International Journal of Pharmaceutics 513 (2016) 191–210

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Review

Design, fabrication and biomedical applications of zein-based nano/micro-carrier systems

Zhang Yong[a,b,c,*], Cui Lili[d], Li Feng[a], Shi Nianqiu[b,e], Li Chunlei[c], Yu Xianghui[a,b], Chen Yan[a,b,*], Kong Wei[a,b]

[a] National Engineering Laboratory for AIDS Vaccine, School of Life Sciences, Jilin University, Changchun 130012, China
[b] Key Laboratory for Molecular Enzymology and Engineering, the Ministry of Education, School of Life Sciences, Jilin University, Changchun 130012, China
[c] State Key Laboratory of New Pharmaceutical Preparations and Excipients, Shijiazhuang 050051, China
[d] Pharmaceutical Biophysics Group, Institute of Pharmaceutical Science, King's College London, 150 Stamford Street, London SE1 9NH, United Kingdom
[e] Department of Pharmaceutics, School of Pharmacy, Jilin Medical University, Jilin 132013, China

ARTICLE INFO

Article history:
Received 11 July 2016
Received in revised form 5 September 2016
Accepted 7 September 2016
Available online 9 September 2016

Keywords:
Biopolymer
Nano/microparticle
Nanocapsule
Microcapsule
Delivery carrier

ABSTRACT

Nano/micro-carrier systems have shown promising application in the biomedical field as various delivery carriers. The composite material and fabrication method determine their microstructures, properties and thus their potential applications. Since approved as tablet coating material by the U.S. Food and Drug Administration (US-FDA), zein has been widely investigated as one of protein-based materials in the past few decades. Zein is renewable, biodegradable and relatively inexpensive in comparison with animal proteins (*e.g.*, gelatin and albumin). This paper reviews the current landscape of zein-based nano/micro-carrier systems, with particular emphasis on nano/microparticles, nano/microcapsules and their design, fabrication, assembly mechanisms and biomedical applications especially for controlled drug delivery. The benefits, challenges and related solutions of zein-based colloidal carrier systems are also discussed. In addition, investigations on the molecular structure, biocompatibility and immunogenicity of zein are summarized and discussed.

© 2016 Elsevier B.V. All rights reserved.

Contents

* Corresponding authors at: National Engineering Laboratory for AIDS Vaccine, School of Life Sciences, Jilin University, Changchun 130012, China.
E-mail addresses: zhangyongking1@gmail.com (Y. Zhang), chen_yan@jlu.edu.cn (Y. Chen).

http://dx.doi.org/10.1016/j.ijpharm.2016.09.023
0378-5173/© 2016 Elsevier B.V. All rights reserved.

1. Introduction

Nano/micro-carrier systems have great advantages over other carriers in terms of robustness, small size, large surface area, versatile surface modification, intracellular uptake and controlled release (Karthikeyan et al., 2012; Luo et al., 2013a; Penalva et al., 2015; Xu et al., 2015; Zou and Gu, 2013). For these reasons, they display great potential in delivering therapeutic agents into the systemic circulation *via* invasive/non-invasive routes. Some preparations in the form of microparticles have already been used in clinical practice and have shown great improvement in patient compliance without negative effects on medical efficacy. For example, triptorelin-loaded microspheres (Lundstrom et al., 2009) and exendin-4-loaded microspheres (Ryan et al., 2013) approved by the US-FDA in 2010 and 2012 for the treatment of advanced prostate cancer and type 2 diabetes, respectively, can dramatically reduce injection frequency *via* sustained drug release. The composition and microstructure of carrier systems usually have a great influence on the *in vivo* behavior of carriers and thus their therapeutic efficacy. Various natural and synthetic polymers (*e.g.*, chitosan, albumin, collagen and poly(lactic-*co*-glycolic acid) (PLGA)) have been investigated to illustrate their potential as nano/micro-carrier systems (Kratz, 2014; Masotti and Ortaggi, 2009; Mora-Huertas et al., 2010). Recently, plant-based proteins have emerged as novel biomaterials with the potential of drug and gene delivery (Reddy and Yang, 2011). Plant-based proteins are easily available and biodegradable. Many of them, such as zein, soybean and wheat proteins, have been consumed as an integral part of human diet.

