Effect of bio-based nanostructures in curcumin bioaccessibility: physical state and carrier oil type

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Curcumin (CUR), a natural phytochemical from *Curcuma longa*, presents a wide range of biological activities such as antioxidant, antimicrobial and antitumoral effects. However, it exhibits very low water solubility and low bioavailability, which limit its food application. To overcome these limitations, nano-scale delivery systems (e.g. nanoemulsions (NE) and solid lipids nanoparticles (SLN)) can be developed to improve its bioavailability and stability. Also, it is essential to assess nanoformulations' behaviour and CUR fate in the gastrointestinal (GI) tract.

This work aimed at understanding the effect of nanoformulations' physical state (NE and SLN) and oil type used in NE (medium chain triglycerides (MCT) and long chain triglycerides (LCT)) on CUR stability, bioaccessibility and effective bioavailability when submitted to an *in vitro* digestion process. Nanoformulations' stability was characterized at each stage of digestion. At the end of digestion, free fatty acids (FFA) release, CUR stability, bioaccessibility and effective bioavailability were determined. Cellular uptake was evaluated using Caco-2 cells.

All nanoformulations showed to be stable until gastric phase, from which an increase of particle size was observed. However, SLN showed to be more stable than NE. Regarding FFA release, both NE released higher FFA amount than SLN. Also, NE-MCT released a higher FFA amount than NE-LCT. Although SLN and NE-LCT promoted similar CUR stability, SLN presented the lowest CUR bioaccessibility and effective bioavailability. NE-MCT exhibited lower CUR bioaccessibility but promoted a higher CUR stability and effective bioavailability when compared to NE-LCT. Thus, it was possible to observe that the physical state and oil chain length have a high effect in nanoformulations' digestibility and on CUR fate in the GI tract.

This work contributed to the progress of the knowledge on the development of different bio-based nanoformulations with improved CUR bioavailability, by collecting essential data on digestion and absorption.

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