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Efavirenz-loaded poly (ethylene oxide)-modified nanoparticles as potential rectal anti-HIV microbicides

Objective

Mucus penetrating nanoparticles (NPs) obtained by dense poly (ethylene oxide) (PEO)-coating are promising platforms for the delivery of drugs to mucosal surfaces. We developed efavirenz (EFV)-loaded poly (lactic-*co*-glycolic acid) (PLGA) NPs modified at the surface with PEO and tested their potential to be used as rectal microbicides in preventing sexual HIV transmission.

Methods

EFV-loaded PLGA NPs produced by nanoprecipitation and modified by surface adsorption of Poloxamer 407 (a surfactant containing PEO) were characterized regarding their technological and *in vitro* biological properties. Further, NPs were evaluated regarding their colorectal distribution and retention, as well as safety after 14 days of once daily rectal administration to mice.

Results

Dense surface modification of PEO-PLGA NPs (200nm) with PEO was confirmed by ^{1}HNMR analysis. Drug association with NPs did not substantially affect the antiretroviral activity of EFV and improved the cytotoxicity profile of the drug. NPs modified or not with PEO were mainly distributed throughout the last two thirds of the colon of mice. However, PEO-PLGA NPs showed significantly improved retention in colonic tissues over non-modified particles 15 min and 2 h after administration (**Figure 1**). EFV-loaded PEO-PLGA NPs were found safe after 14-day rectal administration, as assessed by histological observation and analysis of IL-1b, IL-6, IFN-γ and TNFα levels in rectal lavages.

Conclusions

EFV-loaded PEO-PLGA NPs appear to be safe and able to distribute and retain in the colorectum, potentially contributing to sustained local drug levels that could be useful in preventing rectal HIV transmission.

Figures

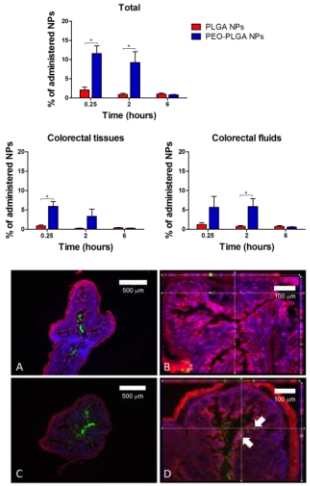

Figure 1: Graphs: Recovery of fluorescent NPs from colorectal tissues at 15 min, 2 and 6h post-administration. Results are expressed as the percentage of the initial amount of NPs. Columns represent mean values and bars the SEM (n=3). (*) denotes a significant difference (p<0.05) when comparing PLGA NPs and PEO-PLGA NPs. Images: Fluorescent microscopy images of Middle colon at 15 min (A,C) and Distal colon at 2 hours (B,D) after rectal administration of PLGA NPs (A,B) and PEO-PLGA NPs (C,D).