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Review

Nanotherapeutics: An insight into healthcare and multi-dimensional applications in medical sector of the modern world

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ABSTRACT

In recent years nanotechnology has revolutionized the healthcare strategies and envisioned to have a tremendous impact to offer better health facilities. In this context, medical nanotechnology involves design, fabrication, regulation, and application of therapeutic drugs and devices having a size in nano-range (1–100 nm). Owing to the revolutionary implications in drug delivery and gene therapy, nanotherapeutics has gained increasing research interest in the current medical sector of the modern world. The areas which anticipate benefits from nano-based drug delivery systems are cancer, diabetes, infectious diseases, neurodegenerative diseases, blood disorders and orthopedic problems. The development of nanotherapeutics with multi-functionalities has considerable potential to fill the lacunae existing in the present therapeutic domain. Nanomedicines in the field of cancer management have enhanced permeability and retention of drugs thereby effectively targeting the affected tissues. Polymeric conjugates of asparaginase, polymeric micelles of paclitaxel have been recmended for various types of cancer treatment .The advancement of nano therapeutics and diagnostics can provide the improved effectiveness of the drug with less or no toxicity concerns. Similarly, diagnostic imaging is having potential future applications with newer imaging elements at nano level. The newly emerging field of nanorobotics can provide new directions in the field of healthcare. In this article, an attempt has been made to highlight the novel nanotherapeutic potentialities of polymeric nanoparticles, nanoemulsion, solid lipid nanoparticle, nanostructured lipid carriers, dendrimers, nanocapsules and nanosponges based approaches. The useful applications of these nano-medicines in the field of cancer, nutrition, and health have been discussed in details. Regulatory and safety concerns along with the commercial status of nanosystems have also been presented. In summary, a successful translation of emerging nanotherapeutics into commercial products may lead to an expansion of biomedical science. Towards the end of the review, future perspectives of this important field have been introduced briefly.

1. Introduction

Nanotherapeutics is a recent application of nanotechnolgy that have wide ranging impact on medical field [1]. Nanomedicine has emerged from nanotechnology, is rather a nascent field of science, whose history dates back to 1959, as predicted by Richard P. Feynman [2]. A nanometer is one millionth part of a millimeter where the word nano means 'dwarf' [3]. Nanotechnology, deals with the investigation, modification, and control of atomic/molecular structures of object ranging, between 1–100 nm in size [4].

The branch of nanomedicine is exploiting a wide range of nanotechnological approaches, including numerous biological devices and

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nano-biosensors. Quantum effects taking place at nano-level have an impact on biological, chemical, physical, optical and mechanical properties which permits scientists to exploit the benefits of such phenomena [5]. Nano medicine also includes newly emerging concepts and applications of molecular nanotechnology for designing of nano-machines called nano-robots. Biological macromolecules and structures or xenobiotic chemical drugs provide basic working power to nanostructures. The most revealing fact about nanomaterials is that their size is similar to many of the biological macromolecules which facilitate the use of nano-materials in *in-vivo* as well as *in-vitro*. Thus, by the unification of nanotechnology with biological material, several diagnostic kits, analytical tools, physiotherapy applications and drug delivery vehicles have been developed till date. Therefore, the nano-therapeutics as a branch of medicine has a vast scope of research and development. Unlike the conventional methods of medication, in this technique the drug attach on nanoparticles which enables it to act more efficiently, and accurately with few side effects. Nanotherapeutics provides new opportunities to improve the safety and efficacy of conventional therapeutics [6,7]. Due to this, different national and international agencies and pharmaceutical companies are investing to generate new drug delivery methods, gene therapies, and *in-vivo* imaging techniques. Nanomedicine sales reached up to $16 in, only in nanotechnology. According to a new report by Grand View Research, Inc. the nanomedicine market is anticipated to reach $ 350.8 billion by 2025 showing significant impact on global economy [8].

Nowadays, the healthcare industry is striving to achieve increased productivity, improved access and higher quality of treatment at lower costs. Chronic, serious neurological disorders such as cancer, diabetes, HIV/AIDS and heart disease have been a challenge for health care professionals. Another challenge includes infectious diseases, where conventional antimicrobial agents used for their treatment develop adverse side effects and multiple drug resistance. Target specificity is one of the major hurdles to get the therapeutic efficiency. Nanoparticles have proved as one of the logical and encouraging tools for delivery of medicine in controlled and targeted manner. Nanomedicine plays a significant role in overcoming these challenge because nanotechnology based formulations enhance pharmacokinetic properties, bioavailability and drug targeting in various disorders. Besides prevention and treatment of diseases, nano medicine possesses potential applications in diagnosis, monitoring therapy, drug discovery, surgery, and gene delivery using molecular knowledge of human system [9–11].

