



Ensuring nutrient bioavailability means getting the best out of foods. Many naturally occurring nutrients present in foods at low levels are known to have beneficial effects on health. However, to contribute their full benefit, they must be absorbed from the food through the walls of the small intestine. Namely, they must be bioavailable to the body! This is not always the case, for physiological and/or physical reasons. Work in the Nestlé Research Centre to understand the mechanisms that control bioavailability opens up new avenues for Nestlé to create innovative products that offer consumers, worldwide, nutrition, health and wellness through foods.

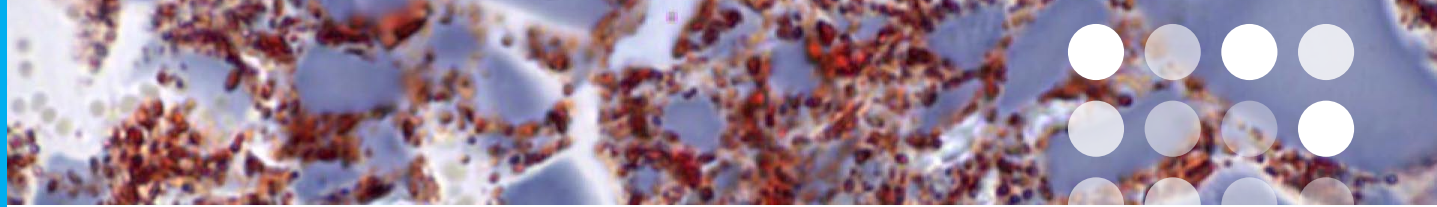
Bioavailability of Nutrients

A Major Research Domain for Nestlé

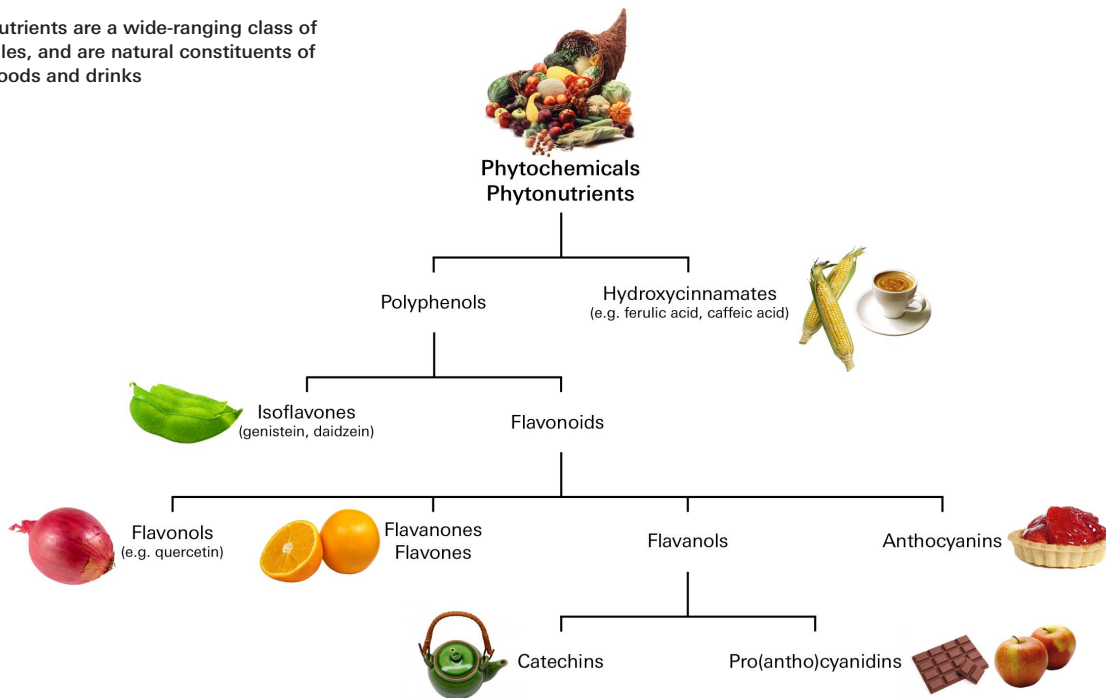
Scientists at the Nestlé Research Centre have been working to understand bioavailability, what affects it, and, through the fine control of specific bioactive ingredients, how to transfer this knowledge into Nestlé products that deliver guaranteed health and wellness benefits. This article cites a selection of Nestlé Research Centre scientific publications. It describes what bioavailability is and why it is a critical field of research for Nestlé, the nutrition, health and wellness company, to fulfil its promise of "Good Food, Good Life".

