Matrix effect and health:
the example of dairy products

European Milk Forum

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The matrix effect is an emerging concept in nutrition

For over half a century, the study of the relationship between diet and health has largely focused on nutrients taken in isolation: fats, carbohydrates, proteins and micro-nutrients. This reductionist approach - linking a nutrient to a health effect - is perfectly legitimate in the case of deficiency diseases: beri-beri is due to vitamin B1 (thiamine) deficiency. Scurvy is linked to vitamin C deficiency and is cured by eating vitamin C-rich citrus fruit.

However, it is not adapted to the multi-factorial chronic diseases affecting the health of populations today. The famous "β-carotene affair" dating back to the 1990s is an example of this. Whereas all the epidemiological studies suggested that consuming β-carotene in the diet had a beneficial effect, the results of the intervention trial conducted with smokers in Finland cast a shadow: the incidence of lung cancer and mortality was higher in the group of subjects who had received a β-carotene supplement[1]. It is fruit and vegetables which are "good for the health" and not β-carotene in isolation, which can be harmful in some cases.

The effects of nutrients on the health can, therefore, be different when combined within the special structures formed by food matrices. The matrix reflects the complexity of foods and takes into account the fact that the sum of the nutrients is not sufficient to explain all the effects of foods in terms of physiology and health[2]. The presence of fibres, proteins and micro-nutrients, bioactives etc. within a complex matrix can lead to interactions between the nutrients. Different foods with the same amount of a component will not necessarily be equivalent in terms of nutrition or health.

The matrix effect is an emerging concept in nutrition which is likely to have a profound effect on the discipline through the many doors it opens both in research and in public health. Examples are starting to stack up, in particular concerning dairy products, which are the most studied food group[3].

[1] Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. N Engl J Med. 1994 ; 330(15):1029-35.

[2] Lecerf JM. Les effets des nutriments dépendent-ils des aliments qui les portent? L'effet matrice. (Do the effects of nutrients depend on the foods containing them? The matrix effect) Cahiers de Nutrition et Diététique. 2015 ; 50 (3) : 158-64

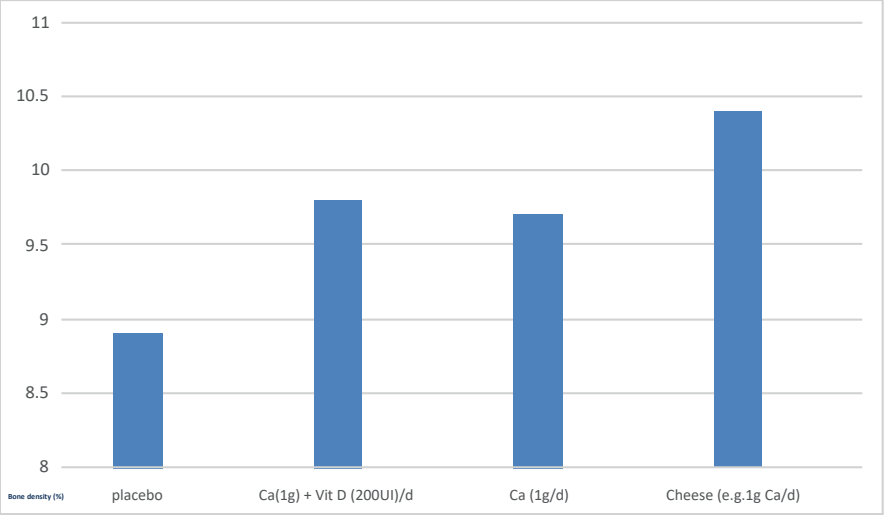
[3] ThorningTK et al. Whole dairy matrix or single nutrients in assessment of health effects: current evidence and knowledge gaps. Am J Clin Nutr. 2017;105(5):1033-1045. doi: 10.3945/ajcn.116.151548.

A nutrient is not enough in itself to make a food

Traditionally, calcium = milk and dairy products. This is essentially true, since dairy products are the main source of calcium in the European diet. However, in terms of health, dairy products are about much more than just calcium. This is reflected in studies comparing the effect of the same amount of calcium in isolation and in the form of a dairy product.