In the light of facts mentioned above, nanotechnology has profound applications in healthcare management (Fig. 1). In past two decades, several nano-therapeutics have been approved by FDA for the treatment of hepatitis, cancer, cardiovascular diseases, neurological diseases, autoimmune diseases, diabetes, high cholesterol, Parkinson's disease, and certain infectious diseases (Table 6) [12]. Moreover, hundreds of nanocarrier based products are currently available at various stages of the preclinical and clinical development [13].

This review highlights the contribution of nanotechnology with intent to aid the researchers in exploring nanocarriers such as polymeric nanoparticles, nanoemulsions, nanogels, solid lipid nanoparticles, nanostructured lipid carriers, dendrimers, nanocapsules, nanosponges in the field of drug delivery. An overview of applications of nanotechnology from different perspectives such as nutrition, diagnosis, biosensor systems, blood purification, tissue engineering and nanotechnology based medical devices including nanorobots are also included. A brief discussion on the significance influence of nanoparticles on the health consequences, regulatory status, safety concerns, and commercial potential has also been given. It is an attempt to provide a bird's eye view to the healthcare professionals about developments in this field.

2. Nanoparticles in drug delivery

Application of nanotechnology in drug delivery has the potential to revolutionize the treatment of various diseases like cancer, diabetes, infection, neurodegenerative diseases, blood disorders and orthopedic problems [14]. Ideally, these strategies are meant to improve the drug absorption, therapeutic concentration, and stability, resulting in effective drug targeting. Reproducibility and long-term release of the drug within the target tissue are other features of nano-based drug delivery systems [15]. Rational design of nanotherapeutics leads to the formulation of nano-platforms of a particular shape, size and surface properties that are indispensable for biological interactions and resultant therapeutic effects [16]. Nanotechnology based formulations possess unique physical and chemical characteristics responsible for a wide range of applications in various disorders [12] (Fig. 2). The nanoformulations reported recently play an important role in the healthcare sector (Table 1). Majority of nano-therapeutic products in the market are available for parenteral administration, while several being meant for oral administration [17]. A significant number of preclinical and clinical trials can be expected to result in the development of new nanotherapeutics intended for non-parenteral routes of delivery such as pulmonary, ocular, nasal, vaginal and dermal. The choice of the route of delivery and associated barriers to be crossed is of particular interest for drug delivery systems (European Commission/ETP) [18]. Over the time, several nanoparticles based formulations were developed to improve the drug delivery system.

2.1. Polymeric nanoparticles

The most commonly used polymeric nanoparticles are fabricated from synthetic polymers. Due to variation in purity and batch-to-batch consistency, natural polymers, resulting in poor reproducibility and controlled release behaviour for the entrapped drug (s). On the other hand, synthetic polymers are available with good to batch reproducibility and purity which facilitates the modification of drug release pattern from polymeric nanoparticles [39]. Nanoparticles prepared using synthetic polymers have been explored extensively for drug delivery (Table 2). Hydrophilic moieties can be encapsulated into synthetic polymer-based nanoparticles by double emulsion technique because it is difficult to maintain the activity of biological molecules in the presence of volatile organic solvents. Widely used synthetic polymers reported for drug delivery include biodegradable aliphatic polymers such as polylactide (PLA), poly lactide-co-glycolide, copolymers (PLGA) and poly (ε- carpolactone), as well as non-biodegradable polymers like polyacrylates and poly (methyl methacrylate) [40].

Polymeric nanoparticles can effectively protect unstable drug moieties from degradation, thereby preventing the side effects of toxic drugs. Natural polymeric nanoparticles are comprised of polymers such as alginate, chitosan, albumin and gelatin [40]. The application of polymeric nanoparticles with dexamethasone or α-tocopheryl succinate palliates cisplatin ototoxicity which resulted from chemotherapy treatment. The nanoparticles that entrap, transport and finally deliver dexamethasone or α-tocopheryl succinate are capable of partially preventing ototoxicity produced from high doses of CDDP [41]. Otherwise, these poorly soluble drugs show severe side effects when systemically administered for longer periods of time. The incorporation of these medicinal products in hydrophobic cavity of nanoparticles provides the desired *in vitro* and *in vivo* effects. Some of the popularly marketed formulations of the polymeric nanoparticles are Decapeptyl®, Gonapeptyl Depot®, Enantone Depot®, and Abraxane [42,43].

2.2. Nanogels

Nanogels, comprising of flexible hydrophilic polymers, can be prepared as plain gels [44]. The drug can be incorporated spontaneously in the nanogel upon swelling in water. As a result, gel collapses, leading to the formation of solid, dense nanoparticles with a decrease in solvent volume. Owing to biocompatibility, high moisture content and desirable mechanical features, nanogels propose unique applications for