The effect of surfactants on the in vitro behaviour of suppositories: spontaneous structure formation effects solubility

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INTRODUCTION: Many drugs have a limited bioavailability when delivered via oral administration. Rectal drug delivery allows for the absorption of drugs by bypassing some major metabolic hurdles [1]. Little is understood about how drug uptake is influenced by the surfactants in the suppository formulation; thus, fundamental research into the effect that formulation components of suppositories have on the bioavailability of drugs delivered rectally is required. Surfactants have played a role in aiding the adhesion of suppository formulations to the rectal wall in a hope to increase drug uptake, but no systematic study into their structure-property relationships pertaining to drug bioavailability has been performed. Insights from a colloid and interface science perspective can elucidate a mechanism of action that is easily controlled through formulation modifications.

METHODS: One hydrophilic (acetaminophen) and two hydrophobic drugs (indomethacin and idronoxil) were formulated into a hard fat suppository using surfactants with a range of HLB values: Tween 80 (HLB 15), TPGS (13.2), Kolliphor EL (12.7) and Myrj S8 (10.8). Each formulation was then introduced into a simulated rectal environment by mixing the drug formulations in simulated rectal fluid [2] at physiological temperature (37 °C). Drug partitioning was measured using UV-Vis spectrophotometry. Synchrotron small angle X-ray scattering (sSAXS) and cryogenic scanning electron microscopy (cryoSEM) were used to characterise the spontaneous formation of hydrated amphiphilic nanostructures of the suppository formulations.

RESULTS AND DISCUSSION: The spontaneous formation of amphiphilic structures upon the hydration of suppositories in simulated rectal conditions was observed to investigate the influence of structure in these two-phase systems on the solubility of hydrophilic and hydrophobic drugs. The spontaneous emulsification or micellisation was observed to be dictated by the properties a range of non-ionic surfactants. Time resolved structural analysis revealed that the more hydrophilic surfactants, those with a higher HLB, were more likely to promote the formation of micelles whereas the more hydrophobic surfactants (low HLB) emulsify the formulation on hydration. As the bioavailability of drugs are closely linked to their solubility, the impact of these structure of the hydrophilic partitioning experiments. It was found that the non-ionic surfactants had no significant impact on the solubility of the hydrophilic drug, acetaminophen. On the other hand, the solubility of the poorly water soluble drugs, were significantly enhanced through emulsification and the maintenance of the lamellar structure within the lipid droplets.

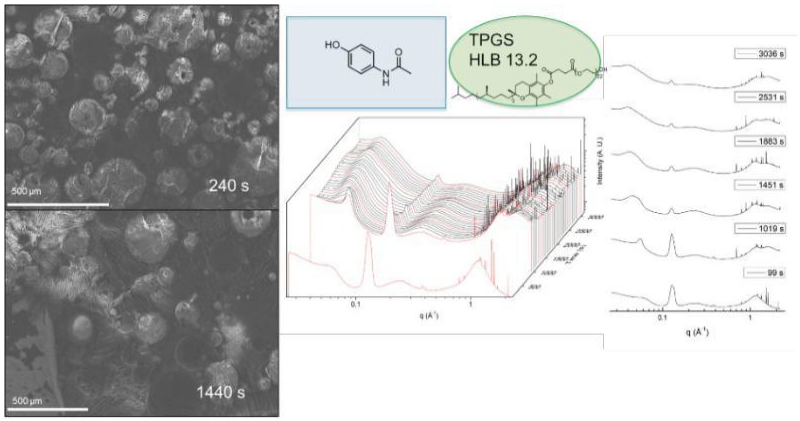

Figure 1. Time resolved structural analysis of the formation of structures during the hydration of suppositories (acetaminophen and TPGS) in simulated rectal fluid. Upon hydration, sSAXS indicate the spontaneous formation of micelles which gradually incorporated increasing amounts of oil over time. The resulting emulsion shown in the cryoSEM images appear very inhomogeneous. This process was repeated for all mixtures.

CONCLUSION: Through fundamental physicochemical studies, understanding the relationship between formulation, structure formation and solubility will allow for the better design and formulation of lipidic delivery systems for pharmaceutical treatments.

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