

Milk's Bioactive Peptides: Are We Disregarding Nature's Miracle?

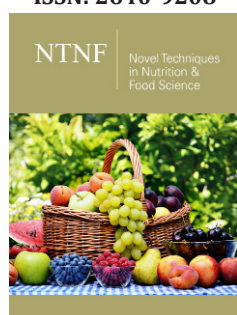
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Abstract

Milk has a great nutritional value due to its amino acid composition and its fat content. However, what makes milk an excellent product for human consumption is the presence of bioactive sequences among their aminoacidic profile. Bioactive peptides derived from milk proteins are well known to retain many biological properties and have therapeutic effects in several health disorders. The main source of these compounds are the peptides formed after protein degradation which can occur during gastrointestinal digestion, food processing or fermentation via enzyme or bacterial activity. In a post-pandemic context, where environmentally and health-safe medications and antimicrobials are constantly pursued, milk-derived peptides could be of significant importance for health, as well as for the pharmaceutical, nutraceutical and dairy industry.

Keywords: Milk; Proteins; Proteolysis; Peptides; Bioactivities

Today's View on Milk

It was not so long ago that the consumption of milk and dairy products was regarded as synonymous to health benefits, for reasons that are well known. However, times have changed, and today milk is often regarded as a bad health option. Indeed, several scientific studies have shown that 1) not all benefits of milk are true (mainly Ca absorption) and 2) the high and regular consumption of milk and dairy products can allegedly cause/aggravate a range of health problems. This last point received greater attention some years ago, when the new Harvard School of Medicine food pyramid was published, in which the consumption of milk and derivatives was strongly reduced to a maximum of 1 or 2 servings per day or, alternatively, supplements of vitamin D and Calcium, having been pointed out that dairy products are not only not essential for a healthy diet, but their high consumption can be a health risk. Consequently, the food markets have adapted to this new vision of milk as the "bad guy" and an ever-growing number of dairy and milk alternatives have emerged. Needless to say, these alternatives are often not as nutritional as milk *per se* and lack several of the advantageous technological features of milk, from foaming ability to taste.

Milk Bioactive Peptides: A Miracle of Nature

As nutritional rich food product, milk contains around 3,5% of proteins. Of these 3,5%, 80% represents the caseins and 20% whey proteins [1], which comprise a wide range of different proteins, such as β -lactoglobulin, α -lactalbumin and several minor (lactoferrin, lysozyme, lactoperoxidase [1]). Besides its high nutritious content, milk proteins present a unique feature, that is largely unique: Their amino acid sequence encodes an array of different bioactivities [2], rendering milk one of the best-known and most successful functional foods [3,4]. In fact, all of milk's proteins present some sort of bioactivity, which is rather phenomenal. The aminoacidic bioactive sequences are often released through digestion

(i.e., proteolysis), producing small peptides that constitute a true miracle of nature, as their unique sequences provide a wide array of different health promoting effects, which are of crucial importance to new born infants and adults alike. Today, these peptide's sequences and their antimicrobial, immunomodulatory, anti-atherogenic, sleep-enhancing effects, antihypertensive, anticholesterolemic, antioxidant, opioid and anticancer activities are all perfectly known [3-8] and more are being discovered. For example, different studies performed with milk derivate peptides, preventient from casein and whey proteins, have demonstrated to diminish cellular damage after atherogenic plaque development [7] and peptides formed after casein proteolysis have demonstrated to have sleep-enhancing properties, increasing sleep duration in mice [8]. It becomes worthy to notice that some of the most reported bioactivities in milk proteins present antibacterial and antiviral activities. This fact can be very significant, particularly in a post-pandemic Era, where zoonotic diseases antibiotic resistance is a major global concern. Furthermore, we don't need digestion anymore, as there are several food technologies that can be used to produce these peptides in a fast and easy manner and use them as novel nutraceuticals or functional foods (Figure 1). The

most common of which are: (i) the use of digestive proteins (e.g., trypsin, pepsin), (ii) microbial activity during fermentation and (iii) the use of enzymes from proteolytic microorganisms [9,10]. Indeed, for some time now, several studies have been focusing on the isolation of specific polypeptide sequences from milk and whey fermentation, with several bioactivities, namely antimicrobial, which can be used both in the food industry and in medicine (e.g., antibiotics and nutraceuticals). Within this context, by-products of the dairy industry, such as whey, may present a low-cost alternative to produce peptides with antimicrobial action that may serve as antibiotics or food disinfecting agents. Lactic Acid Bacteria (LAB) for instance, have been used for thousands of years in food fermentation, which constitutes one of the oldest preservation techniques, and continues to be used today for the manufacture of widely appreciated gastronomic specialties [11]. Many LAB species are also considered very effective probiotics, stimulating a healthier gut microbiome [12-15]. Furthermore, besides decreasing the high lactose content in milk, LAB also produce mainly lactic acid which also plays an important role as an antimicrobial agent in fermented foods.

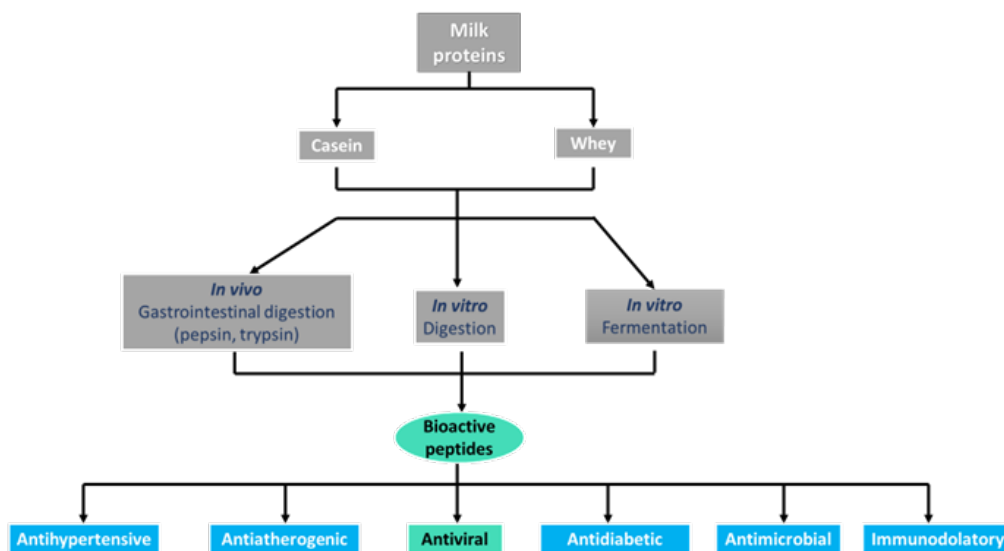


Figure 1: Overview of the available mechanism to release milk-derived bioactive peptides.

Conclusion

Currently, as the food industry is investing more time and money towards the development of more processed forms of vegetable drinks as a replacement of milk and dairy, which most of the time lay a far distance from natural products, we are neglecting important features in milk and dairy that have been at our disposal since the dawn of mankind. The presence of antibacterial and antiviral peptides in fermented milk and whey should be regarded as a more interesting topic, particularly in a time when antibiotic resistance and zoonotic diseases are becoming a worldwide problem, urging us to develop effective alternative therapeutic strategies. Many believe that, in the future challenges that will be undoubtedly posed

to humanity, the use of bioactive peptides as adjuvants and/or as anti-inflammatory, infectious or other therapeutic alternatives, will be a reality in the near or distant future. Milk bioactive peptides are therefore an opportunity worth being pursuit.

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