

ABSTRACT BOOK



Quantification of Efavirenz with Booster Dose of Ritonavir in PEGylated PAMAM G4 Nanocarriers: Pharmacokinetic, Tissue Distribution and Toxicity Studies in Rat

Kharwade Rohini, Mahajan Nilesh, More Sachin

Dadasaheb Balpande College of Pharmacy, Besa, Nagpur, Rashtrasant Tukadoji Maharaj Nagpur

University, Nagpur, (MS), INDIA-440037.

Presenting Author email: rohinismore1@gmail.com

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Aim and Objectives: The present investigations were aimed to develop PEGylated prolong circulating, co-encapsulated Efavirenz (EFV) and Ritonavir (RTV) PAMAM G4 dendrimers (PPG4ER) to improve the pharmacokinetics and efficacy of antiretroviral therapy.

Methodology: The G4 PAMAM dendrimers were synthesized and characterized. Subsequently a RP-HPLC chromatography method was developed in plasma as a simple and sensitive technique. This developed bioanalytical method was validated and applied for pharmacokinetics and tissue distribution studies in Wistar rats by intra-peritoneal route.

Results and Discussion: The drug loaded PEGylated PAMAM dendrimers were 6.472nm in size with narrow size distribution and zeta-potential was -0.273mV with prolonged drug release. The EFV and RTV were separated by a gradient system of mobile phase comprised of Ammonium acetate buffer 25 mM (pH 5.5): and Acetonile:Methanol (70:30) (Fig. 1). The developed RP-HPLC method showed lower limit of detection (LOD) and lower limit of quantification (LOQ) for EFV and RTV which allowed their determination for plasma pharmacokinetic and tissue distribution. The PPG4ER exhibited significant improvement in pharmacokinetics parameters and tissue distribution in lymph node and spleen (Fig.2 and 3).

Conclusion: This PPG4ER can effectively diffuse in various cellular and tissue compartments where the virus harbours. Hence this would be a potential way to completely irradiated the HIV-infection by maintaining its therapeutic efficacy for prolong period of time.

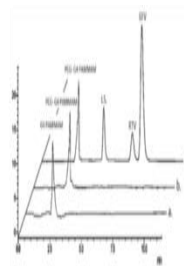


Figure 1 :Chromatogram of G4 PAMAM(a) PEGylated G4 PAMAM(b) and PPG4ER

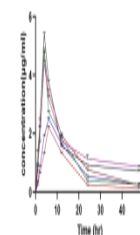


Figure 2 : Plasma pharmacokinetic of EFV

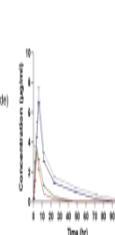


Figure 3: Concentration of EFV in different tissue.

References

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