A NOVEL ALTERNATIVE "MORNING AFTER" LOCAL ADMINISTRATION APPROACH FOR POST-EXPOSURE PROPHYLAXIS OF HIV: DEVELOPING A FORMULATION

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Background: Since 2013 the number of newly diagnosed cases of HIV has practically remained unchanged. 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, thus potentially excluding a significant population exposed in lower to moderate risk scenarios. While the size of this population is unclear, unpublished data from our group shows that it could be as high as 30% of a sexually active population.

Methods: Dolutegravir was selected the antiviral of choice. It was then chemically modified; producing a dolutegravir myristate (MDTG).A two-step nanoprecipitation system was designed. Three testing conditions were assessed; using different coating masses of mPEG5000-LA100**.** Biocompatibility at 24 hours was on Caco-2 and Raw 264.7 cells**.** Uptake at 24 hours was then traced quantitatively and qualitatively by substituting 10% of the total nano-carrier with a Cy5 Blue labelled PEG5000.

Results: MDTG can be precipitated into an unstable nanocrystal .All formulations developed contained a significant drug content with a final average of 215nm in size. 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 in target tissues.

Conclusions: Due to the 14-carbon chain in MDTG, it can be successfully self-assembled into an unstable nanocrystal through a nanoprecipitation set up. 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.