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IMPROVING SOLUBILITY OF DAPIVIRINE BY USING NANOTECHNOLOGY

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INTRODUCTION

Dapivirine (TMC 120) is an investigational antiretroviral compound being developed as a microbicide. It exhibits poor solubility (<0.1 µg/ml at pH 4.5-5 typical of vaginal fluid). After administration, this may lead to suboptimal concentration in the vaginal cavity, resulting in poor prophylactic activity. The objective of this study was to investigate the feasibility of nanosizing approach to increase the solubility of dapivirine.

METHODS

1% (w/v) dapivirine was dispersed in 1% Poloxamer F 68 solution in water. For nanosizing, high pressure homogenization (HPH) was performed using an Emulsiflex C-3 homogenizer. Samples were characterized before and after HPH for particle size distribution (laser diffractometry), apparent solubility (HPLC) and solid state transformation (Infrared spectroscopy, powder X ray diffraction and scanning electron microscopy (SEM)).

RESULTS

SEM micrographs and particle size analysis results revealed significant reduction in the particle size after HPH. While before HPH, the average particle size was 2.5 µm, after HPH it reduced to 0.140 µm. Similarly, particle size distribution was uniform after HPH with >80% particles below 0.5 µm. In addition, as compared to the unmilled samples (before HPH) which showed solubility of < 0.1 µg/ml, after HPH a solubility of 0.42 ± 0.02 µg/ml was observed. Absence of any solid state transformation (as indicated by solid state characterization techniques) during HPH, showed that the solubility improvement was only due to nanosizing.

CONCLUSION

Nanosizing resulted in significant improvement in solubility of dapivirine. Therefore, utilization of nanosized particles of dapivirine can be useful in achieving the required therapeutic concentration after administration.

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