomes faster. The drugs are released by matrix by diffusion, swelling, erosion or degradation. The drug release is controlled by osmotic pressure, mechanical pumping and through electro kinetic transport [8].

Nano-technology based DDS provides drugs to target sites by their ligand attraction process. The NP surface can be decorated by ligands and these ligands can attach to the specific receptors in the surface of targeted cell by bio-recognition. The NPs enter the target cells by receptor mediated endocytosis. Inside the cell NPs are developed in to endosomes. Then endosomes merge with each other to form large endosomes or lysosomes. Finally, therapeutic drugs can be released in response to enzymes or acidic pH with controllable manner by degradation of polymeric NP shell [6]. Ultimately NPs in DDS enhance the ability to use highly toxic, poorly soluble, unstable drugs and maximizing patient comfort.

Different types of NPs

Above mentioned actions can be achieved by different types of NPs. There are mainly two types of NPs; organic NPs such as liposomes, Nano crystals, dendrimers, polymeric NPs, and inorganic NPs such as metal NPs and silica [8,9].

Liposomes are amphiphilic molecules that are able to carry both hydrophobic and hydrophilic drugs. The shape, surface, charge, size and functional groups in liposomes can be easily changed according to the drug and the target site. Drugs can be incorporated in to liposomes by encapsulation method. Liposomes are encapsulated with various drugs such as anticancer drugs, neurotransmitters, antibiotics, and anti-inflammatory drugs. For instance, Doxorubicin which is a highly toxic anticancer drug can be safely and accurately delivered directly to the tumour cells instead of accumulating in the heart and kidney [10].

The Nano crystals can reduce accumulation of carrier particles and directly incorporate the drug to the target site. Nano crystals have the ability to become stable in aqueous dispersion without any stabilizers. Dendrimers are synthetic polymers with well-defined size and structural branched chains. Drugs can be incorporated either to internal surface/ core or surface by covalent bonds and it is decided by the drug and target site [6,11].

The polymeric NPs can deliver drugs to the site of action with minimum toxic levels and it is hydrolysed inside the

body to produce bio-degradable metabolite monomers like lactic acid and glycolic acid. Protein and peptide drugs can be conjugated with polymers such as PEG and it can prevent protein drug degradation in stomach and increase the half-life of drugs in plasma [11]. The polymeric NPs with surface decorated with PEG and target ligands are capable of delivering highly toxic cancer drugs like Doxorubicin to target sites without harming healthy cells. In the treatment of Tuberculosis continuous and frequent drug supply to the cells can be achieved by NPs covered with PEG and attached with drugs such as Rifampicin (RMP), Isoniazid (INH)/Pyrazinamide (PZA). Polymeric NPs, nano gels, liposomes, micelles, dendrimers, and protein NPs are being investigated for use in treatment of several ophthalmic conditions [12,13].

Metal Nano-particles (MNP) such as gold, silver, iron, platinum, and ceramic, are used due to their optical, magnetic, electrical properties and size which leads to less solvent contamination and uniform distribution. In ophthalmology glaucoma can be treated with nano-diamonds with drug (timolol maleate) embedded in contact lenses. Researchers attempt to reduce side effects of platinum used in cancer therapy by using gold NPs [14].

Silica Material such as Xerogels and Mesoporous silica NPs have higher biocompatibility, convenient functionalization and high porous matrix. Phenytoin, Cisplatin, Nifedipine, Doxorubicin, Metronidazole and Heparin are drugs incorporated with Xerogels. Mesoporous silica nanomaterial has high surface area for drug absorption. Anticancer drugs, antibiotics, heart disease drugs are delivered by mesoporous which controls drug release by diffusion method. Silica and magnetic NPs can be successfully used in bone regeneration [10].

Future opportunities

Most applications are still under research, animal testing or only at hypothesis level. Researchers try to improve blood circulation period of NPs by coating their surface with red cell membranes instead of PEG, design NPs with different shapes, ligands, and drug particles, use photosensitive agents that accumulate in tumours, make blood vessels more porous to facilitate penetration by NPs, attach RNA to treat skin cancers and develop monoclonal antibodies and vaccines that are directed against tumours [8,15].

In future Nano-technology based DDS can lead to further advancements in antitumor therapy, gene therapy and radiotherapy. Multi-functional NPs will capable of detecting malignant cell, deliver different drugs at same time, visualize the location by imaging agents, killing cancer cells with minimum side effects and monitor and treat at the same time. NPs will be playing a crucial role in robotic surgery. The NPs can be combined with computer programmes to automate regulation of homeostasis such as blood glucose level and serum calcium level. In immunology, NPs have the potential to act as powerful protectors against foreign particles [16,17].

CONCLUSION

Nano-technologies as DDSs are designed to improve the pharmacological and therapeutic properties of conventional drugs. Current application of NP based drug delivery focus on conditions such as malignancies, diabetics, heart diseases and central nervous system diseases. The NP based drug delivery can be further developed to cure challenging diseases like AIDS. In the future, it may be possible to develop nano-technology treat different disease at the same time by producing multifunctional Nano-particles.

The ultimate goal of NP drug delivery is to improve proper treatment, diagnostics and monitoring with improved performance, effectiveness, safety and patient adherence as well as reduction in the cost.

DECLARATION

Competing interests

The authors declare that they have no competing interests.

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