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Bioaccessibility and associated concepts: need for a consensus

Running title: Bioaccessibility definition

Commentary

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Abstract

Background: The definition of the term 'bioaccessibility' is not clear. In the fields of Nutrition and Food Sciences, the term bioaccessibility was introduced in the context of micronutrients, which can lead to some confusion when applied to macronutrients, the latter requiring hydrolysis (sometimes included in the definition of bioaccessibility).

Scope: In the context of macronutrient digestion, particularly in plant-based food where cell walls play a significant role, it seems coherent to differentiate between the release of nutrients from the food matrix, hydrolysis and absorption.

Key findings and Conclusions: We concluded that the terms bioaccessibility, digestibility and bioavailability have been misused over time and have lost some of their meaning. Therefore, in this study, we suggest a definition for “bioaccessibility” and related vocabulary, as well as a possible classification of the biochemical events occurring during food or feed digestion. It is critical to use precise, specific vocabulary to describe the mechanisms involved while food transits through the different compartments of the gastro-intestinal tract. This goes hand in hand with a recent realisation of the importance of the food matrix, which has an impact on the breakdown of food in the digestive tract and thus on human and animal health.

Keywords: Bioaccessibility, digestion, hydrolysis, mechanisms, nutrients.

1. Introduction

The term "bioaccessibility" is more and more prevalent in the scientific literature as demonstrated by its widespread occurrence in articles (over 6400 articles in Scopus or 4400 in PubMed since 1980), with over 5400 articles that use "bioaccessibility" in their title (see Figure 1). The most recent articles lie in food science, nutrition, chemistry/biochemistry and environmental sciences (85% of the articles identified belonged to the field of nutrition and food sciences), whereas 15 years ago, environmental science and engineering were more dominant. Despite frequent use of the term, its definition does not seem to be clear. There is also a misuse of the term "bioavailability" and both terms are still often assumed to be synonymous.

Furthermore, the terms are used differently between disciplines, for instance human and animal nutrition may utilise terms that have a different and sometimes very specific meaning for each of them. This applies particularly to a notion closely related to bioaccessibility, digestibility.

As a food (or a feed) transits through the gastrointestinal (GI) tract, it undergoes a range of transformations that are both biochemical and physical. First, in the mouth, via mastication, the food matrix is fractured and torn and its components mixed together and with the secreted fluids. Certain nutrients are solubilised into the salivary fluid, some hydrolysed (starch primarily) and new interactions are created. In the gastric and intestinal environments, those processes continue where macronutrients (protein, fat and carbohydrates) are further hydrolysed, small compounds are released and may be absorbed and the remaining matrix reaches the colon where it can be degraded by microorganisms notably via fermentation. It is important to realise that bacteria also synthesise certain compounds (e.g., vitamins) within the gut lumen, and that bacterial hydrolytic activity occurs throughout the GI tract, augmenting mammalian enzyme activity (Wu et al., 2020). These complex and multiscale processes are generally and collectively termed as "digestion" (Bornhorst et al., 2016). However, the word

covers many steps that require to be more accurately named and defined. A sequence of events ought to be followed to allow a food component to reach the bloodstream or lymphatic system (depending on the nature of the molecules absorbed) and be transported to the site (organ or system) where it is metabolised by cells. Therefore, in a nutshell, digestion of food is an orderly, systematic process that includes release and hydrolysis of nutrients, and transport of compounds to the enterocytes. Small, structurally intact compounds coming in contact with the enterocytes may be absorbed (but not all small compounds are absorbable such as structurally altered lysine molecules) (Moughan et al., 1996).

The first step of digestion is the release of nutrients from the food matrix. This process can be key for controlling absorption and the subsequent postprandial responses, particularly for hard or mechanically resistant foods such as those containing intact plant-tissues, such as fruit, vegetables, legumes and nuts. This nutrient release is defined by some as bioaccessibility (Aguilera, 2019; Grundy et al., 2016; Hu et al., 2022; Marze, 2013; Mengucci et al., 2020). However, others refer to bioaccessible nutrients as those able to interact with and be absorbed by the enterocytes, and place less emphasis on food matrix degradation (Carbonell-Capella et al., 2014; Fernandez-Garcia et al., 2009; Hayes, 2018; Thakur et al., 2020). In this regard, the cell wall encapsulating plant cells plays a critical role as it can limit or prevent the release of nutrients from the food matrix. The cell wall also affects other stages of digestion by decreasing the probability of the enzymes binding with their substrate (via for instance an encapsulation mechanism or increase in digestive content viscosity), hindering the release of hydrolysed products from the cell/food matrix and/or interacting with the intestinal mucosa (Grundy et al., 2016). All these processes can have an impact on animal or human physiology, such as transit, post-prandial blood pattern and gut microbiota (Capuano & Pellegrini, 2019; Ratanpaul et al., 2021). Finally, cell wall components (dietary fibre) reaching the distal gut serve as substrates