On bone[4]

195 girls aged 10 to 12 years took part in an intervention trial which lasted two years. The aim was to compare the effect of calcium on bone mass accrual - evaluated by the development of bone density - depending on its source. The girls were divided into four groups: placebo, calcium supplement (1g), calcium (1g) + vitamin D (200UI/d) and cheese, providing the equivalent of 1 g of calcium.
The regular consumption of cheese led to a higher bone mass accrual than the calcium supplement, with or without vitamin D.



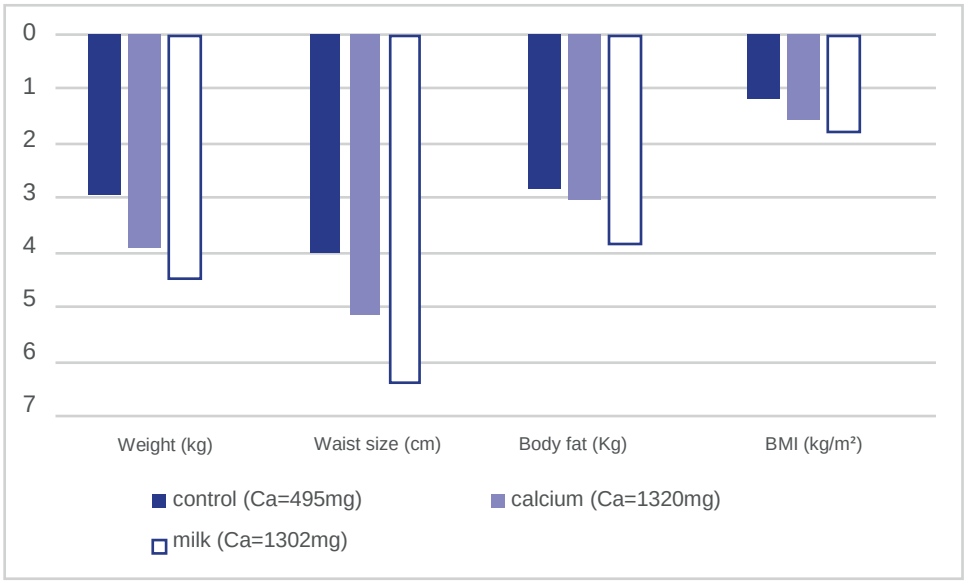
[4] Cheng S et al. Effects of calcium, dairy product, and vitamin D supplementation on bone mass accrual and body composition in 10-12-y-old girls: a 2-y randomized trial. Am J Clin Nutr. 2005;82(5):1115-26

On weight[5]

To study the effect of calcium and its source on weight, 64 overweight women aged 20 to 50 years were randomly separated into three groups. Each group was fed a low-calorie diet (-500 Kcal/day) for 8 weeks providing the same amounts of proteins, fats, carbohydrates and fibres, but with variable amounts of calcium.

- a "control" group with approximately 500 mg of calcium intake;
- and two "calcium" groups both with approximately 1300 mg of calcium intake either in the form of calcium supplements or in the form of milk.

No difference was observed between the control group and the "calcium supplement" group which did not provide any particular benefit. Conversely, the benefits in terms of weight, waist size, body fat and BMI were all greater in the milk group.



In these two examples, it is indeed the matrix effect which explains the differences, since the calcium intakes are identical.

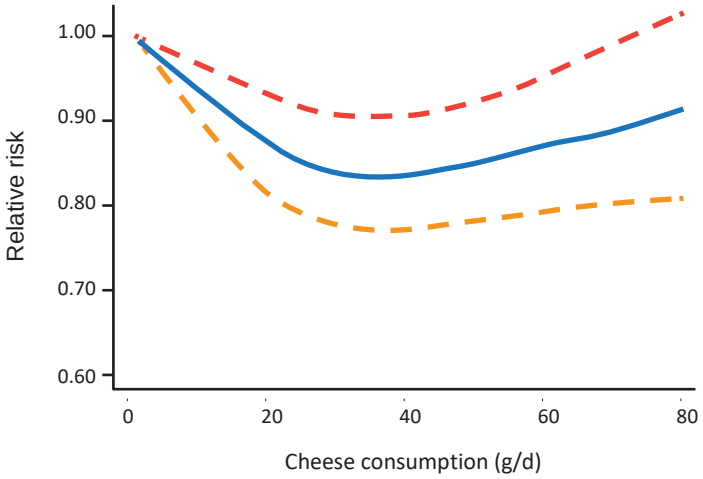
[5] Faghih Sh et al. Comparison of the effects of cows' milk, fortified soy milk, and calcium supplement on weight and fat loss in premenopausal overweight and obese women. Nutr Metab Cardiovasc Dis. 2011;21(7):499-503. doi: 10.1016/j.numecd.2009.11.013.

