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Perspective

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An integrated look at the effect of structure on nutrient bioavailability in plant foods

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Abstract

The true bioavailability of a nutrient being intrinsically coupled to the specific food matrix in which it occurs remains poorly considered in nutrition science. During digestion, the food matrix and, in particular, the structure of food modulate the extent and kinetics to which nutrients and bioactive compounds make themselves available for absorption. In this perspective, we describe an integrated look at the effect of structure on nutrient bioavailability in plant foods. Based on this integrated look, cell wall integrity and the particle size of the plant material during its transit in the small intestine determine the bioavailability of plant nutrients; in turn, cell wall integrity and particle size are determined by the level of oral processing and, accordingly, what subsequently escapes digestion in the upper intestine and is utilized by colon microbiota. Ultimately, the effect on nutrient digestion is linked to food structure through each step of digestion. A consideration of the structure rather than just the composition of foods opens up possibilities for the design of healthier foods.

Keywords: food matrix; structure; digestion; bioavailability; health

INTRODUCTION

Nutrition science has traditionally used a reductionist approach to investigate the link between food and health. Based on this approach, the health potential of foods and diets mainly depends on the content of nutrients or bioactive compounds.[1,2] However, we ingest foods, not nutrients, and foods are not simply vectors for nutrients in the human body (such as a pill is for a drug). Despite the concept of bioavailability (ie, the fact that only a fraction of dietary nutrients is actually available to our body) being long recognized, bioavailability studies still often focus on isolated nutrients or simple vector systems. In other words, the true bioavailability of a nutrient being intrinsically coupled to the specific food matrix in which it occurs remains poorly considered.[3,4] In the present study, we define food matrix as “the whole of the food components, their molecular interactions and spatial organization at different scales”.[5] Digestion comprises the moment where the food matrix mostly exerts this modulating effect on health. Digestion represents a crucial event in the physiological “interface” between food and health. During digestion, the food matrix modulates the kinetics and the extent by which nutrients and bioactive compounds make themselves available for absorption (ie, bioaccessibility). Bioaccessibility is the first pre-requisite for nutrient bioavailability, which also refers to tissue distribution and utilization of the biologically active compound at the relevant site(s).[6]

It is now widely accepted that a diet rich in plant-based food, such as fruits, vegetables, cereals, legumes and nuts, may reduce the incidence of chronic diseases (eg, cancer, diabetes, cardiovascular diseases) and is also beneficial against obesity.[7–10] The beneficial effect of plant-based food derives from the presence of minerals and vitamins, phytochemicals and dietary fibre, as well as from low levels of fat and calories. To optimize the health-promoting effect of plant foods, we must understand how plant matrices interact with our gastrointestinal tract during digestion, as well as how they are modified and how they modify our digestive processes. The plant matrix can modulate the bioavailability of nutrients through its specific composition. For example, food may contain components that interfere with the digestive processes by modulating the catalytic efficiency of digestive enzymes, by precipitating enzymes, substrates or a product of their hydrolysis, or by modifying the colloidal state of digesta (eg, properties of emulsified lipids) or its rheological properties (eg, viscosity).[11,12] In addition to its composition, the plant matrix may modulate the bioavailability of food components through its structure. Although additional structural barriers may exist (eg, subcellular organelles), the continuous network of cell walls is by far the most important structural feature in plant foods. From this perspective, we want to provide an integrated look (Fig. 1) at how structural integrity affects nutrient bioavailability in plant foods.

