Mesoporous Silica and Aluminosilicate Particles as Novel Vaccine Adjuvants for a Recombinant Hepatitis B Surface Antigen (rHBsAg) Vaccine

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Purpose
Mesoporous silica particles are of interest as novel adjuvants. SBA-15 has been reported to enhance the immune response in mice. Our study investigates two other types of mesoporous silica particles: MCM-41 and MSU-F. MCM-41 and MSU-F have significantly different physical characteristics in regards to framework structure, pore size and pore volume. To our knowledge MCM-41 and MSU-F have not been investigated as immunomodulators.

Methods
Silica and aluminosilicate mesoporous particles (MCM-41 and Al-MCM-41) and (MSU-F and Al-MSU-F) were purchased. The vaccine antigen was rHBsAg. Vaccines were prepared by rotisserie mixing rHBsAg with the respective adjuvants for 24 hours at 4°C. Adsorption was assessed by micro BCA assay. Adjuvant particles and vaccines were characterized for particle size distribution (PSD) and charge. HBsAg tertiary structure, in solution and adsorbed, was monitored by intrinsic fluorescence spectroscopy. The vaccines were injected intramuscularly into groups of five female BALB/c mice (age: 5 weeks). Anti-HBsAg IgG antibody concentrations were assessed by ELISA. Soluble rHBsAg and a vaccine with Alhydrogel™ served as controls. PSDs were compared using two-way ANOVA. One-way ANOVAs were used for all other statistical analyses.

Results
For all mesoporous silica and aluminosilicate particles, 24 hours of mixing resulted in stable PSDs for up to 2 weeks, with >96% of the particles under 2.0µm. Zeta potential indicated the particles were negatively charged and statistically similar. Following formulation with antigen, the PSDs were unchanged, and the particles remained negatively charged. In all vaccines, unadsorbed rHBsAg was below the limit of detection (LOD). There was no detectable change in the tryptophan environment of rHBsAg in the adsorbed state compared to the solution state. At day 14, all silica and aluminosilicate groups had at least one mouse with an anti-rHBsAg IgG concentration below the LOD: all mice with MSU-F were below. Aluminosilicate responders were not statistically different from mice that received the vaccine containing Alhydrogel™ at day 14.

Conclusion
Mesoporous silica and aluminosilicate particles did not perform equally with respect to immunomodulation. (Financial support: PhRMA Pharmaceuticals Pre-doctoral Fellowship, TC)