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Review

Caseins as source of bioactive peptides

Sofia V. Silva, F. Xavier Malcata*

Escola Superior de Biotecnologia, Universidade Católica Portuguesa, Rua Dr. António Bernardino de Almeida, P-4200-072 Porto, Portugal

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Abstract

Biologically active peptides are of particular interest in food science and nutrition because they have been shown to play physiological roles, including opioid-like features, as well as immunostimulating and anti-hypertensive activities, and ability to enhance calcium absorption. Hidden or inactive in the amino-acid sequence of dairy proteins, they can be released or activated in vivo during gastrointestinal digestion, or upstream during food processing via specific, enzyme-mediated proteolysis. Caseins, in either milk or dairy products (e.g. cheese), are important sources of those peptides; their biological significance, their impact on human health and the manufacture of novel functional food ingredients therefrom have been subject to intensive research, which will be briefly presented and critically discussed in this review.

Keywords: Dairy products; Proteins; Caseins; Proteolysis

Contents

*Corresponding author. Tel.: +351-2255-80004; fax: +351-22-5090351.
E-mail address: xmalcata@esb.ucp.pt (F.X. Malcata).

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1. Introduction

Casein is the main proteinaceous component of milk, where it accounts for ca. 80% of the total protein inventory. Until recently, the main physiological role of casein in the milk system was widely accepted to be a source of amino acids required by growth of the neonate. However, the dominant physiological feature of the casein micelle system has more recently been proven to be the prevention of pathological calcification of the mammary gland (Holt, 1997).

While no specific physiological property has been proposed for the whole casein system (or its individual fractions, for that matter), various peptides hidden (or inactive) in the amino-acid sequence have been the subject of increasingly intense studies. Much work regarding those peptides, which are known to possess bioactivities, is currently underway regarding their release via selective enzymatic hydrolysis. Until now, such release has been demonstrated primarily in vitro, and to a lower extent in vivo using animal models. Experimental verification of the effectiveness of such bioactive peptides involving human subjects is, however, still scarce. Due to the increasing awareness of the effect of food ingredients upon promotion of health, several publications have arisen that cover recent advances on milk peptide research (Clare, Catignani, & Swaisgood, 2003; Florisa, Recio, Berkhout, & Visser, 2003; Janecka, Fichna, & Janecki, 2004; Kilara & Panyam, 2003; Kitts & Weiler, 2003; Korhonen & Pihlanto, 2003; Lonnerdal, 2003; Meisel & FitzGerald, 2003; Pellegrini, 2003; Pihlanto & Korhonen, 2003; Teschemacher, 2003; Wal, 2002; Walker-Smith, 2003).

This paper intends to provide an overview of the major classes of bioactive peptides putatively derived from caseins, which play a role in the nervous, cardiovascular, digestive and immune systems (Fig. 1), and a brief critical discussion of the most recent data made available in the literature regarding that growing family of molecules.

2. Effect on the cardiovascular system

Functional peptides derived from casein, present in either milk or dairy products, have been shown to have effects in the cardiovascular system, mainly via antithrombotic and antihypertensive features (Tables 1 and 2, respectively).

2.1. Antithrombotic peptides

The mechanisms involved in the clotting of milk, defined as the interaction of κ-casein with coagulating enzyme, and in the clotting of blood, defined as the interaction of fibrinogen with thrombin, have been proved to be similar in nature (Fiat, Migliore, & Jollès, 1993; Jollès, 1975; Jollès & Henschen, 1982). In addition, structural homologies between the undecapeptide (viz. residues 106–116) from cow's κ-casein, on the one hand, and the C-terminal dodecapeptide (viz. residues 400–411) of human fibrinogen γ-chain, on the other, have been duly reported (Jollès, Loucheux-Lefebvre, & Henschen, 1978). Indeed, three amino-acid residues (viz. Ile_{108}, Lys_{112} and Asp_{115}) of the aforementioned undecapeptide of κ-casein are in a homologous position when compared with the human fibrinogen γ-chain (Fiat & Jollès, 1989). Casoplatelins, which are casein-derived peptides (f106–116, f106–112 and f113–116), are inhibitors of both the aggregation of ADP-activated platelets and the binding of human fibrinogen γ-chain to a specific receptor region on the platelet surface (Fiat & Jollès, 1989; Jollès et al., 1986; Schlimme & Meisel, 1995). Furthermore, the κ-casein fragment f103–111 can prevent blood clotting through inhibition of platelet aggregation, but is not able to affect fibrinogen binding to ADP-treated platelets (Fiat et al., 1993).

More recently, it was reported that κ-caseinoglycopeptides from several animal species are a source of antithrombotic peptides. The sequence of amino acids in f106–171 of sheep's κ-casein, known as κ-caseinoglycopeptide, was shown to decrease thrombin- and collagen-induced platelet aggregation in a dose-dependent manner (Qian, Jollès, Migliore-Samour, Schoentgen, & Fiat, 1995). In the plasma of 5-day-old new borns, after breast feeding or ingestion of cow's milk-based formulae, antithrombotic peptides were detected, which had been derived from human and bovine κ-caseinoglycopeptides, respectively (Chabance et al., 1995).

2.2. Antihypertensive peptides

Blood pressure regulation (and hypertension, when it cannot be ensured) is partially dependent on the renin–angiotensin system; renin acts on angiotensinogen, thus releasing angiotensin I that is further converted into the active peptide hormone angiotensin II, a vasoconstrictor, by the angiotensin-converting enzyme (ACE). Angiotensin II inactivates bradykinin (a vasodilator); moreover, it increases the production of aldosterone, which decreases the renal output while increasing water retention (Fiat et al., 1993; Maruyama et al., 1987a; Maruyama, Mitachi, Tanaka, Tomizuka, & Suzuki, 1987b; Tirelli, de Noni, & Resmini, 1997).

Maruyama and Suzuki (1982) reported that tryptic hydrolysates of casein inhibited the in vitro activity of ACE; those peptides derived from casein, known as casokinins, correspond to f23–24, f23–27 and f194–199 of bovine α_{s1}-casein B, as well as to f177–183 and f193–202 of bovine β-casein (Maruyama & Suzuki, 1982; Maruyama et al., 1987a,b; Meisel & Schlimme, 1994).