PLANT STRUCTURE AND NUTRIENT BIOAVAILABILITY IN THE SMALL INTESTINE

The bioavailability of nutrients in the small intestine depends on their accessibility for digestive enzymes and digestive fluids and this depends on food structure. The most striking structural feature of plant foods is the continuous, interconnected network of cell walls. Cell walls are comprised of dietary fibre (DF), which is,

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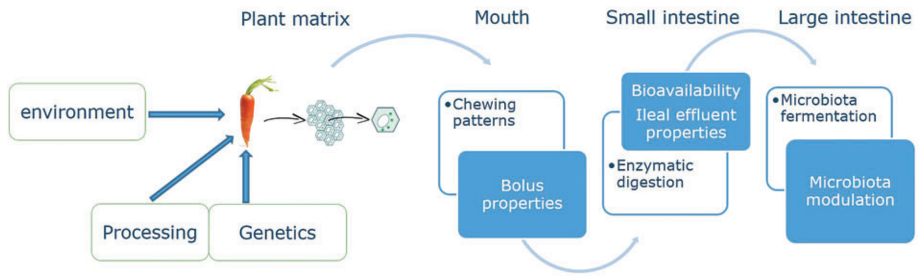

Figure 1. How structural integrity is related to nutrient bioavailability in plant food. The behaviour of plant food during digestion depends on the initial food composition and structure and different steps of digestion are connected with each other through the temporal sequence of the digestive process. Genetics, environment and industrial/domestic processing determine cell wall composition and architecture, including thickness and the density of cell wall material. Those characterstics are translated into precise bolus properties upon mastication. Those bolus properties include the size distribution of particles, the level of integrity of cell walls, their permeability to digestive fluids and the amount of nutrients released. In the small intestine, those bolus properties determine the bioaccessibility of nutrients in the small intestine and therefore the composition and structure of ileal effluents. The characteristics of the ileal effluents determine the effect on the commensal gut microbiota and the pattern of metabolites produced.

by its own definition, resistant to digestion in the small intestine.[13] When cellular integrity is retained, macronutrients are "encapsulated" within cell walls, which shields them from digestive enzymes and bile acids and reduces their digestibility and the absorption of hydrolysis products in the small intestine.[12,14] Unless a solution of continuity is present in the cell wall (eg, in damaged or broken cells), enzymes can only access the intracellular spaces through the natural pores in cell wall. The same holds true for the efflux of micronutrients or products of enzymatic hydrolysis of macronutrients. The degree of shielding depends on the cell wall composition and architecture (ie, its thickness and pore size distribution). Currently, there are no comparative data available on the relative permeability of cell wall material from different botanical sources to digestive enzymes and few data on how technological interventions (ie, thermal treatments) can modify this. Genetics and physiological factors (eg, the ripening stage or degree of maturity), as well as biotic and abiotic stresses, have a large effect on the composition of the cell wall and thus on nutrient bioavailability in plant foods.[15–17] Recently, it was shown how differences in pectin composition among potato lines may be responsible for differences in the rate of starch digestion.[18] Apart from providing a material barrier to enzyme diffusion to their specific substrate, intact cell walls contribute to maintaining a tightly packed intracellular matrix which further decrease digestibility by (i) shielding enzymes to corresponding substrates or (ii) impairing enzyme motility within cytoplasm.[19] Moreover, the size of the plant particle would represent an additional factor with respect to governing nutrient digestibility. This is mostly for two reasons: (i) more nutrients escape from damaged cells on the surface of smaller plant particles compared to bigger particles; this is because smaller particles have more exposed surface compared to bigger particles; and (ii) the diffusion of digestive fluids (and efflux of digested nutrients) to (and from) the core of the particles is slower for bigger particles compared to small particles.[20,21]

