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The antiangiogenic effect of dual-drug loaded polymeric micelles

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Purpose: To evaluate the antiangiogenic effect of individual and mixed paclitaxel (PTX) and rapamycin (RAP) micelles *in vitro*.

Methods: RAP or PTX were conjugated to poly (ethyleneglycol)-*block*-poly(aspartate-hydrazide) to form PEG-RAP and PEG-PTX and characterized by NMR and GPC. Drug conjugates were assembled into individual and mixed micelles. Physically loaded RAP and PTX micelles were also formed. PTX was loaded into PEG2000-*b*-PLA1800 while RAP or PTX: RAP (1:1) was loaded into PEG4000-b-PLA2000. Micelle size was characterized by DLS and loading by RP-HPLC. The antiangiogenic effect of individual and mixed micelles was evaluated in *invitro* Human Umbilical Vein Endothelial Cells (HUVEC) through proliferation, tube formation and migration assays.

Results: PEG-RAP and PEG-PTX were synthesized and characterized by GPC and NMR with individual and mixed micelle sizes between 40-100nm. PEG-RAP and PEG-PTX individual micelles IC50s were 12 nM and 2 nM respectively. Mixed micelles showed synergistic effect in inhibiting the HUVEC cell proliferation. Individual and mixed micelles inhibited HUVEC tube formation and migration with the mixed micelles showing a synergistic effect. Physically loaded PTX and RAP micelles were sized at 36.5 and 33.6 nm respectively. PTX and RAP individual micelles had IC50s of 6.3 nM and 14,051 nM respectively. A synergistic response was observed with PTX: RAP 1:1 micelles. *In vitro* tube formation was significantly inhibited with different concentrations of PTX and RAP in micelles in comparison to individual micelles.

Conclusions: PTX and RAP together, as drug conjugates or physically loaded micelles, demonstrate synergistic antiangiogenic activity.

Biography

Adam WG Alani completed his Ph.D. in the field of Pharmaceutical Sciences on May 2007 from the University of Wisconsin-Madison under the guidance of the late Prof. Joseph R. Robinson. Dr. Alani completed his postdoctoral studies from the same institute in the field of design and synthesis of polymeric micelles for drug delivery and targeting under the guidance of Prof. Glen S. Kwon. Currently, he is an Assistant Professor of Pharmaceutical Sciences at the College of Pharmacy, Oregon State University. Dr. Alani's research focuses on the development of new modalities for targeting angiogenesis in cancer and other disease states.

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