A shift toward a new holistic paradigm will help to preserve and better process grain product food structure for improving their health effects

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Abstract

This review aims at emphasizing the role played by physical characteristics and physico-chemical properties of food matrix on the digestive and metabolic fate, and health effects of grain products. It is today obvious that the food matrix conditions the health effects of food products and that we are able to modify this matrix to control the digestive fate of foods, and the metabolic fate of nutrients and bioactive compounds (reverse engineering). In other words, there is no more to consider nutrition in a quantitative perspective (*i.e.*, a food is a only sum of macro-, micro- and phyto-nutrients) but rather according to a qualitative perspective involving concepts of interaction of nutrients within the matrix, of enzymatic bioaccessibility, bioavailability and metabolic fate in relation with release kinetics in the gastrointestinal tract, and food nutrient synergy. This new perspective on the food health potential also reflects the urge to consider preventive nutrition research according to a more holistic and integrative perspective after decades of reductionist researches based on the study of the health effects of food components in isolation. To illustrate the importance of food structure, a focus has been made on grain-based products such as rice, leguminous seeds and nuts, and on soft technological treatments that preserve food structure such as pre-fermentation, soaking and germination.

1 Introduction: a little history

In 1977, Haber *et al*. (1977)[1] showed in healthy subjects that glycemic response after consumption of apples as whole, puree or juice was all the more faster than the food matrix was unstructured and satiety decreased parallel to the disintegration. It is known that, depending on the kinetic of arrival of carbohydrates in the blood, metabolic response is very different. In addition, an increased satiety contributes to a better control of food intake and ultimately weight. Today, we talk about rapid or slow sugars, this latter property being used by diabetics in their food choices in order to better regulate their blood sugar and insulin levels. In 1986, a study went in the same direction by showing that the act of swallowing foods rich in carbohydrates (sweet corn, apple, white rice and potatoes), rather than chewing, significantly reduced the glycemic response, the effect being similar to the administration of slow carbohydrates.[2] Finally, in 1991, similar results were obtained in humans following consumption of pasta or bread made from the same starting ingredient, *i.e.*, durum wheat, pasta resulting in reduced glycemic and insulin response - *i.e.*, hormonal - compared to bread.[3] Thus, the nutritional property is not contained in the durum wheat as such but in the food matrix shaped by the technological process. These three studies clearly show that, at somewhat constant carbohydrate composition, the nature of the food matrix significantly affects the metabolic response, then the health effect; and therefore that food is not only the sum of its nutrients but a structured matrix that contributes to metabolic and health effects.

It was only much later that we became interested in other nutrients than carbohydrates such as lipids and proteins. The concept of slow and fast proteins was thus proposed for the first time in 1997[4]. Boirie *et al*. (1997)[4] have shown that according to the physicochemical properties of the protein assemblies that are casein and whey, the rate of occurrence of amino acids in the plasma was not the same with a significant effect on the rate of postprandial protein synthesis. Concerning lipids, two years later, Armand *et al*. (1999)[5] showed that, depending on the size of lipid emulsions of identical chemical composition, the rate of digestion was not the same with metabolic consequences resulting in significant potential applications in enteral nutrition for individuals with pancreatic insufficiency and a deficiency of the enzyme lipase.

Besides the main macronutrients that are carbohydrates, proteins and lipids, for other compounds such as vitamins, minerals and phytonutriments (*e.g.*, polyphenols and carotenoids), we now know that for most of them there are both linked (to other compounds of the food) and free moieties. It is also known that depending on the nature of these interactions, speed and location of micronutrient absorption may differ. So there is only one step to broaden the concept of rapid and slow carbohydrates to all nutritional compounds in food. For example, ferulic acid - a polyphenol - is usually present both in free (~1-5%) and bound (~95-99%) form in whole grains. But each fraction has a different digestive fate with different metabolic modes of action, and therefore different health effects, so one can also almost define 'slow' and 'rapid' ferulic acid.[6] However, except for carbohydrate - particularly starch - today one is very far from being able to unravel what are the long-term health effects according to the release kinetics of a particular nutrient.

Therefore, it is no longer sufficient to modify the chemical composition of a food to alter its health effect: the physical structure and physicochemical properties of the matrix must also be taken into account. Yet, this shift from a quantitative nutrition (*i.e.*, a food is a sum of nutrients) to qualitative (*i.e.*, a food is a complex matrix that affects its health value) is relatively recent; and it is only recently that gradually emerges at the international level this awareness by the community of researchers in nutrition and food science. As a result, today, technologists search for controlling the physicochemical characteristics of the food matrices through process technology to control and optimize the health effect of foods (e.g., the degree of starch gelatinization, the degree of fibre solubility when incorporated into the food matrix or the nature of the molecular interactions between nutrient).[7-9] This process is called reverse engineering, i.e., the process that consists of first defining the desired health effect to secondarily design the food in a reverse way.

In the past, nutritionists were first concern whether or not a food contains a given nutrient, generally considered 'good' or 'bad' for health. Then we thought that all was digested in the gastrointestinal tract without really worrying about the kinetics of release of nutrients. But today we know that all the constituent elements of a food are not 100% bioavailable - a fraction thus arrives at the colon - and that their release kinetics can greatly impact the overall health effect of food. Today, research teams in Food Science applied to Nutrition tend to consider the food not as a set of isolated compounds, but as a sum of nested components, interacting with each other, but also with other foods and diet components.[10] This latter perspective is now to link with health effects. This trend also reflects the tendency to consider the nutrition research according to a more holistic and integrative perspective after decades of reductionist research based on the study of the health effects of food components in isolation.[11,12] The reductionist approach has led to the development of functional foods often enriched in one compound recognized as improving a given physiological function.[13] This has not prevented the development of the growing prevalence of unbalanced diet-related chronic and/or metabolic diseases such as obesity, diabetes, cardiovascular disease, hepatic setatosis, osteoporosis and cancer.[12]

The main objective of this review is therefore to discuss the influence of physical and/or physicochemical properties of food matrices on their digestive and metabolic fate and their health effects. Grain-based foods (cereals, legumes, nuts and seeds) are chosen as examples since, among food products, they possess the more solid, structured and compact food structure. In other words, the objective is to highlight that the food matrix, beyond the mere chemical composition, primarily determines the health food effect. There is no more to consider nutrition in a quantitative but qualitative perspective involving notions of interaction of nutrients within the matrix, the notions of enzymatic bio-accessibility, digestive bioavailability and metabolic fate depending on release kinetics within the gastrointestinal tract. First, we will briefly define what bioavailability means in nutrition science, notably as opposed to bio-accessibility.

2 From bio-accessibility to health effects

It is not enough that the food contains a particular beneficial nutrient so that it is fully utilized by the body. Between the food ready for consumption and its health effects, there is digestive fate, bio-accessibility of its components, their intestinal and/or colonic absorption, their metabolism and finally a potential health effect, namely the bioavailability (Fig. 1). The 'path' is long and the percentage of the compound that actually have an effect on the body is very difficult to determine accurately as shown by the few *sensu stricto* bioavailability studies conducted in humans, *i.e.*, using radioactive compounds, such studies being expensive. Notably, the access to the human digestive tract is complicated and does not easily and accurately allow determining bio-accessibility of dietary compounds.

We can distinguish four key steps of food compound fate in the human body (*i.e.*, bioavailability): bio-accessibility at the level of gastrointestinal tract, intestinal absorption, metabolism and final health effect. These four steps primarily depend on both the physical structure and initial physicochemical properties of the food matrix (Fig. 2) and physiological parameters of digestion involving the degree of chewing, gastric emptying rate and time, the viscosity of the bolus and/or hormonal parameters. At this point, some definitions are needed to understand the issues that link structure of the food matrix and health effect. But back first briefly on the concept of food matrix.

2.1 The food matrix

Recall that the term ‘matrix’ comes from the Latin word *matricis*, the latter being derived from *mater* meaning ‘mother’. Thus, a matrix is an element that provides support or structure and that is used to surround, to replicate or build. In the case of food, the matrix thus serves as a carrier or vehicle for bioactive food components. In addition, in the words of Parada and Aguilera (2007)[14]: “The concept of a “food matrix” points to the fact that nutrients are contained into a larger continuous medium that may be of cellular origin (in fruits and vegetables) or a microstructure produced by processing, where they may interact at different length scales with the components and structures of the medium" (page R22). Food matrices are either of natural or synthetic origin as a result of technological treatment applied (Fig. 2). Milk, although being a beverage, is therefore regarded as a full food matrix because interactions between nutrients exist and are likely to influence their release into the digestive tract.

Depending on the structure and physicochemical properties of the matrix, macro- and micronutrients will be more or less bio-accessible, then bioavailable. How nutrients are released into the digestive tract and then absorbed has a very significant impact on their metabolic fate, and therefore on long-term health. In a nutritional perspective, it is important to differentiate the four key steps listed above and not confuse them as has been done in the past: indeed, the proportion of the nutrient contained in the matrix and bio-accessible in the digestive tract is not necessarily equal to the fraction that will exert a health effect, *i.e.*, the bioavailable fraction.

2.2 Biovailability

Duchateau and Klaffke (2008)[15] defines ‘bioavailability’ as follows: “Bioavailability captures, in a single value, the dose fraction of a substance entering systemic circulation to elicit the intended physiological function upon reaching the target site" (page 207). According to Parada and Aguilera (2007)[14], the bioavailable fraction of an ingested compound is "the fraction of ingested nutrient that is available for utilization in normal physiologic functions and for storage" (page R22). The concept of bioavailability therefore implies the notion of physiological target to be reached by the bioactive compound. It is understood that bio-accessible fraction of a nutrient may not fully reach its target. This definition of Parada and Aguilera is the most accepted definition.

2.3 Bio-accessibility

Before being able to exert a beneficial effect in the body, a given nutrient or bioactive food compound must first be bio-accessible within the food matrix. And, in most cases, it is far from 100 % of the compound. According to Parada and Aguilera (2007)[14], bio-accessible fraction of a compound is "fraction that is released from food matrix and is available for intestinal absorption (typically based on *in vitro* procedures)" (page R22), but, should we add, also for the colonic absorption concerning some compounds, e.g., minerals. Due to the obvious difficulties to access the human digestive tract, this fraction is usually measured by *in vitro* digestive systems. Thus, generally, in research articles reporting studies conducted with *in vitro* digesters, the term 'bio-accessible' and not 'bioavailable' should be used. We now understand the key role played by the food matrix but also the digestive process, including mastication that partly deconstructs the food matrix, the physicochemical conditions of digestion such as gastric acidity and stomach emptying rate which depends in part on the size of the food particles coming from mastication. There are compounds in free form that can be easily released from the food matrix as soon as the mastication step; then there is less accessible compounds that become more accessible due to the erosive action of digestive enzymes. The residence time in the mouth, stomach and small intestine plays a very important role vis-à-vis enzymatic bio-accessibility, each step indeed involving enzymatic actions.

For example, chewing time is critical: a food only chewed a little arrive in the stomach in the form of particles with greater size than if chewing would have been longer[16]; accordingly, particle size influences both the rate of gastric emptying toward small intestine and stomach enzyme action *via* pepsin and gastric lipase, but also *via* salivary α-amylase that may continue to act in the stomach as long as the pH is not too acidic, for example into swallowed food bolus.[16]

2.4 Intestinal absorption and metabolic effects

Any fraction bio-accessible in the gastrointestinal tract may not be fully absorbed. For example, raw banana starch digestion releases dextrins which are not absorbed.[17] Indeed, banana starch is uncooked and its digestion may be long so that all products of digestion have not time to be absorbed, and reach the colon.

The metabolic effect of a given nutrient can be therefore defined as the physiological effect resulting from a compound having reached its intended target(s), namely a specific metabolic function such as antioxidant, glycemic or anti-inflammatory effect. The 'metabolic' fraction is actually that used by the body; and metabolic effect strongly depends on the fraction absorbed (Fig. 1).

2.5 Health effects

Considering the health effect of a food compound allows going beyond just the metabolic effect. The health effect of a compound could thus be defined as the potential of the compound to reverse metabolic deregulated or disturbed functions in a positive direction, in other words metabolic functions outside the normal (*e.g.*, increased oxidative stress, hyperglycemia, hyperhomocysteinemia, increased inflammatory status, etc.).

To be complete, this definition should also include the fact that the compound may simply participate in the functioning of a non-deregulated physiological function.

Therefore, the health effect depends on the metabolic fate of the compound, the amount reaching the physiological target and the physiological status of the individual (Fig. 1). In other words, is the individual already subjected or not to one or more diet-related chronic diseases (*e.g.*, obesity, diabetes, osteoporosis, hepatic steatosis, cancer and/or cardiovascular disease) or is it healthy (preventive nutrition)? In either case, the fraction of the compound providing a real health effect will therefore not be the same. Through these theoretical definitions, we understand that there is a huge difference between the amount of a nutrient in a food and the amount that has a real health effect.

Thus, beyond agronomic conditions and/or breeding, the main ways to act on the health value of a food are shaping its food matrix *via* processing (e.g., compactness, nutrient interaction, adding soluble or insoluble fibre) or the modification of the digestive physiology (e.g., satiety feeling, degree of mastication, gastric emptying rate, viscosity of the digesta). However, changing the digestive physiology is mainly realized *via* food: all therefore comes down to food design and formulation.

2.6 Conclusions

The food matrix is therefore a complex structure whose key parameters that affect the digestive fate of nutrients in the digestive tract are not well known. The exception is starch[18] and agro-food industry today knows how to use technological methods to increase the slowly digested and/or resistant starch fractions of foods.