A substantial amount of knowledge has accumulated on the barrier effect of cell wall and particle size on starch digestibility in legumes and cereals,[19–27] although the effect in other starchy foods such as tubers has been comparatively less explored. Similarly, the role of cell wall integrity on lipid digestion has been so far thoroughly investigated in almonds[28,29] and also demonstrated in peanuts,[30] although little is known for other lipid-rich plant foods, such as other tree nuts, seeds or soy. We have recently shown that *in vitro* lipolysis is lower in hazelnut particles (1–2 mm in diameter) compared to hazelnuts oil bodies and that roasting increases lipid digestibility, which is partly explained by the effect of heat on the stability of oil body surface proteins.[31] The effect of roasting on lipid digestibility is shown in Fig. 2A, where the effect of hazelnut particle size on lipid digestibility is also visible. The amount of lipid escaping digestion (still locked into intact cells within hazelnuts particles) (Fig. 2B) is positively correlated to the particle size and is bigger in raw hazelnut particles of 0.5–1.0 mm and particles > 1 mm compared to roasted hazelnut particles of the same size range. The bioaccessibility of lipophilic micronutrients such as carotenoids is also affected by cell wall integrity,[32,33] even though the structural organization of carotenoids within the chromoplasts plays a role.[34] Comparatively, less is known about the effect of structural integrity on plant protein digestion[35–37] and even less is known about the bioaccessibility of low molecular weight, water soluble micronutrients such as vitamin C or polyphenols. With respect to phenolic compounds, the modest bioaccessibility from plant matrixes is partly attributed to interactions with cell wall material.[38,39] The composition of the cell wall material determines the nature and strength of interactions with phenolic compounds,[40,41] whereas the degree of structural integrity may influence the amount of phenolic compounds bound to cell walls by modulating its release from cytoplasm or the total cell wall surface offered to adsorption.

Accordingly, it is clear that the degree of food integrity has a large effect on bioavailability in the small intestine and a high degree of cellular damage will increase the intracellular nutrient bioavailability. Thus, intact (ie, not milled or ground in flour) legumes, nuts and cereals contain less digestible starch, proteins and lipids.[22,28,35] For the same reason, the true metabolizable energy from diets rich in intact plant foods, such as cereals, legumes nuts, fruits and vegetables, is likely lower than that calculated through the current methodologies based on conversion factors that do not take into account the limited digestibility of plant nutrients from intact structures.[42]

EFFECT OF ORAL AND GASTRIC PROCESSING ON PLANT FOOD STRUCTURE

Because cell wall integrity and particle size play such a crucial role with respect to nutrient bioavailability from plant foods, the way that foods are masticated is also very important. Oral processing is the first step of food digestion, by which solid foods are broken down, mixed with saliva and converted into a bolus that can be safely swallowed. Oral processing has evolved to increase the accessibility of nutrients and facilitate the digestion

