Contents lists available at ScienceDirect

Chemical Engineering Research and Design

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

Design and characterization of prednisolone-loaded nanoparticles fabricated by electrohydrodynamic atomization technique

Kampanart Huanbutta[a,*], *Tanikan Sangnim*[b,c], *Sontaya Limmatvapirat*[b,c], *Jurairat Nunthanid*[b,c], *Pornsak Sriamornsak*[b,c]

[a] *Faculty of Pharmaceutical Sciences, Burapha University, Chonburi 20131, Thailand*
[b] *Department of Pharmaceutical Technology, Faculty of Pharmacy, Silpakorn University, Nakhon Pathom 73000, Thailand*
[c] *Pharmaceutical Biopolymer Group (PBiG), Faculty of Pharmacy, Silpakorn University, Nakhon Pathom 73000, Thailand*

ARTICLE INFO

Article history:
Received 16 October 2015
Received in revised form 16 February 2016
Accepted 3 March 2016
Available online 9 March 2016

Keywords:
Electrohydrodynamic atomization
Nanoparticles
Prednisolone

ABSTRACT

Nanoparticles (NPs) have been used for colon-specific drug delivery system due to their specific accumulation in the inflamed tissue in the colon and prolong presence in colon for the treatment of inflammatory bowel disease. The present study aimed to design NPs for colon-specific drug delivery *via* electrohydrodynamic atomization (EHDA). The NPs were prepared by dissolving prednisolone and Eudragit® S100 (EDS) in different solvents using various EDS concentrations and prednisolone/EDS weight ratios. Then, the prepared solution was sprayed using the EHDA machine. The process parameters such as applied voltage, injected distance, feed rate, and drum collector rolling rate were carefully adjusted to obtain blank and drug-loaded NPs. The EDS solution prepared from methanol offered high conductivity (93.51 μs) with low viscosity (4.48 cP), resulting in spherical and small NPs with average diameter of 422 nm. The NPs prepared by using isopropanol and butanol as a solvent were irregular in shape. The sprayed products were changed from particle to fiber when using high concentration of EDS. High-fiber product was obtained when high applied voltage (20 kV) was applied. Size range of the NPs loaded with prednisolone at different concentrations (0.5–3.5%) was 448–660 nm. The maximum drug encapsulation was 91.50%. From the obtained results, the NPs were successfully fabricated by EHDA technique and this showed a promising potential for further drug delivery system development.

1. Introduction

Electrohydrodynamic atomization (EHDA) has gained attention in the field of drug delivery in the past decade; it has been used to fabricate drug carriers including polymeric microparticles, nanoparticles (NPs) and nanofibers used in various pharmaceutical applications (Kenawy et al., 2002; Shen et al., 2011). Theoretically, EHDA is a process where a liquid breaks up into spray droplets under the drive of an electrical field. Various modes of EHDA were reported, of which the stable cone-jet is of specific interest (Xie et al., 2014). Under such mode, liquid flowing through a nozzle maintained at high potential is subjected to an electric field (Fig. 1), which leads to elongation of the meniscus to a form of jet and subsequently the jet deforms and breaks up into fine droplets. The small jet diameter allows rapid evaporation of the solvent and, as a

* *Corresponding author*. Tel.: +66 38102610; fax: +66 38102610.
E-mail address: kampanart@buu.ac.th (K. Huanbutta).
http://dx.doi.org/10.1016/j.cherd.2016.03.004

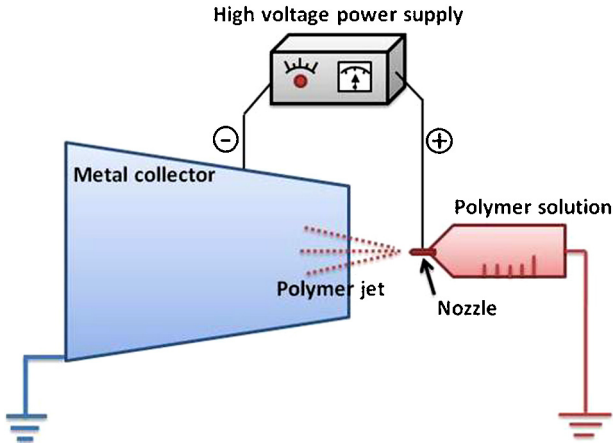

Fig. 1 – Schematic diagram showing nanoparticles fabrication by EHDA.

result, particles are deposited on the collector. Applied voltage, feed rate, distance from the nozzle to collector, drum collector rolling rate, charge and viscosity of sprayed solution are vital parameters to determine product characteristics (Xie et al., 2014). The principal advantages of this technique in drug delivery system are (i) to offer opportunity of heat sensitive drug loading, (ii) the relative rapid and simple way to prepare a several materials into NPs, and (iii) controllable operation factors.

