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Delivery of encapsulated bioactive compounds within food matrices to the digestive tract: recent trends and future perspectives

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ABSTRACT

Encapsulation technologies have achieved encouraging results improving the stability, bioaccessibility and absorption of bioactive compounds post-consumption. There is a bulk of published research on the gastrointestinal behavior of encapsulated bioactive food materials alone using *in vitro* and *in vivo* digestion models, but an aspect often overlooked is the impact of the food structure, which is much more complex to unravel and still not well understood. This review focuses on discussing the recent findings in the application of encapsulated bioactive components in fabricated food matrices. Studies have suggested that the integration of encapsulated bioactive compounds has been proven to have an impact on the physicochemical characteristics of the finished product in addition to the protective effect of encapsulation on the fortified bioactive compound. These products containing bioactive compounds undergo further structural reorganization during digestion, impacting the release and emptying rates of fortified bioactive compounds. Thus, by manipulation of various food structures and matrices, the release and delivery of these bioactive compounds can be altered. This knowledge provides new opportunities for designing specialized foods for specific populations.

HIGHLIGHTS

- Food structure confers specific functionalities to supplemented encapsulated bioactive compounds during processing and digestion.
- Encapsulation of bioactive compounds prevents changes in physicochemical attributes of foods during processing.
- The unique disintegration patterns of foods in the gut impacts how bioactive substances are released and absorbed.

KEYWORDS

Food structure; encapsulation; bioactive compounds; functional foods; food digestion

Introduction

Bioactive compounds are biologically active substances that are extracted from animal- or plant-based sources and have pharmacological or physiological effects that can promote human health. In general, these compounds are produced as secondary metabolites in small quantities and can modulate metabolic processes (Graebin et al. 2019; Khaw et al. 2017; Yang et al. 2016). Bioactive compounds are classified into two major classes based on different chemical structures, i.e., water-soluble compounds (hydrophilic) and lipid-soluble compounds (Lipophilic) (Carbonell-Capella et al. 2014; Galanakis 2017). They are extremely heterogeneous in their chemical structure (polyphenols, carotenoids, tocopherols, phytosterols, organosulfur compounds, and peptides) and have been reported to have several health-promoting activities such as antimicrobial, antioxidant, anti-inflammatory, antidiabetic, among others (Eggersdorfer and Wyss 2018; Oyenih and Smith 2019; Prasad et al. 2022; Ruhee et al. 2020; Szweczyk, Chojnacka, and Górnicka 2021; Tornesello et al. 2020). Bioactive components derived from natural foods are located in complex matrices of lipids, proteins, and/or carbohydrates, which may impede their release into

the gastrointestinal fluids during digestion. In addition, their naturally low levels in various foods and possible chemical interactions with other food constituents significantly decrease bioaccessibility and bioavailability. The concept of isolating bioactive compounds from natural sources to enrich other commonly consumed foods enables achieving higher loading per serve and possibly increase the uptake (Moreno and Ilic 2018; Shahidi 2009).

Scientific understanding of the potential benefits of the bioactive food components has stimulated consumers choice toward natural products with additional health-promoting effect (Betoret et al. 2011; Mollet and Rowland 2002). However, formulating bioactive compounds into fabricated foods encounter many challenges including changes in products' quality, but also losses of bioactivity after consumption because of physical and chemical changes in the bioactive compound within the gastrointestinal tract. In this regard, encapsulation has been regarded as an effective technology to protect bioactive substances within the food products from the peripheral environments, regulate their release in a particular environment, and improve consumer compliance and convenience (Nedovic et al. 2011; Qazi et al. 2015; Rezvankhah, Emam-Djomeh, and Askari 2020; Rodríguez

et al. 2016). Additionally, encapsulation systems can be designed to control the targeted delivery of bioactive compounds in the gastrointestinal environment, thus enhancing their bioaccessibility and bioavailability (Donhowe et al. 2014; Jiang, Liao, and Charcosset 2020; Sabet et al. 2021). The functionality of encapsulated systems is associated with a specific formulation that involves combining the appropriate ratios of carrier materials, functional substances, and one or more biopolymeric emulsifier layers with the right hydrophilic-lipophilic balance (Bao et al. 2019; McClements 2018; Qazi et al. 2015; Zhu 2017). For example, emulsion-based encapsulation systems can entrap bioactive substances into a dispersed phase or be adsorbed onto an oil/water interface. Depending on the emulsion design, it is possible to influence the release rate of the entrapped compound during digestion and absorption (Donhowe et al. 2014; Jiang, Liao, and Charcosset 2020).

To date, most published studies are focused on designing bioactive encapsulation systems and describing their performance under gastrointestinal conditions. However, a few attempts have been made to link bioaccessibility and bioavailability to the structural features of food products and/or to the encapsulation system. Therefore, this review aims to provide a comprehensive overview of the recent advances in the development of food matrices fortified with encapsulated bioactive compounds. The review covers the effects of bioactive fortification on the physicochemical properties of the resulting food matrices during processing, and the impact of food structure on digestion and bioaccessibility of fortified bioactive compounds.

The food structure effect

The food structure usually corresponding to a physical and spatial domain, that contains, interacts directly and/or gives a particular functionality to a constituent or element of the food (Aguilera 2019). This cellular- or colloidal-based dissipative organization is often categorized as soft matter, as its functionality is driven mainly by its internal (i.e., physicochemical and biochemical reactions) and external (i.e., enzymes, pH, thermal fluctuations, and microorganisms) perturbations (Aguilera 2019; Alongi and Anese 2021). The complexity of self-assembled structures in animal- or plant-based foods and structures generated in processed foods revolves around their structural orientation and their chemical composition (Aguilera 2005; Capuano et al. 2018; Flores and Kong 2017; Parada and Aguilera 2007; Ubbink 2012). The rigid and intact structures of native foods, such as plant- and animal-tissue-based fibrous structures, plant-based fleshy materials, and encapsulated plant embryos, not only impact functionality and digestibility but also significantly impact the release of nutrients and the entrapped bioactive compounds (Acevedo-Fani, Dave, and Singh 2020; Cifelli 2021). The processing of these foods affects several physical, chemical, and nutritional attributes *via* the changes their structural arrangements. Processing can be used to develop, from basic raw materials, more complex structures in foods; for example, yogurt, cheese, and ice cream are all

milk-based products with distinctive structures and properties (Dima et al. 2020). Moreover, the processed food is sometimes structurally modified to such an extent that its biological origin is not readily apparent, e.g., the conversion of liquid milk to solid cheese or the transformation of hard grain to fluffy bread. In addition, structural changes continue either during or after processing. Most foods never attain thermodynamic equilibrium, e.g., the softening and loss of crunchiness in fruits as they go through ripening and senescence leads to undesirable product quality (Agarwal et al. 2019; Joardder, Kumar, and Karim 2017). Thus, an understanding of the structural properties of food materials is important for proper control of food processing operations as well as for improvement in the quality of the final product (Karim et al. 2018; Lamothe et al. 2017; Parada and Aguilera 2007).

Figure 1 shows the impact of the interactions among food structures, food components and bioactive substances on processing, product quality and digestion behavior. These interactions are discussed in more detail in subsequent sections.

In-product behavior

Over the last 10 years, a reasonable number of studies has been published dealing with the product quality and shelf-life changes affected by the addition of encapsulated bioactive compounds to a variety of food matrices, including liquid, semi-solid and solid foods. The findings of these studies are summarized in Table 1.

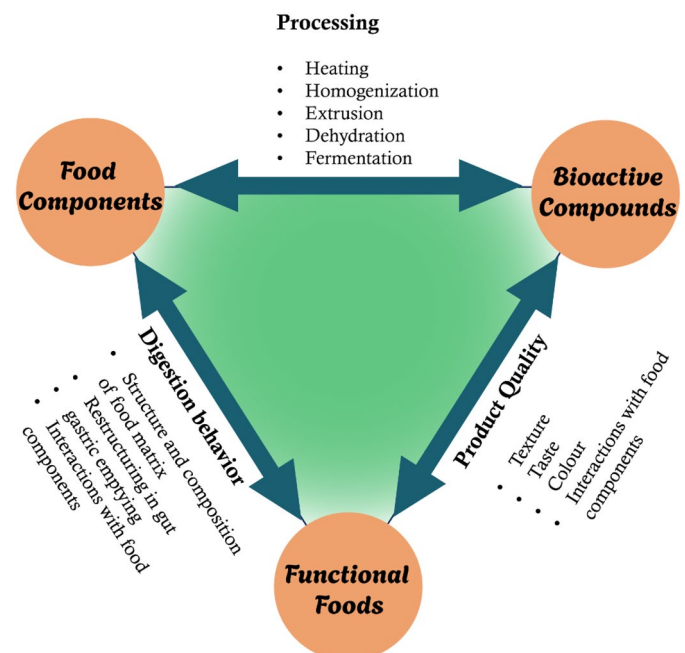


Figure 1. Interactions between fortified food matrices and effects of various factors on the delivery and bioaccessibility of loaded bioactive compounds.

Table 1. Previous investigations on the relationship between the encapsulated bioactive compounds and fortified food matrix.