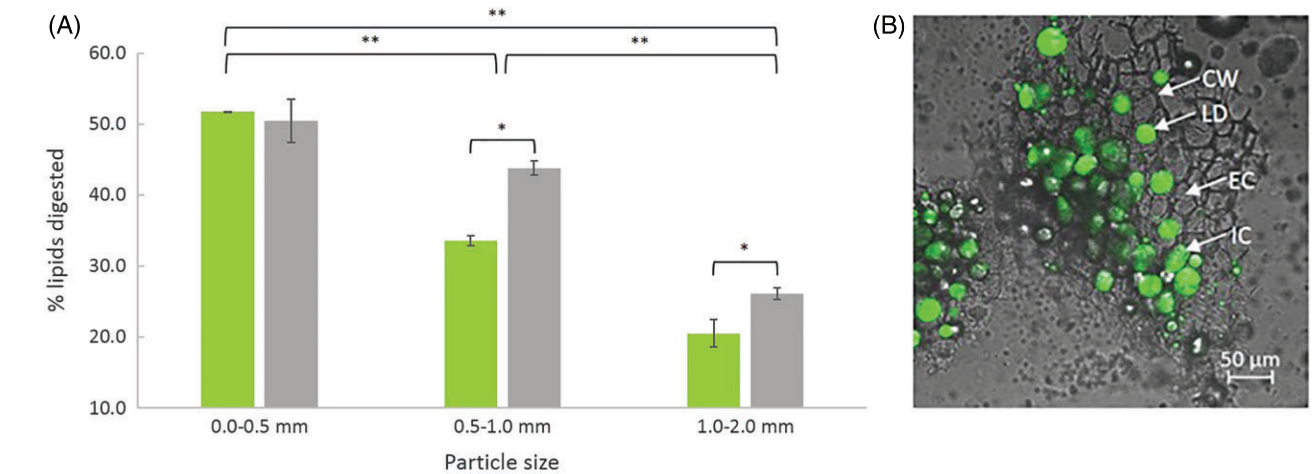

Figure 2. (A) Bioaccessibility percentage of lipids from raw (green bars) and roasted (grey bars) hazelnut particles of different sizes (mean ± SD from duplicate digestions). Percentage of digested lipids was calculated from the amount of undigested lipids recovered at the end of full gastrointestinal digestion from hazelnut particles and extracted with Soxhlet. *Significant difference between raw and roasted particles. **Significant differences among particles of different size. (B) Confocal laser scanning micrograph of raw hazelnut particles at the end of full gastro-intestinal digestion. CW, cell wall; LD, lipid droplet outside cells; EC, empty cells; IC, intact cells. Lipid stained with BODIPY 505/515.

of macronutrients in the gastrointestinal tract.[43] Whether a general assumption can be made that a more thorough comminution would release more nutrients from foods to digestive fluids and thus favour a higher bioavailability of nutrients and energy, as well how this is connected with individual oral behaviour, still remains unclear. The properties of the cell wall material in plant foods ultimately determine the mechanical resistance and failure behaviour during oral processing, and therefore the bolus properties, such as the particle size distribution, the share of broken and intact cells, and the amounts of intracellular macronutrients that are released as a result of mechanical compression by teeth. The properties of the cell wall material that are relevant at this stage comprise the nature of the cell wall constituents and their three-dimensional architecture, the thickness of the cell wall, and the density of the cell wall material (ie, the amount of cell wall material in relation to the tissue, mostly related to cell size).[44] Food processing plays a big role in determining the mechanical resistance and failure behaviour of plant foods, especially thermal treatments, which can alter cell wall composition by solubilizing cell wall components, modify the turgor pressure of plant tissues or induce cells lysis. For example, boiling of carrots softens the tissues by solubilizing pectins in the middle lamella (the cell wall layer that keep adjacent cells adherent).[45] As a result, mechanical failure will preferentially occur along cell walls rather than through them and relatively more intact cells are produced upon chewing compared to raw carrots.[46] Notably, the same effect is not observed in cereals that do not have pectin in the middle lamella, which preserves a strong adherence between adjacent cells after thermal treatments.[47] Another example is nut roasting which decreases nut moisture and increases their brittleness, resulting in smaller particles after chewing.[29] Domestic preparations such as grinding/milling or grating would change the bite size, as well as food geometrical properties, and possibly the way that foods are processed orally, although little or nothing is known in that respect. Similarly, little is known about whether oral processing of heterogeneous foods is different from homogeneous foods. For example, the comminution of whole nuts, seeds, legumes and cereals upon chewing might possibly be different depending on whether those are provided as such or incorporated in a embedding matrix such as bread or a muesli bar. In general, how certain structural features of plant foods are "translated" into certain bolus properties needs to be understood further.

We hypothesize that inter-individual differences in oral processing behaviour comprise a major contributor to inter-individual differences in nutrient bioavailability, especially for intact plant structures where nutrient availability is highly dependent on cellular integrity. Indeed, inter-individual differences in oral processing behaviour have been reported as one of the causes of inter-individual differences in the glycaemic index after the consumption of rice, but not of spaghetti, which is consistent with the fact that cell walls in rice represent a more important barrier to pancreatic amylase compared to the pasta gluten network.[48]

