Nanotechnology in Drug Delivery: Introduction and Recent Developments

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Abstract

Nanotechnology has emerged as one of the very promising fields of biomedical research in the last few decades. Drug delivery is one of the areas where this technology has made remarkable progress. The present article is an attempt to present the brief history of nanotechnology and market forecasts about nanotechnology. The article presents the composition, classification, advantages and examples of nanotechnology assisted drug delivery. Developments in nanotechnology assisted therapeutic applications and the future prospects have also been discussed.

INTRODUCTION

Nanotechnology (nanomaterials and nanoscale devices) for diagnosis, treatment and monitoring diseases is a fast developing area of biomedical research. It is an amalgamation of engineering science with pharmaceutical and medical sciences[1].

1959 Americn Physical Society talk entitled ‘There's Plenty of Room at the Bottom' by physicist Richard Feynman is considered as the first hint about nanotechnology[2].

The term ‘Nanotechnology' was coined in 1980s by K. Eric Drexler[3]. AACR website mentions that this term was actually coined in 1974 by Norio Taniguchi[4]. In Apr, 2001 issue of Modern Drug Discovery, Richard H. Smith has enlisted several speculative applications of nanotechnology[5]. A Lancet editorial has indicated emergence of nanomedicine as a discipline[6].

Drug delivery is one of the most promising fields of nanotechnology[7]. Nanotechnology typically uses particles in 10nm-1µm range[8]. Sinha et al have mentioned that this technology uses particles in the 1nm -100 nm size range[9]. AACR website mentions that nanotechnology components size ranges from 5 to 500 nanometers[4].

NANODRUG DELIVERY SYSTEM

A nanodrug delivery system consists of a core, a particle or emulsion, prepared by chemical methods to function as a carrier. Functional groups are added to the core. Such groups may include therapeutic molecules and ligands for targeting specific locations[4].

Nanotechnology in drug delivery is exemplified by nanocrystals, liposomes, nanoparticle-protein conjugates[10], magnetic nanoparticles, nanogels and biodegradable nanoparticles[8].

ADVANTAGES OF NANOTECHNOLOGY

Nanotechnology may help in increasing the solubility & bioavailability of drugs, new dosage forms and better exploration of less-used drug administration routes for efficient therapeutic outcomes. Nanoparticles with diameter less than 200nm are not screened out of circulation by liver and spleen[3].

Nanotechnology is better suited for drug targeting of individual tissues, cells and cellular receptors and hence, aptly suitable for gene and vaccine delivery. It may also be helpful in designing nanoporous membranes for controlled-delivery drug devices[11].

Nanoscale powders of antiasthma and analgesic drugs are quickly absorbed in the human body in comparison to the traditional drug delivery systems[12].

Nanotechnology is particularly useful in case of drugs with narrow therapeutic indices. It has been shown that self-assemblies (~ 15nm) of phospholipid molecules known as sterically stabilized micelles are helpful in improving efficacy and reducing toxicity of such drugs. The side effect of vasoactive intestinal peptide delivered by this

nanotechnology was completely eliminated as it extravasated specifically in diseased tissues[13]. Nanotech based drug delivery is less toxic as well as inexpensive[8].

Nanotechnology is suited for better drugs delivery to small regions within the human body as such drugs can easily cross biological membranes[14]. Liposomes are effective for drug targeting by chemotherapeutic agents[10].

Some examples[15] of application of nanotechnology are:

- Intracellular drugs delivery through spontaneously forming nanotubes.
- Lipid complexes for i.v. administration of antifungals
- Submicron triglyceride emulsions for parenteral nutrition.
- Accelerated wound healing because of silver nanoparticle antimicrobials as dressings.

Four NanoCrystal based drugs[10] are Rapamune (sirolimus), Emend (aprepitant), TriCor (fenofibrate) and Megace ES (megesterol).

NANOTECHNOLOGY MARKET, INVESTMENTS & FORECASTS

The nanotechnology market has three broad segments: nano-enabled tools, nano-particles/ materials and nano-enabled drugs[2]. A presentation by Amarnath Maitra of University of Delhi (India) available on the internet shows the venture capital investments in various nanotechnology based US industries[16]. Demand for nanotechnology based health care products through 2009 will annually grow by 48 percent[17].

Nanotechnology by 2015 has been estimated to generate $ 1trillion in industry revenues[3]. Nanotech product sales[18] for 2004 were projected to be $20-$50 billion and expected to reach $2 trillion target by the year 2015.