After these theoretical considerations, the effect of grain-based food matrices type on their digestive fate and health effects will be addressed. Indeed, cereals, legumes, nuts and seeds well illustrate the effect of the food matrix on its health effects.

3 Impact of grain food matrices on their digestive fate and health effects

3.1 Grain-based products and food structure levels

The main grain-based foods are cereals (*e.g.*, wheat, rice and maize), pseudo-cereals (*e.g.*, quinoa, amaranth and buckwheat), legumes (*e.g.*, beans and lentils), nuts (*e.g.*, walnuts and almonds) and oilseeds (*e.g.*, linseed and sunflower seeds). Some grains, such as rice, staple food of more than half the world's population, and legume seeds (lentil, bean, chickpea, bean, etc.) are mostly consumed as whole grains not previously processed into flour or meal.

Grain-based foods are generally considered rich in starch, the main source of energy for humans. But this applies especially to cereal grains (~73 g/100 g). Legumes and oilseeds are characterized by their high protein (~26 g/100 g) and fat (~55 g/100 g) content, respectively (Table 1). The ingestion of cereal grains and legumes in the body causes a glycemic response resulting in an increase then a decrease in blood sugar level. The intensity and duration of the glycemic response vary depending on parameters related to the food but also to subject. On the basis of this difference in use by the body of dietary carbohydrates, Jenkins *et al*. (1981)[19] introduced the concept of glycemic index (GI) to characterize and quantify the glycemic response after consumption of different carbohydrate sources. The GI measures the evolution of the glycemic response after consumption of a test food with reference to glucose or white bread. However, the use of glucose as a reference is more relevant than white bread because its manufacturing differs across countries.[20] This has resulted in ranking foods into three categories according to the value of GI obtained: high GI (> 70), low GI (< 55) and moderate GI (55 < IG < 70).

I will focus here to show that, in addition to their nutrient composition, the structure of the grain-based food matrix also influences their nutritional properties. All food will not obviously be addressed and I will focus on some low (rice, legumes, oilseeds and nuts) and highly (breakfast cereal and biscuits) processed grain-based foods. Because bread[20] and pasta[21-23] have already been the subject of many papers, these two products are not presented here.

There are several levels of scale in the structure of foods derived from grains and seeds that may influence the digestive fate of nutrients. The structure will be discussed from the molecule (molecular level) until the particle size of the food during digestion (macroscopic scale), through interactions between the different starch, protein and fibre fractions (microscopic scale). Changes of food structure are derived from changes in product formulation (*e.g.*, adding fibre, adding legume flour, etc.) and/or parameters of manufacturing processes (*e.g.*, water content, temperature and pressure). In addition to changing the digestive fate of starch, the main component of cereal grains or starchy processed foods, the structuring/shaping of a food can also cause changes in the digestive fate of its other components such as protein, fat and fibre.

3.2 Cereal products

The relationship between physical structure and health effects of grain products has mainly been studied through their GI.

3.2.1 Rice grain

Compared to glucose, glycemic index of rice under the form of grain varies from 32 (Bangladeshi variety, traditionally parboiled, 27% amylose) to 139 (Turkish, white, low amylose, boiled).[24] Based on the values reported in Foster-Powell *et al*. (2002)[24] tables, it appears that the GI is highly dependent on the amylose content and cooking time; which seems logical enough: amylose is less accessible to α-amylase than amylopectin because of a more compact structure, and a longer cooking time increases the degree of starch gelatinization, so its water content and its accessibility to α-amylase.

Such an explanation was partly supported by *in vitro* digestion studies. First, Wang *et al*. (2012)[25] showed with ten rice cultivars that rice amylose contents, gel consistency and gelatinization temperatures have significant correlation with the resistant starch contents. However, while the amylose contents could not serve as an indicator to predict starch digestion, cohesiveness has a significant positive correlation with starch digestion index.[25] In seven rice mutants different in resistant starch contents, the degree of hydrolysis showed significant correlation with resistant starch, apparent amylose content, lipid content, and other starch physiochemical properties (gelatinization enthalpy and protein content).[26] However, digestibility was affected mostly by lipid content for mutants with similar resistant starch content. Finally, the integrity of aggregated starch and numbers of round granules observed after cooking contributed greatly to slow starch digestibility.[26] Second, cooking treatment (or thermal history) is an important factor influencing digestion process of rice with pre-soaking, higher water-rice ratio, or longer cooking time favoring higher digestion rate.[27]

Although a high proportion of amylose in a grain of rice is usually associated with lower GI, it appears that the porosity of the rice grains after cooking also plays an important role: thus, three varieties of amylose-rich rice give very different GI of 61, 72 and 91; differences that the authors relate to different degrees of hydration as unraveled by microscopic observations showing more voluminous spaces for water within the matrix of the rice with the highest GI.[28] Otherwise, polishing brown rice (with external envelopes) into white rice does not really cause any significant difference in GI, which remains at around 70.[29] The nutritional benefits of brown rice are therefore based primarily on fibre and protective micronutrients contents from the outer layers of the grain. Finally, cooking methods may also influence rice starch digestibility in the following order for the highest degree of *in vitro* digestibility: autoclaving > electric cooker > microwave oven > stone pot.[30]

These results clearly show that, contrary to common belief, rice is not necessarily a source of slow carbohydrates and may in some cases be a source of very rapid carbohydrates. Its average GI (73 ± 4) remains higher than that of pasta (means of ~50)[29] and is highly dependent on technological processes used in its preparation.

Finally, in addition to the effects of technological processes, the degree of chewing has recently been shown to significantly influence the glycemic response to 30 minutes after ingestion of rice, highlighting the role of particle size - and therefore by the degree of integrity of the physical structure of the food matrix - on physiological effects.[31,32]

Concerning rice digestive process within intestine, studies have been conducted *in vitro* or in pigs. No study in humans could have been found. In pigs, Bornhorst *et al*. (2013)[33] reported that brown and white rice follow distinct breakdown patterns during gastric digestion, bran layer of brown rice influencing its breakdown. This accounts for a slower protein emptying in pigs that had consumed brown rice compared to white rice.[34] In addition, it was previously observed that “the bran layer of brown rice had a profound effect on its gastric digestion, as it inhibited the absorption of moisture and acid leading to decreased texture degradation, thus delaying the rice disintegration as well as dissolution and slowing emptying of solids” (page E450).[35] Thus, non-starch polysaccharide enzymes significantly increased the digestibility of dry matter, and crude protein in early rice grain and brown rice by 16.3 and 27.5%, and 9.1 and 26.4%, respectively.[36]

3.2.2 Other cereal grains

Other minimally processed grain products and/or incorporating more or less whole grain are sweet corn (GI ≈ 52), wheat consumed in the form of grain (*e.g.*, Ebly®, GI ≈ 52), couscous (GI ≈ 65), bulgur (GI ≈ 48) muesli (GI ≈ 57) and breads containing more or less intact cereal grains (mainly consumed in the Scandinavian countries, GI ≈ 53). Their GI is generally less than 70 and usually around 50,[24,29] making them a good source of slow carbohydrates.

3.2.3 Breakfast cereals

Breakfast cereals are products widely consumed worldwide in many different forms. Their study is interesting because unlike the products mentioned above, they are often highly processed and will, in contrast, further emphasize the importance of the structure of the food matrix on its health effects.

One notes that the more drastic are the technological treatments applied to breakfast cereals during their manufacture the higher their GI is, mainly due to a significant breakdown of the physical structure of the initial grain matrix of cereals used. Thus, while the porridge and muesli - that contain little processed cereals - have GI lower than 70 (moderate GI),[24] puffed or flaked cereals have higher GI because of the disintegration of the starting matrix, strong starch gelatinization and the addition of simple sugars (GI generally > 70).[24]

3.3 Leguminous seeds

If there is a food group to which the physical structure of the food matrix plays an important role in the nutritional and health value, it is that of legumes. In our Western countries, these are generally consumed directly after soaking followed by a long cooking time in boiling water.

The matrix structure of legumes before consumption is very different from that of cereals having generally undergone several processing steps. The seeds are composed of a plurality of cells each constituted by a cell wall encapsulating starch granules more or less gelatinized and protein clusters (Fig. 3A). The rigidity of the cell walls limiting the diffusion of water to the starch during cooking is responsible for the partial swelling and gelatinization of the starch grains.[37] In beans, rich in amylose, partial gelatinization retains the crystalline structure of starch.[38] At ileum level in humans, the barrier effect of the cellular structures is illustrated by the presence of intact bean cotyledon cellular structures - that is to say having retained their physical integrity - and the absence of starch grains released from the cells.[38]

The conservation of the physical structure of the beans is also observed *in vitro* after 4 hours of digestion (Fig. 3B).[39] As a barrier to digestive enzymes, the cell walls are more effective than the protein network in pasta. Although this latter surrounds the starch granules, it is degraded in the digestive tract by pancreatic proteases.[40]

The combination of a physical barrier to enzymatic accessibility of the starch by α-amylase and a partly gelatinized starch explains the very slow and gradual release of glucose from legume starch in the blood. It is not surprising that the GI of legumes is generally among the lowest of all the foods, namely between 10 and 50, most often between 30 and 40.[19,24]

In addition to the slow digestion of starch, a significant fraction of the latter is not digested and reaches the colon intact: an estimate made in intubated healthy subjects (to recover the digestion products of white beans at ileum level) showed that about 17 % of the starch was not digested.[38] This value is close enough to the levels of resistant starch measured *in vitro*.[41] Samples collected from the stools show that starch and fibre are fermented in the colon, starch being finally degraded to almost 99%.[38] This is not surprising, the cell walls being composed primarily of dietary fibre fermented in colon.

Legumes also contain anti-nutrients such as phytic acid, lectins, α-galactosides, inhibitors of trypsin and chymotrypsin and tannins. Some, such as bean tannins, can contribute to inhibit the digestion of carbohydrates by inhibiting the enzymatic activity of α-amylase, maltase, saccharase and lactase, and thus affect intestinal absorption of glucose.[42] These anti-nutritional factors may also interact with the proteases and reduce protein digestibility.[43] Indeed, tannins can weaken the digestibility of the proteins forming tannins-proteins complexes that reduce the bioavailability of the amino acids.

Legume-based foods therefore prove to be very interesting from a nutritional point of view, particularly because they are cheap sources of protein, carbohydrates, fibre and many phyto- micronutrients.[44] They are also easy to store for long periods and can be cooked by the majority of the world population. Unfortunately, today they are mainly consumed in developing countries, their preparation time - among other factors - being unsuited to Western lifestyles.

3.4 Nuts and oleaginous seeds

Oilseeds are the third category of foods consumed as grain after cereals and legumes. They are characterized by a high lipid content ranging from 40 (flaxseed) to 70% (pecans) with an average around 55% (Table 1). Their digestive fate has been very little studied, except the almonds in relation to different physiological effects (oxidative stress, glucose, insulin, satiety). It should be known that almonds, with other types of nuts and oilseeds, can reduce serum LDL cholesterol levels[45] and therefore cardiovascular risk[46], although yet considered as important sources of energy. The synthesis of detailed results for this seed can be considered fairly representative of the digestive fate of other seeds of the same type which are of closed composition and physical structure.

As for legumes, it is especially the preservation of the physical structure of almonds during digestion which provides positive nutritional effects (Fig. 4A-D).

It is thus observed, in subjects consuming almonds, intact cotyledon cells in the feces which encapsulate lipids.[47] The cell walls are therefore a very significant factor limiting enzyme bio-accessibility then the digestion and absorption of lipids.[47] Furthermore, an increase in the proportion of almond in a composite meal is correlated with a decrease in blood glucose response.[48] The effect could be explained by the joint action of reducing the rate of gastric emptying and increasing of fibre content of the meal.[48] However, almonds containing mostly insoluble fibre, the effect is likely to be attributed to anti-nutritional factors associated with fibres (*e.g.*, inhibitors of α-amylase activity),[48] and now designated by the more positive term of 'fibre co-passengers'.[49] Finely ground almonds show the higher percentages of release of lipids (39%), protein (45%) and vitamin E (44%) after duodenal digestion, these percentages portending the fundamental role played by the physical structure of the food and in particular the plant cell wall as a physical barrier to the release and digestion of nutrients. Thus, the less almonds are chewed, the more fecal fat excretion, the greater the feeling of satiety and the more slowly the level of plasma insulin declines.[50]

In addition, the particle size significantly influence postprandial blood hormonal response in GLP-1 (glucagon-like peptide-1) which is lower after 25 compared to 40 chews.[50] Finally, more recently, it was shown that there was no effect of the type of grinding almonds (whole, sliced or ground, < 0.5 mm) on blood lipid and α-tocopherol levels after 4 weeks of consumption in hyperlipidemic subjects, chewing probably having leveled the differences in size of the ground particles.[51]

It is interesting to note that, as for almonds, Traoret *et al*. (2008)[52] found higher fat and fecal energy losses after eating whole peanut seeds compared with peanut oil, butter or flour, demonstrating a probably reduced nutrient availability. These results suggest that all oilseeds could exhibit quite similar digestive fate and nutritional properties.

3.5 Conclusions

Compared to cereals consumed as grains (*i.e.*, only a little transformed), legumes and oilseeds (*e.g.*, almond) usually keep a longer physical structure intact during digestion, giving them protective nutritional effects. This effect is attributed to the highly resistant cell walls of these seeds. The slow, gradual and partial degradation of their starch fraction is interesting from several points of view to health, especially for diabetics who find a relevant food to reduce and better manage their postprandial glucose. Thus, legumes have been used to enhance the nutritional quality of pasta providing complementary nutrients to wheat (*e.g.*, amino acids) while maintaining a progressive hydrolysis of starch.[53,54] Legumes also promote satiety[55] and therefore help to avoid snacking between meals, allowing better control of food intake and, ultimately, better control of weight gain. The increase satiety by preserving the physical structure, as for legumes and almonds, is certainly one of the key parameters to be studied in more foods, especially by comparing the evolution of satiety according to their structure or the size of their particles.

