Abstract Submitted
for the MAR12 Meeting of
The American Physical Society

Aggregation behavior of bovine and porcine insulin in presence of inhibitors KIERSTEN BATZLI, BRIAN LOVE, University of Michigan — Insulin aggregation can be problematic when the insulin is in pharmaceutical solution, as well as when aggregates form in insulin pumps or subcutaneously at port sites. Pharmaceutical insulins often include an added stabilizer, such as metacresol, but even with this added compound the protein may degrade, aggregate and become less effective. With greater understanding of the kinetics of aggregation associated with insulin aggregation, a more effective stabilizer may be identified to inhibit aggregation. Bovine and porcine insulin in pharmaceutically relevant concentrations of 5 mg/ml were induced to denature and aggregate at elevated temperature and low pH and the aggregation behavior was characterized as a function of time and temperature by rheology and small angle x-ray scattering (SAXS). Aggregation behavior was probed in both neat solution and with the addition of known inhibiting compounds. The efficacy of the inhibiting compounds at retarding the protein aggregation was found to be related to the hydrophobicity of the compounds and potential inhibitors of interest were identified.

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Date submitted: 11 Nov 2011 Electronic form version 1.4