Design, Characterization, and Transport of Coumarin-6-Loaded Nanoparticles across a Human Placental In Vitro Model
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Purpose
The objective of these experiments was to design and characterize coumarin-6-loaded polymeric nanoparticles (NPs) and study the effect of polymer type, polymer concentration, and the presence of surfactants on particle size, zeta potential, and the transport of the nanoparticles across an in vitro model of human placental trophoblast cells (the BeWo b30 cell line).

Methods
Coumarin-6-loaded NPs were prepared by a modified solvent displacement method. Coumarin-6 (0.1-0.3% (w/w)) and 20-40 mg of a polymer (50:50 poly(D,L-lactide-co-glycolide (PLGA), Resomer® RGP d5055, or Resomer® RGP d50105) were dissolved in acetone prior to nanoprecipitation in purified water. For those nanoparticles prepared in the presence of surfactant, either 0.125% Lutrol® F68 (LUT) or 0.03% α-tocopherol polyethylene glycol-1000-succinate (TPGS) was dissolved in water prior to nanoprecipitation. Nanoparticles were characterized with regard to particle size, particle distribution, and surface charge by dynamic light scattering and laser Doppler velocimetry. Human placental trophoblast cells were cultured as monolayers on Transwell® plates, and nanoparticle solutions were added to the apical side of the cells at time zero in order to determine the maternal-to-fetal apparent permeability (Pe) of the nanoparticles.

Results
Z-average particle size ranged from 145 to 196 nm. Zeta potential values were between -47 and -32 mV. Polydisperisty index values were less than 0.35. The transport of the coumarin-6-loaded NPs across BeWo cell monolayers depended on particle size as well as the presence and type of surfactant. The Pe values for NP transport ranged from $8.0 \times 10^{-7}$ cm/s to $6.3 \times 10^{-6}$ cm/s. The lowest permeability was observed for PLGA NPs prepared with Lutrol F68, and the highest Pe was observed for PLGA NPs without surfactant.

Conclusion
These in vitro results suggest the transplacental transport of polymeric nanoparticles. Nanoparticle size and the transport of NPs across human placental BeWo cells were dependent on polymer concentration, the presence of surfactant in the formulation, and the type of surfactant.

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