for bacterial fermentation, this process can lead to the liberation of more nutrients and energy, which may be utilised either by the host or the gut bacteria (Widaningrum et al., 2022).

On the other hand, hydrolysis corresponds to the cleavage in water, due to the catalytic activity of digestive enzymes, of chemical bonds that link sub-units (i.e., glucose, amino acids, and free fatty acids and glycerol) of macromolecules together (i.e., starch, proteins and triacylglycerols) (Le Feunteun et al., 2021). Hence, amylases hydrolyse glycosidic bonds in starch, proteases and peptidases hydrolyse peptide bonds within proteins and peptides, and lipases hydrolyse the ester bonds of triacylglycerols. A range of enzymes are secreted by the human and the animal, each with their specific activity, in order to degrade polymers into absorbable molecules. The rate and extent (kinetics) at which the hydrolysis takes place rely on the substrate (specific to the enzyme), its availability (easily accessible by the enzyme), the form under which it is present, and the conditions of the food or environment (e.g., pH, enzyme concentration, and presence of compounds that may slow down, such as antinutrients, or enhance the reaction, such as cofactors). With digestion being a dynamic process, the release and hydrolysis of macronutrients can occur in either order, or simultaneously.

This commentary aims to highlight some of the inconsistencies in the concept of bioaccessibility and closely associated vocabulary, particularly when considering macronutrients in plant-based foods, where nutrient release and availability can be a significant issue. Furthermore, the article also offers alternative definitions. Therefore, in this article, we have focussed on plant-based foods as an example given the importance of the structure (food matrix effect), especially the cell wall, in modulating the release and overall digestibility of the nutrients contained within these foods.

2. Bioaccessibility

Early reports of the term "bioaccessibility" describe the "availability" or solubility of elements, such as toxic metal ions, ingested from soil (Davis et al., 1997). It is also found in pharmaceutical sciences and refers to the compounds, often drugs, released into the GI tract and their absorption into the bloodstream (Kholodov et al., 1980). It has then been used by nutritional scientists investigating micronutrients. It has been discussed in food and nutritional sciences in 2002 (Stahl et al., 2002). In that work and in subsequent reports, there is the suggestion, but no clear mention, of the effects of hydrolysis, which does not feature for micronutrients or other biocomponents (Dima et al., 2020). Some definitions only imply the release or solubilisation of a particular food component: "Here bioaccessibility is defined to represent that fraction of the ingested mercury solubilized in the GI tract, while bioavailability denotes the fraction actually absorbed" (Davis et al., 1997). This definition seems to be the one understood by many scientists (Aguilera, 2019; Carbonell-Capella et al., 2014; Hayes, 2018; Hu et al., 2022; Rasera et al., 2023; Thakur et al., 2020). Other authors agree that the term is not clearly defined (Cardoso et al., 2015; Peijnenburg & Jager, 2003).

Recently, Mengucci et al. (2020) stated: "Bioaccessibility kinetics comprise description of both release and transition to absorbable form." What do the authors mean by transition? It could be understood that the food matrix is (physically) transformed but the food compounds, such as proteins, are not necessarily hydrolysed. However, macronutrients require to be hydrolysed by enzymes to be broken down into absorbable compounds. In that case, can we say that the products of proteolysis (amino acids and peptides) are "bioaccessible" (released from the food matrix) given that the hydrolysis is likely to happen mainly outside the food matrix (in the aqueous environment of the lumen and the brush-border membrane of the enterocytes)? And how can we distinguish between release from the food matrix and hydrolysis. On the other hand, some macronutrients, even though not released, can still be hydrolysed (at least partially) by digestive enzymes if the enzymes are able to penetrate the cell wall and reach the

