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Impacts of the structure of infant formulas on their digestive behaviour and hydrolysis: insights from *in vitro* studies and comparison with human milk

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- **Objectives and study:** Human milk lipids are the major source of calories to support infant growth and are delivered under the very specific form of milk fat globules. These micronic droplets (3-5 μm) are based on an apolar core enclosing specifically structured triglycerides. The core is enveloped by a membrane of Milk Polar Lipids (MPL) and proteins. This specific structure is shared by many mammalian milk, including cow's milk. In comparison, infant formulas are submicronic emulsions of vegetable lipids optimized in terms of total fatty acids composition but not biomimetic of human milk structure which may impact their digestive behavior and kinetics of lipolysis. The reintroduction of some cow's milk lipid fractions (MPL or triglycerides) seems a clever approach to mimic human milk natural structure. And yet, very few infant formulas use milk lipids more expensive than vegetable lipids. To assess the benefits of such reintroduction, the structure, digestive behaviour and kinetics of lipolysis of commercial or model infant formulas with or without cow's MPL were determined using an *in vitro* dynamic model of neonatal digestion (DIDGI®) and compared with data obtained on human milks.

- **Methods:** The dynamic digester parameters were based on an exhaustive literature review to mimic the digestion of a 1 month old term newborn. First age infant formulas (IFs) of close compositions but with variable droplets sizes (0.2 to 0.7 μm), all based on vegetable fats *versus* a model IF stabilized by MPL (size 2 μm), were digested. Lipolysis, released fatty acids (FA), lipid classes and the microstructure of the matrices were evaluated before and along digestion. These digestion data were compared with the ones obtained on raw or pasteurized pooled human milks (HMs) (De Oliveira et al., 2016, FRI).

- **Results:** Commercial IFs differed from HMs in terms of chemical composition (specifically regiodistribution), prehydrolysis state and emulsion structure. These initial differences impacted lipolysis kinetics and deconstruction. Model IF with MPL had a structure and interfacial composition closer to HMs. Lipolysis was lower in IFs than in raw HM, before digestion and during gastric phase, and on the contrary higher at the beginning of the intestinal phase, due to the important surface developed by the lipid droplets in commercial or model IFs (14 to 32 m^2/g of lipid) compared to HMs (4 m^2/g of lipid). The profile in released FA from HMs was rich in quickly metabolizable, *i.e.* medium chain and oleic FA, in relation with their specific external distribution on triglycerides. Conversely, palmitic free FA was depleted in HM but remained dominant in IFs (based on vegetable fat). A profile closer to HMs can be obtained in IFs including cow's milk triglycerides.

HMs and model IF with MPL had closer digestive disintegration with the persistence of large entities (droplets or globules) over the digestion underlining the paradoxical metabolic fate of dairy lipids (Bourlieu et al., 2015, EJLST): rapid conveyor of energy through their triglyceride core, but containing some low digestible bioactive complex lipids and proteins in their stabilizing membrane.

- **Conclusion:** The specific structure of HM at several scale levels is a key parameter modulating the profiles of liberated FA, kinetics of lipolysis and colloidal behaviour in gastric phase. The reintroduction of some cow's milk lipids in IFs could help making them more biomimetic of HM digestive behaviour.

- **Conflict of interest:** This project was partially funded by Lactalis.