Encapsulated bioactive compounds	Fortified food matrices	Size	Fortification level	Delivery system	Outcomes	Reference
Epigallocatechin gallate	Fruit Nectar	270 and 220 μm	0.1 g	Microparticle	The chitosan encapsulated EGCG in the fruit nectar was found to be more stable than the alginate coated microparticles, which was attributed to alginate interactions with the phospholipid bilayer.	Istenič, Cerc Korošec, and Poklar Ulrih (2016)
Steppogenin	Apple juice	> 35 nm	1 mL per 9 mL of apple juice	Microemulsion	Comparing enhanced juice with free steppogenin and regular apple juice, nanoencapsulated steppogenin had superior physicochemical and organoleptic qualities and shown effective antibrowning capabilities..	Tao et al. (2017)
Cinnamon extract	Chocolate beverage	162 nm	60 mL colloidal cinnamon nanoparticles and distilled water mixture	Nanoparticle	Despite the fact that the incorporation of nanoparticles significantly improved the suspension stability of chocolate beverages, the stabilization effect of the nanoparticles appeared to be significantly influenced by the characteristics of the beverage raw material.	Muhammad et al. (2019)
Echinacea extract	Acidic beverage	190 nm	0.25 %	Phytosome	Encapsulation not only preserved the bioactive compounds against degradation under external condition provided by acidic beverage but also enhanced the bioavailability.	Molaveisi et al. (2021)
Curcumin	Low-fat milk	63 to 126 nm	30.18 mL of milk and 12.82 mL of Cur-NEs containing 15 mg curcumin	Nanoemulsion	Fortified milk showed significantly lower lipid oxidation than control	Joung et al. (2016)
Fish oil	Fermented probiotic milk	37 nm	0.3 g omega-3 fatty acid per 240 mL	Nanoencapsulation	Nanoencapsulated fish fortified samples showed higher EPA and DHA content, higher survival of probiotic bacteria and overall acceptability.	Moghadam et al. (2019)
Arjuna phenolics	Chocolate vanilla dairy drink	–	0.3 %	Microcapsule	Addition of encapsulated arjuna phenolics markedly affected the physicochemical attributes of the fortified matrix during prolonged storage.	Sawale et al. (2017)
Polyphenols and anthocyanins	Yogurt	–	0.5 g of encapsulated powder in 50 g of yogurt	Microencapsulation	The bioactive compounds encapsulated in yoghurt behaved similarly to those not encapsulated in juice.	Robert et al. (2010)
Olive fruit polyphenols	Greek and European style yogurt	–	500 ppm of 20 % w/w encapsulated polyphenol powder in 10 kg yogurt	Encapsulation	Encapsulated polyphenols did not developed color change during storage which was evident in the yogurt with plain polyphenols	Petrotos et al. (2012)
R. ulmifolius hydroalcoholic extract	Yogurt	79–380 μm	40 mg per 20 g	Microencapsulation	Compared to plain yoghurt and yoghurt with free polyphenols, fortified yoghurt with the encapsulated phenolics displayed somewhat increased antioxidant activity over time.	Martins et al. (2014)
Echium oil and phytosterols	Yogurt	42 μm	2 % w/w	Microencapsulation	Compared to yoghurt without encapsulated bioactive components, yoghurt with microcapsules had better physicochemical properties and increased oxidative stability.	Comunian et al. (2017)
Rubus ulmifolius Schoot flowers phenolics	Yogurt	14 and 88 μm	70 mg of lyophilized microspheres per 125 g of yoghurt matrix	Microencapsulation	The encapsulation protected the theaninangiogenic ability of the polyphenols in the acidic environment of the yogurts compared to free extracts	Oliveira et al. (2017)
Agaricus bisporus extracts	Yogurt	11.34 and 13.42 μm	2.5 mg/50 g	Microencapsulation	Phenolics encapsulated with maltodextrin contribute to the preservation of antiradical activity and overall nutritional properties in yoghurt during storage.	Francisco et al. (2018)
Tocotrienol	Yogurt	–	0.1 % (w/v)	Microencapsulation	The addition of microcapsules to yoghurt reduced changes in texture, color, and viscosity but was ineffective in protecting the encapsulated tocotrienols during storage.	Tan et al. (2018)

(Continued)

Table 1. Continued.

Encapsulated bioactive compounds	Fortified food matrices	Size	Fortification level	Delivery system	Outcomes	Reference
Fish oil/ γ -oryzanol	Yogurt	152 nm	3%/0.1%	Nanoemulsion	Fish oil/ γ -oryzanol incorporated as nanoemulsion into yogurt showed closer sensory attributes scores to plain yogurt	Zhong et al. (2018)
Zeaxanthin	Yogurt	184 and 150 nm	12.5% v/v	Nanoparticle and nanoemulsion	Zeaxanthin nanoparticles and nanoemulsion incorporation resulted in decreased firmness and viscosity	de Campo et al. (2019)
Date palm pollen	Yogurt	–	0.75%, (w/v) of milk	Nanoencapsulation	In comparison to other fortified varieties and the control, yoghurt enhanced with nanoencapsulated date palm pollen displayed the best texture and stronger radical inhibition.	El-Kholy, Soliman, and Darwish (2019)
Sour cherry phenolics	Yogurt	276 nm	5 % (w/w)	Liposome	Liposomal encapsulated phenolics were protected in the yogurt matrix during the storage and especially the spray dried capsules led to an increased total dry solid and reduced syneresis.	Akgün et al. (2020)
β -carotene	Yogurt	148.65–162.45 μ m	2.5 and 5 g/100g	Encapsulation	Carotenoids that were encapsulated greatly increased the yogurt's antioxidant capacity.	Šregelj et al. (2021)
Fish oil	Processed Cheese	0.21 μ m	5 % of the final product	Emulsion	The incorporation of encapsulated fish oil into processed cheese during processing reduces oxidation of omega-3 LC PUFA while maintaining the rheological properties of the processed cheese.	Ye et al. (2009)
Fish oil	Cream cheese	< 21.2 μ m	1.3 % (70% fish oil emulsion)	Emulsion	Addition of fish oil through delivery emulsions changed the microstructure of the cream cheeses and the choice of emulsifier impacted the oxidative stability of the product	Horn et al. (2012)
Polyphenols	Cheese	>100 μ m	–	Multiple emulsion	Addition of encapsulated and unencapsulated polyphenols showed a significant difference in cheese microstructures, moisture and ash content.	Pimentel-González et al. (2015)
Green tea catechins	Low-fat hard cheese	133 nm	0.25 % w/v of cheese	Liposome	The interaction of catechins with food matrix components was protected by encapsulation technique, which also protected against degradation and loss of antioxidant activity.	Rashidinejad et al. (2014)
Saffron extract	Ricotta cheese	190 nm	0%, 0.125%, 1%, and 2% w/v	Nanoliposome	Compared to the control cheese, the cheeses containing encapsulated saffron extract had significantly higher levels of hardness and chewiness	Siyar et al. (2021)
Curcumin	Ice cream	334 nm	0.24% of the final product	Nanoemulsion	Curcumin nanoemulsion incorporated ice cream withstand the processing conditions showing encapsulation efficiency of 93.7%,	Kumar et al. (2016)
Anthocyanins	Margarine	–	–	Microencapsulation	When compared to margarine containing free anthocyanins, margarine containing encapsulated anthocyanins had higher oxidative stability and melting completion temperature with lower onset crystallization temperature.	Zaidel et al. (2014)
Polyphenols	Mayonnaise	90.76–95.35 nm	500 mg per 1 kg	Nanoliposome	Encapsulated polyphenols demonstrated improved phenolic content retention, increased lipid oxidative stability, and reduced changes to the color and sensory properties of mayonnaise.	Rafiee et al. (2018)
Fish oil	Milk, yogurt and salad dressing	1.2 μ m	2% of Milk, yogurt and 20% salad dressing	Emulsion	Fish oil emulsion was more stable in milk than yogurt and salad dressing and this difference was attributed to possible interactions or interchange between the food system and the delivery system	Let, Jacobsen, and Meyer (2007)
β -carotene	Fat-free Tapioca Pudding and yogurt	10.5 μ m	0.528 mg encapsulated β -carotene per 8 g of pudding	Microencapsulation	Both fortified pudding and yogurt matrices significantly decreased the release and micelle incorporation compared to water dispersible β -carotene.	Donhowe et al. (2014)
Gac oil	Milk, yogurt and cake mix	< 30 μ m	20g in milk and yogurt and 160 g per 414 g cake dry mix	Microencapsulation	Encapsulated gac oil showed better retention of color, β -carotene and lycopene and low PV during storage.	Kha et al. (2015)

(Continued)

Table 1. Continued.