intracellular environment (Colosimo et al., 2020; Grundy et al., 2022). This situation is most commonly observed where the substrate is a macromolecular assembly such as a starch granule, lipid or protein body, and therefore more easily retained in the matrix. Le Feunteun et al. (2021) are more specific in their definition: "Proportion of a nutrient that is chemically and physically available for absorption by the small intestine". Given the confusion arising from quite different viewpoints, we suggest that the term "bioaccessibility" be used solely to refer to the ability of an enzyme to access its substrate. This definition would cover an enzyme's ability to diffuse through a porous cell wall and hydrolyse entrapped substrates. So, for this specific example, the nutrients are physically inaccessible (i.e. it is not spontaneously released from the matrix into the gut lumen), but biochemically accessible. It could also cover molecules that are intrinsically resistant to hydrolysis such as resistant starch, that could be bioaccessible but not hydrolysable (in the upper GI tract). This illustrates the complexity of defining "bioaccessibility" particularly regarding the inclusion or not of the hydrolysis step.

The current lack of clarity and consensus in this nomenclature can impact research in this field. This is mostly true when employing *in vitro* methods aimed at unveiling the mechanisms underpinning the various stages of digestion. Bioaccessibility defined as the release of food components is a "theoretical" notion that is best investigated *in vitro* due to the high degree of control over the experimental conditions (more than 75% of the studies encountered in the literature that report the bioaccessibility of food compound(s) were performed *in vitro*). For example, incubation of a food/feed in simulated digestive fluids can easily be performed without enzymes present, enabling the differentiation between macronutrient release and their hydrolysis, which is very difficult and expensive to achieve *in vivo*. In nutritional science, more and more attention has been paid to the role and fate of the food matrix during digestion since it has significant consequences on the absorption of digested compounds, and thereby the postprandial response and subsequent health effects. In that perspective, it is critical to evaluate

the kinetics of enzymes activity (digestion) that rely on the ability of those enzymes to be in contact with their substrate (macronutrients). As mentioned above, in plant-based foods or ingredients, cell walls play an important role in macronutrient release and hydrolysis (Edwards et al., 2021; Grundy et al., 2016).

The question therefore is at what stage of digestion to consider and assess the bioaccessibility of a macronutrient. Is it simply the release of the compound from the matrix, making it available for hydrolysis and subsequent absorption? Or is it the ability of the digestive enzymes to bind to and hydrolyse the substrate? As stated above, it is possible for macronutrient assemblies such as starch granules to be trapped in a matrix, but the enzymes are small enough to diffuse into the matrix and can access and hydrolyse the substrate. Therefore, we propose that the bioaccessibility of a macronutrient be more clearly defined as the proportion of a macronutrient that is accessible by digestive enzymes and hydrolysed to release the absorbable hydrolysis products, irrespective of whether the macronutrient substrate has been released from the matrix or not. The details for this premise are discussed in more detail below.

3. Digestion and digestibility

This brings us to another term closely related to bioaccessibility that has different meanings based on the authors or audience: “digestibility”.

Digestion can be defined as the transformation of the food during digestion, such as swelling or size reduction of particles, and the hydrolysis of macronutrients by digestive enzymes secreted by the human or the animal (Bornhorst et al., 2016; Goodman, 2010). On the other

hand, digestion, especially within the field of animal science, relates to both the enzymatic hydrolysis and microbial fermentation of ingested nutrients, and the absorption of the products from the GI lumen (Stein et al., 2007). Classically, the term "digestibility" refers to the "disappearance" of a compound during its transit through the GI tract, which is a generic term that can refer to a number of different mechanisms. Digestive physiology varies between species, with ruminants having a highly developed foregut, that utilises microbial fermentation to break down the tough cell wall materials to make the nutrients in the feed more bioaccessible and available prior to digestion in the stomach and small intestine (Fujimori, 2021; Karasov & Douglas, 2013). Digestibility is subdivided as apparent, true, real and standardised digestibility. The term "standardised" digestibility is mainly found in animal nutrition. The distinction between those "different types" of digestibility is mainly empirical and based on the method used to determine gut endogenous nutrient losses (Moughan, 2023). It is also nutrient dependent as it applies primarily to amino acids. One issue with the measurement of digestibility, defined as nutrient disappearance, is that disappearance of a nutrient does not necessarily mean that the nutrient has been absorbed.

