Amphiphilic hyper-branched co-polymer nanoparticles for the controlled delivery of novel anti-tumor agents

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INTRODUCTION

In this investigation, we have designed and synthesized an amphiphilic co-polymer with hyper-branched poly(amine-ester) and polylactide (HPAE-co-PLA) to generate nanoparticles (NPs).[1]

EXPERIMENTAL

These NPs have been used to encapsulate a highly active hydrophobic anti-tumor agent, 2-benzoylpyridine 4-ethyl-3-thiosemicarbazone (Bp4eT). Encapsulation in NPs was done in an effort to increase the anti-tumor activity of this agent by facilitating its delivery to tumor cells. We have also examined and optimized the formulation parameters of the NPs that alter their drug-loading capacity and their physical, chemical and biological properties.

RESULTS AND DISCUSSION

The resulting NPs exhibited high Bp4eT-loading capacity and substantial stability in aqueous solution. In vitro drug release studies demonstrated a controlled drug release profile with increased release at acidic pH. Anti-tumor proliferation assays showed that both free drug and drug-encapsulated NPs markedly inhibited tumor cell proliferation in a time- and concentration-dependent manner. Direct microscopic observation revealed that the fluorescent NPs were taken up by cells and localized, in part, in organelles consistent with lysosomes.

CONCLUSION

These results demonstrate a feasible application of the amphiphilic hyper-branched co-polymer, HPAE-co-PLA, as nanocarriers for intracellular delivery of potent anti-tumor agents.

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KEYWORDS: nanoparticles, anti-tumor agents, Bp4eT, lysosomes.

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