

## Essentials of Bioaccessibility and Bioavailability for Applied Nutritional Practices

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### Abstract

Nutrients are partially bioaccessible to be extracted from their matrix. They may be partially lost by processing to a meal and by metabolism after absorption from the GI tract. Numerous steps in this cascade have an impact on the nutrient amount which will finally be bioavailable for an effect. Daily allowances are defined and widely recommended to obtain such an effect. However, these needs are derived from observation of healthy populations and are increased to cover needs for special consumer and patient groups or for pregnancy. Daily allowances are subject to frequent changes whenever new scientific evidence arises as is the case for vitamin D. This article describes reasons why generally reasonable recommendations may fail occasionally are found among the variation of genes, age, gender, or race, as well as epigenetics, which all contribute to the individual expression of metabolic capacity and thus to differences in individual bioavailability.

### Genetic Basis and Impact of Age and Gender on Bioavailability

Orally administered medicines or food will be either incorporated readily as physiological substrates or identified as xenobiotics which, as being foreign, have to be eliminated as efficiently as possible. Highest activities of metabolizing enzymes are observed in liver after birth and decline with increasing age. Enzymes' inducibility begins in the earliest embryonic stage and reaches high rates before birth.

Peptic digestion is incomplete in the first two years of life. Antiseptic effect of acidity in the stomach develops within a few hours after birth. In full-term babies, gastric acidity changes within one hour from 6.1 to 5.4, within 2 hours to 3.1 and within six hours to 2.2. pH increases afterwards for 10 days and goes down again only slightly. Pre-term born babies have a gastric pH >4 for 80% to 90% of time, the acidity only rising with age. An increase in gastric pH to 4 is observed for infants between 1 and 12 months with chronic diarrhea and protein malnutrition, combined with bacterial overgrowth essentially with Gram-negative bacilli, in 57% of the cases. The bacterial overgrowth happens at the moment of the evolution of the disease to a chronic state. Breast-fed babies do not have bacterial overgrowth of gram-negative Bacilli. Acid output similar to adults is reached by 24 weeks.

Oligo elements such as iron and copper are differently absorbed by boys or girls: Preadolescent fasting men absorb 35.2% of an iron loading dose, preadolescent fasting women 45% and 14.8% or 24.7% respectively from a dose taken in a meal. Serum ferritin differed only marginally in this study. This result explains the higher prevalence of iron anemia in boys aged 11-15 (12.1%) compared to equally aged girls (6.1%) [1]. Besides gender influence on iron absorption, it is to be noted that long-term use of PPI pharmacotherapy can cause a decreased iron bioavailability. In acidic conditions, iron will exist in the stomach in the form of hexaaquairon (III) ion,  $[\text{Fe}(\text{H}_2\text{O})_6]^{3+}$ . As pH raises, i.e. as a result of  $\text{pK}_a=2.2$ , this aquo-complex will be deprotonated to  $[\text{Fe}(\text{H}_2\text{O})_5(\text{OH})]^{2+}$ , and to  $[\text{Fe}(\text{H}_2\text{O})_4(\text{OH})_2]^{+}$  as a result of  $\text{pK}_a=3.5$ , to finally become  $[\text{Fe}(\text{H}_2\text{O})_3(\text{OH})_3]^0$  as a result of  $\text{pK}_a=6.0$ . Already at weakly acidic pH and increasingly above approximately pH 5, significant amounts of secondary colloidal iron (III) hydroxides and an amorphous red brown ferric hydroxide precipitate are formed. Ferric iron will condensate through forming hydroxo bridges after elimination of water from the aquohydroxo complexes. These mechanisms occurring at natural pH render ferric iron more and more insoluble

and unsuitable for absorption. As related to copper absorption, it is higher in women aged 20-59 (71%) than in men of the same age (64%). This difference does not exist in adults aged 60-83. Contraceptives in women aged 20-39 increase plasma levels of copper and ceruloplasmin, but not its absorption [2-7].

Gastric acidity and secretion of pancreatic enzymes as well as intestinal motility are gender-dependent. Acidity is 5-fold more active in men than in women. Endocrine secretion of digesting enzymes is much more situation adapted in females whereas in males it is continuous. High progesterone levels in the hormonal cycle, in pregnancy or under contraceptive medicines inhibit intestinal motility. As a result of hormonal changes pregnant women often suffer from heartburn induced by reduced esophageal sphincter pressure and heartburn due to sex hormones, essentially progesterone. In this patient group, short term acid neutralizers or  $\text{H}_2$  antagonists should be preferred instead of PPIs in possibly meal-free phases in order to omit the risk of incomplete protein digestion and the risk of predisposition to immune responses of the child. This risk is indeed confirmed in studies correlating the incidence of allergy and asthma of babies with anti-ulcer consumption of their mothers during pregnancy [8].