Plant food material that is broken down in the mouth can be disintegrated further in the gastric compartment by the simultaneous action of a low pH, mixing and the enzyme pepsin. During passage through the stomach, the combined action of soaking in an aqueous environment and a low pH may cause swelling of the cell wall and the partial dissolution of pectin from the cell walls of the plant material. This dissolution of pectin from middle lamella may contribute to the disintegration of the plant particles upon mixing induced by peristaltic contractions, such as a decrease in the average particle size, as reported for carrot cubes and raw almonds.[49] Clearly, the rate of disintegration is inversely proportional to the particle size because it will take longer for the gastric juice to travel to the core of a comparatively larger particle. In addition, pectin dissolution from primary cell wall may also increase of the permeability of the cell wall. Both particle size reduction and the enlargement of cell wall pores may increase the digestibility of intracellular material even though we did not find any increase in starch digestibility from isolated, intact kidney beans pre-soaked in gastric juice for 2 h,[19] which suggests a limit effect of gastric juice on cell wall permeability. The particle size distribution of boluses at the moment of swallowing and the amount of macronutrients released from fractured cells would also modulate digestive physiology, such as the extent of gastric sieving, the rate of gastric emptying, hormone secretion and ileal break, and also their consequences on gastrointestinal motility.[14]

PLANT STRUCTURE AND MICROBIOTA

Ultimately, all of the nutrients that escape digestion in the small intestine will enter the colon where they interact with the colon microbiota. Nowadays, it is common to refer to humans as superorganisms, where the human part is complemented by our complex symbiotic microbiota.[50] The interplay between the gut microbiota and the host plays an important role in host health. The gut microbiota acts as an additional digestive organ that metabolises the remnants of small intestine digestion, producing a range of dietary-derived metabolites that can impact health in a variety of ways.[51,52] On the one hand, the type of microbiota population determines which metabolites are produced from the material that enters in the colon. On the other hand, the composition of the diet will change the bacterial population in the colon. In general, a DF-rich diet will shift the bacterial population towards a more beneficial composition.[53] Because the microbiota feeds on what escapes digestion in the upper gastrointestinal tract, a direct link exists between behaviour in the upper intestine and colon fermentation.

In the first place, as we have seen above, the level of structural integrity is positively correlated with the amounts of carbohydrate, protein, phenolic compounds and lipid "dietary waste" that escape digestion in the small intestine and thus are available to the gut microbiota. Although it is already known that resistant starch (RS, ie, starch that escapes digestion in the upper gut) is actively fermented by the commensal gut microbiota, with beneficial effects on host health[54–56], it is not clear whether type I RS (basically, gelatinised starch encapsulated within intact cells) behaves differently compared to other forms of resistant starch such as type II RS (native, ungelatinized starch) or type III RS (retrograded starch). Some evidence indicates that different types or resistant starch or starch differing in their degree of crystallinity might be possibly fermented with different kinetics and may exert a differential prebiotic effect.[57,58] Moreover, the composition of the material that enters the colon may affect the order of utilization of the available nutrients by generating a temporal hierarchy based on which more accessible or preferred nutrients are metabolized first. This is sometimes referred to as hierarchical preference.[59] Thus, the presence of a substantial amount of type I RS (those encapsulated into intact cell walls) in the ileal effluents of subjects consuming a diet rich in intact plant structures, such as whole seeds and nuts, intact legumes and cereals, would possibly change the hierarchy of utilization of polysaccharides, with the fermentation of cell wall material being delayed to distal parts of the colon. The simultaneous presence in the large intestine of undigested and potentially metabolizable lipids, such as those delivered as physically encapsulated lipids in whole soybean or nuts, may also modulate the utilization of non-digestible carbohydrates by the gut microbiota. Together with RS, a variable amount of undigested dietary protein or lipids will reach the large intestine upon the intake of plant foods. Lipids might be metabolized by colonic bacteria in physiologically active metabolites such as conjugated linoleic acids and short chain fatty acids, which may have systemic effects once absorbed.[60,61] However, very little is known about the fate of lipids in the large intestine and how lipid utilization is modulated by the utilization of DF material. Proteins are also fermented by commensal microbiota, especially in more distal segments of the colon, which is considered detrimental because of the production of microbial metabolites such as ammonia, *p*-cresol, phenols, amines and H_2S.[62,63] However, certain tryptophan derivatives are considered as potent ligands of the aryl hydrocarbon receptor (AhR), a cytosolic receptor that plays a crucial role in the establishment/maintenance of intestinal homeostasis, which includes maintaining the integrity of the epithelial barrier, protection from pathogens, and regulation of commensal gut microbiota.[64] Recently, it was shown in mice that a tryptophan-containing diet might ameliorate DSS-induced acute colitis and regulate epithelial homeostasis through AhR,[65] which suggests that tryptophan-rich plant proteins consumed in an intact plant matrix may provide a precursor of AhR ligands to gut microbiota. Finally, structural differences in the plant material will be reflected in the total amount of phenolic compounds transported to the large intestine as associated with the cell wall material. Phenolic compounds can beneficially modulate gut microbiota[66] or they can be metabolized into bioactive compounds such as equol, urolithins, enterolactone and enterodiol with local or systemic effects.[67]