When trying to differentiate the different set of events that occur during digestion (travel of a complex food within the GI tract up to the absorption of molecules and ions by the enterocytes) the definition of digestibility can lead to imprecision. Indeed, the term covers not only the hydrolysis and transformation of the food but also absorption and fermentation. So, different compartments of the GI tract with distinct roles are designated within a single definition. The same applies to the nature of the processes studied (biochemical, mechanical, physical and physiological) and the scales. Digestibility in that context seems to describe the physiological response of the animal and not so much the degradation of the food/feed matrix.

Biochemical reactions, through the hydrolysis by enzymes, cannot occur if the enzyme is not in contact with its substrate. In the strict biochemical sense of the term, digestion signifies

hydrolysing polymers (e.g., protein and starch) into their constitutive, absorbable units (amino acid and glucose) (Goodman, 2010). The hydrolyses of those macronutrients will eventually provide energy via different metabolic pathways, based on the nutrients and the physiological state of the human or animal. Once again, there does not seem to be a consensus around the meaning of "macronutrients". According to Le Feunteun et al. (2021), "the term macronutrient refers to the biopolymers initially present in foods (starch, lipid, protein) that need to be hydrolysed by GI secreted enzymes to be converted into nutrients. Sugars and fibres, which are not hydrolysed by GI secreted enzymes, are therefore not included in this definition." Furthermore, some macronutrient polymers are naturally resistant to hydrolysis. For example, some proteins with a high degree of secondary structure can resist hydrolysis (Foegeding & Davis, 2011; Salazar-Villanea et al., 2016). Some starches with higher levels of ordering or crystallinity can resist hydrolysis by endogenous digestive enzymes. Thereby, these components may well be rendered bioaccessible to digestive enzymes, but their availability for uptake is hindered by their molecular structure (Butterworth et al., 2022; Dhital et al., 2019).

Furthermore, in animal science, the distinction is often made between digestible nutrients and digestible energy (Święch, 2017). In human nutrition, energy is often given as calories as determined using the Atwater general factor system. The use of the generalised factors assumes that there is no effect of food type on nutrient digestibility, which is not the case. Following this, 1 g of carbohydrate and protein provides 4 kcal, and 1 g of lipid provides 9 kcal. Furthermore, the susceptibility to hydrolysis of many of these compounds or nutrients can be altered through processing or cooking, altering molecular structure (Aguilera et al., 2019; Groopman et al., 2015). Hence consumption of identical raw or cooked foods can have very different postprandial nutrient responses. Determining metabolizable energy of a food, by actually measuring the nutrient response *in vivo*, though also empirical, seems to give a better appraisal of the energy actually utilised from a food (Gebauer et al., 2016).

4. Precise and accurate definitions to enable the description of mechanisms

How can we improve our understanding of the mechanisms behind digestion if we are not able to describe them with appropriate, specific terms? As discussed above, currently, the release, hydrolysis and absorption of nutritional components are incorporated into a single definition. Therefore, the word "bioaccessibility" is neither precise nor accurate.

The release, as we refer to as bioaccessibility, of food components results from a highly integrated complex process, governed by various mechanisms, occurring at different scales. Before (native and processed ingredients) and during digestion, molecules from foods or feeds interact together to form structures that have physicochemical properties and behaviours that can be studied at different levels (nano-, micro-, meso- and macroscale). It is necessary to investigate these interactions to understand and eventually predict the physiological impact of the ingestion of a food or a feed. One way of doing this is to analyse its nutrient content while following its evolution and transformation throughout its transit in the GI tract. This can be done for individual nutrients (e.g., proteins and generated amino acids and peptides) while also examining the overall matrix degradation. By doing so, both quantitative and qualitative data can be obtained: i) quantitative measurements of macronutrient hydrolysis (kinetics: rate and extent), and potentially the "energy" that can be obtained by the organism following digestion, and ii) qualitative information that complements the former by giving an appraisal of the overall food matrix (e.g., network generated between molecules, coagulation or precipitation of certain compounds, cell wall integrity).

This knowledge is also valuable for studying the microbiota since the delivery form of food components to the terminal small intestine and colon affects bacterial activity. Compounds that are available to microorganisms can be fermented, although the repertoire of enzymes they

possess is much more diverse than the endogenous enzymes secreted by mammals and thereby results in a greater degradation of the food/feed matrix (Flint et al., 2012). The nature and organisation of dietary fibres, the main substrates of the microbiota, within the cell wall matrix determine how they are fermented as it relies on the enzymes having access (bioaccessible?) to them (Bulut et al., 2023; Puhlmann & de Vos, 2022). The resulting hydrolytic products can then be metabolised either by the host or the gut bacteria, offering a further complication to the accurate interpretation of these terms.

