Abstract

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Title of thesis: Effects of Proteins on Apparent Drug solubility in Fasted State Stimulated Colonic Fluids

This thesis investigates the influence of proteins on the apparent solubility of drugs in fasted state stimulated colonic fluids. The investigation was conducted on a selection of compounds with varying physicochemical and plasma protein binding properties. Precisely, three different compounds named as Nilotinib, Carvedilol and Ritonavir were analyzed for their apparent solubility in three distinct protein sources: bovine serum albumin, mucin from dehydrated porcine gastric mucin type II, and collected porcine intestinal mucus.

Accurate reversed-phase high-performance liquid chromatography was developed and employed as the analytical method to determine the concentration of the apparent drug solubility of the investigated compounds.

The research on the solubility of poorly soluble compounds in simulated colonic fluids has been restricted. Additionally, factors such as the impact of proteins remains unexplored in biorelevant media, which could be critical for enhancing our understanding of drug solubility and protein binding in the colon.

The results of the study demonstrate that the presence of proteins in colonic fluids can significantly influence drug solubility. Specifically, the presence and increased concentration of proteins can enhance the apparent solubility of certain drugs with low water solubility.

These discoveries hold significant implications for pharmaceutical development, emphasizing the need to consider the influence of proteins in the colonic environment during the design of new drugs. The thesis contributes valuable insights into the intricate relationship between proteins and drug solubility in the colon.

The study also highlights the need for further research in this area, in order to better understand the mechanisms by which proteins affect drug solubility in the colonic environment.