Ethanol Effects on Apparent Solubility of Poorly Soluble Drugs in Simulated Gastric Fluid
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Purpose
To study potential consequences of concomitant drug and ethanol intake on apparent drug solubility (S_{app}) in gastric media using small scale dissolution testing in acidic media with or without small amounts of solubilizing lipids and 20% v/v ethanol.

Methods
S_{app} was measured with the µDiss profiler Plus (pION, Woburn, MA) for three bases, three acids and three non-ionizable drug molecules in four different media reflecting the gastric fluid. The media used were HCl-NaCl solution (pH 2.5) and Fasted state simulated gastric fluid (FaSSGF - pH 2.5 with 80 µM taurocholate and 20 µM lecithin) with and without 20% ethanol. Powder was weighed in excess to vials and preheated media (37°C) was added at the start of the experiment. The dissolution was performed in triplicates and monitored using fiber optic probes scanning the suspensions until a plateau representing the S_{app} of the compound in the media was reached. Resulting dissolution profiles were analyzed using a nonlinear biphasic curve fitting function in GraphPad Prism 6 (GraphPad Software, San Diego, CA).

Results
Compounds with basic functional groups all exhibited high apparent solubility due to ionization effects at the low pH used in this study resulting in a relatively high apparent solubility in all media studied. However, the solubility was partially suppressed in media containing ethanol leading to lower S_{app} as compared to ethanol-free media. The three acidic compounds (tofremamic acid, indomethacin and indoprofen) were neutral at the pH studied and showed similar behavior as the non-ionizable compounds. The acidic and non-ionizable compounds showed on average eight times higher apparent solubility compared to media without ethanol. Further it was revealed that the lipid content in FaSSGF is too low to effectively solubilize most of the studied compounds.

Conclusion
Concomitant intake of ethanol and drug products may significantly increase the dissolution rate and apparent solubility of lipophilic, poorly soluble acidic and non-ionizable compounds, whereas dissolution of cationic drug molecules will mostly be a result of ionization.