It is clear, through the example of legumes, that one cannot be based solely on the chemical composition of food to assess its health effect. The physical structure of the matrix interacts to qualitatively change the digestive fate of its nutrients.

The relation linking the structure of foods derived from grains and seeds and the effects on blood glucose is difficult to establish because of the number and the variety of factors that may be involved. They can be related to food (composition and structure), the physiology of the digestion and the intra and inter-individual variability. The health status of the individual (healthy or diabetic) is also involved in the way glucose is used by the body.[56,57]

In this context, it is extremely difficult to predict the *in vivo* digestive fate of a food by *in vitro* methods that cannot simulate all the parameters influencing the digestion of starch *in vivo*.[58,59] Efforts are now being made to improve these methods and couple them with mathematical models estimating the reality to the closest.[60]

From the viewpoint of the food, if it is desired to ultimately direct its shaping to control the digestive fate of starch, it is important to characterize the food matrix at the various scales of structure and at all stages of life of food (production, preparation, storage, chewing, gastric and intestinal fates) and connect this structure to data digestibility. Variations in the structure of a starchy food can be obtained by changes in the formulation (additions of fibre, legumes, *etc.*) and/or in the technological processes, which may have additive or antagonistic effects. The shaping, however, should not affect the nutritional quality of the food (*e.g.*, loss of essential amino acids) or safety (allergenicity).

4 Slow carbohydrates, pre-hydrolysis and pre-fermentation of grain products

The nutritional quality of plant-based foods can be improved by many more or less drastic technological processes. Among the drastic methods are especially distinguished extrusion cooking and refining. These two treatments usually decrease the nutritional value of plant products by drastically reducing the levels of bioactive compounds of interest (reducing nutrient density) through refining or by deconstructing the original food matrix and gelling starch excessively (extrusion-cooking at high pressures). Today, less drastic technological treatments are sought to preserve both the physical structure of plant products (effect on satiety) and nutrient density of bioactive compounds such as fibre, vitamins, minerals and phytonutrients. Moreover, due to the functional properties of certain ingredients, we know how to make more slowly digestible starch (slow carbohydrates) to reduce the glycemic response. Among technological treatments reported as less drastic or as preserving a certain naturalness of the food, pre-fermentation and/or germination are widely used, particularly in developing countries, to increase the nutrient density in bioactive compounds by releasing bound fraction in the food matrix or generating, *via* bacterial metabolism, novel compounds of interest.

4.1 Holistic *versus* reductionist approach to food

Undeniably, technological treatments alter the physical structure of the food matrix and hence its nutritional value, either positive or negative. There is obviously no question of eating cereal grains or legumes without hydrothermal treatment because starch has to be gelatinized, even slightly, to be digestible. However, excessive refining followed by recombination of isolated ingredients generally leads to energy-dense foods and of lower nutritional quality, even very poor as in the case of white bread. Technological processes should be therefore used wisely to maximize the nutritional value of plant products and not degrade it.

The reductionist approach used in research in food science and human nutrition mostly explains this fact (Fig. 5)[12]. The food was indeed reduced to a single sum of compounds leading both to study each compound alone and to restrict/reduce food nutritional value to some compounds only. The role of the food matrix in the nutritional effect of plant foods has been largely neglected leading to fractionation-recombination processes of food ingredients and/or excessive refining.

Instead, a holistic approach to food considers the food matrix as a complex structure that plays a role on the health effects of food through the satiety potential, different nutrient release kinetics and possible synergistic effects of the compounds in the human body (Fig. 5). According to this view, food is a complex set of macro-, micro- and phyto-nutrients in permanent complex interaction: in other words, a holistic vision of the food means that 1+1 > 2 and not 1+1 = 2.

I will present some examples of soft technologies allowing improving the health potential of plant products, in particular through the modification of the physical and physico-chemical properties of food matrices, specifically cereals and legumes. Indeed, in these foods, beyond the single chemical composition, physical structure of the food matrix plays an important role in their health and nutritional effects (see above).

4.2 Increasing the content in slow carbohydrates and resistant starch

Carbohydrates are the most important part of the energy (~45-55%), especially in the form of starch mainly *via* grain products, legumes, bananas and potatoes.

Generally, one ranks starch of plant products in three fractions: rapidly digestible, slowly digestible and resistant[41]. Depending on the speed of digestibility, starch therefore does not provide the body with the same nutritional benefits. For example, the rapid fraction can be interesting during exercise since quickly mobilized (*e.g.*, for a runner), the slow fraction before exercise for intense efforts over the long term (*e.g.*, the eve of a soccer match) and resistant starch provides the body with butyric acid after fermentation in the colon, the latter serving as fuel for cells of the colonic mucosa.

Based on the knowledge gained in the digestive fate of starch of various foods and its physicochemical properties, we today know how to increase the levels of slow carbohydrates and resistant starch in foods. Technological means are numerous. They all have in common to act on the physical structure of either food matrix or starch. The literature on the subject is oversized and we therefore restrict ourselves here to a brief summary.

4.2.1 Slow carbohydrates

Regarding the increase in the content of slow carbohydrates, one can modify either directly the food or digestive physiology by slowing the rate of absorption of sugars. At the basis of the reduction of starch digestion kinetics, there is either a reduction of its accessibility to enzymes or the slowing of the diffusion of the digestion products of starch (dextrins and glucose) to absorptive mucosa. This can be achieved at macroscopic (mm), microscopic (μm) and molecular (nm) levels of the food, i.e., by increasing or maintaining the size of the particles during digestion (thus promoting food matrices with high cohesive structure), by encapsulation of the starch with protein networks modeled by technology (pasta) or natural fibrous networks (legumes), and by modifying the chemical structure of the starch, namely limiting its degree of gelatinization thus reducing its porosity and enzyme accessibility; increasing the amylose content (unbranched polymer that are less accessible to α-amylase than amylopectin); or alternatively to complex starch with lipids, the amylose-lipid complexes being digested more slowly. We also know how to create artificial fibre networks in food to reduce the accessibility of starch to α-amylases, as has been shown with bread and galactomanannes from guar gum[61] or β-glucans[62-64] (Fig. 6A-B). One could also reduce the glycemic response of the bread by increasing the density of the crumb.[65] However, it has been shown that, whatever the percentage of β-glucan (from barley) used (4 to 8%), if their molecular weight is low, they have no significant effect on the reduction of glycemic response.[66]

One can also change the digestive physiology *via* two principal mechanisms such as slowing the rate of gastric emptying or increase the viscosity of digestive effluents to slow the rate of diffusion of the degradation products of starch to the absorption zones, but also to slow the rate of diffusion of the α-amylases to the food, the network of fibre forming a dense matrix around the food. The means used are mainly viscous fibre (especially soluble arabinoxylans and β-glucans, guar gum, *etc.*: see Fig. 6B) or the formulation of starchy foods with a matrix structure which keeps longer during digestion to slow the rate of gastric emptying. For example, breads with whole and/or more or less intact cereal grains can be baked or more compact food structures can be developed, this latter solution having been little tested up today. The best known example of compact matrix structure preserved during digestion is that of pasta through the extrusion process.[67,68] Others have shown that barley under the form of flakes rather than finely milled renders starch more resistant to digestion in the ileostomy subjects.[69] The thickness of oat flake was also tested (1 *versus* 0.5 mm): thicker flakes significantly reduced the glycemic and insulinemic responses compared to finer flakes.[70] This result was also observed with linguine pasta types of different thickness.[3] In the case of the viscosity effect of fibre, Wood *et al*. (1994)[71] evaluated that 79-96 % of changes in plasma glucose and insulin could be attributed to the viscosity.

4.2.2 Resistant starch

Review on the subject are many and I invite the reader to refer to them; the goal here is mainly to show that it is today known how to control the digestive fate of starch.[72-75]

Regarding the increase of the resistant starch content, its digestion in the small intestine is prevented so that it is fermented in the colon in order to act as a prebiotic, namely a compound that promotes, through its fermentation, development of bacterial flora in favor of health;[76] that is to favor increased production of butyric acid. Furthermore, according to the structure and nature of the resistant starch, one can generate more or less butyric acid[77], a volatile fatty acid with important nutritional properties, for example its anti-carcinogenic effect.

As for slow carbohydrates, the technological means used are now well developed. One can simply directly add, during formulation of foods, resistant starch of commercial type (chemically modified resistant starch type 4, RS4); or one may favor the presence of native crystalline non-gelatinized starch (naturally occurring under the form of starch grains, *e.g.*, in raw potatoes, green bananas, or high-amylose maize variety, RS2); or still one can promote retrogradation of starch (resistant starch which forms by retrograding amylose, RS3); finally, there is also starch physically inaccessible, present for example in seeds or legumes or in unground whole grains (RS1).[72]

4.3. Reducing plasma hyperlipidemia

The reduction in plasma hyperlipidemia - especially for patients at risk of cardiovascular disease or subjects with hyperlipidemia - mainly concerns cholesterol and triglycerides. As for glucose from starch, it is today known some simple ways to reduce hyperlipidemia, *via* mainly the increase - in food or diet - of the soluble viscous fibre content, also potentially capable of binding lipids.[78] Note also that the cell structure of oilseeds (flax, sunflower...) and nuts (almond, walnut...) favors a reduced accessibility of lipids and a feeling of prolonged satiety and may participate in cardiovascular protection despite a significant energy input.[79]

For example, the addition of 6 g of partially hydrolyzed guar gum in 200 g of yoghurt in healthy subjects significantly reduces postprandial serum hypertriglyceridemia.[78] In another study, the consumption of bread made from 6 g of β-glucan (oat soluble fibre) by overweight and moderately hypercholesterolemic subjects results in significantly lower levels of plasma cholesterol associated with lipoprotein.[80] These results were confirmed on several occasions thereafter[81].

The mechanisms involved were studied *in vitro* using a digester and the results showed that partially hydrolyzed guar gum reduced bio-accessibility of triglycerides and cholesterol in a dose-dependent manner.[82] The primary mechanism involved is an effect of de-emulsification of lipid by the guar gum. In addition to this mechanism, the authors suggest the effect of another mechanism they call flocculation depletion: in short, partially hydrolyzed guar gum has no surface activity and is therefore not adsorbed to the surface of lipid droplets, leaving a space without polymers around the droplets which would promote coalescence and flocculation of the latter.[82] But the emulsification of fat by bile salts is essential for their proper digestion step. Concerning more specifically cholesterol, soluble fibre can trap or sequester bile salts in the intestine, thus reducing their re-absorption and thus their return to the liver. The reduction of concentrations of hepatic bile acid activates the enzyme CYP7A1 (cholesterol 7 α-hydroxylase or cytochrome P450 7A1) that converts cholesterol into bile acids: it follows a reduction in plasma cholesterol associated with lipoproteins *via* an accelerated transfer of this cholesterol to the liver. It has also been shown *in vitro* on rat intestines that β-glucans could reduce lipid absorption, particularly through inhibition of genes regulating intestinal absorption and lipid synthesis.[83]

But it seems that we should also take into account the physicochemical properties of viscous fibres used, such as molecular weight: thus, oat β-glucan with a molecular weight of 210,000 is 50% less efficient than β-glucans with a molecular weight of 2,210,000 or 530,000 vis-à-vis the reduction of serum cholesterol associated with low density lipoproteins.[84]

4.4 Pre-hydrolyzing fibre

In the nutritional properties of food products of plant origin, soluble/insoluble fibre ratio is important, each fibre type having its own physicochemical properties. The trend today is to seek to increase the proportion of soluble fibre, especially in cereal products, not only for their ability to increase the viscosity of digestive effluents in the upper gastrointestinal tract, but also for their faster fermentation in the colon. One was especially concerned with the pre-hydrolysis of arabinoxylans and β-glucans, these two types of fibre having both soluble and insoluble fractions in the cereal products.

We can consider the pre-hydrolysis of fibre from two angles: pre-hydrolyzing initially insoluble fibre to make them soluble and increase the soluble/insoluble ratio; or pre-hydrolyzing already soluble fibre, thus reducing their molecular weight, to change their physicochemical properties, such as their ability to bind compounds and their viscous potential, or even change the speed of their colonic fermentation.

Generally, the more the fibres are pre-hydrolyzed the less their viscous effect in the gut.[85] Thus, a smaller reduction in serum cholesterol associated with low density lipoprotein[84] or in glycaemia[86-88] with lower molecular weight β-glucans was measured. For example, without glucanases, β-glucans tend to increase the viscosity of the digesta and the ability to form gels, which disrupts intestinal motility and decreases digesta, enzymes and other compounds mixtures; and they also tend to form a fibrous physical barrier to the diffusion/mobility of digestive enzymes to their substrates and increase the thickness of the unstirred layer at the absorptive surface of the intestinal microvillus, thereby limiting the absorption of nutrients.