Secondly, the structure of what enters the large intestine can also modulate the microbial population and its activity and represents a neglected dimension in the complex relationship between the diet and gut microbiota.[57] These structural differences will modulate bacterial utilization by creating different micro-environments for bacterial growth, as well as different levels of accessibility of attractive substrates with respect to bacterial colonization and enzymes. Particle size, porosity and the total surface area of DF particles may therefore affect the fermentation rate, although how this reflects differences in the microbial utilization of DF is not clear. Although a more intense fermentation (and higher production of short chain fatty acids) was reported for smaller wheat bran particles compared to larger wheat bran particles[68] as well as for smaller mango particles compared to larger mango particles,[69] the opposite was observed for carrots and banana particles.[69,70] Because the size distribution of plant particles at the end of duodenal digestion is correlated with particle size distribution after oral processing, we hypothesize that the latter can affect gut microbial fermentation through the patterns of particle sizes produced in the mouth. The physical architecture of non-digestible polysaccharides within cell walls also represents a potential determinant. Technological interventions, such as thermal treatments or fermentation, can alter the composition and structural organization of the cell wall. Soaking of cell wall material in the digestive fluids of the small intestine loosens the cell wall structure, making the cell content more accessible to bacterial enzymes.[46,71]

CONCLUSIONS AND FUTURE PERSPECTIVES

The structural features of food can affect the bioavailability and the digestibility of nutrients at different interconnected levels, during the oral phase, during digestion and absorption in the upper intestine, and during bacterial fermentation in the large intestine, and all these levels are connected with each other via the temporal sequence of the digestive phases. It is clear that a reductionist approach to nutrition, which considers the nutritional properties of foods only in correlation with their composition, is naive and another dimension should be added to account for the variability in health benefits that we can obtain from the nutrients and bioactive compounds in our diets.[72,73] In particular, an intact food structure in minimally processed foods may contribute to modulating the bioavailability of nutrients, which represents an additional mechanism for the health-promoting effect of plant-based foods. Food structure is scarcely considered by health authorities in their nutritional guidelines mainly because of a lack of simple and appropriate methodologies that account for its structural properties. This problem may be circumvented, for example, by developing more holistic indices that include food structural properties next to nutrient composition,[73] by a broad classification of foods in groups based on the level of processing,[72] or by developing, for example, a database with food-specific or food group-specific conversion factors. This last approach is used by the Atwater specific system for calorie calculation, which takes into account the specific food product/category in which the nutrient occurs when defining the energy conversion factor for that nutrient.[74] Including the effect of structure in the evaluation of nutritional quality of food would represent a first step towards a more holistic approach to nutrition, which considers the whole of a diet rather than the sum of its nutritive components.[3] Modifying the structure rather than just the composition of foods (eg, through reformulation) opens up new opportunities for the design of healthier foods.

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