Absorption, digestibility and bioavailability are distinct terms to bioaccessibility, even though they all describe different events underlying to the absorption of nutrients via the enterocytes. **Absorption** corresponds to the uptake of molecules and ions by the enterocytes; **digestibility** the hydrolysis and sets of transformation occurring to the food matrix as discussed above, release of nutrients and uptake by the enterocytes (classically defined as nutrient disappearance), and **bioavailability**, the use of the nutrients and other food compounds by the organism. “Bioavailability” has been usually described as the uptake of nutrients from the GI tract in a structural form that is utilisable for metabolism (Fuller, 2012). Some authors use the terms “digestibility” and “bioavailability” synonymously.

Following our suggested use of the term “bioaccessible”, possible scenarios, that remain to be elucidated for a wide range of foods and feeds, can be classified (see Figure 2) as follows:

-**Bioaccessible and hydrolysable** – nutrients are released from the food matrix and are hydrolysed into smaller molecules

-**Not bioaccessible and hydrolysable** – enzymes can diffuse into the food matrix (e.g. through cell walls), hydrolyse the substrate and the products diffuse out of (are released from) the matrix.

-Not bioaccessible and not, or only partially, hydrolysable – nutrients remain encapsulated within the food matrix and the enzymes cannot access them.

-Bioaccessible and not, or partially, hydrolysable – nutrients are solubilised (or released from the food matrix) but their molecular structure, or interactions with other food compounds or agents could prevent/restrict hydrolysis and/or absorption (e.g., anti-nutrients binding essential minerals or inhibiting enzymes). In that latter category are included molecules that are resistant to hydrolysis because of their structure, such as certain proteins, resistant starch, and soluble fibres. Some of those fibres and compounds may be fermented by bacteria and contribute, to various degrees, to the availability of nutrients and energy depending on diet and species.

The gut microbiota

Several aspects concerning the profuse and diverse microbiota that is found throughout the human and the animal GI tract can be emphasised here, with particular activity being found in the ileum and colon.

The first aspect is that bacteria secrete a range of enzymes that could be active in food/feed digestion (their influence has been largely overlooked), in addition to the mammalian enzymes (Cerqueira et al., 2020; Flint et al., 2012; Kaoutari et al., 2013). Released nutrients can be absorbed by bacteria and fermented, with short chain fatty acids or simple organic acids being produced and absorbed by the host as nutrients (and in some cases as physiological regulators). The microorganisms can also synthesise compounds that are released into the GI tract (e.g., cobalamin) (Roth et al., 1996).

The second aspect relates to bioaccessibility. Nutrients once released from the food matrix, are hydrolysed (macronutrients are thus converted into absorbable molecules) and enter the soluble pool in the gut lumen and then are accessible for cellular absorption. But these newly produced

molecules may be absorbed by two types of cell: the enterocyte (in the small intestine) or a bacterium. In the latter case, the molecule will be fermented or metabolised and the resultant product of process will enter the soluble pool and once again become accessible for enterocyte absorption. For example, various enzymes can lead to the release of glucose from starch which will enter the gut soluble pool (Cerqueira et al., 2020). Glucose molecules may be absorbed by the enterocyte or by a bacterium and, in this case, be fermented to generate short-chain fatty acids (Gromova et al., 2021). So, in this context, bioaccessibility is not restricted to accessibility by enterocytes (host).

Moreover, bacteria can increase the bioaccessibility of macronutrients by degrading the cell wall of plant-based foods or feeds (Puhlmann & de Vos, 2022; Rastall et al., 2022). Nutrients encapsulated within the food matrix can then become available for hydrolysis and/or absorption. However, this is likely to take place primarily in the lower small intestine and colon where the populations of bacteria are denser, and the amount of nutrients released will depend on the integrity of the cell walls (Widaningrum et al., 2022). Any macronutrients released in the colon are likely to be used mainly for bacteria (potentially beneficial for the host) as endogenous enzymes are less active in that compartment and the absorption of products of digestion is low. On the other hand, certain micronutrients can be used directly by the host (e.g., vitamin and minerals such as iron) (Mayneris-Perxachs et al., 2022).