The processes of getting rid of xenobiotics, independently of the source, are qualitatively described in chronological steps. To cope with metabolic variability some genetic items have to be understood. Frequently, just one mutation on a single nucleotide (SNM, single nucleotide mutation) in a genotype results in a modification of this capacity and gives rise to polymorphisms. Ethnic groups show typical phenotypes which are related to diverse "detoxifying" and "digesting" capacities.

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The influence of genes on food “digestion” and vice versa is scientifically explored by the “omics” sciences such as nutrigenetics, nutrigenomics, proteomics, and metabolomics. The effect of genes in determining race phenotypes will slowly decrease with evolution, recombination of genetic codes, adaption and changing food habits from local traditional to international multicultural meals. Influence is also exerted the other way round, i.e. from food on genes. Thus, the need of diagnostic tools and interventions on an individual level (personalized medicine, personalized nutrition) is evident.

### Loss of Nutrients in the Course of Processing, Intake, and Metabolism

Nutrients, unlike pure substances used for parenteral nutrition, must be liberated from the food stuff matrix first. Primary raw material from plants or animal sources is cut into smaller pieces, washed, processed using different amounts of ingredients (water, butter, vegetable oil, spice) and heat. These processes contribute enzymatically or physico-chemically to degradation. In the GI tube, impacts of acidity and digestive enzymes determine the extent of liberation of the nutrient from the matrix.

Depending on the biochemical and eventually microbiological stability, only a part of the nutrient amount is available, after eating, for absorption. It will decrease further after having been distributed, metabolized (mainly in the liver, first-pass effect) and excreted. These losses have to be assessed in feeding decision support if individuals should respond to a nutrient dose.

Bioaccessibility describes the extent, quantity, or fraction to which nutrients are extractable from a food stuff matrix in the course of processing and become available for absorption from the gut in its chemical form. The nutrient gets bioaccessible by mastication, and through the mixture with amylase and the gastric juice. The bioaccessibility of a nutrient may differ depending on the production and processing of the product, e.g. cooking a vegetable increases the bioaccessibility of potassium. The awareness about bioaccessibility of nutrients is essential for investigations about nutrition and health benefits.

Bioavailability describes the extent to which a nutrient or pharmaceutical active ingredient will reach systemic circulation and be available for metabolic use and effect. If a nutrient is also used as an intravenous injection, the ratio of the amounts orally taken and intravenously administered describes the individual absolute bioavailability. If bioavailability is compared from one person to another, it represents the inter-individual systemic bioavailability. Finally, the bioavailability of one substance compared to a second one, e.g. a gold standard in clinical trials, is referred to as relative bioavailability and relevant for the concept of the glycaemic index.

### Application of the Bioavailability Concept: Glycemic Index

It may be convenient to compare food from various sources for equivalence. An Italian brand of pasta has a specified composition. A generic industrial brand or fresh home-made pasta may have another composition and therefore be different. It would be equal or a copy, if the recipe and the raw material would be the same in either one of the products. Otherwise it should be considered as an alternative to the original. As well, freshly prepared pasta and reheated pasta differ in the extent of carbohydrates cleavage. Therefore, reheated pasta is likely to be more bioavailable than fresh pasta.

In medicines, excipients are considered to have no effect, thus the concept of bioavailability is only applied for active ingredients. The method of choice to prove bioequivalence is to monitor the blood levels of the active ingredient as a function of time. If areas under the curve (AUC) correspond to each other, bioequivalence is approved. In practice, original and alternative are assessed as being bioequivalent, if their lead substances have the same biological effect [9,10].

The amount of an active ingredient ingested is measured from the area under the curve (AUC) from a plasma level-time plot. The same applies for blood glucose measured after ingestion of food or in a polydose test. It describes, as a simplification of relative bioavailability used currently in pharmacokinetics, the fraction of food absorbed and detectable as glucose in systemic circulation. Glucose is liberated directly from 100 g carbohydrates and indirectly from other monosaccharides contained in the portion, which are converted to glucose by isomerization. This liberated glucose is expressed as per cent of the glucose plasma level after ingestion of 100 g pure glucose. Various carbohydrate sources lead to various glucose levels after polysaccharides hydrolysis. Not only carbohydrates, but glucose released from glycogen of muscle tissues or from the liver, glycogenic amino acids, and fatty acids in catabolic metabolism such as hunger or cachexia contribute to the plasma glucose level. In low-carb diet, the strategy to avoid high plasma glucose levels should in turn limit insulin peaks and additional adipose deposits [11].

### Examples of Glycemic Index (GI) of a Selection of Foodstuff

- Fructose: GI=19
- Sucrose: GI=65
- Honey: GI=61
- Lactose: GI=45
- Milk (full fat): GI=41
- Brown rice: GI=55
- White rice: GI=44 (converted)/56 (long-grain)/72 (short-grain)
- Potatoes: GI=70
- Spaghetti (white, al dente): GI=46
- Pizza Margherita (dough, tomato, mozzarella): GI=80 Pizza

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