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Lipid Digestion – Key to the Ability of Milk-like Emulsions to Promote Oral Drug Delivery

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Lipid Digestion – Key to the Ability of Milk-like Emulsions to Promote Oral Drug Delivery

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Milk is a staple of the human diet and is an essential nutrient source for all mammalian infants. The fat content of milk comprises 98% triglycerides emulsified with milk fat globular membrane material and native proteins. Digestion of these triglycerides in the intestines yields monoglycerides and fatty acids that are absorbed through the intestinal wall. Lipophilic molecules such as drugs and nutrients can be dissolved in the milk fat globules but fat digestion can result in further dissolution or precipitation of incorporated drugs and nutrients. Digestion of milk fats also leads to the formation of intricate liquid crystalline structures that evolve throughout digestion,[1,2] which may also affect the release of incorporated drugs and nutrients. The process of lipid digestion is therefore key to the fate of lipophilic molecules dissolved in the fat globules of the milk emulsion and directly controls milk's ability to act as an excipient for lipophilic drugs and nutrients.

In this presentation, small angle X-ray and neutron scattering techniques (SAXS and SANS, respectively) will be used to probe the structural transformations occurring during the digestion of milk fats and the subsequent effects on incorporated drugs. Synchrotron SAXS reveals that the liquid crystalline structural transformations occurring during the digestion of milk fats are robust with respect to heat treatment, freezing and powdering/reconstitution of milk.[3] It will also be established that milk-substitutes such as infant formula and vegetable juices do not necessarily replicate milk-like structures during digestion. The distribution of digestion products within fat globules at different extents of digestion will be examined with SANS combined with selective deuteration of milk digestion products. Finally, the incorporation of the amphiphilic antimalarial drug OZ439[4] into milk and infant formula will be outlined and the influence of lipid digestion on the solubility and bioavailability of OZ439 will be discussed.

1. Salentinig et al. Formation of Highly Organized Nanostructures during the Digestion of Milk. *ACS Nano* 2013, 7 (12), 10904-10911.
2. Salentinig et al. Self-Assembly Structure Formation during the Digestion of Human Breast Milk. *Angew. Chem. Int. Ed.* 2015, 54 (5), 1600-1603.
3. Clulow/Salim et al. A closer look at the behaviour of milk lipids during digestion. *Chem. Phys. Lipids* 2018, 211, 107-116.
4. Clulow et al. The Curious Case of the OZ439 Mesylate Salt: An Amphiphilic Antimalarial Drug with Diverse Solution and Solid State Structures. *Mol. Pharm.* 2018, in press, DOI:10.1021/acs.molpharmaceut.8b00173

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