Encapsulated bioactive compounds	Fortified food matrices	Size	Fortification level	Delivery system	Outcomes	Reference
<i>Garcinia</i> fruit extract	Bread	20–100 μm	2 g in 100 g of wheat flour	Microencapsulation	Breads containing microencapsulates had significantly better qualitative characteristics than breads containing water extract. Due to the efficient encapsulation of WPI, bread with WPI encapsulates had significantly higher volume, softer crumb texture, and highly desirable sensory attributes.	Ezhilarasi et al. (2013)
Green tea extract	Bread	8–141 μm	2 g per 100 g of wheat flour	Microencapsulation	The volume and crumb firmness of the encapsulated green tea polyphenols-enriched bread were almost identical to the control but had better sensory attributes.	Pasrija et al. (2015)
Oleic acid and garlic phenolics	Bread	110–140 nm	0.65 mL/100 g of dough	Liposome	When compared to pure garlic phenolics, nanocapsules in bread formulation retard liposomal thermal decomposition.	Pinilla, Thys, and Brandelli (2019)
Curcumin	Bread	13.35 nm	20.75 g per 1 kg	Nanoemulsion	Curcumin nanoemulsion incorporated into bread formulation as the replacement of margarine showed an increase in the total strain and the elasticity of the crumb of bread compared to the control bread	Bagale et al. (2022)
Green tea extract	Biscuits	500 and 780 nm	2 g/100 g flour	Microencapsulation	Microparticles proved to be very effective in stabilizing the catechins during thermal treatment	Gómez-Mascaraque et al. (2017)
Beetroot pomace phenolics	Biscuit	–	10.8 % of dry matter	Microencapsulation	Pomace phenolics enhanced some nutritional properties and changed the color of baked goods, particularly when used as encapsulates.	Hidalgo et al. (2018)
Cocoa hulls polyphenols	Biscuit	6.4 μm	0.32 %	Microencapsulation	The use of maltodextrin for encapsulation resulted in the most stable powder with a total phenolic content that was unaffected by the baking process.	Valentina A. Papillo, Arlorio, et al. (2019)
Polyphenols	Cookies	–	10, 15, 20 %	Pumpkin protein isolate	Hardness color and sensory attribute of the cookies were significantly impacted by different level of the fortified encapsulates bioactive compounds.	Čakarević et al. (2021)
Oliver leaves extract	Meat system	0.3 to 20 μm	100 mg oleuropein/kg	Polyglycerol ester of polyricinoleic acid and sodium caseinate	Improvement of binding properties and texture of meat system.	Robert et al. (2019)
Fish oil	Beef Burger	–	15% of the fat	–	Increasing encapsulated fish oil inclusions did reduce cook loss but resulted in greater texture modification compared to controls.	Keenan et al. (2015)
Cinnamon extract	White and milk chocolate	191 nm	0.5, 1, 1.5, 2% (w/w)	Nanoparticle	Cinnamon extract nanoparticles containing chocolates showed minor differences in moisture content, hardness, color, and flow behavior, but not in particle size or melting properties.	Muhammad et al. (2018)
Fish oil	Energy Bars	–	5% of the final product	Emulsion	The casinate protective layer around Fish oil increased the distance between pro-oxidants in the surrounding matrix that enhanced the oxidative stability of energy bars	Nielsen and Jacobsen (2009)
Fish oil + Brown Seaweed extracts	Granola Bars	0.9 μm	5% of the final product	Emulsion	The coating material repelled the pro-oxidative ions in the water phase, reducing the interaction with the interface thus higher oxidation stability of oils in baked granola bars	Hermund et al. (2016)
Betanin	Gummy candy	36 nm	10 % w/w	Nanoliposome	The betanin nanoliposomes reinforced the gel matrix by reducing water activity and enhancing the interaction between gelatin chains, which led to an improvement in the texture of gummy candies in terms of hardness, gummyness, and chewiness.	Amjadi et al. (2018)

Beverages

In recent times, the functional beverages have become the most active functional food category due to convenience and the possibility to meet consumers' demands. However, the physicochemical environment of the beverages (e.g., low, high pH, moisture, salts etc.), their compositions (e.g., fruit pulp, chocolate, stabilizers, etc.) and their processing conditions can be challenging that might negatively affect the fortified bioactive compounds (Aadil et al. 2019; Ozdal, Yolci-Omeroglu, and Tamer 2020). Micro/nanoencapsulation has improved the sensory characteristics of functional beverages, including flavor, shelf-life stability, and controlled flavor release. In addition, the incorporated encapsulated bioactives improved the health-promoting properties of the beverages (Ozdal, Yolci-Omeroglu, and Tamer 2020). Tao et al. (2017) developed a steppogenin, loaded microemulsion to increase its solubility and stability in aqueous solution and studied microemulsions' ability to prevent oxidation of fresh apple juice. The steppogenin's (a natural flavanol) water solubility increased up to 3000-fold using a microemulsion and significantly inhibited browning of fresh apple juice. In another investigation, (Istenič, Cerc Korošec, and Poklar Urih 2016) tested the storage stability of epigallocatechin gallate in free form, entrapped into liposomes, and into alginate and chitosan microparticles loaded with epigallocatechin gallate liposomes in a fruit nectar. Compared with the free form, both delivery systems had the ability to stabilize epigallocatechin gallate in the liquid food during storage.

Dairy-based products

Since ancient times, dairy products have been the primary source of nutrients such as protein, fat, vitamins, and minerals, making them the most popular and highly consumed products worldwide (Eržen, Kač, and Pravst 2014; Pereira 2014; Scholz-Ahrens, Ahrens, and Barth 2020). This also makes them appropriate vehicles for the addition or modification of a variety of nutrients and health-enhancing substances. Dairy-product-based foods can be classified into three main categories: liquid (milk and fermented milk products), semi-solid (yogurt and a few varieties of soft cheese), and solid (mostly cheeses). However, the stability and the effective integration of isolated bioactive compounds have a detrimental impact on sensory attributes and preservation. Additionally, heat, light, oxygen, an acidic or basic pH, and water can make these bioactive chemicals vulnerable, which leads to undesirable changes in the products (Augustin and Sanguansri 2015; Bao et al. 2019; Cifelli 2021; Raikos and Ranawana 2017). Encapsulation with a properly chosen coating material can overcome these challenges, with little to no impact on the physicochemical and organoleptic qualities of the product.

For liquid milk products, the addition of several type of encapsulation systems have been investigated. For example, Moghadam et al. (2019) added nano-encapsulated fish oil consisting of omega-3 fatty acids into a probiotic fermented milk. Authors found that the fermented milks containing

nano-encapsulated fish oil increased probiotic bacterial counts, decreased the oxidation of eicosapentaenoic acid and docosahexaenoic acid, without negatively affect the sensorial attributes of the product. Similarly, Joung et al. (2016) assessed the radical scavenging activity of a curcumin nanoemulsion in a low-fat milk. The radical scavenging activity was not significantly affected by the water content, but was significantly increased by the surfactant concentration, indicating that a high surfactant concentration might make it easier for curcumin to dissolve in the oil phase, which would then increase the antioxidant activity. In a different study, the inclusion of both free and encapsulated arjuna herb phenolics had a significant impact on the physicochemical characteristics of the fortified matrix during long-term storage. However, changes in quality characteristics occurred less frequently in the sample containing encapsulated arjuna phenolics than in the other samples, indicating that the encapsulated form was successful in improving the storage stability of dairy drinks (Sawale et al. 2017).

The fundamental steps in the production of fermented dairy products (i.e., cheese and yogurt) include coagulation or gelation of milk proteins. Caseins and whey proteins, the two primary proteins found in milk, can be destabilized by enzymes such as rennet to coagulate the caseins, heat to denature the whey proteins, and acid to coagulate the caseins. Gelation is an irreversible because milk protein undergoes rearrangements, fusion, and syneresis during and after gelation (Fagan et al. 2017; Lucey 2008; Panthi et al. 2019). These structures in a coagulated protein system entrap milk fat as well as related nutrients and bioactive compounds. Tan et al. (2018) investigated the impact of storage and the yogurt matrix on the stability of tocotrienols encapsulated in chitosan–alginate microcapsules. The texture, color, and viscosity of the yogurt matrix were not significantly altered by the addition of tocotrienol microcapsules, and the tocotrienol microcapsules demonstrated greater resistance to oxidation during heat treatment than the unencapsulated tocotrienols. However, both the heat treatment and the acidity of the yogurt caused the rapid loss of α -tocotrienol in the fabricated microcapsules. Another study used yogurt as a delivery system for liposomal powdered phenolics from sour cherries. Compared with the control yogurt, the spray-dried liposomal powder resulted in an increased total dry solid and an increased water-holding capacity, which reduced syneresis in the fortified yogurt. Moreover, the total phenolic content was found to be highest in the yogurt samples that incorporated encapsulated sour cherry phenolics (Akgün et al. 2020). Ye et al. (2009) evaluated the lipid oxidation, sensory stability, and microstructure of processed cheese enriched with fish oil emulsion. The addition of emulsified fish oil substantially changed the microstructure of the processed cheese, and it was hypothesized that this change in microstructure and the choice of emulsifier for preparing the emulsions contributed to the oxidative stability of the processed cheese.

Green tea catechins and epigallocatechin gallate that were encapsulated in soy lecithin-based liposomes were added to low-fat hard cheese (Rashidinejad et al. 2014). During cheese processing, liposomes were retained in the curd

rather than partitioning into the whey. However, the interaction of the catechins with the components of the cheese was protected by the encapsulation, which also protected them against degradation and loss of antioxidant activity. Similarly, grape polyphenols that were encapsulated by multiple emulsions and added to Chihuahua cheese were compared, in terms of structure and physicochemical properties, with the control cheese and cheese with free grape polyphenols (Pimentel-González et al. 2015). Even though the inclusion of encapsulated polyphenols had an impact on the cohesiveness, moisture content, and ash content of the cheese, the encapsulation proved to be more effective at protecting the polyphenols and the cheese displayed physicochemical traits that were comparable with those of traditional cheese.

Starch-based foods

Starch is composed of two types of molecule: linear glucose polymer (amylose) and branched polymer (amylopectin) (Singh, Dartois, and Kaur 2010; Wang and Copeland 2013). Different ratios of these two molecules and their orientation within the granules provide starch with considerable variability in functional properties, such as water absorption, swelling, pasting, gelation behavior, and vulnerability to enzymatic degradation (Singh, Kaur, and Singh 2013; Zhu 2017).

