The Influence of Surfactants on passive Diffusion and active efflux of Drugs

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Non-charged detergents are used as excipients in drug formulations. Until recently they were considered as inert compounds, enhancing drug absorption essentially by improving drug solubility. However, many detergents insert into lipid membranes, although to different extents, and change the lateral packing density of membranes at high concentrations. Moreover, they bind to the efflux transporter P-glycoprotein (and most likely to related transporters and metabolizing enzymes with overlapping substrate specificities). If their affinity to P-glycoprotein is higher than that of the co-administered drug they act as modulators or inhibitors of P-glycoprotein and enhance drug absorption. Inhibition of Pgp and related proteins can, however, cause severe side effects. We first review the membrane binding propensity of different non-charged detergents (including poloxamers) and discuss their ability to bind to Pgp. Secondly we interpret literature data on drug uptake enhancement by non-charged detergents obtained *in vivo* and *in vitro* by analyzing them on a molecular level. The present analysis provides the tools for an approximate and simple *a priori* estimate of the membrane and Pgp binding ability of non-charged detergents based on a modular binding approach.

Reference
Anna Seelig and Grégori Gerebtzoff, Expert Opinion on Drug Metabolism & Toxicology, in Press