Health and wellness through bioactive elements and molecules in foods

Nestlé research in nutrition over the years has broadened and deepened knowledge within and outside the Company on the health benefits of the classical essential nutrients. More recent research has focussed on the more specific health benefits offered by non-classical nutrients, namely naturally occurring molecules from plants like sterols, carotenoids and polyphenols.



Phytonutrients are a wide-ranging class of molecules, and are natural constituents of many foods and drinks



Among these, polyphenols are currently a focus of research. They are a wide-ranging class of molecules, are natural constituents of many foods and drinks, often as red, orange, blue, purple or brown colour pigments, and are strong antioxidants broadly considered to be beneficial to health with a multitude of effects to protect most tissues in the body (1). In relation to polyphenols, a number of review articles address the question of their bioavailability (2-4). So what is bioavailability? Why is it important? And what is Nestlé Research doing about it to present both classical and non-classical nutrients alike in appropriate forms in foods to optimise their physiological activity?

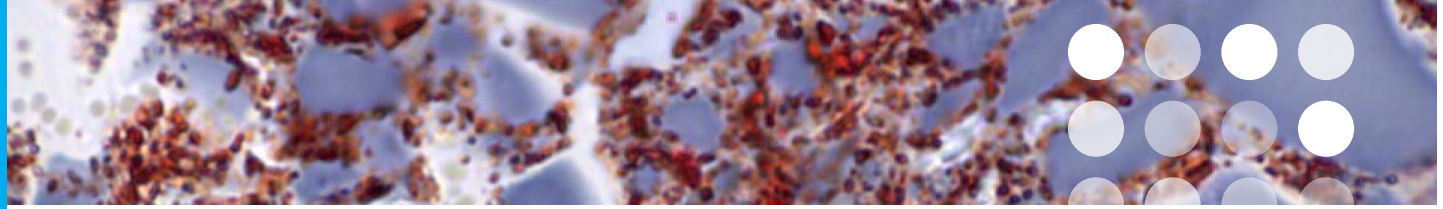
Bioactive molecules: the message on the package

If you look at the labels of food and drink products and in particular their lists of ingredients, you will see, for example, that one product may contain 50 mg of anthocyanins (the natural red colours in fruits) or 20 mg of soya isoflavones, both polyphenol antioxidants. Another may contain 3 mg of lycopene (a carotenoid from tomato) active in maintaining a youthful skin quality. Even if the names may not be familiar, this should be great news for all consumers who want nutrition, health and wellness

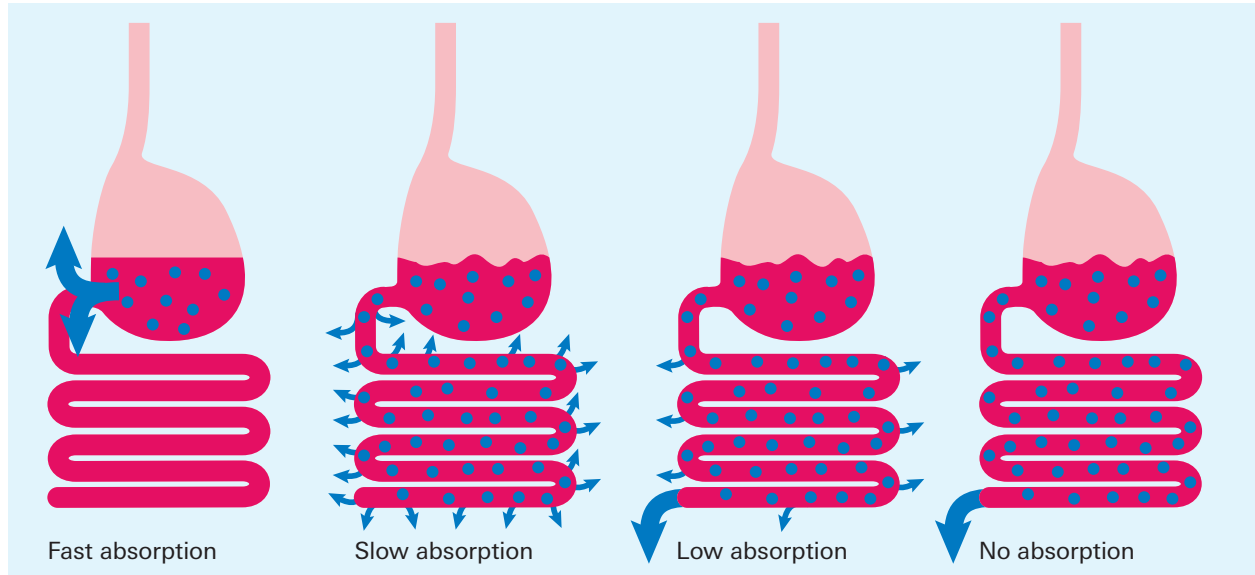
from their foods and drinks. But before we start rejoicing, we have to stop and think! The amount of a health-promoting active ingredient indicated on the package is one side of the story. The amount of that ingredient that reaches the target tissues in the body to exercise its benefit is the other side.