Inflammatory bowel diseases (IBD) are relapsing and chronic inflammatory disorders of the intestinal mucosa, with an organ-susceptibility for the colon (Mowat et al., 2011). Conventional drug delivery systems are not completely successful when applied for the treatment of IBD (Friend, 2005). Aside from incidences where therapy fails due to insufficient drug deposition at the site of action, adverse drug effects have also limited therapeutic outcome. These adverse effects are thought to be related to the lack of selective drug release at the inflamed colon. Nanoparticulate systems for colonic drug delivery exhibit that size-dependency of particles impacts their epithelial uptake and a preferential accumulation in the inflamed colon has been found (Lamprecht, 2009). Lamprecht et al. (2001) demonstrated that high binding to the inflamed tissue of Lewis rat colon was found for 100-nm particles. This is because thicker mucus layer produced in the ulcerated regions increasing adherence of the small particles.

Prednisolone is a synthetic corticosteroid drug that is particularly effective as immunosuppressant and anti-inflammatory drug. It has been used to treat a number of different conditions such as IBD, inflammation (swelling), severe allergies, adrenal problems, arthritis and asthma (Gionchetti et al., 2002; Porter, 2011). For treatment of IBD, administration of prednisolone at a large and frequent dose for a long period causes significant and prolonged absorption of the drugs from the small intestine, often leading to toxic side effects (Campieri et al., 1997). Therefore, the specific delivery of drugs to diseased parts should be developed. Furthermore, prednisolone is a class II substance according to the Biopharmaceutics Classification System; it is a poorly water-soluble drug (Vogt et al., 2007). Consequently, the improvement of the dissolution rate of prednisolone by different techniques such as solid dispersion, nanoparticle preparation and liquisolid compacts can offer more rapid and complete absorption (Chen et al., 2015; Spireas and Sadu, 1998; Zakeri-Milani et al., 2011).

To extensively target drug to the colon, nanocarriers made of pH-dependent polymer have been applied. In the gastrointestinal tract, from the stomach to the colon, intraluminal pH varies progressively up to 7. In order to obtain pH-sensitive NPs, Eudragit® S, a polymer of methacrylic acid and methyl methacrylate, which dissolves when the pH is above 7, was used to control the release of entrapped drug (Damge et al., 2010; Makhlof et al., 2009). Therefore, the aim of this study was to design and optimize formulation and processing factors influencing the characteristics of NPs prepared by EHDA technique.

2. Materials and methods

2.1. Materials

Eudragit® S100 (EDS) (lot number B041005026) was a gift from Evonik Degussa (Thailand) Co., Ltd., Thailand. Methanol (lot number 14080041) was purchased from RCI Labscan Ltd., Thailand. Ethanol (lot number J32T04) was obtained from Mallinckrodt Baker, Malaysia. Butanol (lot number K35977190619) was purchased from Merck, Germany. Isopropanol (lot number V1A707131A) was received from Carlo Erba Reagents, France. Prednisolone (lot number R25301) was a gift from Bangkok Lab & Cosmetic Co., Ltd., Thailand. All other chemicals were of reagent grade and used without further purification.

2.2. Characterization of EDS solution

The prepared EDS solutions were characterized by several techniques to reveal the effect of the polymer solution properties on the NPs. The conductivity of each EDS solution was measured by conductivity meter (model ECtestr11+, Eutech Instruments Pte Ltd., Singapore). The viscosity was examined by viscometer (model DV-III Ultra, Brookfield, USA). The surface tension was measured by sessile drop method using a drop shape instrument (model FTA 1000, First Ten Angstroms, USA). All experiments were performed in triplicate.

2.3. Preparation of NPs

To prepare the blank NPs, various concentrations of EDS were dissolved in several solvents, including methanol, ethanol, isopropanol, butanol and mixtures of ethanol/water. The EDS solution was then sprayed using EHDA machine (Bangkok Cryptography, Thailand). For the drug-loaded NPs, prednisolone was dissolved in the EDS solution before spraying. The drug:EDS weight ratios were varied at 0.5:5, 1.5:5, 2.5:5 and 3.5:5. As presented in Table 1, the processing parameters such as applied voltage, injected distance, feed rate, and drum collector rolling rate were carefully adjusted to obtain blank

Table 1 – Conductivity, viscosity and interfacial tension of 5% (w/v) EDS in different solvents.

Solvent	Conductivity (μS)	Viscosity (cP)	Interfacial tension (mN/m)
Methanol	93.51 ± 2.56	4.48 ± 1.10	22.82 ± 0.35
Ethanol	31.64 ± 0.74	5.76 ± 0.37	21.71 ± 0.19
2-Propanol	9.13 ± 0.09	10.88 ± 0.37	20.46 ± 0.25
t-Butanol	N/A[a]	N/A[a]	N/A[a]

[a] EDS did not completely dissolve in t-butanol.