Zein was approved in 1985 by the US-FDA as a generally recognized as safe excipient for tablet and pellet coating (Anonymous, 1985). Zein is a family of alcohol-soluble prolamins isolated from corn (Gorham, 1821). According to solubility and sequence similarity, it is divided into 4 groups: α-zein (19 and 22 kDa), β-zein (14 kDa), γ-zein (16 and 27 kDa), δ-zein (10 kDa) (Esen, 1987; Thompson and Larkins, 1989). It should be noted, however, that these zein proteins may have different molecular weights when different extraction methods are used. Among these 4 types, α-zein and γ-zein, respectively, comprise about 80% and 15% of the total fraction of zein mass (Wilson, 1991). Zein primarily consists of hydrophobic and neutral amino acids but also contains some polar amino acid residues (*e.g.*, glutamine) (Coleman and Larkins, 1999). Thus, zein is soluble only in limited solvents such as aqueous alcohols and alkaline solution (John, 2002). Commercially available zein may contain fewer xanthophyll pigments, which therefore leads to its yellow color (Kale et al., 2007; Moros et al., 2002). Details of the amino acid composition, extraction and purification methods and physicochemical properties of zein can be found in other publications (John, 2002; Rishi and Munir, 2001).

Over the past few decades, zein has been investigated as various carriers, such as nano/microparticles, nano/microcapsules, films, nanofibers, hydrogel and implants, for delivery of bioactive agents (Corradini et al., 2014; Paliwal and Palakurthi, 2014; Zhang et al., 2015a,b). This paper focuses on the current landscape of zein-based colloidal nano/micro-carrier systems with emphasis on their design, preparation, assembly mechanisms and biomedical applications. Moreover, the benefits, limitations and related solutions in both fabrication and applications are also discussed. Investigations on the molecular structure, biocompatibility and immunogenicity of zein are also reviewed and discussed.

2. Fundamental aspects of zein

2.1. Structure

The structure of zein is closely related to its physicochemical properties and the self-assembly mechanism of various zein-based colloidal carrier systems. Structural studies on zein have mainly focused on α-zein and γ-zein, probably due to their high fractions in total zein mass. The primary and secondary structures of α-zein and γ-zein can be easily determined by various techniques (*e.g.*, chromatography, circular dichroism, fourier transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR)). α-zein is reported to have a high α-helix content of 35–60%, which is varied with a number of factors such as temperature, pH and solvent compositions (Cabra et al., 2006; Forato et al., 2003). γ-zein contains 33% α-helix and 31% β-sheet in its physiological states (Bicudo et al., 2005). However, in the presence of reducing agent dithiothreitol, γ-zein displays an increased α-helix content of about 55% accompanied by a decrease in β-sheet content to 6% (Bicudo et al., 2008, 2005). Similar to α-zein, the secondary structure of γ-zein is also solvent dependent (Bicudo et al., 2008). Of note, the N-terminal part of γ-zein contains eight proline-rich repetitive sequences of PPPVHL, which can form an extended left-handed amphipathic helix (polyproline II conformation). This proline-rich hexapeptide is a type of cell-penetrating peptides, which could be used as a carrier to improve the cellular uptake of drugs and genes (Fernandez-Carneado et al., 2004).

Several models for the tertiary structure of α-zein have been suggested. The first one is based on the repeat sequence units and α-helix content analysis of zein in methanol (Fig. 1a) (Argos et al., 1982). In this model, 9 adjacent and antiparallel helices formed a cylindrical surface capped by glutamine residues. This structure was stabilized by both van der Waals forces and intramolecular

Download English Version:

https://daneshyari.com/en/article/6481856

Download Persian Version:

https://daneshyari.com/article/6481856

Daneshyari.com