A further aspect is that bacteria can metabolise some molecules that have been released into the gut lumen altering their molecular structures and thus rendering the molecules more bioactive (e.g., certain phenolic compounds) (Rodríguez-Daza et al., 2021).

Therefore, the term “bioaccessibility” can also be used to describe the extent to which the food matrix and the macromolecules imbedded within the food matrix are accessible to both mammalian and bacterial enzymes. Therefore, the term as currently used has two distinct meanings, dependent upon the situation. It is suggested that “bioaccessibility” could be used to

refer to the latter phenomenon, with the term "solubilisation" being used to infer a nutrient that has been released from the food matrix, and that has entered the GI tract soluble pool. Just because a molecule has entered the latter pool, it does not mean that it is bioaccessible. For instance, certain peptides are soluble but not absorbed.

5. Conclusion

The challenge faced by scientists working in the field of nutrition (and this is also true for other disciplines) is to use terms that can be understood by themselves but also by different communities. Both "bioaccessibility" and "digestibility" are somehow too generic and combine different notions belonging to biochemistry, biophysics, biomechanics, physiology and nutrition. Ideally, it should be possible to describe processes taking place during digestion that can be translated at different scales (e.g., nutrients, food, tissues/cells, and host) without losing their meaning.

The terms bioaccessibility, digestibility, bioavailability have often been confused over time and have lost some of their meaning, particularly when comparing different published studies. Therefore, in our view these should be the definitions:

-**Bioaccessibility**:

For macronutrients: luminal accessibility of a food compound to enzymes (digestive from the host or of bacterial origin) that become potentially available for absorption. This covers both scenarios where the hydrolysis step can occur either before (scenario 2 in Figure 2) or after release of the substrate from the food matrix (scenario 1 in Figure 2). In this instance, the hydrolysis requires to be differentiated from the release as certain food compounds may resist digestion. Therefore, some nutrients may enter the soluble pool in the GI tract lumen but not be hydrolysable or absorbable (e.g., certain peptides, scenario 4 in Figure 2).

For micronutrients: release of potentially absorbable food components from the food matrix or macromolecular assembly, into the GI tract lumen, allowing them to reach the site of absorption (enterocytes or microbial).

-**Digestibility**: the luminal disappearance of a nutrient (hydrolysis for macronutrients) during its passage through the GI tract.

Note: true, apparent, real and standardised digestibility are long-standing terms used in both human and animal nutrition, but have very specific meanings depending upon what and how fractions of gut endogenous nutrient flow are determined.

-**Bioavailability**: the amount of an ingested nutrient that is released from the food matrix during digestion, hydrolysed, absorbed via the GI tract, transported and distributed to cells and tissues in a chemical form that is available for utilization in metabolic functions or for storage. The term should therefore cover the uptake of a compound into the circulation or lymphatic system and the reaching of target organs and tissues. In fact, many scientists consider it to refer to the extent and rate at which the active moiety (nutrient, drug or metabolite) enters the systemic circulation, thereby reaching the site of action. This is different from bioefficacy where the moiety is taken up by the target organ where it exerts its biological activity which in turn manifests itself in the phenotypic function of an organ.

Note: here we assume that a molecule that is not able to reach its target tissue is not bioavailable.

Overall, defining bioaccessibility may well be nutrient dependent. For macronutrients, it refers to when they are accessible to hydrolytic enzymes (host or bacteria). For micronutrients, it could be when they are made accessible for absorption by release from the food matrix. Their "bioavailability" for uptake is then dependent on their susceptibility to hydrolysis (macronutrients) or interactions (sequestration) with other compounds which prevent absorption (micronutrients).

