



Investigation Of Quil-a Release From Cubosomes Using A Photonic Crystal Slab Sensor

Nielsen, Line Hagner; Sørensen, Kristian Tølbøl; Crosio, Marco ; von Halling Laier, Christoffer; Boisen, Anja; Kristensen, Anders

Publication date:
2018

Document Version
Peer reviewed version

[Link back to DTU Orbit](#)

Citation (APA):
Nielsen, L. H., Sørensen, K. T., Crosio, M., von Halling Laier, C., Boisen, A., & Kristensen, A. (2018). *Investigation Of Quil-a Release From Cubosomes Using A Photonic Crystal Slab Sensor*. Abstract from Controlled Release Society Annual Meeting & Exposition 2018, New York, New York, United States.

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Investigation of Quil-A release from cubosomes using a photonic crystal slab sensor

Line Hagner Nielsen, Kristian Tølbøl Sørensen, Marco Crosio, Christoffer von Halling Laier, Anja Boisen, Anders Kristensen

Department of Micro and Nanotechnology, Technical University of Denmark, Kgs. Lyngby, Denmark

Learning objectives:

1. Explain the idea behind a photonic crystal slab (PCS) sensor
2. Describe the value of being able to measure co-release of an antigen and adjuvant from vaccine formulations
3. Discuss pros and cons of this obtained release profile of Quil-A from the cubosomes

INTRODUCTION:

Now-a-days, in vaccine delivery, subunit antigens are often utilized due to safety reasons¹. These subunit antigens are not that strong immunogenically and therefore, it is necessary to deliver them together with an adjuvant, and often also a particulate system¹. One of the common adjuvants investigated is Quil-A which is a heterogeneous mixture of triterpenoid saponins². There is an increasing focus on the importance of obtaining co-delivery (and thereby co-release) of the antigen and adjuvant for an optimal immune response³, and therefore, investigation of the release of the adjuvant is important. The aim of this study was to investigate the release of Quil-A from cubosomes by monitoring the resonance wavelength shift of a photonic crystal slab (PCS) sensor (Fig. 1).

METHODS:

The cubosomes were prepared by dissolving the glycerol monooleate Dimodan® in ethanol (5.33 w/v%) and mixing it with an aqueous solution of dextran (stabilizer) and Quil-A (2.63 and 0.035 mg/mL, respectively). Subsequently, the solution was spray dried on a Büchi mini spray dryer. The size of the particles in aqueous suspension was measured by dynamic light scattering. Polymeric PCS sensors were fabricated defining a 100 nm grating of period 368 nm into a low-refractive index (RI) polymer, coated by a 300 nm thin high-RI polymer. In order to separate released compounds (dextran and Quil-A) from the cubosomes, a nanoporous membrane filter (pore size of 30 nm) was integrated into a custom fluid well, made from CO₂-laser cut poly(methyl methacrylate) (PMMA) and adhesion-bonded onto the sensor. To relate resonance wavelength shift with Quil-A concentration, a standard curve was created in milli-Q water in the range of 50-800 µg/mL. Subsequently, cubosome powder with Quil-A was placed on the filter on top of the PCS sensor and 15 µL of milliQ water was added to determine the release of Quil-A over time.

RESULTS:

The powder of cubosomes was produced and when re-dispersing the particles in aqueous solution, cubosomes with a size of 257±8 nm was formed. The standard curve of Quil-A was found to be linear in the range from 50-800 µg/mL. Subsequently, it was found that 87.2±1.1 % of Quil-A was released from the cubosomes within the time range of 30 min (Fig. 2).

CONCLUSIONS:

We have shown that a PCS sensor can detect Quil-A release from particulates in a fast and reproducible manner.

ACKNOWLEDGEMENTS:

The authors would like to acknowledge the Danish National Research Foundation (DNRF122), Villum Fonden (Grant No. 9301) for Intelligent Drug Delivery and Sensing Using Microcontainers and Nanomechanics (IDUN), and Innovation Fund Denmark (POLYNANO – Strategic Research Center in Precision and Nano-Scale Polymer Mass Fabrication, Grant No. 10-092322).

REFERENCES:

1. Foged, C. Subunit Vaccines of the Future: The Need for Safe, Customized and Optimized Particulate Delivery Systems. *Ther. Deliv.* 2011, 2(8):1057–77.
2. Kersten GF, Teerlink T, Derks HJ, Verkleij AJ, van Wezel TL, Crommelin DJ, Beuvery EC. Incorporation of the major outer membrane protein of *Neisseria gonorrhoeae* in saponin-lipid complexes (iscoms): chemical analysis, some structural features, and comparison of their immunogenicity with three other antigen delivery systems. *Infect Immun.* 1988, 56(2):432-38.
3. Kapadia CH, Tian S, Perry JL, Sailer D, Luft CJ, DeSimone JM. Extending antigen release from particulate vaccines results in enhanced antitumor immune response. *J Control Release.* 2018, 269: 393-404.
4. Hermansson PG, Sørensen KT, Vannahme C, Smith CL, Klein JJ, Russev MM, Grützner G, Kristensen A. All-polymer photonic crystal slab sensor. *Opt. Express.* 2015, 23:16529–39.

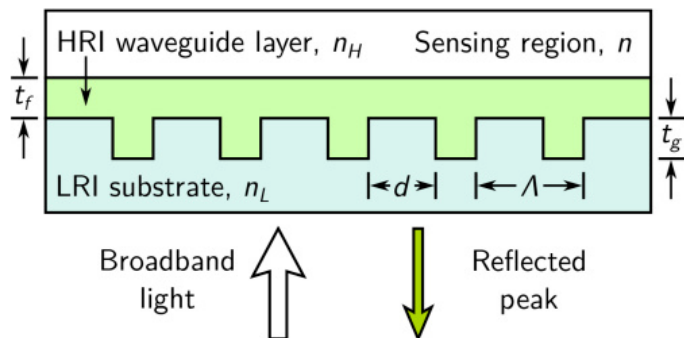


Fig. 1: Schematic illustration of photonic crystal slab (PCS) sensor⁴.

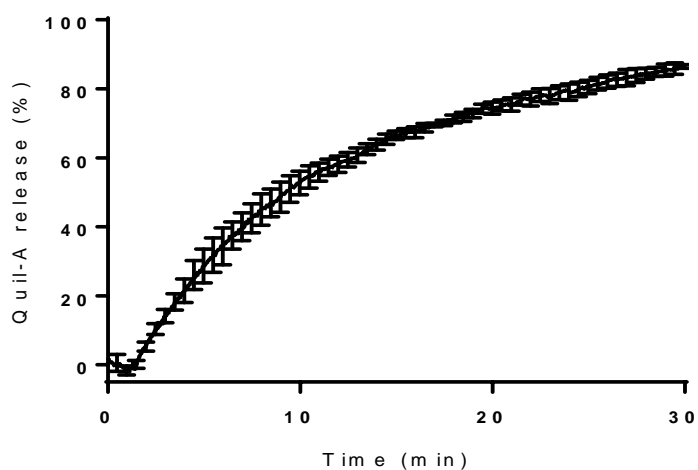


Fig. 2: Release curve of Quil-A from the cubosomes in milli-Q water measured using a PCS sensor. The curve is representing mean \pm SD in triplicates.