Bioactive molecules: their tribulations in the body

Taking lycopene as an example, it has to find its way from the food, through the body after consumption, to reach the skin, in order to have its beneficial effect. On a molecular level, this is like the labours of Hercules! Once consumed, the active molecule must survive the hostilities of gastric acidity and enzymes before reaching the intestine. There, it must present its “biometric” passport to a molecular gatekeeper to be allowed through into a sort of ante-chamber where it must undergo a further series of molecular identity checks to open a second door that gets it into the bloodstream. The circulating blood carries it around the body where it “visits” all the different tissue and cell types in the body. When it reaches the skin cells of the dermis and epidermis, another set of doorkeepers check it again, and this time let it into the cell to do its healthy work (5).



Bioavailability depends on ensuring efficient absorption through the wall of the small intestine



● Bioactive substance

These multiple controls along the pathway from the product in the package to the target tissue are part of the mechanism by which the body protects itself against the invasion of potentially dangerous pathogens and contaminants. But even for a “friendly” molecule, the body’s defences take no chances.

Bioavailability definition and consequences

The bioavailability of an active ingredient is the quantity that reaches the target tissue, compared to the amount in the original product. Many factors affect the fraction reaching the target tissue. These include the age, health status, gender and individual genetics of the consumer, as well as the complexity of the food matrix, other foods ingested at the same time, rate of gastric emptying and intestinal transit time. When taken together these and other factors can result in variations of bioavailability from 0 to 100% (5).

So can we make a parallel between foods and pharmaceuticals? The answer is, Yes and No! To do its job, any active molecule must reach its target. But most pharmaceuticals provide the active molecule in high concentration so that it reaches the target tissue by finding its way through the body’s molecular screening system outlined

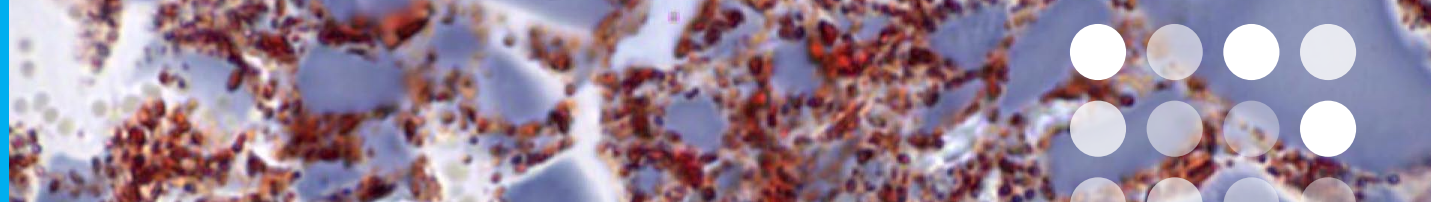
above. With natural active substances in foods, the challenge is to work within a narrow window of quantities, originally from food, so that there is enough to ensure that a part of the active substance reaches its target, but not so much that the amount starts to have negative side effects (5).

Innovative solutions via improving the intestinal transport of bioactive ingredients and their delivery to target tissues throughout life.