The starch matrix has been shown to better protect hydrophilic and hydrophobic food ingredients from degradation under high temperature processing compared with lipid and protein food matrices, which undergo degradation (Fathi, Martín, and McClements 2014; Zhu 2017); however, the direct addition of bioactive compounds to cooked foods is still not possible, because of their easy thermal degradation/oxidation (Papillo, Arlorio, et al. 2019). Additionally, in a complex food, the way in which proteins and lipids interact with starch throughout the processing and digestion of meals might alter the quantities of glucose and active ingredients that are released (Lu et al. 2019; Singh, Dartois, and Kaur 2010). To overcome the environmental influence, the encapsulation has shown promising results in protecting the payload. Papillo, Arlorio, et al. (2019) added microencapsulated cocoa husk polyphenols to model biscuits to increase their stability during baking. After baking, the antioxidant activity of all the biscuits was decreased considerably compared with that of the equivalent powder at 0 min. The biscuits containing polyphenol microencapsulated with maltodextrin, which served as a stabilizing agent in preventing the heat-labile polyphenols from degradation, had the highest total phenolic content and the highest antioxidant activity. In contrast, the biscuits containing extract that was not microencapsulated had little stability. In a different study, the oxidative stability of granola bars supplemented with a multilayered fish oil emulsion was examined in the presence of novel brown-seaweed-based antioxidants. The bars made with the secondary emulsion method produced fewer oxidation products, which could probably be attributed to the thicker interfacial layer, which would act as a barrier to the

penetration and diffusion of molecular species that support oxidation in lipids during the baking of granola bars (Hermund et al. 2016).

The integration of bioactive compounds has been proven to have an impact on the structural characteristics of the finished product in addition to the protective effect of encapsulation on the fortified bioactive compound (Delfanian and Sahari 2020; Tolve et al. 2023). For instance, the presence of gluten protein during bread baking gives distinctive viscoelastic properties to the dough, allowing the dough to expand during fermentation while also retaining the majority of the gas inside the dough structure. The direct addition of organic acids to the dough can significantly reduce the mixing time and make the dough weaker (Lu et al. 2021; Su et al. 2019). Ezhilarasi et al. (2014) studied the effect of both unencapsulated and microencapsulated *Garcinia* fruit extract on the quality of bread. The direct addition of the *Garcinia* fruit extract significantly lowered the volume of the bread because of the presence of hydroxycitric acid, which directly affected the dough development and ultimately resulted in the poor bread volume. In contrast, microencapsulation improved the resistance of the dough to the effects of acid and assisted in maintaining the volume of the dough at a specific level, producing a bread with a softer crumb texture and better sensory attributes. Even though there is a wealth of information on the use of starch-based encapsulation methods for bioactive substances, a thorough approach examining the interactions between the starch matrix and the encapsulated bioactive ingredients is still required. With the appropriate physicochemical properties and controlled release applications, it will be possible to build superior functional products.

Meat products

The meat industry is paying increased attention to the incorporation of bioactive compounds in order to create various meat products that are both nutritious and of high quality. As well as the successful replacement of synthetic antioxidants and antimicrobials in recent years, meat products incorporating bioactive-loaded oil-in-water emulsions have also demonstrated an improvement in the fat content to fulfill consumer demand (Domínguez et al. 2021; Keenan et al. 2015; Robert et al. 2019). The partial substitution of native saturated animal fat with bioactive-loaded emulsions containing healthier unsaturated fats/lipids from other sources is arguably a healthier option but creates considerable hurdles in terms of texture, lubricity, and mouthfeel in comminuted products (Nacak, Öztürk-Kerimoğlu, Yıldız, Çağındı, and Serdaroğlu et al. 2021; Nieto and Lorenzo 2021; Serdaroğlu, Öztürk, and Urgu 2016). Robert et al. (2019) encapsulated olive leaf extract in a double emulsion and introduced it into a meat system as a fat replacer. Because of the enhanced double emulsion dispersion within the meat matrix, the substitution of pork backfat with the double emulsion greatly improved the binding and textural qualities of the meat system. Additionally, encapsulated olive leaf extract also enhanced the oxidative stability and

oleuropein degradation, resulting in meat systems with reduced concentrations of thiobarbituric acid reactive substances and lower peroxide values compared with the control. Another study compared the effects of using encapsulated and unencapsulated fish oil to partially replace the fat in beef burger patties (Keenan et al. 2015). In addition to altering the fatty acid profile, the inclusion of encapsulated fish oil resulted in greater texture modification with reduced cooking loss compared with the control. Despite these published studies, this area of meat-based foods with added encapsulated bioactive compounds has not been extensively investigated. Thus, further research to explore the in-product interactions of the bioactive compounds with the other elements of the surrounding matrix is required, as this will aid in the development of meat products that have better consumer acceptance.

Lipid/fat-based foods

Lipid/fat-based foods are complex colloidal systems consisting of highly organized, self-assembled microstructures that can generally be affected by various factors such as water content, processing conditions, fat/lipid composition, and storage conditions. These foods have been used as an important template for the delivery of lipophilic bioactive compounds. However, most of the studies to date have focused on the direct fortification of these isolated health-promoting compounds, which undergo various transformations during processing and storage. Encapsulation is an effective method for protecting these chemicals from degradation while also improving their stability in the matrix and ensuring end-product functionality. Zaidel et al. (2014) investigated the storage and stability characteristics of margarine, i.e., a water-in-oil emulsion, containing both nonencapsulated and encapsulated anthocyanins from roselle and red cabbage. When compared with nonencapsulated anthocyanins, margarines containing encapsulated anthocyanins had superior attributes, as evidenced by their high melting completion temperature, low onset crystallization temperature, and higher stability during storage. In another study, Rafiee et al. (2018) evaluated the effect of phenolic compounds containing nanoliposomes on the oxidative stability, microbial spoilage, and sensory properties of mayonnaise samples during storage. In addition to improving the phenolic component retention, the slower, more gradual release of the polyphenols from the nanoliposomes resulted in significantly fewer alterations in color metrics and sensory characteristics than did the free phenolic compounds.

Mostly these studies focused on the influence of initial structures of food systems. However, the inclusion of other food components, such as the combination of protein, lipids, and polysaccharides in a single meal composition, may lead to far more complicated chemical interactions and structural organization at the macro-, meso-, and microscopic level. As a result, real fortified food matrices (i.e., noodles, curries, cereals) that are part of our common diet might be a future study path to examine.

Behavior of encapsulated bioactive compounds during digestion

The process of the disintegration and consequent absorption of nutrients in the human gut is directly affected by the microstructural arrangement of the food (Aguilera 2019; Kong and Singh 2008; Rein et al. 2013). The complex structure of the meal is disrupted throughout the digestion process, reducing its particle size by comminution and trituration. Thus, for the design and production of innovative foods with particular targeted behaviors within the body, it is crucial to understand the relative relevance of the gut disintegration processes in relation to the composition and structure of the foods (Acevedo-Fani, Dave, and Singh 2020; Somaratne et al. 2020).

The structural breakdown of foods takes place in the mouth, stomach, and small intestine – the three primary parts of the digestive system. Depending on their physiology/anatomy and the structure of the ingested food, each of these digestive organs contributes differently to the breakdown process. All the fragments of the ingested food, regardless of their texture, and size, are processed in a specific way and vary a lot from one person to another. These variations in fragmentation are influenced by the individual person's behavior and masticatory system, i.e., total ocular area $\approx 214.7\text{cm}^2$, including lips, cheeks, palate, tongue, and teeth, number of teeth and chewing cycles, bite force applied by jaw muscular activity, amount of saliva produced to bind the masticated food into a coherent and slippery bolus, and the different phases of the foods including solids, semi-solids, or even liquids (Liu et al. 2017; van der Bilt 2009). Additionally, factors such as age, gender, ethnic groups, and oral health may vary the process of chewing (Chen 2009). During the chewing process, saliva moistens the food particles and converts them into a slippery bolus that can pass easily down the alimentary canal. Unlike solid foods, liquid foods do not undergo a large amount of chewing and mastication and have comparatively very short residence times in the oral cavity (Minekus et al. 2014). Additionally, the nature of the liquid, i.e., viscosity because of dispersed particles, the ratio of water to fat, and rheological attributes of emulsions mixed with salivary proteins, significantly influences the structural properties of the bolus (Liu et al. 2017; van der Bilt 2009).