Moreover, the incorporation of xylanases during baking increasing bread AXOS (arabinoxylan-oligosaccharides) levels, which have particular prebiotic properties, and generally have a positive effect on digestive health.[89] However , the pre-hydrolysis of wheat arabinoxylans by adding xylanases during kneading of the bread was tested in insulinoresistant subjects, but no significant effect was observed on lowering blood glucose and insulin responses compared to normal bread.[90]

Enzymes hydrolyzing fibrous compounds known to bind or sequester minerals or trace elements were also added to increase mineral bioavailability. Phytic acid and the majority of fibre have indeed a high capacity to bind minerals.[91] Thus, the bioavailability of minerals has been tested *in vitro* with bread with or without xylanase and fungal phytase: the addition of enzymes increases the solubility of complexed minerals (from 1.4 to 2.5 times higher), while only solubility and dialysability of zinc is increased three times by the presence of xylanase.[92]

On the physiological effect of the increase in the soluble/insoluble fibre ratio in cereal products in humans, the work is, to our knowledge, inexistent. But given the results presented above, one can imagine that optimized pre-hydrolysis of fibre of some cereal products may be promising on health effects. This pre-hydrolysis is also naturally produced in sourdough bread where active acidity activates some enzyme activities (see below).

4.5 Pre-hydrolyzing phytonutrients

Given the ability of phytic acid to complex minerals and to reduce their intestinal absorption, it has been sought to limit this effect, in particular *via* its pre-hydrolysis. This can be done using a pre-fermentation step of foods containing the most, such as cereals and legumes, but also *via* soaking and germination. Pre-fermentation indeed activates phytases (at acidic pH) which pre-hydrolyze phytic acid. But we can also promote its pre-hydrolysis *via* technological processes as hydrothermal treatment in the presence of lactic acid[93] or via the incorporation of exogenous phytase as those from the yeast *Saccharomyces cerevisiae*,[94] *Aspergillus oryzae*,[92] *Bifidobacterium pseudocatenulatum*[95] or from lactic acid bacteria[96] such as *Pediococcus pentosaceus*.[97] In humans, it has thus been shown that degradation of phytic acid *via* sourdough fermentation resulted in higher absorption of iron (13.6%) compared to other cereal products not including a fermentation step and pre-hydrolysis of phytic acid, such as in chapattis (7.4% iron absorption) or in extruded products (5.6% iron absorption).[98] While the fermentation may cause the almost complete disappearance of the phytic acid, the extrusion cooking allows only a partial hydrolysis of about 20 %.[98] Note, however, that despite the chelating effect of phytic acid, the mineral intake *via* bread made from whole-meal flour is such that the supply to the body will always remain greater than that obtained with white bread without phytic acid, this latter being very poor in minerals.

Phytates pre-hydrolysis, apart from increasing mineral bioavailability and content of free *myo*-inositol (*myo*-inositol is a lipotrope and may therefore participate in preventing excessive hepatic lipid deposition)[99], could also contribute to suppressing the proliferation of colorectal cancer cells: the compound involved here is a hydrolyzate of phytic acid rich in IP3 (*myo*-inositol triphosphate) whose efficiency is higher than that of phytic acid (IP6) with respect to cell proliferation.[100]

However, to our knowledge, it seems that no product containing phytases has found application in the food market.[101]

The same type of approach has been tested for polyphenols - including tannins - considered - as well as phytic acid - as being potentially anti-nutrients. Thus, addition of tyrosinase oxidase (polyphenol oxidase from mushroom) following the reduction of the levels of phytic acid with phytase improves the *in vitro* bio-accessibility of iron, the degree of improvement depending on the applied technological pretreatment, namely: no processing, cooking, soaking or germination (the strongest effect: about 2% to 10%).[102]

The case of ferulic acid, found mainly in cereals, also deserves special attention. Indeed, it exists both in free (1-5%) and bound (95-99%) forms in cereal brans, particularly in the aleurone layer[6]. Given the many potential positive effects to the body of free ferulic acid (antioxidant potential[103-105] and anti-carcinogenic[106], hypoglycaemic[107], anti-inflammatory[108], anti-atherogenic[109] and hypolipidemic[110] effects), it has also therefore been sought to pre-hydrolyze it within foods to obtain a greater fraction of free ferulic acid, usually absorbed in the upper gastrointestinal tract - while the bound fraction directly reach the colon, where it can be utilized by the microorganisms fermenting the dietary fibre fraction.[111-112] Differences in metabolic fate of free and bound fractions of ferulic acid therefore led me to formulate the concept of rapid and slow ferulic acids, which could be probably extended to all phenolic acids.[6] According to Rosa & Micard (2013)[113]: "The feruloyl esterase thus appear as very effective tools to release free ferulic acid from feruloylated oligosaccharides of grain fractions, but their action is still more effective when combined with methods able to deconstruct the complex structure of the cereal matrix".

4.6 Soaking, pre-fermentation and germination

Germination, presoaking and pre-fermentation were primarily concerned by developing countries of Asia, Africa and Latin America because they are cheap ways to get food with high nutritional density *via* modifications of the physical structure, physicochemical properties and bioactive compound contents of the food.[114] The literature on this subject is plethoric. However, recently, we have been interested in the pre-fermentation and germination as a means of improving the nutritional quality of cereal products in developed Western countries.[115-117] One of the main advantages of pre-ferment is to promote the development of various enzymatic activities which either generate new bioactive compounds or release fractions of compounds originally linked to other components, making them more potentially bioavailable, or hydrolyze components known as anti-nutrients such as phytic acid (known to limit the bioavailability of many minerals) *via* activation of phytases, or even degrade dietary fibre, making them more fermentable. The increase in percentage of free fractions of some nutrients through the pre-fermentation will therefore potentially impact on health, including increasing the bioavailable fraction in the small intestine.

In general, the pre-fermentation primarily relates to cereal grains[118] and legumes seeds,[119] although this method is also applied to fruits and vegetables to produce, *e.g.*, wine from grapes or sauerkraut from cabbage.

4.6.1 Germination and soaking

Germination is to boost development and metabolic activities of seeds that were dormant. This is achieved by changing the conditions of temperature, moisture and light. Reactivation of metabolism results in the recovery of enzymatic activities that generate new compounds, hydrolyze fractions linked to other micronutrients or even degrade compounds considered as anti-nutritional such as phytic acid. In addition, germination alters the physical structure of the grain or seed, in particular softening it. Germination can also be used to enhance the functionality of some proteins, making them more soluble or simply to increase the protein content. For example, oat grains germination for 24 hours results in an increase in lysine content of almost 30% and a significant decrease in starch content (from 60 to 20%) with an increase in levels of soluble sugars, while the phytic acid content decreases from 0.35 to 0.11%.[120] Germination can thus improve the nutritional value of proteins that can be hydrolyzed to polypeptides, essential amino acids and more easily assimilated free amino acids, as has been shown with lentils and peas compared to bean.[121]

Germination is therefore a simple way to increase the nutritional value of grains and seeds.[117] A study has also shown that you can increase the total polyphenol content and thus ultimately the antioxidant potential of several types of seeds (wheat, lentil, radish, mustard, broccoli, sunflower, onion, etc.) after 7 days of germination.[122] Studies on the effect of germination on the nutritional density of foods are plethoric and all cannot be described here: what we need to remember is that this procedure improves the nutritional potential of grains and seeds increasing the levels of various nutrients and bioactive compounds and/or increasing the digestibility of some nutrients for various types of food, as has been demonstrated, for example with soybean[123] and sesame seeds.[124]

Soaking treatment is a domestic technology which comprises soaking the seeds in water to soften the texture and reduce the cooking time. Soaking is therefore also part of many technological treatments such as boiling, canning, germination and fermentation. As for germination, these conditions reactivate seed metabolism and therefore the enzymatic activities.

A study of legume seeds and pearled millet can highlight the respective effects of soaking and germination on the degradation of phytic acid which is at least 2.5 times higher with germination (32-56% *versus* 13-19%).[125] Germination also tends to further increase the calcium, zinc and iron contents of seeds and grains, while the differences between soaking and germination were leveled for magnesium, manganese and copper.[125] It is otherwise interesting to note that soaking can reduce the levels of β-galactosides - at the origin of flatulence (16-27%) - and trypsin inhibitor (12%) - an anti-nutritional factor, the latter being solubilized then eliminated *via* the steep water. Concerning another type of legume, fenugreek, soaking improves the protein and starch digestibility and mineral bioavailability.[126] Similarly, soaking improves the metabolic utilization of various minerals in rats consuming cooked beans (calcium, phosphorus and magnesium)[127] or pea flour (zinc and magnesium).[128]

The combination of soaking and germination is a common practice to increase the digestibility and palatability of legume seeds - which are also associated with flatulence.[44,129] However, soaking can also lead to loss of nutrients by solubilization, as for carbohydrates and minerals, but also for free polyphenols, being likely to cause a reduction in the percentage of their bioavailability or a reduction of the antioxidant potential of food. A specific method of soaking (autolysis) applied to wheat and its milling fractions allows producing free amino acids from the aleurone layer of bran, especially branched amino acids (leucine, isoleucine and valine), arginine and lysine, and the γ-amino-butyric acid, for which many positive biological activity (reduction of blood pressure, vascular dilation effect, etc.) have been reported.[130] Derivatives milling byproducts could then potentially be used to fortify foods.

4.6.2 Pre-fermentation

The fermentation is mainly to promote bacterial activity (*e.g.*, *Saccharomyces cerevisiae* and *Lactobacillus rhamnosus*) in acidic medium to generate a large number of metabolic changes within food. The best known are the ethyl/alcoholic (e.g., alcoholic beverages and bread) and lactic acid (e.g., sauerkraut and yogurt) fermentations.

As for germination or soaking, pre-fermentation in liquid medium is a widespread method and applied primarily to grains and seed type food, especially in Africa, Asia and Latin America, but also to fruit purees (*e.g.*, *Makumbi* in Zimbabwe) and milks (*e.g.*, *hodzeko* in Zimbabwe).[131] These products are very varied and include malt, alcoholic and non-alcoholic beverages and porridges. Numerous studies show that fermentation improves the nutritional quality of foods, including increased levels of essential amino acids (*e.g.*, lysine, methionine and tryptophan), vitamins, polyphenols and minerals. The fermentation may also inhibit the activity of pathogenic bacteria causing diarrhea.

Pre-fermentation applied to cereal products or different fractions of wheat - bran or whole-meal flour, including bread - brings them undeniable nutritional plus-value, that is to delay the rate of starch digestion and thus to reduce the glycemic response (due to a slowing of the rate of gastric emptying in the presence of increased levels of organic acids), and to modulate levels and bio-accessibility of many bioactive compounds, to improve mineral bioavailability (*via* increased phytic acid degradation), to produce indigestible carbohydrates, to change the accessibility of the fibrous matrix to intestinal microbiota or to partially degrade gluten (*via* activation of proteases by acidification), which could potentially make bread more acceptable for people with celiac disease (gluten intolerance), and finally to increase protein digestibility[116].

For example, in humans, the consumption of pre-fermented whole-grain barley flour enhances iron bioavailability of 94 % (from 3.0 to 5.5%), this difference being also observed using an *in vitro* digester.[132] However, if the acidity associated with the fermentation process can reduce the rate of gastric emptying and absorption of glucose, other studies show that the fermentation increases the *in vitro* starch digestibility - and also that of proteins - and reduces the resistant starch content, as has been shown for sorghum dough (endosperm protein restricting accessibility of the starch would be affected by the fermentation and render the starch more accessible), commonly used in the semi-arid tropical countries as the basis of various cereal products, giving them a better nutritional value.[133] As with soaking, the fermentation may increase the nutritional value of cereal bran by increasing the levels of bioactive compounds, as has been shown with rye bran where folates and ferulic acid levels are increased.[134]

If cereal pre-fermentation can provide such health benefits, one can easily imagine that the extension of this method to other food products could be very promising from a health perspective in humans. For example, a fermented food made from fruits, oil seeds (nuts) and vegetables rich in polyphenols - trade name Regulat® - improves some parameters of the immune system such as intracellular glutathione level of lymphocytes, monocytes and natural killer cells and brings positive effects on antioxidant and anti-inflammatory systems in healthy subjects compared to placebo.[135]

Otherwise, the pre-fermentation may pre-hydrolyze anti-nutrients such as tannins and increase the percentage digestibility of protein and starch, as has been shown *in vitro* with two sorghum cultivars.[136] Moreover, the fermentation of sorghum gruel with added wheat phytases and mushroom polyphenol oxidase reduces by 39% the content of phytic acid and 57 % of the total polyphenol content: it follows an increase in the *in vitro* bio-accessability of iron from 1 to 3%.

It should also be noted that the fermentation can degrade bioactive compounds of interest, as has been shown with alkylresorcinols in sourdough bread made from wheat and whole rye.[137] The alkylresorcinols are phenolic lipids which have potentially positive nutritional properties (antioxidant or reduce plasma cholesterol).

The combination of germination and sourdough fermentation was also tested, including rye, where these processes reduce the levels of prolamins and provide an interesting way to produce cereal foods for people intolerant to gluten.[138] The advantage of these natural fermentations is that they use an enzyme pool that may lead to more efficient hydrolysis of gluten than a single enzyme. The combination fermentation-germination therefore seems to optimize the increase of bioactive compounds levels in cereals: for example, the fermentation of germinated rye increased folates, free phenolic acids, total polyphenols, lignans and alkylresorcinols levels more significantly compared to the single fermentation,[139] or even increases the *in vitro* protein digestibility of a mixture of grain flour of breadfruit and soybean and reduces the content of phytic acid more efficiently than the single fermentation or germination.[140] Another study showed that the fermentation was more effective than soaking to reduce the phytic acid content of whole-grain brown rice.[141]

4.7 Conclusions

Today, with relatively simple technologies (that could also be called mild/soft *versus* conventional and drastic hydrothermal treatments at high pressures), it is therefore known how to increase the levels of slow carbohydrates and bioactive compounds of some foods, including cereal and legume seeds. These modifications are based on a reduction of the enzymatic availability of the starch, the activation of endogenous enzymes in the food and/or the use of exogenous hydrolytic enzymes. From the standpoint of preventive nutrition, these treatments are used to develop foods reducing hyperglycemia and/or hyperlipidemia, increasing mineral bioavailability and/or concentrations of bioavailable antioxidants or reducing the allergenic potential of some proteins. Moreover, these treatments allow a relative preservation of the initial physical structure of the plant food matrix as opposed to fractionation-refining then recombination of isolated ingredients.

