INTRODUCTION

Since 2013 the number of newly diagnosed cases of HIV has practically remained unchanged (1). Current post-exposure prophylaxis (PEP) involves an oral administration, often with considerable side effects. Under WHO guidelines, PEP in a sexual exposure (PEPSE) is limited to only high-risk scenarios (2). The size of the population exposed to low to moderate risk scenarios is unclear.

METHODS

- Dolutegravir was selected as the antiviral of choice. It was then chemically modified, producing a dolutegravir myristate (MDTG) (Figure 1).

- A two-step nanoprecipitation system was designed (Figure 2). Three testing conditions were assessed, using different coating masses of mPEG5000-LA100 (Figure 3).

- Biocompatibility at 24 hours was on Caco-2 and Raw 264.7 cells. Uptake was traced by substituting 10% of the total nano-carrier with a Cy5 Blue labelled PEG5000. (Figure 3).

AIM

The overarching aim of this project is to develop a nanoparticle-based PEPSE with a significant drug loading, for local rectal administration after a low to moderate risk sexual exposure.

RESULTS

- MDTG can be precipitated into an unstable nanocrystal (Figure 4).

- All formulations developed contained a significant drug content with a final average of 215μm in size (Figures 5-6).

- The coated formulation with 0.22mg was chosen to test further as it carried a significant drug content.

- In vitro data suggests biocompatibility and internalization of the formulation in target cells. Therefore providing potential for drug delivery (Figures 7-9).

CONCLUSIONS/FUTURE WORK

- Due to the 14-carbon chain in MDTG, it can be successfully self-assembled into an unstable nanocrystal through a nanoprecipitation setup. Once in this form, it can be coated with a polymer agent, in a second nanoprecipitation.

- Nanoformulations with a high drug content (above 50% wt%) of MDTG were developed. In vitro data suggests that uptake is higher in Raw 264.7 macrophage than Caco-2 cells at 24 hours. Target cells for this formulation are macrophages and antigen presenting cells, thus the results are encouraging.

- More complex in vitro models such as Caco-2/M cells co-culture need to be investigated to provide more physiological relevant uptake data.

REFERENCES

1. C. Sanders 1, V. Taresco2, R. Cavanagh1, M.J. Stocks1, P.M. Fischer1, C. Alexander1, P. Gershkovich1
1School of Pharmacy, University of Nottingham, Nottingham UK. 2School of Chemistry, University of Nottingham, Nottingham, UK.
Contact email: pavel.gershkovich@nottingham.ac.uk