The heterogeneous particles of the bolus are further hydrolyzed by the gastric secretions, which convert the dispersed nutrients into more readily bioavailable forms (Kong and Singh 2009). The rate of digestion of the bolus is determined by the time required for the gastric secretions to reach the walls of the surrounding matrix and free the bioactive compound from the matrix (Figure 2) (Bornhorst and Singh 2014; Guo et al. 2020; Lentle and Janssen 2011). Depending on the starting pH and buffering ability of the food, the pH in the stomach steadily decreases and may vary from one food to another (Acevedo-Fani et al. 2021; Luo et al. 2021; Qazi, Ye, Acevedo-Fani, and Singh, 2021, Qazi et al. 2022). Similarly, gastric emptying depends upon the properties of the meal consumed, such as viscosity, density, and particle size. Both propulsion and retropulsion processes,

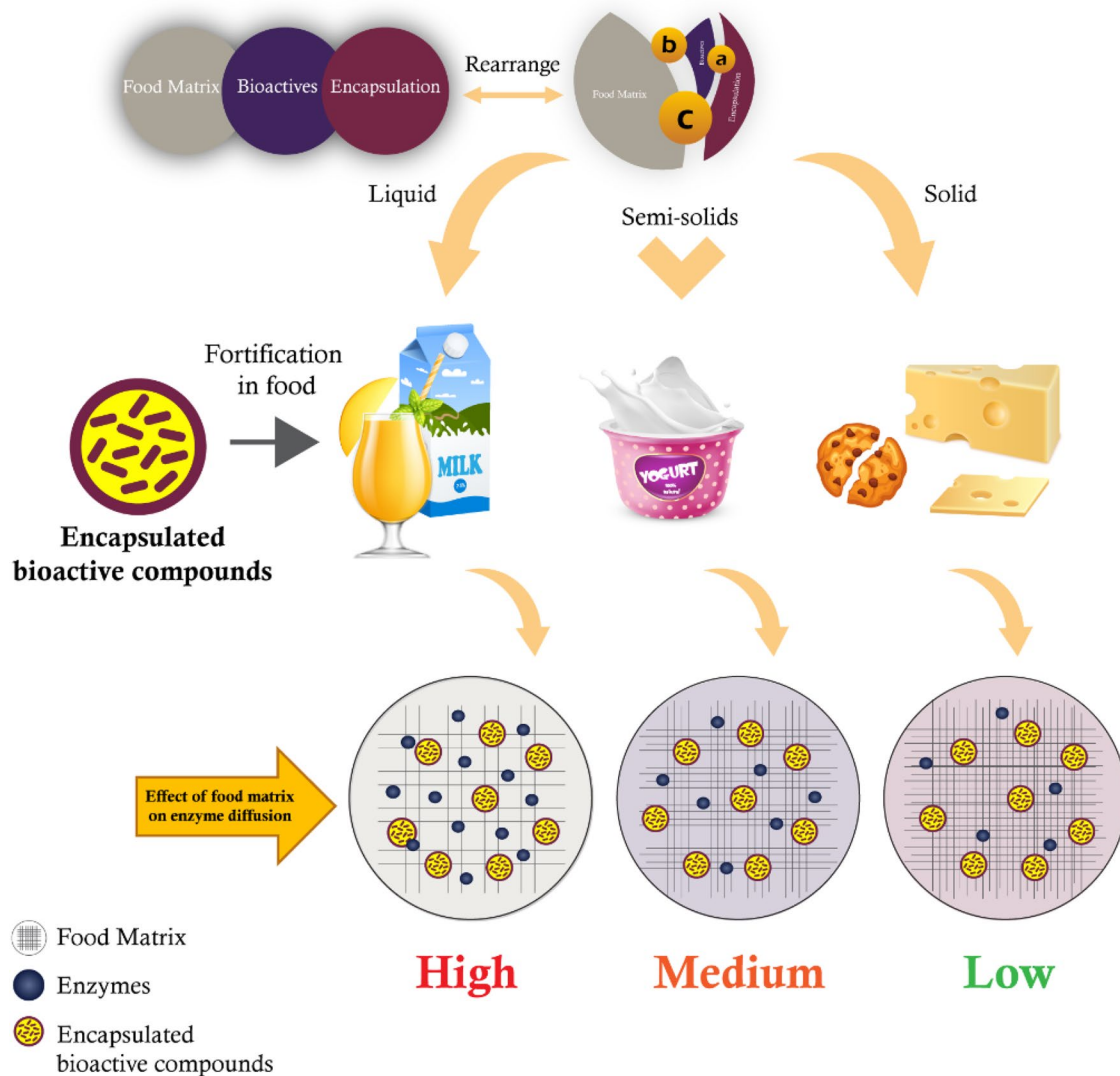


Figure 2. Effect of different types of food matrix on the penetration of digestive enzymes.

along with the gastric juice, attempt to reduce the size of the food to fine particles and to empty them into the first part of the small intestine, i.e., the duodenum. Additionally, *in vivo* studies (Egger et al. 2017; Miranda and Pelissier 1981; Ye et al. 2019) and a dynamic *in vitro* human gastric simulator (HGS) have shown that the stomach juice and the mechanical grinding can cause liquids such as milk to coagulate, which prolongs their digestion rate and their duration within the stomach (Mulet-Cabero et al. 2019; Ye 2021).

Following gastric digestion of the food, its digestion is continued in the small intestine, where the macromolecules are predominantly broken down and water and nutrients are absorbed (Campbell, Berry, and Liang 2019; Li et al. 2020). The segmentation and peristaltic movement patterns in the small intestine help to mix the chyme and increase its interaction with the villous surfaces (Feher 2017; Nadia et al. 2021).

Pancreatic and bile secretions play a pivotal role in the digestion in the small intestine, firstly, by drastically changing the pH of the gastric chyme with bicarbonate ions to pH \approx 5–7 (Bakala N’Goma et al. 2012), and secondly, by

enzymatically (i.e., amylase, proteases, peptidases, lipases, and esterase) cleaving the protein, starch, and lipids that remained unhydrolyzed during the gastric phase (Singh and Gallier 2014). Pancreatic proteases are divided into trypsin, chymotrypsin, elastase, and carboxypeptidases A and B. Pancreatic lipase is the major contributor to the digestion of lipids and fats in food (MacFarlane 2018; Minekus et al. 2014). The pancreatic lipase, colipases, cholesterol esterase, phospholipase, etc. catalyze the mono- or diglycerides, fatty acids, and cholesterol. Similarly, pancreatic α -amylase hydrolyzes the 1–4 α linkages in starch (Nadia et al. 2021; Patricia and Dhmoon 2019). Another major factor in intestinal digestion is the bile salts produced by the liver and stored in the gall bladder. They are rigid, biological surfactants that are synthesized from cholesterol. Their major function is to reduce the surface tension and to conjugate with the products of lipolysis, i.e., phospholipids and monoglycerides, resulting in emulsification, the formation of a cylindrical disk called a micelle, and its transportation across the brush border membrane (Salvia-Trujillo et al. 2017; Sarkar, Ye, and Singh 2016; Vitek and Haluzik 2016). Following digestion in

the small intestine, the undigested material, such as dietary fiber, enters the colon, where it is fermented by the residing microbiota (Wong et al., 2012). Thus, the unique pattern of the disintegration of food during digestion and the release of fortified or enriched bioactive compounds deserves special attention in order to understand and design a food matrix that with superior health benefits. In the last 10 years, scientific advances Table 2 lists the *in vitro* digestion studies of several encapsulated bioactive compounds that were enriched into real/model foods. In the following sections, we give more detail about a few of these examples.

Digestion of liquid foods

Healthy dairy- and plant-based beverages, sports and energy drinks, fermented beverages, and many more comparable items are always in high demand from consumers. To cater for the increasing consumer demand for healthier beverages, food industry is continually developing various fortified beverages that are stable, have good shelf life, and are appealing to consumers (Ahmad and Ahmed 2019; Ansari and Kumar 2012; Puiggròs et al. 2017).

As liquid foods generally lack structures that need to be broken down, they empty from the stomach rapidly without a lag phase, thus resulting in a minimum matrix effect (Siegel et al. 1988; Ye 2021). The alterations in liquid foods are mostly brought about by interactions between the constituent parts of the food and bodily fluids, or between the constituent parts when they are in a gastrointestinal environment (McClements et al. 2008; Singh and Acevedo-Fani 2022). A simple liquid matrix, such as isotonic beverages, has a set of easily digestible carbohydrates and a well-balanced mineral composition, is a suitable carrier for supplementing functional ingredients. Wyspiańska et al. (2019) designed an isotonic drink that was fortified with inulin- or maltodextrin-microencapsulated soybean isoflavone to investigate the impact of the microencapsulation process on the stability and antioxidant activity of isoflavones during a simulated *in vitro* gastrointestinal digestion. The isotonic beverage had no matrix effect on the delivery of the microcapsules. Although using inulin as a carrier resulted in capsules with a superior surface structure and better storage stability, the isoflavone levels in all samples were found to be significantly affected by the acidic and basic environments in the gut. To circumvent environmental impacts that such fortified beverages experience during digestion, a number of delivery methods have been suggested. To evaluate the release behavior, a model beverage was prepared by combining various curcumin-loaded lipid-based encapsulation systems. The curcumin nanoemulsion showed increased instability immediately after incorporation into the beverage, whereas the beverage stability relative to the pH remained unaffected in the presence of solid lipid nanoparticles and nanostructured lipid carriers. Furthermore, the beverage containing solid lipid nanoparticles had higher curcumin bioaccessibility than the other beverages, implying that lipid digestion products from liquid lipids bound with the salts in the beverage, preventing

the formation of mixed micelles (Gonçalves, Vicente, and Pinheiro 2023).