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Table

Table 1: Summary of the definitions of "bioaccessibility" found in the literature and their limitations

Definitions	References*	Limitations
Solubility of compounds or nutrients	Davis et al., 1997	Some food compounds may be released from the food matrix but may not be soluble in the aqueous environment of the digestive tract (e.g., hydrophobic compounds including lipids, aggregates or precipitate)
Release of nutrients from the food matrix	Aguilera, 2019 ; Butterworth et al., 2022 ; Grundy et al., 2022 ; Hu et al., 2022 ; Marze, 2013 ; Mengucci et al., 2020.	It does not cover the fact that some macronutrients are accessible to digestive enzymes but still enclosed within the food matrix (e.g., enzymes that can penetrate the cell wall of plant-based foods).
Release of nutrients from the food matrix and the hydrolysis of macronutrients - nutrients thus become potentially available for absorption	Capuano & Pellegrini, 2019 ; Carbonell-Capella et al., 2014 ; Cardoso et al., 2015 ; Colosimo et al., 2020 ; Edwards et al., 2021 ; Grundy et al., 2016 ; Le Feunteun et al., 2021 ; Rasera et al., 2023 ; Stahl et al., 2002 ; Thakur et al., 2020	Both release and hydrolysis are included in this definition which does not permit to discriminate between these two aspects of the digestion process. This general definition could be suitable for micronutrients but not so much for macronutrients.
Compounds released into the gastrointestinal tract and their absorption into the bloodstream	Dima, et al. 2020 ; Kholodov et al., 1980 ; Fernandez-Garcia et al., 2009 ; Hayes, 2018 ; Peijnenburg & Jager, 2003	Degradation of the food matrix, including hydrolysis by digestive enzymes, is not clearly identified in this definition whereas the absorption step is added.

*The list of references is not exhaustive, only a few examples (previously cited in the article) are given

Figures

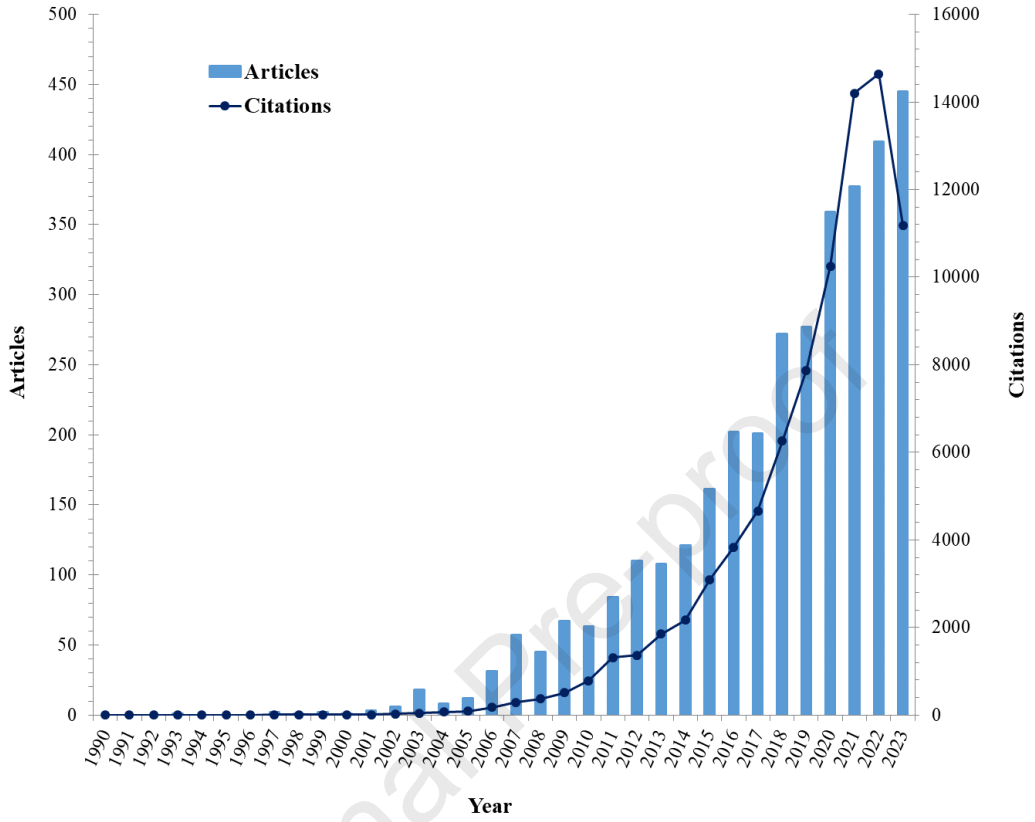

Figure 1: Titles present in the literature containing the word “bioaccessibility” and the citation trend over the past 30 years (sources: Scopus and Pubmed).

