Well-defined, size-tunable, multifunctional micelles for efficient paclitaxel delivery for cancer treatment.

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Public Summary:
We have developed a well-defined and biocompatible amphiphilic telodendrimer system (PEG-b-dendritic oligocholic acid) which can self-assemble into multifunctional micelles in aqueous solution for efficient delivery of hydrophobic drugs such as paclitaxel. In this telodendrimer system, cholic acid is essential for the formation of stable micelles with high drug loading capacity, owing to its facial amphiphilicity. A series of telodendrimers with variable length of PEG chain and number of cholic acid in the dendritic blocks were synthesized. The structure and molecular weight of each of these telodendrimers were characterized, and their critical micellization concentration (CMC), drug-loading properties, particle sizes, and cytotoxicity were examined and evaluated for further optimization for anticancer drug delivery. The sizes of the micelles, with and without paclitaxel loading, could be tuned from 11.5 to 21 nm and from 15 to 141 nm, respectively. Optical imaging studies in xenograft models demonstrated preferential uptake of the smaller paclitaxel-loaded micelles (17-60 nm) by the tumor and the larger micelles (150 nm) by the liver and lung. The toxicity and antitumor efficacy profiles of these paclitaxelloaded micelles in xenograft models were found to be superior to those of Taxol and Abraxane.

Scientific Abstract:
We have developed a well-defined and biocompatible amphiphilic telodendrimer system (PEG-b-dendritic oligo-cholic acid) which can self-assemble into multifunctional micelles in aqueous solution for efficient delivery of hydrophobic drugs such as paclitaxel. In this telodendrimer system, cholic acid is essential for the formation of stable micelles with high drug loading capacity, owing to its facial amphiphilicity. A series of telodendrimers with variable length of PEG chain and number of cholic acid in the dendritic blocks were synthesized. The structure and molecular weight of each of these telodendrimers were characterized, and their critical micellization concentration (CMC), drug-loading properties, particle sizes, and cytotoxicity were examined and evaluated for further optimization for anticancer drug delivery. The sizes of the micelles, with and without paclitaxel loading, could be tuned from 11.5 to 21 nm and from 15 to 141 nm, respectively. Optical imaging studies in xenograft models demonstrated preferential uptake of the smaller paclitaxel-loaded micelles (17-60 nm) by the tumor and the larger micelles (150 nm) by the liver and lung. The toxicity and antitumor efficacy profiles of these paclitaxel-loaded micelles in xenograft models were found to be superior to those of Taxol and Abraxane.