European Journal of Pharmaceutics and Biopharmaceutics 163 (2021) 23–37

Contents lists available at ScienceDirect

European Journal of Pharmaceutics and Biopharmaceutics

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

Microparticle encapsulation of a tuberculosis subunit vaccine candidate containing a nanoemulsion adjuvant via spray drying

Mellissa Gomez [a], Michelle Archer [b], David Barona [a], Hui Wang [a], Mani Ordoubadi [a], Shabab Bin Karim [a], Nicholas B. Carrigy [a], Zheng Wang [a], Joseph McCollum [b], Chris Press [b], Alana Gerhardt [b], Christopher B. Fox [b,c], Ryan M. Kramer [b], Reinhard Vehring [a,*]

[a] Department of Mechanical Engineering, University of Alberta, Edmonton, AB, Canada
[b] Infectious Disease Research Institute, Seattle, WA, USA
[c] Department of Global Health, University of Washington, Seattle, WA, USA

ARTICLE INFO

Keywords:
Nano-encapsulation
Physical stability
Gel microparticles
Vaccine spray drying
Adjuvant emulsion

ABSTRACT

Spray drying is a technique that can be used to stabilize biopharmaceuticals, such as vaccines, within dry particles. Compared to liquid pharmaceutical products, dry powder has the potential to reduce costs associated with refrigerated storage and transportation. In this study, spray drying was investigated for processing an adjuvanted tuberculosis subunit vaccine, formulated as an oil-in-water nanoemulsion, into a dry powder composed of microparticles. Applying *in-silico* approaches to the development of formulation and processing conditions, successful encapsulation of the adjuvanted vaccine within amorphous microparticles was achieved in only one iteration, with high retention (>90%) of both the antigen and adjuvant system. Moisture-controlled stability studies on the powder were conducted over 26 months at temperatures up to 40 °C. Results showed that the powder was physically stable after 26 months of storage for all tested temperatures. Adjuvant system integrity was maintained at temperatures up to 25 °C after 26 months and after one month of storage at 40 °C. The spray-dried product demonstrated improved antigen thermostability when stored above refrigerated temperatures as compared to the liquid product. These results demonstrate the feasibility of spray drying as a method of encapsulating and stabilizing an adjuvanted vaccine.

1. Introduction

An important aspect of disease control is intervention by inducing widespread protective immunity through vaccination. Liquid pharmaceutical formulations, such as vaccines, usually must be kept refrigerated during transportation and storage in order to maintain their potency. Widespread global immunization is limited because vaccines often require refrigeration to remain effective [1]. Exposure to higher temperatures can lead to loss of potency of the active pharmaceutical ingredient and the possible formation of unsafe byproducts. Eliminating the refrigeration requirement would facilitate greater global distribution through cost reduction of storage and transportation. This would be especially beneficial towards interventions for diseases that are prevalent in population-dense locations that lack the required infrastructure to maintain refrigeration. Thermostability can be improved by converting a liquid product into a solid dosage form that can be rehydrated for administration as needed. Desiccation processing methods, such as spray drying, have been widely used in the food processing, chemical, and pharmaceutical industries to preserve temperature-sensitive components [2]. Spray drying produces a dry powder made up of microparticles through the drying of atomized droplets via a drying gas. Once the solvent has evaporated, the dried particles are separated from the drying gas, e.g. via a cyclone.

Thermostability of vaccines can be improved by stabilization via spray drying. Experimental dry powder vaccines have been developed for the intervention of measles [3], influenza [4–7], anthrax [8], herpes [9], whooping cough [10], and tuberculosis [11,12]. The immunogenicity of spray-dried vaccines can be maintained provided an appropriate stabilizing excipient(s) and drying conditions are used. Successfully stabilized dry powder vaccines have been reported to elicit similar immunogenicity profiles as their liquid counterparts after reconstitution when administered in animal models [3,4,7,10]. Ideally,

* Corresponding author at: University of Alberta, 116 St & 85 Ave, Edmonton Canada.
E-mail address: reinhard.vehring@ualberta.ca (R. Vehring).

https://doi.org/10.1016/j.ejpb.2021.03.007
Received 8 September 2020; Received in revised form 10 March 2021; Accepted 13 March 2021
Available online 19 March 2021