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Synthesis and characterization of novel lipid prodrugs of ganciclovir

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Purpose: The objective of this study is to synthesize several long carbon chain lengths of mono and di-ester conjugated lipid prodrugs of ganciclovir (GCV) and to characterize prodrugs with respect to their yield, purity, melting point (MP), NMR and cytotoxicity.

Materials and methods: Long chain mono and di-conjugated lipid prodrugs of GCV were synthesized following the conventional method. All prodrugs were ester conjugated to parent drug, GCV. Synthesized prodrugs were identified on TLC and purified by flash chromatography (solvent mixture; dichloromethane and methanol). Prodrugs obtained were recrystallized with cold diethyl ether. Final yield and melting point for the synthesized prodrugs was determined. Prodrug purity was determined with HPLC. Synthesized prodrugs were characterized with 1H and 13C NMR spectroscopy. Mass spectrometry was used to determine their molecular weights. Prodrug cytotoxicity studies were conducted on ARPE-19 cell lines.

Result: Three different carbon chain length (C5, C9 and C12) of mono and di-ester conjugated lipid prodrugs of GCV were synthesized. The MPs for prodrugs were found to be lower than GCV and purity was found to be > 96%. Characterization of the prodrugs with 13C NMR shows a distinct ester conjugation peak signal in at 172 ppm in lipid prodrug which was absent in GCV. The mass of each individual prodrug was determined with mass spectroscopy and a sodium adduct of the prodrug was observed.

Conclusion: Long chain conjugated mono and di-ester prodrugs of GCV were successfully synthesized and characterized. Prodrugs are of high purity and have negligible toxicity towards ARPE-19 cells.

Biography

Hoang M. Trinh has completed her Bachelor's of Pharmacy from University of medicine and pharmacy, Vietnam and is currently a graduate student at the University of Missouri-Kansas City. She has contributed in one book chapter. She has presented at national and international conferences. She was elected treasurer for Pharmaceutical Science Graduate Student Association (PSGSA) -UMKC student organization for 2013-2014 and is a member of AAPS organizations.

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