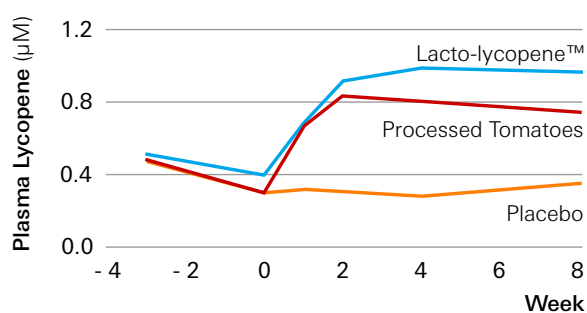
Research on bioavailability in the Nestlé Research Centre

In fact, bioavailability is an extremely complex subject, situated on the interface between the biological and physical sciences, bringing together human physiology on the one side and food structures on the other.

Physiology: Many of the physiological aspects involved are described above. Compared to macronutrients where the intake is always high, micronutrients have a much lower and relatively narrow beneficial intake



range. Their bioavailability depends on five pharmacokinetic processes summarised by LADME... Liberation from the food matrix after consumption, Absorption into the systemic circulation, Distribution to body tissues, Metabolism by biochemical conversion and Excretion from the body (5). The situation is further complicated by the fact that the active substances reaching the tissues may already be first or second order metabolites rather than the intact molecules as present in the food (6). Nestlé scientists are among the world's leading players in methods to assess the bioavailability of phytochemicals, adding human studies through genomics and proteomics to the range of in-silico and in-vitro methods. They expect that much more detailed information on bioavailability will emerge in the next decade and provide a firm basis for exploiting the health benefits of phytochemicals in foods (5) and moving towards the individualised diet (7).



NRC developed a specific process to optimize bioavailability of lycopene through a suitable galenic form for nutritional supplement

Stable isotope tracers: When isotope labelled tracers were first used in the 1930s to study the metabolism of food components, this heralded the era of modern nutrition, transforming it from a science of observation to an investigative science. Radioactive isotopes were the first to be used because technologies already existed to quantify their presence in different body tissues and fluids. However, the use of isotope tracers in human studies had to wait for the development, in the 1980s, of mass spectrometers sensitive and selective enough to analyse trace amounts of stable isotopes. Since this time, Nestlé scientists have developed a number of sophisticated methods using stable isotope labelled tracers in foods to measure the efficiency of absorption of specific nutrients in human subjects, from babies to the elderly (8). Most of these have used inorganic mass

spectrometry to determine the bioavailability of minerals and trace elements from foods and how this is enhanced or diminished by different food components. Stable isotope studies have shown that, in young adult women, calcium absorption from certain mineral waters is as efficient as from milk, which can have important consequences for preventive measures against osteoporosis later in life (9). Also in young women, magnesium bioavailability was shown to be enhanced when the water is consumed with a meal, perhaps because of a slower gastrointestinal transit time (10). Other studies include mineral and trace element absorption in the elderly (11) and in infants (12), as well as investigating food constituents that increase or decrease absorption of iron in infants from wheat- and soy-based infant cereals (13, 14).

Delivery systems: Phytosterols, such as sitosterol, are the equivalent in plants to cholesterol in humans and, as such, have a similar chemical structure. They inhibit cholesterol absorption into the body when co-ingested with cholesterol-containing foods. However, they are capricious, and spontaneously crystallise when isolated in vegetable oils. The crystals are not bioavailable. They transit through the whole digestive system without being absorbed, so their potential health benefit is lost. One of the centres of expertise in the Nestlé Research Centre works on the creation of delivery systems, namely food systems that provide the necessary physico-chemical environment to stabilise "difficult" molecules. In the case of phytosterols, this means holding them in a soluble form by preventing crystallisation. As with minerals and trace elements, stable isotope labelling is used to test the performance of delivery systems. In the case of phytosterols, this is with ^2H and ^{13}C labelled cholesterol as the tracer molecules. Isotope ratio mass spectrometry with a gas chromatography-combustion interface, permits the precise measurement of ^2H and ^{13}C isotope enrichment in the different body pools and, as such, gives a measure of the efficiency of different food matrices for phytosterols in reducing blood cholesterol levels. A high bioavailability is obtained when phytosterols are solubilised in low-fat milk (15, 16). This is one of several examples of targeted delivery systems specifically created by NRC scientists to ensure that low levels of individual bioactive molecules in food products are efficiently absorbed in the digestive system to fully express their health benefit potential for the consumer.