In contrast, because of their instability under gastric conditions, e.g., creaming of oil/fat, protein aggregation, and the high viscosity of carbohydrates, some fortified liquid foods can remain in the stomach for longer periods of time (Araiza-Calahorra et al. 2020; Liu et al. 2016; Niu et al. 2020; Steingøtter et al. 2017; Wang et al. 2021; Ye 2021). Liquid food such as milk have unique digestion kinetics because of their protein content, with completely distinctive properties. The coagulation of caseins in the stomach, driven by pepsin, and the acidic environment led to a protracted gastric digestion, resulting in slower release of the fortified ingredients (Hodgkinson et al. 2018; Mudgil and Barak 2019; Qazi et al. 2022). In contrast, whey proteins are digested and absorbed in the intestine more quickly. Recent research has demonstrated that altering the processing conditions, i.e., homogenization, heating, etc., can vary the interactions between the milk proteins and the other constituents, hence changing the kinetics of milk digestion (Egger et al. 2017; Huppertz and Chia 2021; Mulet-Cabero et al. 2020; Mulet-Cabero et al. 2019; Ye et al. 2017; Ye et al. 2019). The gastrointestinal digestion of recombined milk systems fortified with curcumin nanoemulsion was investigated using an HGS (Qazi et al. 2022). The milk systems reconstituted from low-heat, medium-heat, and high-heat skim milk powders had significantly different disintegration behaviors in the stomach because of the different degrees of casein/whey protein complexes formed during the processing of the milk. In contrast to the low-heat and medium-heat milk proteins, the high-heat-treated milk proteins produced a loose and soft curd under dynamic gastric conditions, which led to a quicker outflow of the curd fragments and entrapped curcumin nanoemulsions. Thus, both the release of free fatty acids and the bioaccessibility of curcumin during intestinal digestion were affected by these variations in the gastric digesta profiles. Milk proteins have high surface activity and can partially or completely displace low-surface-active emulsifiers from the surface of emulsion droplets, making oil droplets in the beverage more susceptible to lipase action, which can accelerate the formation of mixed micelles in the small intestine. Niu et al. (2020) showed that, when used as a food system, a high-protein beverage improved the absorption of an enriched coenzyme-Q10-loaded nanoemulsion by boosting the lipolytic activity, in comparison with a coenzyme-Q10 nanoemulsion and coenzyme Q10 dissolved in oil. Whey protein and milk protein concentrates were effective in replacing the modified starch used to encapsulate the coenzyme-Q10, making them more susceptible to lipolysis, resulting in increased free fatty acid release and mixed micelle formation during the intestinal phase. Likewise, beverages made by structurally modifying milk proteins during fermentation, such as drinking yogurt, have been shown to alter the digestion kinetics and the release of entrapped phenolics in the gastrointestinal tract (Altin, Gültekin-Özgülven, and Ozcelik 2018).

In recent years, there has been a surge in consumer interest in replacing dairy milk with plant-based milks in the diet, demonstrating several health benefits to health-conscious

Table 2. Summary of *in vitro* digestion studies of different encapsulated bioactive compounds fortified real/model food matrix.

Encapsulated bioactive compound	Fortified food matrices	Size	Fortification level	Delivery system	Type of <i>in vitro</i> digestion	Outcomes	Reference
Isoflavones	Isotonic drink	2 to 10 µm	250 mg	Microencapsulation	Static	Isoflavone levels in all samples were found to have significantly decreased during gastric phase and was dependent on the food matrix and the pH prevailing in the process.	Wyspiańska et al. (2019)
Curcumin	Model Beverage	150 nm	38 µg/mL	Nanoemulsion, solid lipid nanoparticles and nanostructured lipid carriers	Static	When compared to beverages with free curcumin, the integration of lipid-based nano delivery systems increased curcumin's bioaccessibility while showing that the components present in the beverage impact lipids digestion and impacting the mixed micelles formation.	Gonçalves, Vicente, and Pinheiro (2023)
Mangiferin	Milk	135 nm	2%, 4%, 6% and 8%	Nanoparticles	Static	Addition of mangiferin nanoparticles slowed glycemic index of milk due to suggested hydrophobic bindings between mangiferin and carbohydrates and protein.	Samadarsi, Mishra, and Dutta (2020)
Curcumin	Milk	187 nm	0.03% of lipid fraction	Nanoemulsion	Semi-dynamic	High heated milk showed faster disintegration in the gastric phase and higher curcumin release and bioaccessibility compared to medium and low heated curcumin nanoemulsion fortified milk systems.	Qazi et al. (2022)
Coenzyme Q 10	High protein beverage	~200 nm	1250 g of nanoemulsion per 5 kg batch	Nanoemulsion	Static	In comparison to a coenzyme Q10 nanoemulsion and coenzyme Q10 dissolved in oil, a high-protein beverage as a food system increased the lipolytic activity, which improved the absorption of an enriched coenzyme-Q10-loaded nanoemulsion.	Niu et al. (2020)
β-carotene	Fat-free Yogurt	10.5 µm	0.528 mg encapsulated β-carotene per 8 g of yogurt	Microencapsulation	Static	Fortified yogurt matrix and the encapsulation method significantly decreased the release and micelle incorporation	Donhowe et al. (2014)
Zeaxanthin	Yogurt	184 and 150 nm	12.5% v/v	Nanoparticles and nanoemulsion	Static	Zeaxanthin bioaccessibility was found to be lower in both fortified with zeaxanthin nanoparticle and nanoemulsion, and this was connected to the wall material and food matrix.	de Campo et al. (2019)
Rutin	Yogurt	–	2.5 mg/g	Encapsulation	Semi-dynamic	The strong interaction between the encapsulated rutin and yogurt matrix protected the rutin during gastrointestinal digestion and increased solubility in the small intestine.	Acevedo-Fani et al. (2021)
Curcumin	Yogurt	64–102 µm	1.6 mg per 100 ml yogurt	Microparticles	Static	Yogurt matrix slowed down the curcumin release which was linked with the composition, pH profile and viscosity of the emptying digesta.	Ye et al. (2021)
Cinnamon leaf extract	Yogurt	–	0.8 % (w/v)	Encapsulation	Static	The beneficial compounds that can stop protein denaturation were unable to stabilize the proteins before the yoghurt was digested as a result of the physical entrapment of cinnamon leaf extract in agar and yoghurt matrix.	Tang et al. (2022)

(Continued)

Table 2. Continued.

Encapsulated bioactive compound	Fortified food matrices	Size	Fortification level	Delivery system	Type of <i>in vitro</i> digestion	Outcomes	Reference
Green tea catechins	Hard low-fat cheese	165 nm	125, 250 and 500 mg kg ⁻¹		Static	Catechin recovery was much higher for the 500 mg kg ⁻¹ catechin-enriched cheese than for the other two fortified cheeses. The increased breakdown of protein-catechin association by digestive enzymes in the cheese containing 500 mg kg ⁻¹ enriched catechin resulted in more unbound catechin available under the same digesting circumstances.	Rashidinejad et al. (2015)
Capsaicinoids	Whey protein emulsion gels	0.5 µm	0.02 wt%	Emulsion	Semi-dynamic	The matrices of the gels affected the characteristics of the gastric digesta which in turn influenced the lipolysis in intestinal digestion and the bioaccessibility of incorporated capsaicinoid.	Luo et al. (2021)
Curcumin	Yogurt and cheese gels	187 nm	0.03% of lipid fraction	Nanoemulsion	Semi-dynamic	Yogurt like gel showed a higher bioaccessibility compared to the cheese like gel and these change was linked with the structural changes of gels in the stomach affecting the composition of gastric digesta which changed the FFA release and curcumin bio-accessibility in the small intestine.	Qazi et al. (2021)
Curcuminoids	Yogurt and Rice	1–15 µm	0.05 %	Microencapsulation	Dynamic	Fortified rice showed higher curcuminoid bioaccessibility than yoghurt and was also 2- and 1.5-times more bioaccessible than the ingredient alone.	Valentina Azzurra Papillo, Arlorio, et al. (2019)
β-carotene	Whole milk, oat meal and whole milk-oatmeal	560 nm	0.1 %	Emulsion	Semi-dynamic	Microstructural changes of meal matrices as a result of macromolecule interactions influenced the lipid emptying rate, which was further linked with the retention of β-carotene during the GI digestion.	Molet-Rodríguez et al. (2023)
Tuna Oil	Orange Juice, Yogurt, cereal bar	–	0.8g microcapsules (25% oil loaded) per 38.2g of yogurt	Microencapsulation	Static	Microencapsulated tuna oil fortified cereal bars showed higher digestion of PUFA due to presence of higher dietary fiber content compared to other two food matrices.	Shen et al. (2011)
β-carotene	Almond butter	–	1.8 mg/g	Microencapsulation	Semi-dynamic	Despite of higher recovery of β-carotene in the small intestine the incorporation into micelle fraction was much lower for encapsulated system in food matrix, which was associated with the influence of coating material	Roman, Burri, and Singh (2012)
β-carotene	Murumuru Butter	35 nm	0.06 g/100g	Nanostructured lipid carriers	Dynamic	The amount of fatty acid release as a result of lipolysis in each gut compartment was linked with the bioaccessibility of β-carotene.	Gomes et al. (2019)
β-carotene	Rice starch hydrogels	0.26 µm	0.3%, w/w of lipid fraction	Emulsion	Static	Emulsion filled hydrogels showed faster digestion of lipid droplets than conventional emulsions which subsequently resulted in higher bioaccessibility of β-carotene	Mun, Kim, and McClements (2015)

(Continued)

Table 2. Continued.