However, a functional food alone cannot solve everything and prevent all metabolic deregulation associated with overeating: they must register under balanced diets promoting dietary diversity and consumption of less refined foods combining lower energy density and higher nutrient density (in the form of bioavailable bioactive compounds).

Such a shift in the transformation of plant products can only be done by developing a more holistic vision of the food that more respect its natural complexity, and therefore its long-term health potential.[12,142-144]

5 Food structure modification for optimum health effects?

5.1 Natural *versus* reconstructed food matrices

A careful examination of the scientific literature tends to show that it would be preferable for health to preserve the initial food structure or at least to modify it in a less drastic way: indeed, in general, the more the initial and natural food is manufactured, the more it loses its initial matrix cohesion and at the same time its full health potential: in other words, these foods appear to have a less solid and compact matrix that disintegrates faster during digestion and releases nutrients faster with a reduced effect of satiety; while most natural matrices retain good structural cohesion due to pre-existing interactions; and these interactions are apparently stronger than those artificially reconstructed. Moreover, the preservation of an intact and natural food matrix or moderately processed can contribute to a prolonged feeling of satiety, stronger than with recombined products - as has been shown with carrots[145] - and thus contribute to a better control of weight gain.

Indeed, food matrices can be of natural origin - more or less transformed - or coming from the recombination of originally isolated ingredients from natural food matrices (Fig. 2).

Scientific literature suggests that the matrices of natural origin and only a little processed gradually release nutrients in the digestive tract, while very processed or recombined matrices appear to be digested faster. Probably the interactions between nutrients in natural matrices are stronger than in highly processed foods. Some matrices obviously need to be processed before consumption; however, between consuming unprocessed and highly processed foods, there may exist an intermediate path that is to be applied to food matrices, *i.e.*, softer and less drastic technological processes to preserve the nutritional value of food (what is called 'minimal processing').

The physical structure therefore plays a major role in the digestive fate of grain products and seeds. It interacts with particular stages of digestion as the degree of mastication, the rate of gastric emptying, satiety, enzyme accessibility and digestive motility. If the chemical composition of the food is important, it is clear that it is primarily physical and physicochemical characteristics of the matrix (particle size, cohesion of the matrix, porosity, interaction between nutrients, etc.) that first determine digestive fate of the food.

A question arises: should we focus on functional and reconstructed foods or on natural foods? In this regard, it may be useful to better highlight, through comparative studies, health effects of natural food *versus* reconstructed matrices on the basis of identical chemical composition. However, it remains that recombining ingredients to create new foods is an essential aspect of creativity that man needs. I think the main issue, as unraveled by literature linking diet-related chronic diseases and adhesion to ultra-processed foods[146], is to based our diet on natural complex and minimally processed foods, not on those made of re-combined ingredients.

5.2 Differential release kinetics *versus* differential health effects

Unlike macronutrients - such as starch - virtually no study has tried to link the differences in release kinetics of a micronutrient in the gut with metabolic and health effects. For example, to the best of my knowledge, the following question has never been addressed: has the kinetic to which a given mineral is released and absorbed within gut a real impact on the mineral status, bone health, etc.? Moreover, the problem of polyphenols bioavailability appears of nutritional value: indeed, because of their generally initial low bioavailability, it is reasonable to assume that an increase - even small - of their bioavailable fraction in the small intestine will result in significant metabolic effects. For example, ferulic acid in wheat is only a little bioavailable (< 5%): an increase, would that double, must necessarily have undeniable health effects because of all the health effects reported for ferulic acid used as free and isolated compound.[147]

This is probably true for any compound originally very few bioavailable. In the field of reverse engineering, it is therefore important to address the right issues in relation to the desired nutritional effects. For example, one might ask if there are *slow* and *rapid* B vitamins - like for starch - and whether or not differences in kinetics are reflected by real optimized health effects. This also means that a significant amount of micronutrients reaches the colon, but we do not really know for which nutritional effects?

5.3 Technological processes: the 'good' and the 'bad'…

In addition, deconstructing food matrices, isolating ingredients or compounds and recombining them to form a new food may seem like a waste of time, money and energy for little obvious health benefits. It also follows a rather high associated carbon cost with these treatments for the environment. Paradoxically, however, these recombined and processed foods are often cheaper than natural foods having preserved intact their matrix structure.

Technological treatments can also improve the health value of foods, e.g., by destroying anti-nutritional factors or by increasing the bio-accessibility of some micronutrients in the digestive tract, like carotenoids in processed tomatoes. Therefore, technology is also a way to optimize and better control the health effects of some foods. Thus, canning and fermentation can promote the release of bioactive compounds initially bound to other components. Technological processes may also contribute to create new more compact food matrices, which generally maintain a structural condition for longer time during digestion, limiting enzymatic bio-accessibility of some nutrients, like pasta, sources of slow carbohydrates whereas the initial semolina cooked as such is rather a source of rapid carbohydrates. It was also shown that one can make breads with more dense and compact crumb and reduce the glycemic response.[65] From a technological point of view, the margin for change - increase or decrease - the bioavailability of nutrients is therefore very wide; but for which health benefits?

The structural characteristics of the food matrix therefore determine its health effect, as it affects the kinetics of release of nutrients and the amount absorbed in the upper gastrointestinal tract. In view of the scientific literature, it is no longer possible today to rely solely on the chemical composition of foods to assess their nutritional value.

6 Perspectives

6.1 To control food digestion: for which benefit?

Food formulation with controlled release matrices of nutrients during digestion seems a promising area for future research. However, progress in this area can only be done when we have accumulated enough significant and convincing *in vivo* data linking differences in release kinetics and health effects. But today, apart from carbohydrates and to a lesser extent proteins and lipids, we do not know much. One issue could be, at first, to apply the approach used for starch (fast and slow sugars) more systematically to lipids and proteins.

6.2 Toward more *in vitro* digestion procedures

Before creating new food matrices which we could control the digestive fate, one must understand and study in detail the digestive fate of food: however, as paradoxical as it may seem, as noted above, we know pretty little thing about such an issue (the difficulty to access the digestive tract probably have contributed to this fact!). As highlighted by Norton *et al.* (2007)[8]: "All foods pass through a common unit operation, the gastrointestinal tract, yet it is the least studied and least understood of all food processes. To design the foods of the future, we need to understand what happens inside people in the same way as understanding any other process." (page 84).

The fate of food in the digestive tract is indeed extremely complex and depends on physical, physico-chemical and hormonal parameters. To simulate it with *in vitro* digesters in order to approach this complexity may appear at first sight as illusory and impossible since digestive parameters also depend on the individual and their genetic profile. The *in vivo* reality therefore being not modeled to perfection, it is advantageous to use *in vitro* standardized and simple digesters integrating mastication and gastric emptying, two key steps to deliver nutrients to the small intestine, the major site of absorption.

In particular, one would hope, in a near future, greater harmonization of the *in vitro* digestion systems used with the creation of an international standard that would raise a large number of data obtained in the same conditions to compare them. Indeed, today there are nearly as many *in vitro* digestion systems as laboratories working in this field. One should also define some standard diets within which we would study the digestive fate of a particular nutrient in a food or a given new matrix. Such standardization would get long to achieve, but once accepted, would quickly gather essential nutritional data on the bioavailability of nutrients according to new food matrices; and we will get an indication of their potential *in vivo* release kinetics. The collection of these data will then enable the development of *in silico* models that can predict and simulate the digestive fate of various types of food matrices, which will save time and money...

6.3 Toward a more holistic approach…

Willingness to study the digestive fate of a single nutrient in a reductionist approach and connect it to a single metabolic or health effect, then seek to control through technological processes its digestive fate has its limits. Functional foods have not made it possible to reduce public health problems related to unbalanced nutrition.[12] The prevalence of obesity and chronic diseases (including cancer, cardiovascular disease and type 2 diabetes) are increasing in developed countries but also in developing countries, where the nutrition transition has often been more rapid. This type of approach is certainly useful for identifying mechanisms of action of metabolites or to solve specific health problems (*e.g.*, type 2 diabetes and slow carbohydrates) but it should not be used first.[12]

It is also very important to better understand how the food is degraded in the digestive tract ('black box'). However, along with this reductionist approach, should be developed in food and nutritional sciences more holistic approaches considering the food as a whole (*i.e.*, the whole package). Food is not the only sum of its parts and should not be considered as a drug[148]. It contains a set of macro and micronutrients released in the gastrointestinal tract according to a variety of kinetics; and often synergistic action of several components is more effective than that of an isolated component then reincorporated in food at high doses - as has been demonstrated with antioxidants. The holistic approach should also consider the food in interaction both with other foods of the diet and digestive environment during digestion, which is another level of complexity.

Abbreviations

GI, Glycemic index

RS, Resistant starch

References

1 G. B. Haber, K. W. Heaton, D. Murphy and L. F. Burroughs, *Lancet*, 1977, **2**, 679-682.

2 N. W. Read, I. M. Welch, C. J. Austen, C. Barnish, C. E. Bartlett, A. J. Baxter, G. Brown, M. E. Compton, K. E. Hume, I. Storie and et al., *Brit. J. Nutr.*, 1986, **55**, 43-47.

3 Y. Granfeldt, I. Bjorck and B. Hagander, *Eur. J. Clin. Nutr.*, 1991, **45**, 489-499.

4 Y. Boirie, M. Dangin, P. Gachon, M. P. Vasson, J. L. Maubois and B. Beaufrere, *Proc. Natl. Acad. Sci. USA*, 1997, **94**, 14930-14935.

5 M. Armand, B. Pasquier, M. Andre, P. Borel, M. Senft, J. Peyrot, J. Salducci, H. Portugal, V. Jaussan and D. Lairon, *Am. J. Clin. Nutr.*, 1999, **70**, 1096-1106.

6 A. Fardet, *Nutr. Res. Rev.*, 2010, **23**, 65-134.

7 I. Norton, P. Fryer and S. Moore, *AIChE J.*, 2006, **52**, 1632-1640.

8 I. Norton, S. Moore and P. Fryer, *Obesity Rev.*, 2007, **8 Suppl 1**, 83-88.

9 J. E. Norton, G. A. Wallis, F. Spyropoulos, P. J. Lillford and I. T. Norton, *Annu. Rev. Food Sci. Technol.*, 2014, **5**, 177-195.

10 M. L. Slattery, *Am. J. Clin. Nutr.*, 2008, **88**, 14-15.

11 D. R. Jacobs, Jr, M. D. Gross and L. C. Tapsell, *Am. J. Clin. Nutr.*, 2009, **89**, 1543S-1548S.

12 A. Fardet and E. Rock, *Adv. Nutr.*, 2014. In press

13 A. Fardet and E. Rock, *Med. Hypotheses*, 2014, **82**, 181-186.

14 J. Parada and J. M. Aguilera, *J. Food Sci.*, 2007, **72**, R21-R32.

15 G. Duchateau and W. Klaffke, *Food Biophys.*, 2008, **3**, 207-212.

16 G. M. Bornhorst and R. P. Singh, *Compr. Rev. Food Sci. Food Saf.*, 2012, **11**, 101-118.

17 N. Faisant, A. Buleon, P. Colonna, C. Molis, S. Lartigue, J. P. Galmiche and M. Champ, *Brit. J. Nutr.*, 1995, **73**, 111-123.

18 J. Parada and J. M. Aguilera, *Food Sci. Technol. Int.*, 2011.

19 D. J. A. Jenkins, T. M. S. Wolever, R. H. Taylor, H. Barker, H. Fielden, J. M. Baldwin, A. C. Bowling, H. C. Newman, A. L. Jenkins and D. V. Goff, *Am. J. Clin. Nutr.*, 1981, **34**, 362-366.

20 A. Fardet, F. Leenhardt, D. Lioger, A. Scalbert and C. Remesy, *Nutr. Res. Rev.*, 2006, **19**, 18-25.

21 M. Petitot, C. Brossard, C. Barron, C. Larré, M.-H. Morel and V. Micard, *Food Chem.*, 2009, **116**, 401-412.

22 E. Kim, J. Petrie, L. Motoi, M. Morgenstern, K. Sutton, S. Mishra and L. Simmons, *Food Biophys.*, 2008, **3**, 229-234.

23 A. Fardet, J. Abecassis, C. Hoebler, P. M. Baldwin, A. Buleon, S. Berot and J. L. Barry, *J. Cereal Sci.*, 1999, **30**, 133-145.

24 K. Foster-Powell, S. H. Holt and J. C. Brand-Miller, *Am. J. Clin. Nutr.*, 2002, **76**, 5-56.

25 L. Wang, B. J. Xie, G. Q. Xiong, X. Du, Y. Qiao and L. Liao, *Carbohydr. Polym.*, 2012, **87**, 1038-1044.

26 X. L. Shu, L. M. Jia, H. X. Ye, C. D. Li and D. X. Wu, *J. Agric. Food Chem.*, 2009, **57**, 7552-7559.

27 H. J. Chung, H. S. Lim and S. T. Lim, *J. Cereal Sci.*, 2006, **43**, 353-359.

28 L. N. Panlasigui, L. U. Thompson, B. O. Juliano, C. M. Perez, S. H. Yiu and G. R. Greenberg, *Am. J. Clin. Nutr.*, 1991, **54**, 871-877.

