Editorial

New Trends in Pharmaceutical Nanotechnology

INTRODUCTION

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The emergence of nanoscience and nanotechnology, which is the creation of materials and tools at the nanometer scale, has had a great influence in pharmaceutical research, particularly in the field of drug delivery. Despite the therapeutic efficacy of numerous drugs used nowadays in clinics, some of these present several technological limitations, such as poor solubility and lack of specificity to the target tissue or organ, leading to adverse effects. Several efforts have been made in order to develop systems able to promote a more controlled release, carrying appropriate amounts of therapeutic agents to the site of action, with consequent minimal side effects due to the absence of deposition of drugs on healthy tissues, improving their bioavailability and efficacy.

Nanomedicine has been defined as the application and further development of nanotechnology to solve some problems in medicine and may radically change the method of production and administration of drugs. Nanotechnology plays an important role in therapy by enabling the use of lower effective doses as well as increasing therapeutic indices and safety profiles.

The most popular and prospective strategies used in pharmaceutical nanotechnology include polymer-drug conjugates, nanoemulsions, dendrimers, micelles, liposomes, solid lipid nanoparticles and polymeric nanoparticles for controlled, sustained and targeted drug delivery across various physiological drug barriers. However, nanocarriers itself act mainly by passive targeting and thus, to increase their specificity of action several approaches have been studied such as the attachment in the carrier surface of antibodies or their fragments and other molecules, which bind specifically to markers expressed in the diseased organ or tissue.

Considering the route of administration, oral route is preferable because it is noninvasive. However, this is a destructive route for many drugs, such as proteins and peptides, due to the acid condition of the stomach and first pass metabolism, leading to reduced bioavailability [1, 2]. Nonetheless, other alternative routes have been investigated, such as the mucosal delivery. In comparison with other routes, mucosal delivery serves as a more acceptable alternative route. Drugs absorbed through oral cavity, nasal cavity, lungs or genital tract overcome the first-pass metabolism, increasing bioavailability. Additionally, for *in loco* treatments, mucosal delivery is also safer and easier than the invasive administration [3]. Ocular administration of drugs remains also a challenging route due to their defense mechanisms, such as lacrimation and blinking. In this case, the use of colloidal carriers, namely, polymeric and lipid nanoparticles, is considered as a promising strategy for enhancing the bioavailability of ophthalmic drugs [4]. Regarding lung delivery, nanoparticles loaded with therapeutic agents administered via inhalation takes advantage of the ease and non-invasive nature of administration, the large alveolar surface area for rapid uptake, prolonged local action and a lower effective dose, resulting in lower risk of toxicity compared to systemic drug delivery [5, 6]. Drug delivery to the brain is a challenge due to the protective effects of blood-brain barrier. Nanotechnology has been used in order to find solutions to effectively deliver drugs to the brain [7]. Nasal mucosa has also been studied as an administration route for targeting the central nervous system, particularly, the brain.

Nanotechnological tools are able to safely replace the viral vectors by less immunogenic nanosized carriers [6]. Another broad application of nanotechnology is the delivery of antigens for vaccination [8].

Beyond the encapsulation of active pharmaceutical substances, imaging agents have been incorporated in these nanosystems. Sometimes, both imaging agent and drug are encapsulated in one nanocarrier to compile diagnosis and therapy, also called nanotheranostics, in the same drug delivery system. These nanotechnologies allow the development of personalized medicine [9].

Focusing the current knowledge, nanotechnology assumes an important place for therapeutics and diagnosis and shows a promising future. Some formulations based on nanocarriers are in the market, many others are in clinical trials and an intense research in this field has been performed in order to improve this systems.

The current status and future perspectives of nanotechnology in pharmaceutical development will be addressed in this special issue through different approaches.

NANOSCALE FORMULATIONS AND DIAGNOSTICS WITH THEIR RECENT TRENDS

At the beginning, Mukherjee *et al*. provides an overview about the application of nanotechnology in therapy and diagnosis [10]. Nanotechnology has been designed to overcome challenges due to the development and fabrication of nanostructures. This nanosized systems are able to carry and deliver active substances in a controlled and targeted way. Nanocarriers can be designed with dual purpose, allowing treatment and diagnosis. Thus, therapeutic index of many conventional free drugs are efficiently increased. In this revision, several recent developing and modifying nanoproducts for the detection, analysis, and treatment of diseases with their patents along with various diagnostics kits are discussed.

POLYMERIC NANOCARRIERS FOR DRUG DELIVERY

Nanotechnology offers suitable drug delivery systems for cancer treatment. Nanoparticles injected in the blood stream can selectively be accumulated in tumor due to the enhanced permeation and retention effect. Polymeric nanoparticles have been extensively studied, proving to be a very promising drug delivery system. Osteosarcoma is one of the most serious malignancies with great incidence in children and teenagers. Various polymeric nanoparticles have been developed to overcome the difficulties in drug delivery to osteosarcoma. Chen *et al*. present an overview about on the development of polymeric nanoparticles for anticancer drug delivery in osteosarcoma treatment and briefly describes challenges and opportunities for future [11].