Encapsulated bioactive compound	Fortified food matrices	Size	Fortification level	Delivery system	Type of <i>in vitro</i> digestion	Outcomes	Reference
Curcumin	Starch gels	187 nm	0.03% of lipid fraction	Nanoemulsion	Semi-dynamic	The initial structures of the starch gels and further changes in the stomach significantly impacted the release of entrapped curcumin nanoemulsion into the intestine.	Qazi et al. (2023)
Beetroot juice polyphenols	Cookies	–	10, 15, 20 %	Microncapsulation	Static	The gastrointestinal digestion produced novel peptides that improved the bioactive properties of enriched products <i>via</i> synergistic action with active compounds from beetroot juice.	Čakarević et al. (2021)
Curcumin	Gellified fish product	0.5 µm	0.5 g/100 g of mince	Microparticles	Static	Curcumin bioaccessibility in fish gels incorporated with Curcumin-gelatin microparticles was comparable to that of commercial curcumin loaded fish gels; however, complexation of free curcumin with water soluble protein in fish gel comparatively decreased antioxidant activity.	Gómez-Estaca, Gavara, and Hernández-Muñoz (2015)

consumers (Fructuoso et al. 2021; McClements and Grossmann 2021; Sethi, Tyagi, and Anurag 2016). Typically, plant-based milks are produced utilizing size-reduction techniques that entail mechanical, chemical, or enzymatic breakdown of the original plant tissue structure (McClements and Grossmann 2021; Reyes-Jurado et al. 2021). However, they differ greatly from dairy-based milk systems in terms of their protein structures and interactions with fortified bioactive chemicals during processing and digestion (Fructuoso et al. 2021). Very few studies that have evaluated fortified plant-based milk systems are available. Zheng et al. (2019) compared the efficacy of curcumin crystals dispersed in water (control) with three delivery systems produced using the pH-shift method: curcumin nanocrystals; curcumin-loaded nanoemulsions; and curcumin-loaded soy oil bodies (commercial soymilk). The curcumin-loaded nanoemulsion and the soymilk had a homogeneous appearance and good stability. However, there were noticeable differences in terms of aggregation during the gastrointestinal digestion. In particular, the soymilk was considerably more prone to aggregation in the stomach than the nanoemulsions, which appeared to be more prone to aggregation in the mouth. However, by the end of the digestion, both systems produced curcumin that was relatively stable and bioaccessible. In contrast, curcumin nanocrystals had low bioaccessibility because there were fewer mixed micelles to solubilize the curcumin molecules. Similarly, Zheng, Zhou, and McClements (2021) encapsulated curcumin in the oil bodies of plant-based milk analogues (coconut, cashew, almond, and oat milks) using the same pH-driven method. Overall, the lipids in the plant-based milk were digested reasonably quickly during the first 20 min of the intestinal phase but more slowly thereafter. These differences were attributed to the different

compositions and structures of the lipids. Furthermore, the concentration of curcumin in the mixed micelle phase was much higher in the plant-based milks than in the control. It is interesting to note that, regardless of the lipid makeup of the oil bodies, the bioaccessibility of the curcumin was very consistent across all the plant-based milks. Recent research utilizing the dynamic gastric model, i.e., the HGS, has demonstrated that different plant-based milk systems go through various physicochemical changes in the gastric compartment (Wang et al. 2021; Wang et al. 2022; Wang, Ye, and Singh 2020). These changes have been shown to have a significant impact on the gastric emptying of nutrients in the small intestine, which can further influence the bioaccessibility of fortified bioactive compounds. The two studies that were presented earlier used a static approach to *in vitro* digestion, ignoring the dynamism that occurs in the actual gut. Therefore, in the future, thorough *in vitro* and *in vivo* studies will be needed to understand how plant-based milk matrices affect bioactive delivery.

Digestion of fortified semi-solid food matrices

The viscoelastic behavior of semi-solid matrices is substantially greater than that of liquid matrices, and semi-solid matrices contain a sophisticated biopolymer network that can hold a lot of water (Aguilera 2019; Alsanei, Chen, and Ding 2015; Devezeaux de Lavergne et al. 2015). Assemblies made during processing frequently contain fortified elements, which must be released during digestion for them to be further absorbed in the gut (Augustin and Sanguansri 2015; Dupont et al. 2015; Parada and Aguilera 2007). Additionally, these food structures, defined during

processing, undergo further structural reorganization during digestion, which impacts on the release of enriched bioactive compounds from the food structure (Mao et al. 2017; Qazi et al. 2021). Semi-solid foods, as opposed to liquid foods, spend a longer time in the oral cavity, where they first undergo transformation during mastication and salivation. Increased surface exposure during mastication because of increased mouth fragmentation increases the likelihood that bioactive substances that were previously contained will be released. Meanwhile, the salivary secretion also lubricates and wets the food after it has been chewed, creating a cohesive bolus that is ready for swallowing (Chen 2009; Minekus et al. 2014; Mun and McClements 2017). Apart from its role in bolus formation, saliva contains various proteins, enzymes, and electrolytes, which play a significant role in the emulsification and disintegration of food assemblies. Both *in vitro* and *in vivo* trials to understand the oral breakdown of semi-solid foods into small particles have been conducted. Luo et al. (2019) investigated the breakdown behavior in the mouth of capsaicinoid-containing whey protein emulsion gel structures; 18 human subjects chewed the gels, i.e., soft/elastic gel, semi-solid gel, and hard/brittle gel. The bioactive diffusivity was higher in the soft and semi-solid gels, as they went through a greater degree of fragmentation because of their loose structures. Luo et al. (2021) extended this work by subjecting the whey protein soft and hard emulsion gels to *in vitro* gastrointestinal digestion to evaluate the influence of the gel structures on the bioaccessibility of capsaicinoids. The hard gel had lower levels of lipid digestion and disintegrated more slowly than the soft gel because of the larger gastric particles and oil droplet sizes and the increased fat content in the digesta. It was found that the degree of lipid digestion was positively linked with the bioaccessibility of the capsaicinoids.

As previously discussed, liquid milk undergoes significant modifications during the gastric phase by forming a curd, which influences the release of fortified bioactive compounds; however, semi-solid dairy gel matrices such as yogurt and cheese, which are formed by the acid and rennet coagulation of milk proteins during processing, can alter the digestion kinetics and nutrient release in the gastrointestinal cavity. Our recent study investigated the *in vitro* digestion of yogurt- and cheese-like model gels that were fortified with curcumin nanoemulsion (Qazi et al. 2021). Although these gels had similar rheological and compositional profiles, their disintegration behaviors during dynamic gastric digestion had a significant impact on gastric emptying. After 240 min, all the curd particles from the acid-coagulated gel had disintegrated and none remained inside the gastric chamber (Figure 3). In contrast, the curd particles from the rennet-coagulated gel were rebuilt into a dense protein network under the influence of the gastric fluids and the gastric chamber was filled with numerous compact structured clots by 240 min (Figure 3). These alterations in the curd structures and gastric emptying rates during the gastric phase influenced the compositional profile of the digesta, which changed how the oil droplets were delivered and digested. This, in turn, affected the bioaccessibility of the associated lipophilic curcumin during the intestinal phase.

The release and delivery of these bioactive compounds can also be changed by fortifying them in various food matrices. Using a protein-rich food (yogurt) and a carbohydrate-rich food (rice), Papillo, Arlorio, et al. (2019) studied the gastrointestinal absorption of microencapsulated curcuminoids coated with gum Arabic/maltodextrin. The gastric degradation of curcuminoids in yogurt was less than that in rice, but the bioaccessible fraction of curcuminoids was much higher in the presence of the rice matrix compared with the yogurt matrix. Similarly, by combining two or more food elements, these food matrices can be made more complex. Another study investigated the digestion dynamics of a stirred yoghurt matrix enriched with the flavonoid rutin, as well as how interactions between the food matrix and rutin influenced the flavonoid's release and bioaccessibility throughout digestion (Acevedo-Fani et al. 2021). The results showed in comparison to co-digestion of an unfortified yoghurt with a rutin vegetable capsule, fortification of the yoghurt with a casein-rutin co-precipitate improved rutin protection and solubility during gastrointestinal digestion. Molet-Rodríguez et al. (2023) investigated the effects of whole milk, oatmeal, and whole milk-oatmeal containing β -carotene emulsions on the rate at which the stomach emptied, the digestibility of the lipids, and the retention of β -carotene. Changes in the microstructure of the meal matrices brought on by interactions between macromolecules had an impact on the rate of lipid emptying. Both the whole milk-oatmeal and the oatmeal had delayed lipid emptying, which was probably caused by the presence of β -glucan, which increases viscosity. Both the amount of fat emptied at each time point and the retention of β -carotene were linked by the *in vitro* small intestinal digestion. Furthermore, the introduction of oil-in-water emulsions into the complex meals enhanced the retention of β -carotene during the *in vitro* small intestinal digestion, leading to speculation that milk and oat flake components may prevent β -carotene from degrading during transit in the gut.

Vegetable butters as a potential matrix for the delivery of encapsulated bioactive compounds have also been explored. Roman, Burri, and Singh (2012) used *in vitro* digestion models, i.e., a static shaking water bath and an HGS, to study the release and bioaccessibility of β -carotene from fortified almond butter. β -Carotene oil (oil) and whey protein isolate-alginate-chitosan capsules (capsule) containing β -carotene oil were studied. In comparison with the shaking water bath model, peristalsis in the HGS model resulted in a greater release of β -carotene from the almond butter enriched with oil. In contrast, during intestinal digestion, more β -carotene was released from the almond butter enriched with capsules. However, more β -carotene was found in the micelle fraction of the almond butter that had been fortified with oil, pointing to the potential role of the coating material in preventing the β -carotene in the fortified almond butter from being absorbed into the body.

Despite several studies, many untested semi-solid food matrices must be investigated in the future if they are to be potentially employed for the delivery of these bioactive compounds.

