Nanoparticles in Theranostics

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INTRODUCTION

Nano relates to the size of the objects, particularly very small sized. It is one billionth of a meter/gram or 10-9 of the meter/gram. Nanoscience is the application or the study of the nano particle and it is utilised in various fields like material science, engineering, chemistry, biology, and physics.[1] In the medical science nano particles can be used for theranostic purpose. The term 'theranostic' was coined by Funkhouser in 1998.[2] 'Theranostics' combines therapy and diagnostics and defines ongoing efforts to develop more specific, individualized therapies for various diseases, and to combine diagnostic and therapeutic capabilities into a single agent. The rationale arose from the fact that diseases, such as cancer, are immensely heterogeneous, and all existing treatments are effective for only limited patient subpopulations and at selective stages of disease development. The hope was that a close marriage of diagnosis and therapeutics could provide therapeutic protocols that are more specific to individuals and, therefore, more likely to offer improved outcomes.[2]

HISTORY

The principle of nanoparticle was applied in medical science for the first time by Speiser in 1960s. Since then it has found a wide application in drug delivery particularly as vaccine carriers for slow and sustained release of the drug.[3] In 2016, Nobel prize was awarded to the three scientists in Chemistry viz. Jean-Pierre Sauvage from University of Strasbourg France, Sir J. Fraser Stoddart from Northwestern University, USA and Bernard L. Feringa from University of Groningen, Netherlands "for the design and synthesis of molecular machines" which use nanotechnology.[4]

Initially the nanoparticles found use in the therapeutics and later these found application in diagnostics by using fluorescence associated marking of biological tissues. With advancement, nanoparticles have been used in gene therapy, identification of pathogens for diagnosis, detection of protein, DNA probing, biological molecule purification and segregation, contrast enhancement in diagnostic scanning like Positron Emission Tomography (PET),

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Magnetic Resonance Imaging (MRI), and Computerized Tomography (CT).

PHARMACOKINETICS

Nanoparticles passage across the biological membrane, like clearance from the circulation, depends upon their size. Nanoparticles <10nm are easily cleared by kidney or through extravasation, whereas size larger than this may be phagocytosed by mononuclear phagocyte system/ reticular endothelial system. When the nanoparticles reach the circulation, they have the tendency to adsorb nonspecific proteins. This is known as opsonisation in which this nanoparticle is made more noticeable to phagocytic system. Pegylated spherical nanoparticles of size <100nm to >200nm showed different protein adsorption properties and differ in their pharmacokinetics. <100 nm sized particles remain inside the circulation for prolonged period of time and have reduced hepatic filtration. Other factor which affects this property is the polarity of nanoparticles. Neutral and negatively charged particles have less immunogenicity than positively charged particles. Based on the above characteristics nanoparticles show optimal activity if they are in the size range of 10-250 nm and are either neutral or negatively charged. Before designing, one should consider the factors affecting bio-distribution and clearance of the nanoparticles.[5]

DELIVERY SYSTEM

The nano technology used for delivering the drugs is the modern drug delivery system which aims to deliver the drug at the right place at the right time. In this system the drug is directed to desired site by two mechanisms either passive or active targeting. In passive drug targeting, there is highly selective ligand receptor interaction and the drug is preferentially accumulated at the desired site passively like in the tumour cells. There are multiple hindrances in this for nano-particles in the way to their site like mucosal barriers, nonspecific uptake and delivery. In active drug targeting, ligands are specific and selectively identified by the receptor hence more specific and precise delivery occurs to the targeted tissue. The advantages of active targeting are that bioavailability and uptake of poorly soluble agents is increased, more specific targeting is achieved, and nonspecific toxicity is prevented.[5]

DISADVANTAGES

Minimal alteration in the existing property of the nanoparticle can have harmful consequences in pharmacological properties. Larger variation in the structure of nanoparticle will adversely affect its performance; it will work differently in lab settings than at actual cellular level. Nanoparticle stability is another challenge. It should remain stable in solution in due time and no aggregate should form. Nanoparticles adversely affect clinical trials in terms of time and cost, additionally contributing to toxicity. Hence nanoparticles should be inert.[6]

APPLICATION

Nanoparticles have enormous applications in theranostics like in drug delivery, cell specificity, internalization within the tissues, delivery of vaccines, in gene therapy, transport of peptides/nucleic acid/other molecules, and gene slicing. In diagnostics it can be used as radio contrast enhancer in imaging procedures. It has the potential for free radical scavenging, photosensitizers, stimulating the host immune response and production of antibodies to reduce the toxicity, bio-conjugation with polymer, diagnosis of micro metastasis of the tumours, the treatment of non-communicable diseases like insulin dependent diabetes mellitus, the treatment of incurable disease like HIV-AIDS/Tuberculosis, identification of proteins, elimination of plasma opsonins and increase in circulation time, use together with ultrasound in thrombolysis known as sonothrombolysis, targeting of brain/tumour tissue, delivery of artificial growth factors, for production of reactive oxygen species to destruct targeted tissue, transfection, chemotherapy, pharmacogenomics in drug development process, artificial red blood cells, clearing the blood circulation, non-viral transfection, delivery of antibodies/ antibiotics/enzymes, bioassay and many more.[3,5-13]

CONCLUSION

Nanoparticles' utility in medical science is a boon. When a new drug is discovered or invented, aim is to achieve maximum benefit with minimal adversity, which is possible with nanotechnology. Medical science has achieved numerous milestones from precise and early diagnosis of the disease to the treatment of highly fatal cancer.In theory, a nanoparticle based theranostic agent can deliver therapeutics to a diseased area and can use its imaging function to improve diagnosis and to monitor therapeutic response. Despite the promise, the related proofs are so far inadequate and should be the main focus of the future investigation.[2]

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