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

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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. 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. One of the common adjuvants investigated is Quil-A which is a heterogeneous mixture of triterpenoid saponins. 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, 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.
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REFERENCES:

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