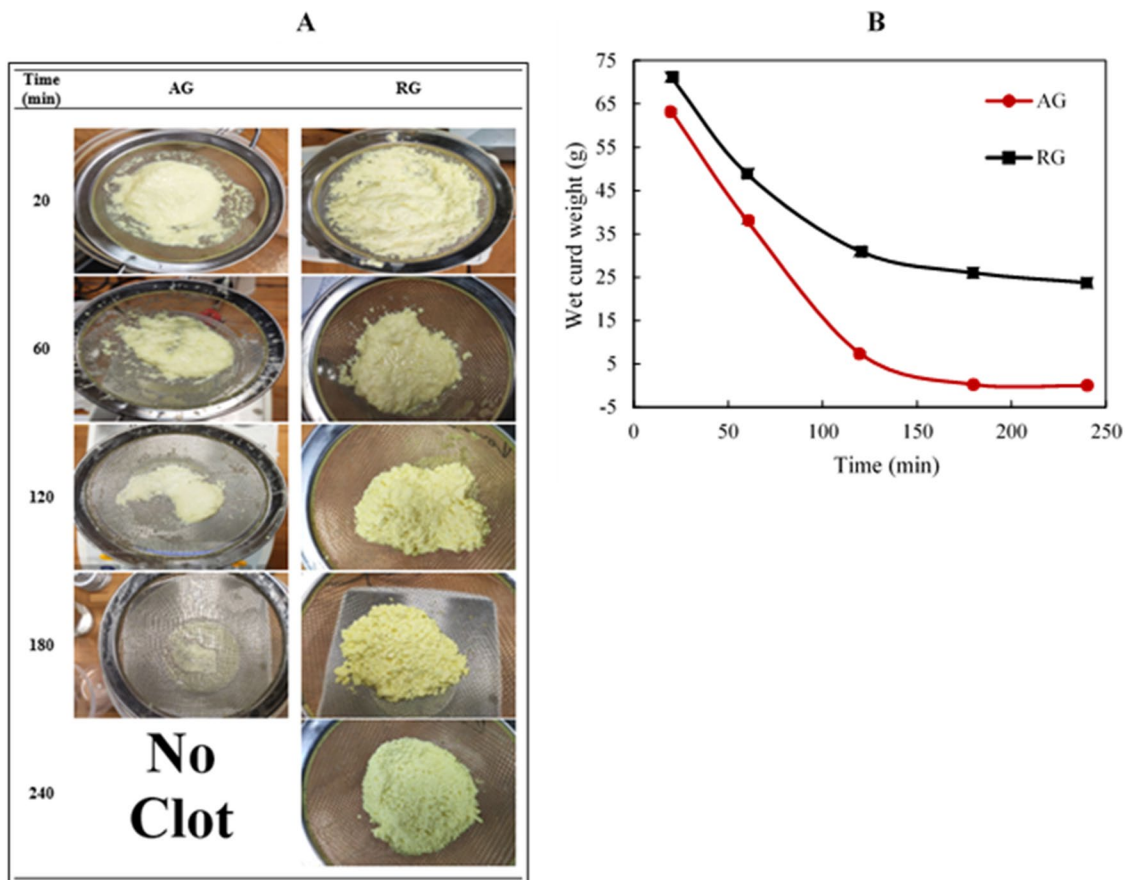


Figure 3. Images (a) and changes in wet weight (b) of curds formed by AG (acid gel) and RG (rennet gel) within the gastric chamber at selected time points. AG: acid gel, RG: rennet gel. [adapted from Qazi et al. (2021)].

Digestion of fortified solid food matrices

Natural and processed solid foods vary greatly in their structure and texture and these properties have a significant impact on the release of nutrients and active ingredients in the gut. Solid food matrices are usually low-moisture, semi-crystalline or crystalline structures. It is thought that the rate at which nutrients can dissolve into a solution for absorption is determined by how quickly the solid food matrices undergo disintegration, when the food particulates break into small fragments, allowing the nutrients that are held therein to dissolve into the gastric fluids (Kong and Singh 2008). Solid food begins to break down in the mouth during mastication, when saliva containing amylase is combined with the food to create a swallowable bolus that is then transported into the stomach by the esophagus. Compared with oral mastication, the gastric phase has greater complexity because of influencing factors such as fed/fast state, gastric acid, enzymatic reactions, and hydrodynamic and mechanical forces. These factors have been shown to significantly affect the restructuring of the food matrix, which further plays a major role in the release and bioavailability of active ingredients from food in the small intestine (Acevedo-Fani, Dave, and Singh 2020; Acevedo-Fani and Singh 2021; Somaratne et al. 2020; Ye et al. 2019).

Čakarević et al. (2021) assessed the physicochemical and sensory properties of cookies fortified with pumpkin-protein-

isolate-encapsulated beetroot juice polyphenols at three different levels, i.e., 10%, 15%, and 20%. The addition of the encapsulate increased the overall phenolic and betalain content and significantly improved the stability during storage. After gastrointestinal digestion, new peptides were created, which, in combination with the active ingredients in the beetroot juice, improved the bioactive properties of the enriched products. Mun, Kim, and McClements (2015) investigated the influence of rice starch hydrogels on the bioaccessibility of emulsified-lipid-solubilized β -carotene. To evaluate the bioaccessibility of β -carotene, the rice starch hydrogels loaded with β -carotene emulsion were compared with unencapsulated β -carotene-loaded starch gels and emulsions. Their study showed greater bioaccessibility of encapsulated β -carotene in the hydrogels compared with the other two systems, which was attributed to the protective effect provided by the surrounding hydrogels against aggregation of the lipid droplets during digestion. However, the composition of these gels could have altered the release behavior, ultimately altering the lipid digestibility. Mun et al. (2016) extended this work by studying the influence of methylcellulose (0–0.2%) on the digestion of rice starch hydrogels loaded with encapsulated β -carotene. In this case, the lipid digestion and the bioaccessibility of β -carotene decreased with increasing concentration of the indigestible polysaccharide (methylcellulose). It is interesting to note that most of the research carried out on the digestion of starch gels has

been conducted using static models of *in vitro* digestion, which do not provide detailed information regarding the behavior of the gels in the stomach and how this affects the bioaccessibility of the bioactive compounds. In a recent study, curcumin-nanoemulsion-loaded corn starch gels made from waxy, native, and high amylose corn starches were examined in detail for their microstructure, physicochemical characteristics, and *in vitro* gastrointestinal digestion (Qazi et al. 2023). The addition of curcumin nanoemulsion to the gels significantly changed their initial physicochemical characteristics. In the dynamic gastric phase, the breakdown and the emptying from the stomach of the waxy gel were slowed down, despite its higher amylopectin content, because of its higher adhesive nature, which trapped the majority of the nanoemulsified oil droplets inside the gel fragments. The different rates of starch hydrolysis, the release of free fatty acids, and the related bioaccessible percentage of curcumin were further linked to this heterogeneity in the compositional and structural profiles of the gastric digesta. In another study, Gómez-Estaca, Gavara, and Hernández-Muñoz (2015) investigated the bioaccessibility of curcumin after subjecting fish gels containing encapsulated curcumin micro-particles to an *in vitro* gastrointestinal digestion. When applied to a gelatinized fish product, the bioaccessibility and the antioxidant activity of the gelatin-encapsulated curcumin were reduced, indicating that curcumin may be able to form more stable complexes with some digested water-insoluble fish proteins that would lower these characteristics.

Conclusions and future outlook

Consumer's interest in functional food products is increasing because they offer supplement-level concentrations of health-promoting substances. However, despite this increasing interest, few efforts have been made to integrate encapsulated bioactive compounds into actual or model food systems; little dynamic *in vitro* and *in vivo* research has been carried out to assess their effectiveness after oral administration. The food structure is a key component that, in most cases, not only relates to a spatial physical domain that holds, interacts with, or confers specific functionalities to supplemented bioactive compounds during processing, but also controls their release in the gastrointestinal system. The intricate processing and preservation procedures can affect not only where bioactive chemicals are absorbed but also how well they interact with other dietary components. These modifications to these structural features of foods cause distinctive disintegration patterns, which eventually affect how bioactive compounds are released and absorbed in the gut. Several types of foods, such as dairy- and starch-based food systems, have been shown to have a longer residence time in the stomach, which alters the composition and the emptying pattern of the gastric digesta into the small intestine.

Although many studies reveal a possible connection between initial food structure and release and bioaccessibility of the nutrients and bioactive substances, much of the focus has been on the influence of initial structures of model food systems and *in vitro* disintegration in the gastrointestinal

tract. Much of the research involved relatively simple model systems, such as starch/lipid and protein/lipid based food systems. However, the inclusion of other food components, such as the combination of protein, lipids, and polysaccharides in a single meal composition, may lead to far more complicated interactions and structural organization at the macro-, meso-, and microscopic level. More realistic food matrices (i.e., noodles, pasta, breads) that are part of our common diet need to be considered for future studies. Additionally, it is important to explore how different bioactive chemicals, encapsulating materials, and delivery systems interact with distinct food matrices during processing and digestion. Moreover, utilizing advanced dynamic gastrointestinal models and noninvasive technologies like real-time MRI and hyperspectral imaging may offer valuable insights into food structure changes during digestion.

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Authors' contributions

Haroon Jamshaid Qazi prepared the original draft and edited the manuscript. Aiqian Ye critiqued and edited the original draft of the manuscript. Alejandra Acevedo-Fani and Harjinder Singh critically reviewed the manuscript. All authors listed have made a substantial, direct, and intellectual contribution to the conception and design of the manuscript and read and approved the final manuscript for publication.

Disclosure statement

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