29 F. S. Atkinson, K. Foster-Powell and J. C. Brand-Miller, *Diabetes Care*, 2008, **31**, 2281-2283.

30 S. H. Han, S. W. Lee and C. Rhee, *Eur. Food Res. Technol.*, 2008, **227**, 1315-1321.

31 V. Ranawana, J. A. Monro, S. Mishra and C. J. K. Henry, *Nutr. Res.*, 2010, **30**, 246-254.

32 V. Ranawana, C. J. K. Henry and M. Pratt, *Nutr. Res.*, 2010, **30**, 382-391.

33 G. M. Bornhorst, K. Kostlan and R. P. Singh, *J. Food Sci.*, 2013, **78**, E1383-E1391.

34 G. M. Bornhorst, L. Q. Chang, S. M. Rutherfurd, P. J. Moughan and R. P. Singh, *J. Sci. Food Agric.*, 2013, **93**, 2900-2908.

35 F. Kong, M. H. Oztop, R. P. Singh and M. J. McCarthy, *J. Food Sci.*, 2011, **76**, E450-E457.

36 W. Li, S. Yu and J. Sun, *Chin. J. Rice Sci.*, 2004, **18**, 86-88.

37 P. Wursch, S. Del Vedovo and B. Koellreutter, *Am. J. Clin. Nutr.*, 1986, **43**, 25-29.

38 L. Noah, F. Guillon, B. Bouchet, A. Buleon, C. Molis, M. Gratas and M. Champ, *J. Nutr.*, 1998, **128**, 977-985.

39 S. Mishra and J. Monro, *Food Chem.*, 2012, **135**, 1968-1974.

40 A. Fardet, C. Hoebler, P. M. Baldwin, B. Bouchet, D. J. Gallant and J. L. Barry, *J. Cereal Sci.*, 1998, **27**, 133-145.

41 H. Englyst, S. Kingman and J. Cummings, *Eur. J. Clin. Nutr.*, 1992, **46**, S33 - S50.

42 A. Carmona, L. Borgudd, G. Borges and A. Levybenshimol, *J. Nutr. Biochem.*, 1996, **7**, 445-450.

43 C. Nergiz and E. Gokgoz, *Int. J. Food Sci. Technol.*, 2007, **42**, 868-873.

44 S. Satya, G. Kaushik and N. S. N., *Mediterr. J. Nutr. Metabol.*, 2010, **3**, 183-195.

45 M. Wien, D. Bleich, M. Raghuwanshi, S. Gould-Forgerite, J. Gomes, L. Monahan-Couch, K. Oda, *J. Am. Coll. Nutr.*, 2010, **29**, 189-197.

46 T. Y. Li, A. M. Brennan, N. M. Wedick, C. Mantzoros, R. Nader, F. B. Hu, *J. Nutr.*, 2009, **139**, 1333-1338.

47 P. R. Ellis, C. W. Kendall, Y. Ren, C. Parker, J. F. Pacy, K. W. Waldron and D. J. Jenkins, *Am. J. Clin. Nutr.*, 2004, **80**, 604-613.

48 A. R. Josse, C. W. C. Kendall, L. S. A. Augustin, P. R. Ellis and D. J. A. Jenkins, *Metabolism*, 2007, **56**, 400-404.

49 J. M. Jones, in *Dietary fibre: new frontiers for food and health*, J. W. van der Kamp, J. M. Jones and B. V. McCleary Topping D. L. editors, Wageningen Academic Pub, 2010, pp. 365-378.

50 B. A. Cassady, J. H. Hollis, A. D. Fulford, R. V. Considine and R. D. Mattes, *Am. J. Clin. Nutr.*, 2009, **89**, 794-800.

51 J. M. Frecka, J. H. Hollis and R. D. Mattes, *Eur. J. Clin. Nutr.*, 2008, **62**, 1231-1238.

52 C. J. Traoret, P. Lokko, A. C. R. F. Cruz, C. G. Oliveira, N. M. B. Costa, J. Bressan, R. C. G. Alfenas and R. D. Mattes, *Int. J. Obesity*, 2008, **32**, 322-328.

53 M. Petitot and V. Micard, in *Food Biophys.*, Springer New York, 2010, vol. 5, pp. 309-320.

54 M. Petitot, C. Barron, M.-H. Morel and V. Micard, *Food Biophys.*, 2010, **5**, 284-299.

55 S. H. Holt, J. C. Miller, P. Petocz and E. Farmakalidis, *Eur. J. Clin. Nutr.*, 1995, **49**, 675-690.

56 K. N. Englyst and H. N. Englyst, *Brit. J. Nutr.*, 2005, **94**, 1-11.

57 Y. Granfeldt, X. Wu and I. Bjorck, *Eur. J. Clin. Nutr.*, 2006, **60**, 104-112.

58 A. C. Dona, G. Pages, R. G. Gilbert and P. W. Kuchel, *Carbohydr. Polym.*, 2010, **80**, 599-617.

59 J. Singh, A. Dartois and L. Kaur, *Trends Food Sci. Technol.*, 2010, **21**, 168-180.

60 J. Parada and J. M. Aguilera, *LWT-Food Sci. Technol.*, 2011, **44**, 1739-1744.

61 C. S. Brennan, D. E. Blake, P. R. Ellis and J. D. Schofield, *J. Cereal Sci.*, 1996, **24**, 151-160.

62 L. Cleary and C. Brennan, *Int. J. Food Sci. Technol.*, 2006, **41**, 910-918.

63 L. J. Cleary, R. Andersson and C. S. Brennan, *Food Chem.*, 2007, **102**, 889-897.

64 F. Finocchiaro, B. Ferrari, A. Gianinetti, F. Scazzina, N. Pellegrini, R. Caramanico, C. Salati, V. Shirvanian and A. M. Stanca, *Int. J. Food Sci. Nutr.*, 2012, **63**, 23-29.

65 P. Burton and H. J. Lightowler, *Brit. J. Nutr.*, 2006, **96**, 877-882.

66 P. S. Thondre and C. J. K. Henry, *Int. J. Food Sci. Nutr.*, 2011.

67 C. Hoebler, M. F. Devaux, A. Karinthi, C. Belleville and J. L. Barry, *Int. J. Food Sci. Nutr.*, 2000, **51**, 353-366.

68 C. Hoebler, Karinthi A, Devaux M-F, Guillon F, Gallant D J G, Bouchet B, Melegari C, and Barry J-L, *Brit. J. Nutr.*, 1998, **80**, 429-436.

69 G. Livesey, J. Wilkinson, M. Roe, R. Faulks, S. Clark, J. Brown, H. Kennedy and M. Elia, *Am. J. Clin. Nutr.*, 1995, **61**, 75-81.

70 Y. Granfeldt, A. C. Eliasson and I. Bjorck, *J. Nutr.*, 2000, **130**, 2207-2214.

71 P. J. Wood, J. T. Braaten, F. W. Scott, K. D. Riedel, M. S. Wolynetz and M. W. Collins, *Brit. J. Nutr.*, 1994, **72**, 731-743.

72 E. Fuentes-Zaragoza, M. J. Riquelme-Navarrete, E. Sánchez-Zapata and J. A. Pérez-Álvarez, *Food Res. Int.*, 2010, **43**, 931-942.

73 M. G. Sajilata, R. S. Singhal and P. R. Kulkarni, *Compr. Rev. Food Sci. Food Saf.*, 2006, **5**, 1-17.

74 D. L. Topping, M. Fukushima and A. R. Bird, *Proc. Nutr. Soc.*, 2003, **62**, 171-176.

75 D. L. Topping, I. Segal, A. Regina, M. A. Conlon, B. H. Bajka, S. Toden, J. M. Clarke, M. K. Morell and A. R. Bird, in *Dietary fibre: new frontiers for food and health*, J. W. van der Kamp, J. M. Jones and B. V. McCleary Topping D. L. editors, Wageningen Academic Pub, 2010, pp. 311-321.

76 E. Fuentes-Zaragoza, E. Sanchez-Zapata, E. Sendra, E. Sayas, C. Navarro, J. Fernandez-Lopez and J. A. Perez-Alvarez, *Starch/Stärke*, 2011, **63**, 406-415.

77 M. Stewart, A. Becker and J. Slavin, in *Dietary fibre: new frontiers for food and health*, J. W. van der Kamp, J. M. Jones and B. V. McCleary Topping D. L. editors, Wageningen Academic Pub, 2010, pp. 339-349.

78 S. Kondo, J. Z. Xiao, N. Takahashi, K. Miyaji, K. Iwatsuki and S. Kokubo, *Biosci. Biotechnol. Biochem.*, 2004, **68**, 1135-1138.

79 M. Wien and L. Monahan Couch, *Agro Food Industry Hi-Tech*, 2011, **22**, 36-39.

80 N. Reyna-Villasmil, V. Bermudez-Pirela, E. Mengual-Moreno, N. Arias, C. Cano-Ponce, E. Leal-Gonzalez, A. Souki, G. E. Inglett, Z. H. Israili, R. Hernandez-Hernandez, M. Valasco and N. Arraiz, *Am. J. Ther.*, 2007, **14**, 203-212.

81 U. Tiwari and E. Cummins, *Nutrition*, 2011, **27**, 1008-1016.

82 M. Minekus, M. Jelier, J. Z. Xiao, S. Kondo, K. Iwatsuki, S. Kokubo, M. Bos, B. Dunnewind and R. Havenaar, *Biosci. Biotechnol. Biochem.*, 2005, **69**, 932-938.

83 L. A. Drozdowski, R. A. Reimer, F. Temelli, R. C. Bell, T. Vasanthan and A. B. R. Thomson, *J. Nutr. Biochem.*, 2010, **21**, 695-701.

84 T. M. Wolever, S. M. Tosh, A. L. Gibbs, J. Brand-Miller, A. M. Duncan, V. Hart, B. Lamarche, B. A. Thomson, R. Duss and P. J. Wood, *Am. J. Clin. Nutr.*, 2010, **92**, 723-732.

85 P. J. Wood, *J. Cereal Sci.*, 2007, **46**, 230-238.

86 A. Regand, S. M. Tosh, T. M. S. Wolever and P. J. Wood, *J. Agric. Food Chem.*, 2009, **57**, 8831-8838.

87 A. Regand, Z. Chowdhury, S. M. Tosh, T. M. S. Wolever and P. Wood, *Food Chem.*, 2011, **129**, 297-304.

88 S. M. Tosh, Y. Brummer, T. M. S. Wolever and P. J. Wood, *Cereal Chem.*, 2008, **85**, 211 LP-217.

89 W. F. Broekaert, C. M. Courtin, K. Verbeke, T. Van de Wiele, W. Verstraete and J. A. Delcour, *Crit. Rev. Food Sci. Nutr.*, 2011, **51**, 178-194.

90 J. Lappi, E. Selinheimo, U. Schwab, K. Katina, P. Lehtinen, H. Mykkänen, M. Kolehmainen and K. Poutanen, *J. Cereal Sci.*, 2010, **51**, 152-158.

91 H. W. Lopez, F. Leenhardt, C. Coudray and C. Remesy, *Int. J. Food Sci. Technol.*, 2002, **37**, 727-739.

92 D. T. Ramonaltyte, G. Juodelklene, L. Basinskiene and V. Zlauklene, *Proceedings of 4th International Congress 'Flour-Bread 07' and 6th Croatian Congress of Cereal Technologists, Opatija, 24-27 October*, 2007, pp. 217-224.

93 E.-L. Bergman, K. Fredlund, P. Reinikainen and A.-S. Sandberg, *J. Cereal Sci.*, 1999, **29**, 261-272.

94 L. Mi-Hyeon, L. Ok-Hee, C. Jong-Eon, K. Hyun-Mi, K. Il-Chul, L. Hwanghee Blaise, I. Suhn-Young and B. Suk, *Biotechnol. Lett.*, 2008, **30**, 2125-2130.

95 M. Haros, N. G. Carlsson, A. Almgren, M. Larsson-Alminger, A. S. Sandberg and T. Andlid, *Int. J. Food Microbiol.*, 2009, **135**, 7-14.

96 M. Anastasio, O. Pepe, T. Cirillo, S. Palomba, G. Blaiotta and F. Villani, *J. Food Sci.*, 2010, **75**, M28-M35.

97 P. Raghavendra, S. R. Ushakumari and P. M. Halami, *Beneficial microbes*, 2011, **2**, 57-61.

98 R. F. Hurrell, M. B. Reddy, J. Burri and J. D. Cook, *Brit. J. Nutr.*, 2002, **88**, 117-123.

99 A. Fardet and J.-M. Chardigny, *Crit. Rev. Food Sci. Nutr.*, 2013, **53**, 535-590.

100 S. Ishizuka, K.-i. Saitoh, T. Suzuki, J.-S. Lee and H. Hara, *Food Chem.*, 2011, **125**, 1219-1225.

101 R. Greiner and U. Konietzny, *New Biotechnol.*, 2009, **25**, S109-S109.

102 E. Matuschek, E. Towo and U. Svanberg, *J. Agric. Food Chem.*, 2001, **49**, 5630-5638.

103 Z. H. Zhao and M. H. Moghadasian, *Food Chem.*, 2008, **109**, 691-702.

104 A. R. Sudheer, S. Muthukumaran, N. A. Devipriya, H. Devaraj and V. P. Menon, *Toxicology*, 2008, **243**, 317-329.

105 S. Y. Ou, G. M. Jackson, X. Jiao, J. Chen, J. Z. Wu and X. S. Huang, *J. Agric. Food Chem.*, 2007, **55**, 3191-3195.

