Toxicology: Open Access

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Toxicology: Nanoparticles Toxicology in Drug Delivery

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Abstract

Nanoparticles have revolutionized biomedicine especially in the field of drug delivery due to their intriguing properties such as systemic stability, level of solubility, and target site specificity. It can, however, be both beneficial and damaging depending on the properties in different environments, thus highlighting the importance of Nano toxicology studies before use in humans. Different types of nanoparticles have been used in drug delivery, and this review summarizes the recent toxicity studies of these nanoparticles.

Keywords: Nanoparticles; Nanotoxicology; Toxicity assessment; Protein nanoparticles; Metal nanoparticles; Lipid

Introduction

Nanoparticles: The hallmark of managing patients with drug toxicities is primarily to assess and treat compromises in airway, breathing, and circulation: intubate and mechanically ventilate patients with respiratory compromise; establish intravenous access, hydrate with intravenous fluids for hypotension; and obtain labs to assess the underlying etiology of the compromise [1]. This chapter provides information on the prevention, prognosis, common pitfalls in diagnosis and management, and treatment algorithms of diseases caused by drug toxicities [2]. Initial treatment of all toxin ingestions should focus on managing airway, breathing, circulation, and neurologic deficits of toxicology. Some patients presenting with severe intoxications can require prolonged ventilation or ICU support [3]. The prognosis depends on the type of ingestion and organ system primarily affected. nanotechnology has been rapidly developed and applied in medicine and pharmaceutical products. Nanoparticles have been intensively studied and proposed for medical uses, especially for drug delivery due to the unique characteristics of these nanoparticles such as particle sizes and surface area per unit volume. However, these specific characters may induce adverse side effects in clinical practice leading to unexpected or delayed toxicity [4]. In this chapter, the following topics will be discussed. Firstly, benefits and toxicities of different types of biological origin or chemical nanoparticles in drug delivery will be discussed including carbon nanotubes, quantum dots, metal nanoparticles, liposomes, polymeric micelles, polymeric nanoparticles, dendrimers, and fullerenes. Secondly, biotransformation, biodistribution, and clearance of these nanoparticles in drug delivery system will be reviewed as these nano-formulation [5].

Methods

Marqibo, commercialized by Spectrum pharma, previously Talon Therapeutics, is a 100 nm Liposome containing vincristine sulfate, a microtubule polymerization inhibitor. It has been approved since 2012 for treatment of acute lymphoblastic leukemia (ALL), using several intravenous injections at a dose of 2.25 mg/m^2. Preclinical studies have shown a higher circulation time of Marqibo compared with free vincristine, optimized delivery to target tissue, facilitated dose intensification without increased toxicity. Clinical studies carried out on patients with ALL showed that the MTD was 3-5 mg, two times larger than that of free vincristine. When it was administered intravenously at a dose of 2.5 mg/m^2 on 13 patients, it resulted in a clearance of 345 mL/h, higher than that of 189 mL/h observed with free vincristine, a higher MTD, a superior antitumor activity, a larger amount of vincristine delivered to tumors tissues compared with free vincristine. Marqibo was also tested clinically for treatment of large B-cell lymphoma and non-Hodgkin Lymphoma, commercialized by Teva Pharma, previously named Cephalon, is a non-pegylated 190 nm liposome with a membrane of phosphatidylcholine and cholesterol containing doxorubicin, which is a toxic anthracyclic used for solid and hematologic tumour treatments. It has been approved in Europe and Canada since 2000 for first line treatment of metastatic breast cancer (MBC) using intravenous administration repeated every three weeks at a dose of 60-75 mg/m^2 in combination with 600 mg/m^2 of cyclophosphamide. Clinical assessment of this treatment on 297 patients indicates that it improves the therapeutic index of doxorubicin by significantly reducing cardio-toxicity and grade 4 neutropenia while providing comparable antitumor efficacy Compared with non-liposomal doxorubicin, Myocet is characterized by higher EHL, AUC and lower clearance Moreover, unwanted toxicity due to PEG (swelling on the palms of hand and soles of feet, hand-foot syndrome) or to doxorubicin (cardiac or gastrointestinal toxicity) can be avoided However, the absence of PEG also induces undesired phagocytosis of Myocet by mononuclear phagocytes resulting in lower EHL, AUC and higher clearance than with the pegylated liposome formulation Doxil. Myocet has also been tested for a combined treatment of MBC with docetaxel and trastuzumabor with gemcitabine as well as for treatments of relapsed/refractory myeloma, several different types of lymphoma and sarcoma actors may implicate on their toxicities and their uses in clinic.

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