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Review

Boosting the bioavailability of hydrophobic nutrients, vitamins, and nutraceuticals in natural products using excipient emulsions

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ABSTRACT

Many highly hydrophobic bioactives, such as non-polar nutrients, nutraceuticals, and vitamins, have a relatively low or variable oral bioavailability. The poor bioavailability profile of these bioactives may be due to limited bioaccessibility, poor absorption, and/or chemical transformation within the gastrointestinal tract (GIT). The bioavailability of hydrophobic bioactives can be improved using specially designed oil-in-water emulsions consisting of lipid droplets dispersed within an aqueous phase. The bioactives may be isolated from their natural environment and then incorporated into the lipid phase of *emulsion-based delivery systems*. Alternatively, the bioactives may be left in their natural environment (e.g., fruits or vegetables), and then ingested with *emulsion-based excipient systems*. An excipient emulsion may have no inherent health benefits itself, but it boosts the biological activity of bioactive ingredients co-ingested with it by altering their bioaccessibility, absorption, and/or chemical transformation. This review discusses the design and fabrication of excipient emulsions, and gives some examples of recent research that demonstrates their potential efficacy for improving the bioavailability of hydrophobic bioactives. The concept of excipient emulsions could be used to formulate emulsion-based food products (such as excipient sauces, dressings, dips, creams, or yogurts) specifically designed to increase the bioavailability of bioactive agents in natural foods, such as fruits and vegetables.

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1. Introduction

Many natural and processed foods contain hydrophobic bioactive agents that may have beneficial effects on human health when consumed as part of a regular diet, including nutrients (such as certain triacylglycerols), vitamins (such as vitamins A, D, and E), and nutraceuticals (such as carotenoids, curcumin, flavonoids, and coenzyme Q10) (Aluko, 2012; Huang, Yu, & Ru, 2010; McClements, 2010). However, the potential health benefits of these dietary bioactives are often not fully realized because of their low or variable oral bioavailability (Fernandez-Garcia et al., 2012; Rein et al., 2013; Zou, Liu, Liu, Xiao, & McClements, 2015a). Numerous factors may contribute to the poor bioavailability profiles of hydrophobic bioactives, but these can often be divided into three major categories: poor bioaccessibility; low absorption; transformation into an inactive form. The dominant factors that limit the bioavailability of a bioactive agent in a specific food have to be established before a successful strategy can be developed to improve its bioavailability profile (McClements & Xiao, 2014; Zou et al., 2015a) (See Table 1).

In general, there are two major approaches that can be used to improve the bioavailability of hydrophobic bioactives in foods (Fig. 1). The first approach is to isolate the bioactive components from their natural environment (such as a fruit or vegetable) and then to incorporate them into a suitable delivery system (McClements, 2015b). A wide range of colloidal delivery systems have been developed to encapsulate bioactive agents and have been reviewed in detail elsewhere, such as molecular complexes, microemulsions, emulsions, liposomes, solid lipid nanoparticles, biopolymer particles, and microgels (Huang et al., 2010; Marze, 2013; McClements, 2010; Norton, Espinosa, Watson, Spyropoulos, & Norton, 2015; Ting, Jiang, Ho, & Huang, 2014; Velikov & Pelan, 2008). Emulsion-based delivery systems are particularly suitable for this purpose because they are already widely used in the food industry, and because of their ease of fabrication from widely used food ingredients and processing operations. Delivery systems must be carefully designed to ensure they are compatible with the food they are to be incorporated into, cost-effective, safe, robust, and efficacious. Colloidal delivery systems are particularly suitable for applications where the hydrophobic bioactive is initially present within an underutilized waste-stream, such as the peel of a fruit or vegetable that would normally be discarded. The second approach for increasing bioavailability is to leave the bioactive components within their natural environment (such as fruits or vegetables), but consume them with specially designed "excipient foods" (McClements & Xiao, 2014). An excipient food may have no bioactivity itself, but it boosts the bioavailability of bioactive agents that are consumed with it by altering their bioaccessibility, absorption, or transformation within the gastrointestinal tract (GIT). Oil-in-water emulsions are particularly effective vehicles for developing excipient foods because of the great flexibility in designing their compositions and structures. Thus, an "excipient emulsion" can be defined as an emulsion that increases the bioactivity of bioactive agents in foods that are co-ingested with it, without necessarily having any intrinsic bioactivity itself. In summary, oil-in-water emulsions can either be used as delivery systems or as excipient systems. For delivery systems, the hydrophobic bioactive agents are encapsulated within the oil phase of the emulsion, but for excipient systems a bioactive-free emulsion is consumed with a bioactive-rich food.

The purpose of this article is to highlight the major factors that limit the oral bioavailability of hydrophobic bioactive agents from fruits and vegetables, and then to describe how excipient emulsions can be developed to overcome these hurdles. This knowledge could be used to develop a new range of excipient food products specifically designed to increase the bioavailability of bioactive agents from natural products (such as fruits, vegetables, cereals, meats, or fish), e.g., excipient sauces, dressings, dips, creams, or beverages.

2. Characterizing factors limiting oral bioavailability

The major factors that limit the oral bioavailability of bioactives in fruits and vegetables can be characterized using the recently developed *Nutraceutical Bioavailability Classification Scheme* (NuBACS), which has recently been discussed in detail elsewhere (Zou et al., 2015a; McClements et al., 2015). Briefly, this scheme divides the limiting factors into three categories based on the physiochemical or physiological mechanisms limiting bioavailability (Fig. 2): bioaccessibility (B^*); absorption (A^*); and transformation (T^*). Each of these categories is given the symbol "(+)" when it is a non-limiting factor and "(−)" when it is a limiting factor. The precise mechanism involved for limiting the bioavailability is described by utilizing sub-categories within each major category. For bioaccessibility, the sub-categories are poor liberation from the food matrix (L), poor solubility in the gastrointestinal fluids (S), and interactions that promote insolubility (I). For absorption, the sub-

Table 1
Summary of the main factors limiting the bioavailability of bioactive agents as characterized by the nutraceutical bioavailability classification system (NuBACs).

Major classes	Sub-classes				
Bioaccessibility (B^*)	Liberation (L)	Solubilization (S)	Interactions (I)		
Absorption (A^*)	Mucus layer (ML)	Tight junction (TJ)	Membrane permeability (MP)	Active transporters (AT)	Efflux transporters (ET)
Transformation (T^*)	Chemical (C)	Metabolism (M)			