The effect is not necessarily what one might expect from the nutrient composition

For a long time, saturated fatty acids were thought to increase the level of “bad” cholesterol and the risk of cardiovascular disease. As full-fat cheese and dairy products contain saturated fatty acids (in variable amounts depending on the products), one might expect them to have a negative effect. However, this is not the case.

Cheese is associated with a reduction in the risk of cardiovascular disease[6]

A recent meta-analysis of 15 cohort studies confirms that overall, eating cheese is associated with a significant 10% reduction in the risk of cardiovascular disease (14% for coronary diseases, 10% for strokes). A dose-response analysis shows that “optimum” consumption is around 40g/day.



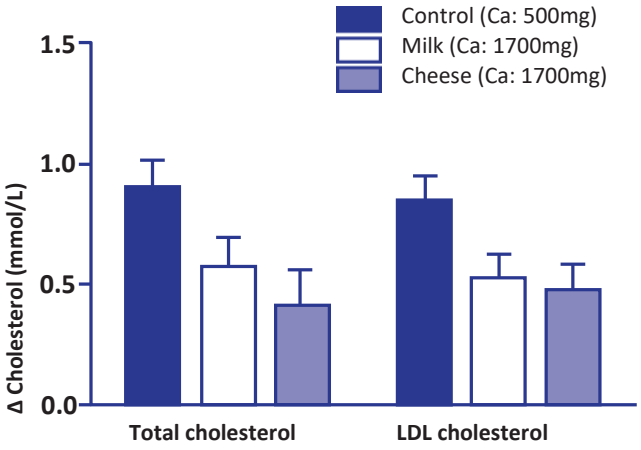
The matrix modulates the saturated fatty acid response[7]

To understand these results, researchers fed 15 healthy subjects 3 diets very rich in saturated fatty acids, each lasting 15 days: control, milk and cheese diets. The three diets were comparable in terms of calories, proteins, carbohydrates, fibre, fats and saturated fatty acids but the milk and cheese diets contained much more calcium.

As expected, the total cholesterol and LDL cholesterol (the “bad” cholesterol) levels increased in all three diets as compared to the start of the study. However, the increase was significantly less with the dairy product diets.

[6] Chen GC et al. Cheese consumption and risk of cardiovascular disease: a meta-analysis of prospective studies. Eur J Nutr 2017 56 (8): 2565-75

[7] Soerensen KV et al. Effect of dairy calcium from cheese and milk on fecal fat excretion, blood lipids, and appetite in young men Am J Clin Nutr. 2014;99(5):984-91. doi: 10.3945/ajcn.113.077735.



The matrix modulates lipid metabolism

The authors of the study followed this reasoning through to its logical conclusion: they measured the quantity of fats eliminated in the stools. The results were clear: the milk and cheese diets significantly increased the excretion of fats in the stools in relation to the control diet. The quantity of fats in the stools in directly linked to the blood cholesterol levels: the more it increases, the lower the cholesterol level.

	Energy excreted (Kcal/d)	Fats excreted (g/d)
Control Ca=500mg/d	170 +-8	3.9 +- 0.3
Milk Ca=1700mg/d	202 +- 13*	5.2 +- 0.4**
Cheese Ca = 1700mg/d	193+-14*	5.7 +- 0.4**

*p<0.05

Thus, full-fat dairy products, particularly cheese, certainly contain saturated fatty acids, but they also contain many other nutrients which can interact and modulate the effect. In this case calcium in the dairy matrix binds to fatty acids and this leads to a reduction in the absorption of fats by the intestine. This has positive consequences on cholesterol and on the risk of cardiovascular disease.