106 K. Kawabata, T. Yamamoto, A. Hara, M. Shimizu, Y. Yamada, K. Matsunaga, T. Tanaka and H. Mori, *Cancer Lett.*, 2000, **157**, 15-21.

107 E. H. Jung, S. R. Kim, I. K. Hwang and T. Y. Ha, *J. Agric. Food Chem.*, 2007, **55**, 9800-9804.

108 A. Murakami, Y. Nakamura, K. Koshimizu, D. Takahashi, K. Matsumoto, K. Hagihara, H. Taniguchi, E. Nomura, A. Hosoda, T. Tsuno, Y. Maruta, H. W. Kim, K. Kawabata and H. Ohigashi, *Cancer Lett.*, 2002, **180**, 121-129.

109 D. L. Rakotondramanana, M. Delomenede, M. Baltas, H. Duran, F. Bedos-Belval, P. Rasoanaivo, A. Negre-Salvayre and H. Gornitzka, *Bioorg. Med. Chem.*, 2007, **15**, 6018-6026.

110 M. Sri Balasubashini, R. Rukkumani and V. P. Menon, *Acta Diabetol.*, 2003, **40**, 118-122.

111 P. Vitaglione, A. Napolitano and V. Fogliano, *Trends Food Sci. Technol.*, 2008, **19**, 451-463.

112 N. N. Rosa, A.-M. Aura, L. Saulnier, U. Holopainen-Mantila, K. Poutanen and V. Micard, *J. Agric. Food Chem.*, 2013, **61**, 5805-5816.

113 N. Rosa and V. Micard, in *Structure des aliments et effets nutritionnels*, ed. A. Fardet, Souchon, I., Dupont, D., Quae publisher, 2013, p. 472.

114 M. J. R. Nout, *Food Microbiol.*, 2009, **26**, 685-692.

115 D. Lioger, F. Leenhardt and C. Rémésy, *Industrie Céréales*, 2006, **149**, 14-22.

116 K. Poutanen, L. Flander and K. Katina, *Food Microbiology*, 2009, **26**, 693-699.

117 F. Hübner and E. K. Arendt, *Crit. Rev. Food Sci. Nutr.*, 2013, **53**, 853-861.

118 J. K. Chavan and S. S. Kadam, *Crit. Rev. Food Sci. Nutr.*, 1989, **28**, 349-400.

119 L. Iocheva, R. V'Lcheva and S. Antonova-Nikolova, *Khranitelno-Vkusova Promishlenost*, **3**, 2004, 13-15.

120 B. Tian, B. Xie, J. Shi, J. Wu, Y. Cai, T. Xu, S. Xue and Q. Deng, *Food Chem.*, 2010, **119**, 1195-1200.

121 Y. H. Kuo, P. Rozan, F. Lambein, J. Frias and C. Vidal-Valverde, *Food Chem.*, 2004, **86**, 537-545.

122 B. A. Cevallos-Casals and L. Cisneros-Zevallos, *Food Chem.*, 2010, **119**, 1485-1490.

123 H. Shi, P. K. Nam and Y. Ma, *J. Agric. Food Chem.*, 2010, **58**, 4970-4976.

124 K. Zyla, M. Mika, T. Fortuna, B. Szymczyk and M. Czubak, *Electro. J. Polish Agric. Univ.*, 2005, **8**, http://www.ejpau.media.pl/volume8/issue4/art-53.html.

125 D. Sushma, B. K. Yadav and J. C. Tarafdar, *J. Food Sci. Technol.*, 2008, **45**, 344-348.

126 S. Hooda and S. Jood, *J. Food Biochem.*, 2003, **27**, 165-176.

127 T. Nestares, M. Barrionuevo, M. Lopez-Frias, C. Vidal and G. Urbano, *J. Agric. Food Chem.*, 2003, **51**, 515-520.

128 G. Urbano, S. Frejnagel, J. M. Porres, P. Aranda, E. Gomez-Villalva, J. Frias and M. Lopez-Jurado, *Eur. Food Res. Technol.*, 2008, **226**, 105-111.

129 B. Bartolomé, I. Estrella and T. Hernandez, *Z. Lebens.-Unters. Forsch.*, 1997, **205**, 290-294.

130 Y. Nogata and T. Nagamine, *J. Agric. Food Chem.*, 2009, **57**, 1331-1336.

131 T. H. Gadaga, A. N. Mutukumira, J. A. Narvhus and S. B. Feresu, *Int. J. Food Microbiol.*, 1999, **53**, 1-11.

132 C. Eklund-Jonsson, A.-S. Sandberg, L. Hulthén and M. L. Alminger, *Open Nutr. J.*, 2008, **2**, 42-47.

133 A. E. O. Elkhalifa, B. Schiffler and R. Bernhard, *Nahrung-Food*, 2004, **48**, 91-94.

134 K. Katina, A. Laitila, R. Juvonen, K.-H. Liukkonen, S. Kariluoto, V. Piironen, R. Landberg, P. Åman and K. Poutanen, *Food Microbiol.*, 2007, **24**, 175-186.

135 C. Schoen, A. Schulz, J. Schweikart, S. Schütt and V. von Baehr, *Nutrition*, 2009, **25**, 499-505.

136 I. A. G. Hassan and A. H. Eltinay, *Food Chem.*, 1995, **53**, 149-151.

137 A. Winata and K. Lorenz, *Cereal Chem.*, 1997, **74**, 284-287.

138 J. Loponen, P. Kanerva, C. Zhang, T. Sontag-Strohm, H. Salovaara and M. G. Gänzle, *J. Agric. Food Chem.*, 2009, **57**, 746-753.

139 K. Katina, K.-H. Liukkonen, A. Kaukovirta-Norja, H. Adlercreutz, S.-M. Heinonen, A.-M. Lampi, J.-M. Pihlava and K. Poutanen, *J. Cereal Sci.*, 2007, **46**, 348-355.

140 C. C. Ariahu, U. Ukpabi and K. O. Mbajunwa, *Plant Foods Hum. Nutr.*, 1999, **54**, 193-206.

141 J. F. Liang, B. Z. Han, M. J. R. Nout and R. J. Hamer, *Food Chem.*, 2008, **110**, 821-828.

142 A. Fardet, *Adv. Nutr. Food Technol.*, 2014, **1**, 103.

143 A. Fardet, *Cereal Foods World*, 2014, **59**, 224-229.

144 A. Fardet, *J. Nutr. Health Food Eng.*, 2014, **1**, 1-2.

145 S. A. Moorhead, R. W. Welch, M. Barbara, E. Livingstone, M. McCourt, A. A. Burns and A. Dunne, *Brit. J. Nutr.*, 2006, **96**, 587-595.

146 C. A. Monteiro, J. C. Moubarac, G. Cannon, S. W. Ng and B. Popkin, *Obes. Rev.*, 2013, **14**, 21-28.

147 S. Y. Ou and K. C. Kwok, *J. Sci. Food Agric.*, 2004, **84**, 1261-1269.

148 D. R. Jacobs and L. C. Tapsell, *Nutr. Rev.*, 2007, **65**, 439-450.

149 G. Mandalari, R. M. Faulks, G. T. Rich, V. Lo Turco, D. R. Picout, R. B. Lo Curto, G. Bisignano, P. Dugo, G. Dugo, K. W. Waldron, P. R. Ellis and M. S. J. Wickham, *J. Agric. Food Chem.*, 2008, **56**, 3409-3416.

150 A. Surget and C. Barron, *Ind. Cér.*, 2005, **145**, 3-7.

151 U.S. Department of Agriculture, Agricultural Research Service, Nutrient Data Laboratory, USDA National Nutrient Database for Standard Reference, release 18, http://www.nal.usda.gov/fnic/foodcomp/Data/SR18/reports/sr18page.htm, 2005.

152 C. W. C. Kendall, A. Esfahani, A. R. Josse, L. S. A. Augustin, E. Vidgen and D. J. A. Jenkins, *Nutr. Metabol. Cardiovasc. Dis.*, 2011, **21**, S34-S39.

Figure Legends

Fig. 1 From food matrix to health effects

Fig. 2 From raw materials to bioavailability

Fig. 3A-B (A) Cross section of white bean cotyledon cells by optic microscopy: the starch grains are embedded in cells separate with rigid cell walls (source: INRA Library); (B) Cross section of red bean before and after 4 hours of *in vitro* digestion (U: beans before digestion ; D: beans after digestion: beans keep their physical structure).[39] © 2012, Elsevier.

Fig. 4A-D Cross sections of almond seeds after bucco-ileal digestion;[149] A-C: cross section by optic microscopy after 3 hours of *in vitro* gastro-duodenal digestion (A), after 3.5 hours of digestion in human (B: ileal contents) and after 12 hours of digestion in human (C: ileal contents); D: cross section by transmission electronic microscopy after 12 hours of *in vivo* digestion: both intact and fractured cells can be observed. © 2008, American Chemical Society.

Fig. 5 Holistic *versus* reductionist view of grain products (with permission from Surget & Barron for image of whole-grain wheat)[150]

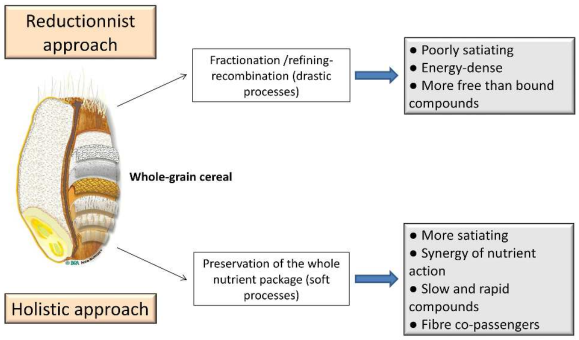
Fig. 6A-B Scanning electronic microscopy of a bread piece. (A) Common wheat bread with visible starch granules (S) and the gluten protein network (M); (B)similar bread containing 6 g/100 g of guar gum showing starch granules embedded by compounds identified as galactomannans,[61] these latter limiting starch accessibility to digestive α-amylases. © 1996, Elsevier.

Table 1 Main nutritional characteristics of grain products

	Water[a]	Starch[a]	Proteins[a]	Lipids[a]	Fibres[a]	Glycaemic Index[b]
Whole-grain cereals	10.1	72.5	12.3	3.4	11.0	51
Legumes	10.9	46.0	25.7	7.4	14.0	25
Nuts & Seeds	5.2	8.1	18.7	54.5	12.0	4[c]

[a]Means calculated from 7, 4 and 8 types of cereal grains (soft wheat, *durum* wheat, brown rice, maize, oat, barley and rye), leguminous seeds (common bean, lentil, soya bean and chickpea), and nuts and seeds (sesame seed, linseed and sunflower seed, walnut, Pecan nut, hazelnut, almond and peanut), respectively (From USDA Food Tables (2005));[151] [b]Means calculated from GI tables by Foster-Powell *et al*. (2002)[29] and Atkinson *et al.* (2008)[24] with glucose as reference food (GI = 100) ; [c]From Kendall *et al.* (2011)[152]

Table of contents entry:



A holistic approach of grain products will help preserve their food structure and nutrient density, then their health potential.