LIPID-BASED NANOCARRIERS FOR MUCOSAL DRUG DELIVERY

Mucosal routes of drug delivery, which includes buccal, ocular, intranasal, pulmonary, rectal and vaginal, are considered as convenient and safe. However, the efficiency can be compromised by physiological mechanisms and by this way nanocarriers have attracted attention. Lipid-based nanocarriers attract much attention due to their great biocompatibility, cell membrane affinity and physicochemical properties. Additionally, modification strategies of this nanocarriers are widely investigated and show great improvement of drug bioavailability. Huang *et al*. performed a general review about the use of nanoparticles in mucosal delivery [12].

NANOPARTICLES IN OCULAR DRUG DELIVERY SYSTEMS

The conventional formulations for ocular application may have limited therapeutic efficacy due to the physiological mechanisms of cleaning, which reduces the contact time of drug with mucosa and prevents the penetration of drug through ocular tissues. Additionally, repeated administrations can lead to the appearance of side effects. In this review, Almeida *et al*. discuss some strategies, such as the use of polymeric and lipid nanoparticles to overcome the weaknesses of ocular conventional formulations [13]. In fact, this strategy have demonstrated an increase in residence time and ability to penetrate through ocular mucosa.

NOSE TO BRAIN DELIVERY: NEW TRENDS IN AMPHIPHILE-BASED "SOFT" NANOCARRIERS

The blood brain barrier can be the major obstacle for a conventional approach because it represents the only direct access to cell's brain. It is possible to reach the brain with alternative routes to intravenous administration, that however are invasive, risky, and expensive techniques requiring surgical expertise especially for multiple dosing regimens. Nasal mucosa is a potential route of administration for targeting the central nervous system, particularly, the brain. Colloidal carriers has become a revolutionary approach to enhance nose to brain delivery. In this paper Carafa *et al*. present vesicular carriers (liposomes and niosomes) and micelles in nose to brain delivery [14].

NANO-THERAPEUTICS FOR THE LUNG

Pulmonary drug delivery is often the route of choice for treatment of lung diseases. Inhalation of aerosolized compounds is a popular, non-invasive route for the targeted delivery of therapeutic molecules to the lung. However these drugs administered by pulmonary route through conventional aerosols are rapid cleared by the mucociliary system and alveolar macrophages. Nanocarriers assist in several aspects of pulmonary drug delivery: achieve therapeutic effects in lung at a lower drug dose, enhance delivery of hydrophobic molecules, protect against rapid degradation or immune inactivation and enhance nanoparticles internalization. Thus, Nguyen *et al*. made a revision about the state of the art of nanotechnology for pulmonary drug delivery and lung regeneration, as well as associated challenges, emerging advances and future perspectives [15].

BIOCOMPATIBLE MATERIALS CONSTITUTED MICRONEEDLE ARRAYS FOR VACCINATION

Nowadays most of the vaccines are inoculated through injection bearing intrinsic disadvantages, such as needing professionals, waste metal needle pollution and infection and low vaccination compliance. To overcome these drawbacks various microneedles have been developed and widely tried on delivering vaccines due to many prominent advantages. Biocompatible material-constituted microneedle arrays (bioMMAs) that are fabricated with biocompatible materials in the form of matrix or of formulated micro/nanoparticles, such as liposomes, PLA/PLGA/chitosan nanoparticles, hydrogels, polyelectrolyte multiplelayers (PEMs), plasmids, and nonvirulent pathogens, have proven an effective and stable vaccine adjuvant-delivery system. In this revision performed by Wang and Wang various types of bioMMAs used as a vaccine adjuvant-delivery system are introduced to show the update advancement and their diverse utilities and potential applications in the vaccine related field [16].

MAGNETIC RESONANCE NANO-THERANOSTICS FOR GLIOBLASTOMA MULTIFORME

Glioma represents a large category of brain tumors, and accounts for about 80% of malignant brain tumors. The most common and also most aggressive glioma is glioblastoma multiforme. Difficulties with early detection, post-surgical recurrences, and resistance to chemotherapy and/or radiotherapy are important reasons for the poor prognosis of glioblastoma multiforme. The development of nanocarriers for concomitant therapeutic and imaging applications has recently won considerable attention. This strategy potentially allows an approach that combines treatment and diagnosis in individual patients, which has been termed nanotheranostics. In this work Lin *et al*. revised recent research and progress in use magnetic resonance based nanotheranostics, more specifically, for glioblastoma multiforme diagnosis, therapy, targeting and improve drug delivery, as well as outstanding challenges [17].

ACKNOWLEDGEMENTS

The Executive Guest Editors would like to express their gratitude to authors for their interesting contributions and to reviewers for their useful comments and suggestions.

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