



Preparation of Heat-Denatured Macroaggregated Albumin for Biomedical Applications using a Microfluidics Platform

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Albumin is widely used to improve the efficacy, decrease the toxicity, or alter the pharmacokinetic profile of active compounds. Macroaggregated albumin (MAA) is a common albumin microparticle, which is predominately used for lung perfusion imaging when labeled with the radionuclide ^{99m}Tc . These microparticles are formed by heat denaturing albumin in bulk solution; as a result, there is limited control over the size of the particles formed. In this work, we developed an integrated microfluidics platform to create more tunable and precise MAA particles, so-called microfluidic-MAA (M2A2). Prepared using off-stoichiometry thiol-ene chemistry, these chips consist of a flow focusing region followed by an extended and water heated curing channel (85°C). M2A2 particles with diameters between 70 and 300 μm with coefficients of variation between 10-20% were reliably prepared by adjusting the flow rates of the dispersed and continuous phases. To demonstrate a biomedical application of M2A2, particles were labeled with ^{111}In and their distribution was assessed in healthy mice using nuclear imaging. ^{111}In -M2A2 behaved similarly to ^{99m}Tc -MAA; lung uptake was seen early on, and the particles were cleared over time by the renal and reticuloendothelial systems. M2A2 represents an elegant and controllable method to prepare albumin microparticles, and it demonstrates one of many diverse applications for microfluidics in the world of pharmaceutical sciences.