A report entitled “The Impact of Nanotechnology In Drug Delivery: Global Developments, Market Analysis And Future Prospects” examines the business opportunities being created by nano-engineered drug delivery market[14].

In 2005, Science predicted that nanotechnology will revolutionize the diagnostics, imaging and therapy segments of healthcare. National Science Foundation (USA) has predicted that by 2010 nanotechnology based-drug delivery applications will account for half of all the pharmaceutical sales[8].

DEVELOPMENTS IN NANOTECHNOLOGY-BASED THERAPEUTIC APPLICATIONS

Khademhosseini and Langer have comprehensively discussed nanobiotechnology in drug delivery and tissue engineering. Developing nanotechnology into clinical therapy is a challenging task[19].

In a recent article, Jin and Ye have highlighted nanotechnology in in vitro and in vivo drug and gene delivery[20].

CANCER

Nanoparticles of paclitaxel stabilized by albumin are approved by FDA for use in chemotherapy refractory metastatic breast cancer[10]. Sinha et al have discussed the utility of bioconjugated nanoparticles for anticancer drugs delivery[9]. Recently, findings on use of synthetic nano-low density lipoproteins as targeted drug delivery vehicle for glioblastoma multiforme have appeared[21]. In mice receiving injections of human epithelial cancer cells, the nanoparticle-based therapy using folic acid and methotrexate was found to have delayed tumour growth 10 times better than methotrexate alone[22]. Ehdaie has reviewed nanotechnology in cancer research with reference to progress in NCI's Alliance for Nanotechnology[23]. Nanoparticles specfically targeting cancer cells can be heated up under the influence of magnetic field to kill cancer cells[12].

DIABETES MELLITUS

Martinac and Metelko[24] have disscused potential and applications of Nanotechnology in diabetes mellitus.

Polyethylcyanoacrylate nanospheres as biodegradable polymeric carriers have been found good for oral insulin delivery in streptozotocin-induced diabetic rat model[24].

SmartCell technology may help diabetics to maintain their glucose levels without needing blood sample glucuse monitoring and injecting insulin. The rise in blood glucose will result in breakage of protein matrix of SmartCell and subsequent release of insulin proportionate to blood glucose[24].

RESPIRATORY DISORDERS

Polymeric nanoparticles with polylactide-co-glycolide have demonstrated clear advantages over traditional drug carriers in case of intermittent chemotherapy in experimental

tuberculosis[25].

OPHTHALMIC DISORDERS

Dendrimers have a potential for treatment of ocular disorders[26].

AIDS

VivaGel is an antiHIV drug based on dendrimer technology[12].

MISCELLANEOUS DEVELOPMENTS

NanoVic with Monash University, Eiffel and MiniFAB is developing nanotechnology solutions for transdermal delivery of vaccines, peptide hormones and other drugs through stratum corneum layer of the skin. NanoVic is also developing drug delivery microneedles from biocompatible polymers[11].

Nanospheres of poly(acrylic acid) have the ability to absorb substantial amounts of drugs in case of drug overdosage in a few minutes time. These nanospheres have a potential as fast-acting antidotes and can reduce drug-overdosage mortalities[27].

Nanomaterials can be embedded in dosage forms to help detection of counterfeit drugs[28].

QBI Life Sciences has developed polymeric micelles for placement of micelle/biotin / lipid complex on solid support[29].

CURRENT CLINICAL TRIALS

It has been proposed that a new stent of nanoporous particle with better polymer for drug release may prove safer and more efficacious alternative (particularly in case of high-risk coronary artery disease patients such as diabetics) as compared to drug-eluting stents currently available in the market[30].

PATENTS

More than 100 Nanopharmaceutical patents[3] were granted by US patent office during 2001-05. United States Patent 6933331 entitled “Nanotechnology for drug delivery, contrast agents and biomedical implants” has been granted for nanoscale powders as composite and device components[31].

REGULATORY CONTROL

The US FDA regulates foods, cosmetics, drugs and devices some of which may be either nanotechnology-based or contain nanomaterials[32].

FUTURE APPLICATIONS

Construction of a nanorobot with insulin in inner chambers and glucose-level sensors on the surface is also being tried. This nanorobot may act as nano-artificial pancreas[24].

Jin and Ye have emphasized nanotechnology for improving controlled and sustainable drug delivery in solid tumors and for neurodegenerative diseases[20].

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