References

1. Kroon, P., Williamson, G. (2005), Polyphenols: dietary components with established health benefits, *J Sci Food Agric.*, 85, 1239-1240
2. Holst, B., Williamson, G. (2004), A critical review of the bioavailability of glucosinolates and related compounds, *Nat Prod Rep.*, 21, 425-447
3. Manach, C., Williamson, G., Morand, C., Scalbert, A., Rémésy, C. (2005), Bioavailability and bioefficacy of polyphenols in humans. I. Review of 97 bioavailability studies, *Am J Clin Nutr.*, 81 (suppl), 230S-242S
4. Manach, C., Williamson, G. (2005), Bioavailability and bioefficacy of polyphenols in humans. I. Review of 93 intervention studies, *Am J Clin Nutr.*, 81 (suppl), 243S-255S
5. Holst, B. and Williamson, G. (2004) Methods to study bioavailability of phytochemicals. In Bao, Y.P. and Fenwick, G.R. (eds.) *Phytochemicals in Health and Disease*. Marcel Dekker, New York, pp 25-56.
6. Kroon, P.A., Clifford, M.N., Crozier, A., Donovan, J.L., Manach, C., Williamson, G. (2004), How should we assess the effects of exposure to dietary polyphenols in vitro? *Am J Clin Nutr.*, 80, 15-21
7. Mutch, D.A., Wahli, W., Williamson, G. (2005), Nutrigenomics and nutrigenetics: the emerging faces of nutrition, *FASEB.*, 10, 1602-1616
8. Kastenmayer, P., Davidson, L., Galan, P., Cherouvrier, F., Hercberg, S., Hurrell, R. (1994), A double stable isotope technique for measuring iron absorption in infants, *BJN.*, 71, 411-424
9. Couzy, F., Kastenmayer, P., Vigo, M., Clough, J., Munoz-Box, R., Barclay, D.V., (1995), Calcium bioavailability from a calcium- and sulfate-rich mineral water, compared with milk, in young adult women, *Am J Clin Nutr.*, 62, 1230-1244
10. Sabatier, M., Arnaud, M.J., Kastenmayer, P., Rytz, A., Barclay, D.V., (2002), Meal effect on magnesium bioavailability from mineral water in healthy women, *Am J Clin Nutr.*, 75, 65-71
11. Couzy, F., Kastenmayer, P., Mansourian, R., Guinchard, S., Munoz-Box, R., (1993), Zinc absorption in healthy elderly humans and the effect of diet, *Am J Clin Nutr.*, 58, 690-694
12. Davidson, L., MacKenzie, J., Kastenmayer, P., Agget, P.J., Hurrell, R.F., (1996), Zinc and calcium apparent absorption from an infant cereal: a stable isotope study in healthy infants, *BJN.*, 75, 291-300
13. Davidson L., Kastenmayer, P., Szajewska, H., Hurrell, R.F., Barclay, D.V., (2000), Iron bioavailability in infants from an infant cereal fortified with ferric phosphate or ferrous fumarate, *Am J Clin Nutr.*, 71, 1597-1602
14. Davidson, L., Galan, P., Kastenmayer, P., Cherouvrier, F., Juillerat, M.A., (1994), Iron bioavailability Studied in infants: The influence of phytic acid and ascorbic acid in infant formulas based on soy isolate, *Ped. Res.*, 36, 816-822
15. Pouteau, E.B., Monnard, I.E., Piguët-Welsch, C., Groux, M., Sagalowicz, L., Berger, A., (2003), Non-esterified plant sterols solubilised in low fat milks inhibit cholesterol absorption: A stable isotope double-blind crossover study, *Eur J Nutr.*, 42, 154-164
16. Gremaud, G., Dalan, E., Piguët, C., Baumgartner, M., Ballabeni, P., Decarli, B., Leser, M.E., Berger, A., Fay, L. B., (2002), Effects of non-esterified stanols in a liquid emulsion on cholesterol absorption and synthesis in hypercholesterolemic men. *Eur J Nutr.* 41, 54-60