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

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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 reasons[1]. 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 system[1]. One of the common adjuvants investigated is Quil-A which is a heterogeneous mixture of triterpenoid saponins[2]. 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 response[3], 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 CO_2-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.

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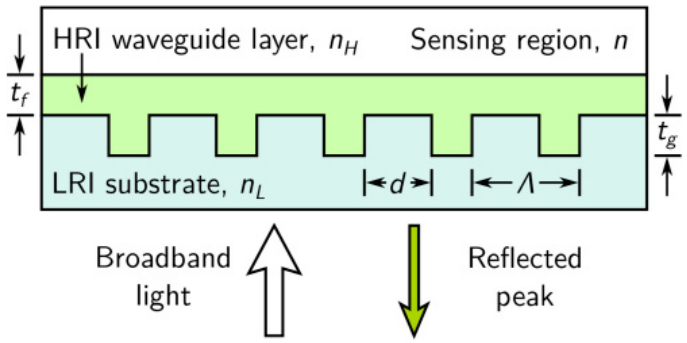

Fig. 1: Schematic illustration of photonic crystal slab (PCS) sensor[4].

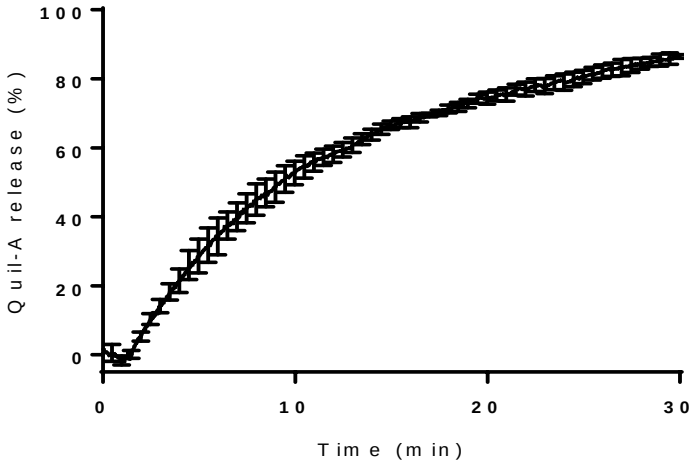

Fig. 2: Release curve of Quil-A from the cubosomes in milli-Q water measured using a PCS sensor. The curve is representing mean±SD in triplicates.