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Echogenic liposomes for image-guided drug delivery

Christy Holland[a] and David McPherson[b]
[a]University of Cincinnati, Biomedical Engineering, MSB, 231 Albert Sabin Way, Cincinnati, OH 45267-0586, USA
[b]University of Texas Health Science Center, 6431 Fannin St., MSB 1.252, Houston, TX 77030, USA

Echogenic liposomes (ELIP) are under development to enable ultrasound-controlled drug delivery. Ultrasound-triggered release of hydrophilic and lipophilic agents was assessed from circulating ELIP in vitro using color Doppler ultrasound (6 MHz). Calcein, or recombinant tissue plasminogen activator (rt-PA), both hydrophilic agents, or papaverine, a lipophilic agent, were each loaded into ELIP and diluted in 0.5% bovine serum albumin. Ultrasound-triggered release of calcein, rt-PA or papaverine from ELIP was determined relative to detergent and untreated controls. Calcein concentration was measured by fluorimetry and release of rt-PA was assayed with a chromogenic substrate and a spectrophotometric method. Papaverine concentration was quantified by absorbance spectrophotometry and the amount of papaverine associated with P-ELIP was determined using a spin column filtration technique. Dynamic changes in echogenicity were assessed with low output B-mode ultrasound (0.04 MI) as mean digital intensity. Treatment with color Doppler ultrasound resulted in a statistically significant amount of calcein and rt-PA release from liposomes ($p < 0.01$), but did not induce papaverine release ($p > 0.05$). The differential efficiency of ultrasound-mediated pharmaceutical release from ELIP for water-soluble and lipid-soluble compounds suggests that water-soluble drugs are better candidates for the design and development of ultrasound-controlled drug delivery systems.