Since the diets were strictly controlled, this work demonstrates the reality of the matrix effect and the need to take it into account when evaluating the health effect of a food.

There are different kinds of matrices

For calcium

The most well-known example is no doubt calcium, for which intestinal uptake is higher when it is provided by dairy products in comparison to most vegetable products apart from cabbage. For calcium, it is better to drink milk than eat spinach, simply because the dairy matrix contains other nutrients such as phosphopeptides and lactose which potentiate calcium uptake whereas spinach contains oxalates which inhibit calcium uptake.

Or proteins

- **Animal vs. vegetable**[8]

The "Framingham Offspring" cohort studied the relationship between the consumption of foods that are a source of protein, physical activity, muscle mass and functional decline over a 9-year follow-up period.

Overall, when there is a high level of physical activity, foods that are sources of animal protein (meat, poultry, fish, dairy products) and vegetable protein (pulses, seeds, soya) are linked to higher muscle mass, in particular in women.

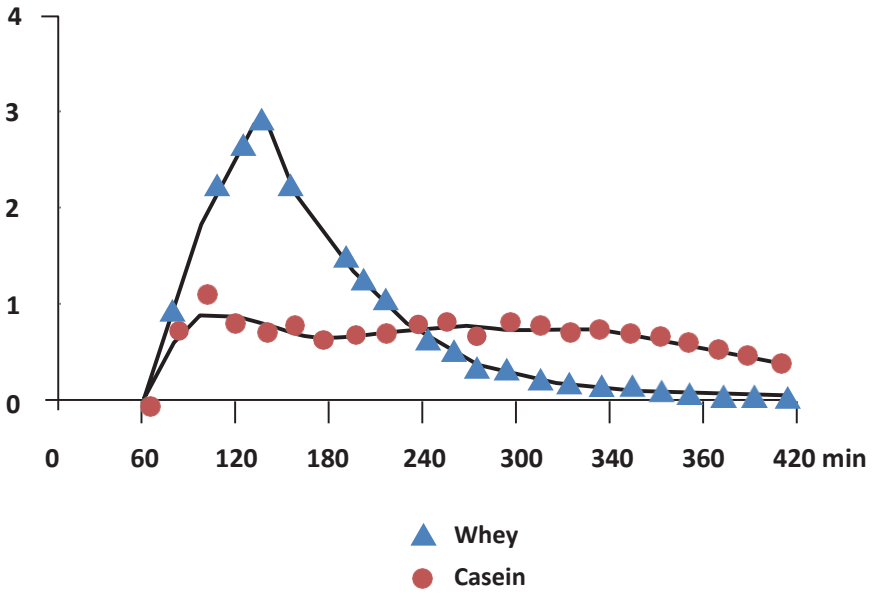
However, when physical activity is limited, only foods that are sources of animal protein are linked to muscle mass.

In active people, consuming both animal and vegetable proteins reduces the risk of cognitive decline. In less active people, foods that are sources of vegetable proteins do not have any beneficial effect, unlike foods of animal origin. Among the latter, the most "effective" are poultry and dairy products.

[8] Bradlee ML et al. High-Protein Foods and Physical Activity Protect Against Age-Related Muscle Loss and Functional Decline. J Gerontol A Biol Sci Med Sci. 2017;73(1):88-94

- **Milk vs. soya**[9]

There are two types of proteins in dairy products, casein, which is slowly digested over an extended period, and whey protein, which more rapidly digested. The “fast” proteins of the whey lead to an early spike of amino acids in the blood, which is very effective in inducing protein synthesis. The “slow” casein proteins have a weaker effect but over an extended period. This perfect complementarity within the dairy matrix goes some way to explaining the greater effect of milk on protein synthesis in the elderly as compared to soya.