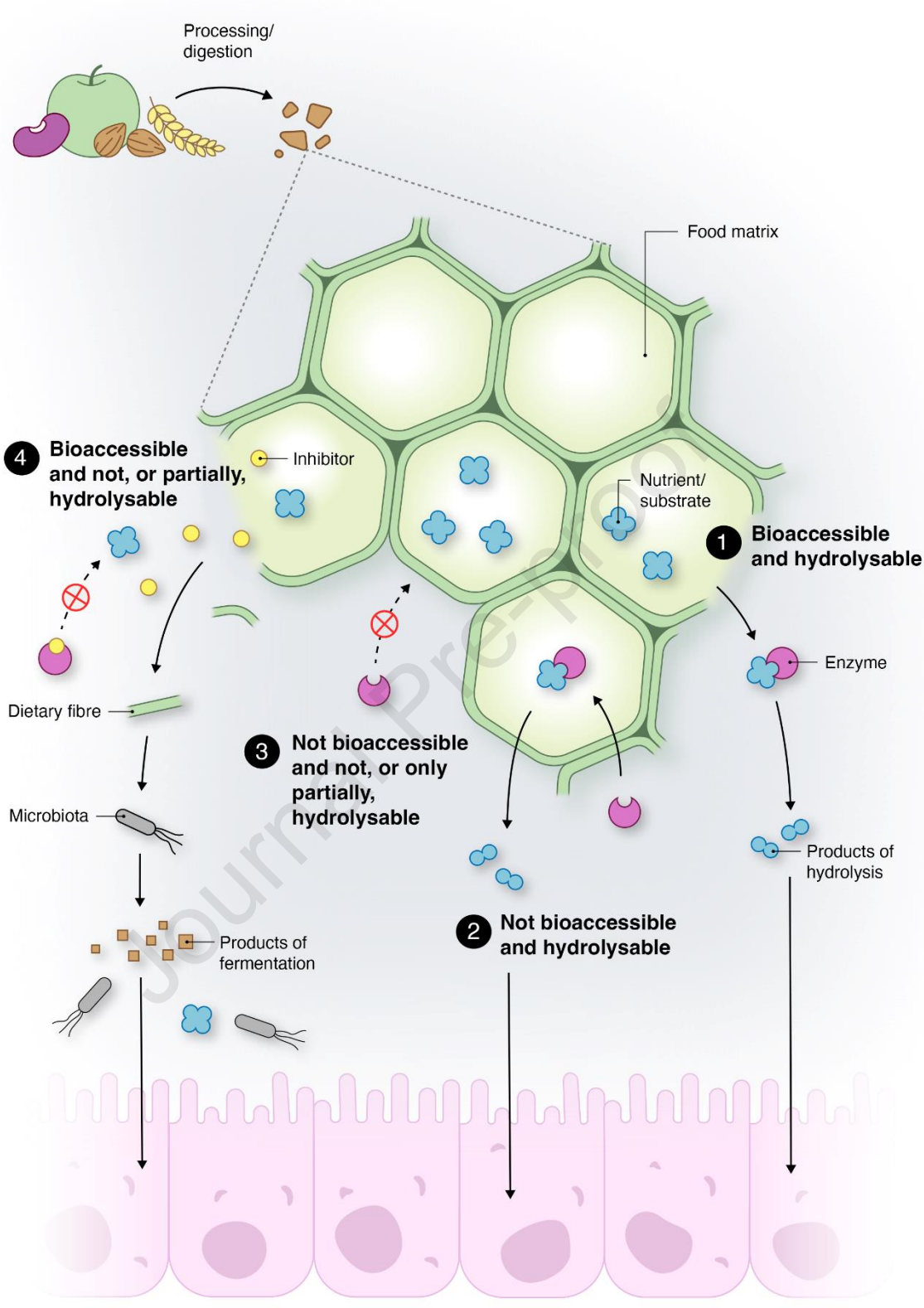

Figure 2: Schematic representation of the 4 scenarios identified for the bioaccessibility and hydrolysis of nutrients (biopolymers) in a plant-based food.

Highlights

- Different definitions of “Bioaccessibility” are found in the literature
- A clear definition is necessary to understand the set of events occurring during digestion
- Four main scenarios related to “Bioaccessibility” can be identified
- Some definitions are suggested

Author Contributions

Myriam M.L. Grundy: Conceptualization, Writing - original draft, Writing - review & editing.

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Pete Wilde: Conceptualization, Writing - original draft, Writing - review & editing.