Figure n°1

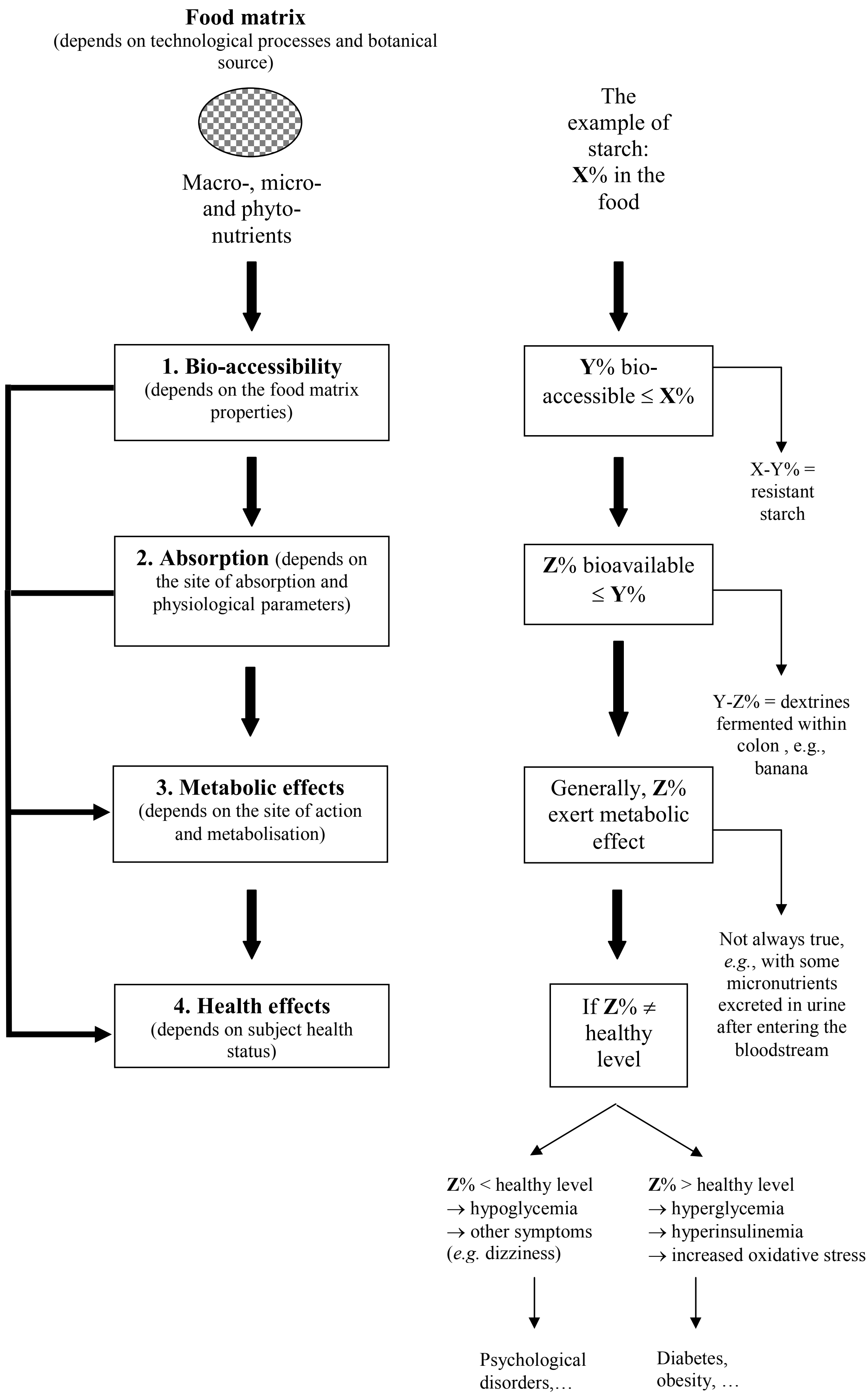
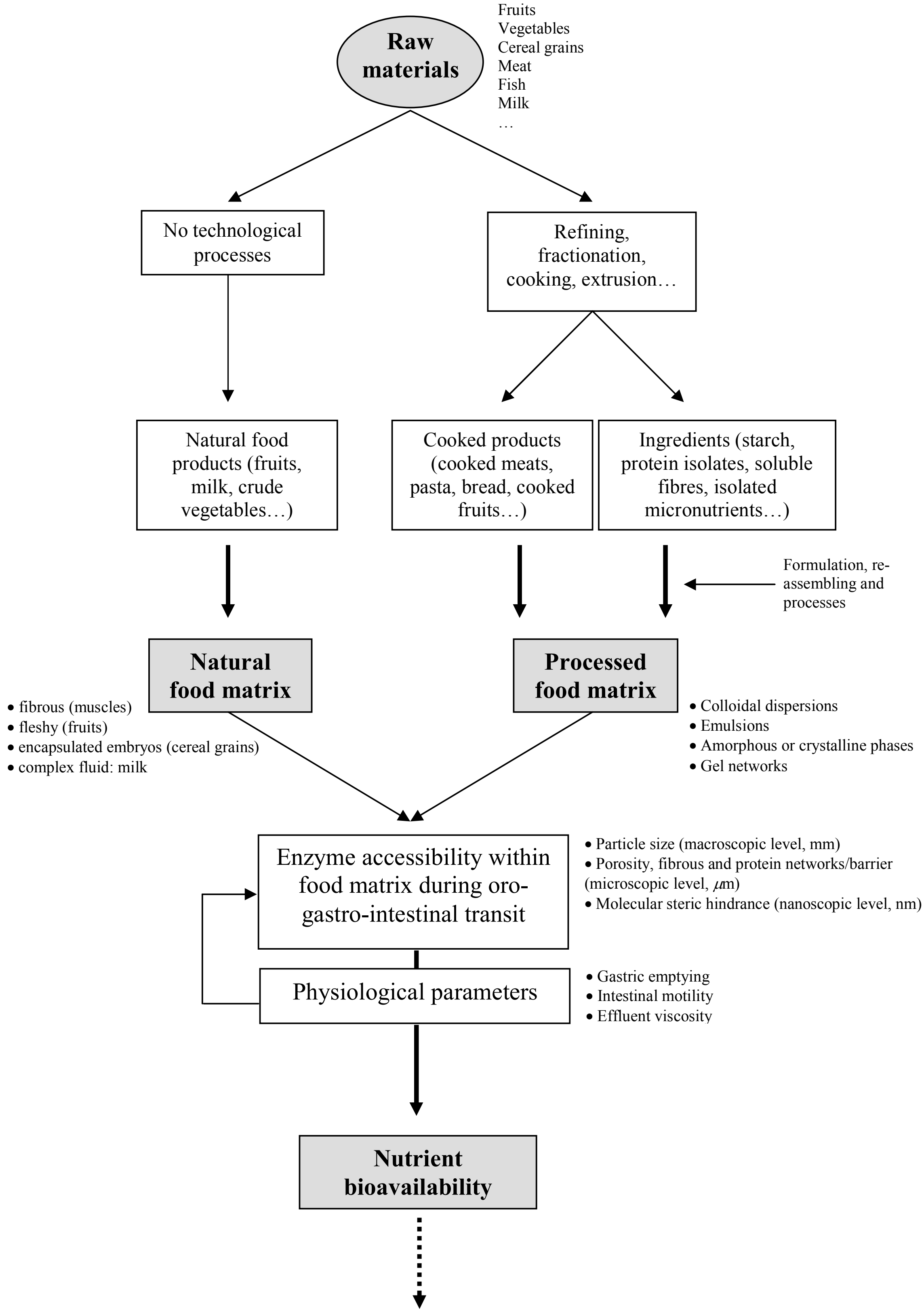
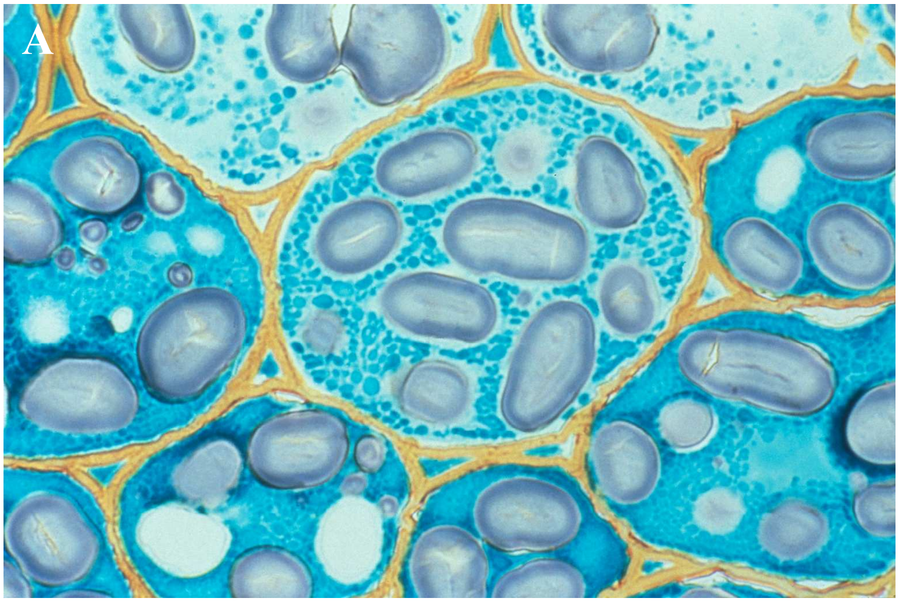

Food matrix
(depends on technological processes and botanical source)
Macro-, micro- and phyto-nutrients
The example of starch: X% in the food
1. Bio-accessibility (depends on the food matrix properties)
Y% bio-accessible ≤ X%
X-Y% = resistant starch
2. Absorption (depends on the site of absorption and physiological parameters)
Z% bioavailable ≤ Y%
Y-Z% = dextrines fermented within colon , e.g., banana
3. Metabolic effects (depends on the site of action and metabolisation)
Generally, Z% exert metabolic effect
Not always true, e.g., with some micronutrients excreted in urine after entering the bloodstream
4. Health effects (depends on subject health status)
If Z% ≠ healthy level
Z% < healthy level → hypoglycemia → other symptoms (e.g. dizziness)
Z% > healthy level → hyperglycemia → hyperinsulinemia → increased oxidative stress
Psychological disorders,…
Diabetes, obesity, …

Figure n°2


Raw materials
Fruits
Vegetables
Cereal grains
Meat
Fish
Milk
…
No technological processes
Refining, fractionation, cooking, extrusion…
Natural food products (fruits, milk, crude vegetables…)
Cooked products (cooked meats, pasta, bread, cooked fruits…)
Ingredients (starch, protein isolates, soluble fibres, isolated micronutrients…)
Formulation, re-assembling and processes
Natural food matrix
• fibrous (muscles)
• fleshy (fruits)
• encapsulated embryos (cereal grains)
• complex fluid: milk
Processed food matrix
• Colloidal dispersions
• Emulsions
• Amorphous or crystalline phases
• Gel networks
Enzyme accessibility within food matrix during oro-gastro-intestinal transit
• Particle size (macroscopic level, mm)
• Porosity, fibrous and protein networks/barrier (microscopic level, µm)
• Molecular steric hindrance (nanoscopic level, nm)
Physiological parameters
• Gastric emptying
• Intestinal motility
• Effluent viscosity
Nutrient bioavailability

Figures 3A-B



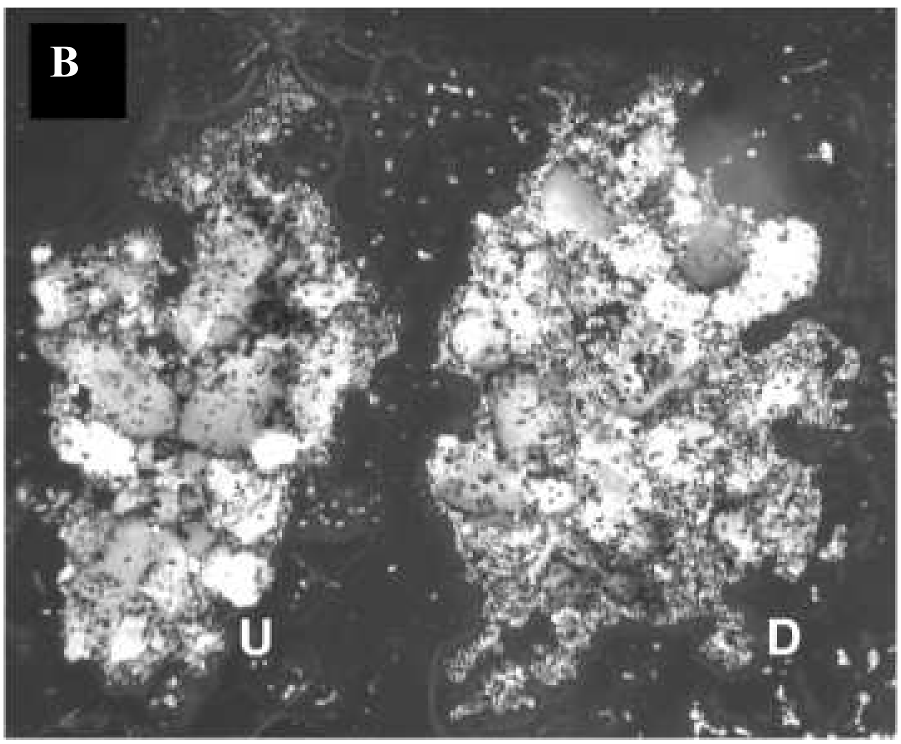
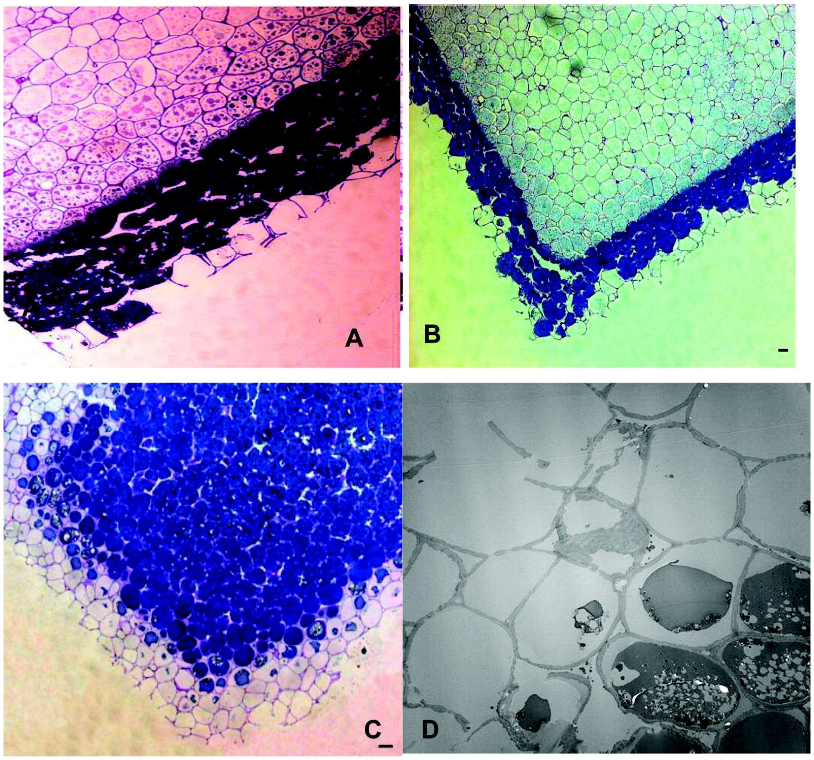


Figure 4A-D



Reductionnist approach

Whole-grain cereal

Fractionation (refining)-recombination (drastic processes)

- More or less isolated compounds
- Reconstructed/recombined foods
- Possible supra-nutritional doses

- Poorly satiating
- Energy-dense
- More free than bound compounds

Preservation of the whole package (soft processes)

- Packages of functional compounds (antioxidants, lipotropes…)
- Nutrient interaction
- Food structure preservation
- Nutritional doses

- More satiating
- Synergy of nutrient action
- Slow and rapid compounds
- Fibre co-passengers

Holistic approach

Figure 6A-B