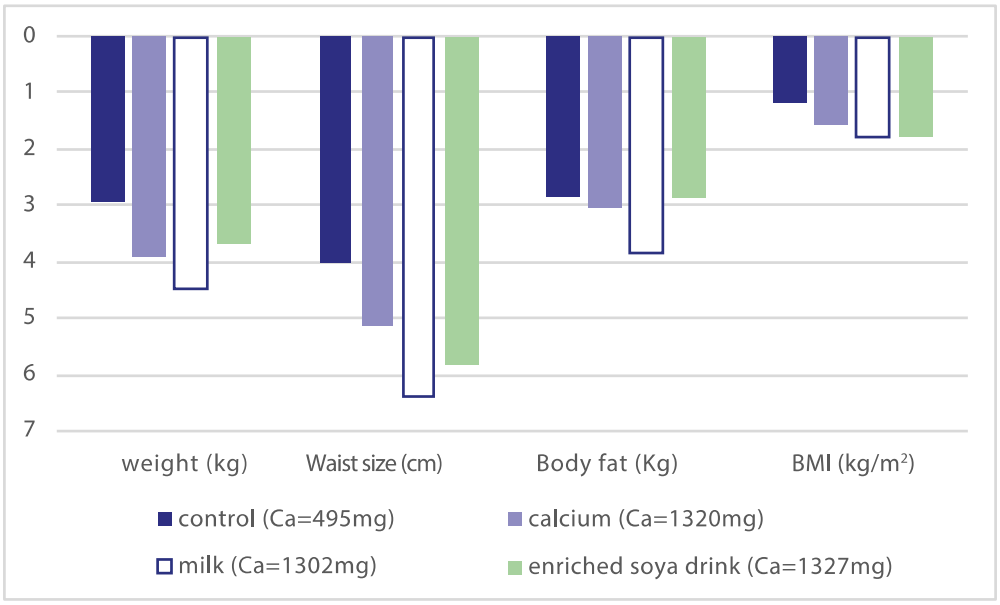
Therefore, the concept of interaction between nutrients in the food should be considered.

9 Dangin M et al. Influence of the protein digestion rate on protein turn-over in young and elderly subjects. J Nutr 2002; 132:3228S-33S

Foods are not simply assemblies of nutrients

It could be tempting to try to create “neo-foods” by piling up nutrients and mixing it all together. This forgets that a food is composed of many different components (for example, there are over 2,000 in milk), organised according to extremely complex physical and chemical structures. This means that it is not enough simply to add a nutrient to obtain an effect.

This is demonstrated by the study cited above (5), concerning the effect of calcium and its source on weight, and in which there were in fact four groups: the “control” group (500 mg of calcium), the two calcium groups (1300mg/d) by supplement or from milk, and another calcium group (1300mg/d) with calcium-enriched soya drink. Each group was fed a low-calorie diet (-500 Kcal/day) for 8 weeks providing the same amounts of protein, fats, carbohydrates and fibres, but with variable amounts of calcium.
After eight weeks, all the women had lost several kilos in weight and centimetres around their waists. The calcium supplements did not provide any particular benefit and the enriched soya drink did not do much better: only the waist measurement was significantly improved in relation to the control group. Conversely, the benefits in terms of weight, waist size, body fat and BMI were all greater in the milk group.



It is the milk matrix which makes the difference, since the calcium and protein intakes were identical with the milk and the enriched soya drink.

The matrix effect: a new paradigm revolutionising nutrition

Researchers have been presenting work concerning the matrix effect for several years. They consider that the nutritional value of a food is not limited to the sum of its nutrients, but varies according to the structure of the nutrients, the matrix and the interconnections with the other components in the food. “We eat food, not just nutrients. The way in which the latter are intricately linked has a real impact on their bioavailability,” explains Jean-Michel Lecerf, head of the nutrition department at the Institut Pasteur in Lille.

For example, yogurts and cheeses have a more beneficial effect on bone health, body weight and the reduction of cardiovascular diseases than their nutrients considered in isolation. Marie-Caroline Michalski, research director at Inra, illustrates this argument with another case: “Almonds contain a lot of fats, but some is not absorbed by the intestine despite chewing. As these fats are not used, they therefore do not contribute to energy consumption.”

Recent scientific advances in nutrition and food sciences allow us to analyse our diet differently. Food is no longer considered simply as the sum of its components, but as a complex physical structure which influences the digestive fate of the nutrients, their metabolic effects and ultimately, their long-term effects on health.

It is no longer a question of considering nutrition using solely the nutrient approach, which is reductionist, but from a new holistic perspective, at the interface of food science and human nutrition.