Review

ACE-inhibitory activity and ACE-inhibiting peptides in different cheese varieties

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Abstract – During the ripening of cheese, a large number of peptides are formed from casein. Some of these peptides have been shown to exert an antihypertensive effect due to their angiotensin-I-converting enzyme (ACE)-inhibitory activity. Recently, several studies have investigated the ACE-inhibiting potential of cheese, and various ACE-inhibiting peptides have been isolated and identified from different cheese varieties. The present review focuses on the occurrence of two tripeptides, Val-Pro-Pro and Ile-Pro-Pro, in cheese. These tripeptides were first described in fermented-milk products and have been demonstrated to exert a blood pressure-lowering effect in humans with mild hypertension. The influence of cheesemaking and ripening on the release of ACE-inhibiting peptides is revealed. Finally, the antihypertensive potential of cheese with high ACE-inhibitory activity is discussed with regard to the bioavailability of the peptides involved.

ACE-inhibitory activity / ACE-inhibiting peptide / tripeptide / VPP / IPP / cheese / cheese ripening

Résumé – Activité inhibitrice et peptides inhibiteurs de l’ACE dans différentes sortes de fromage. Au cours de la maturation du fromage, un grand nombre de peptides sont formés à partir de la caséine. Quelques-uns d’entre eux sont réputés exercer des effets antihypertenseurs en raison de l’activité inhibitrice de l’enzyme de conversion de l’angiotensine I (ACE). Récemment, plusieurs études ont examiné le potentiel inhibiteur d’ACE du fromage, et divers peptides inhibiteurs de l’ACE ont été isolés de différentes sortes de fromage puis identifiés. La présente revue porte sur la présence de deux tripeptides Val-Pro-Pro (VPP) et Ile-Pro-Pro (IPP) dans le fromage. Ces tripeptides sont parmi les premiers à avoir été décrits dans les produits laitiers fermentés et sont réputés

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ACE 抑制活性 / ACE 抑制肽 / 三肽 / VPP / IPP / 干酪 / 干酪成熟

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exercer un effet antihypertenseur chez les patients présentant une légère hypertension. Cette revue porte aussi sur l’influence de la fabrication et de l’affinage du fromage sur la libération des peptides inhibiteurs de l’ACE, sur le potentiel antihypertenseur du fromage avec une activité inhibitrice élevée de l’ACE de même que la biodisponibilité des peptides en question.

activité inhibitrice de l’ACE / peptide inhibiteur de l’ACE / tripeptide / VPP / IPP / fromage / affinage de fromage

1. INTRODUCTION

Due to its composition, cheese is of major significance in human nutrition [114]. During ripening, cheese is exposed to various enzymatic processes, mainly driven by specialized bacteria that contribute to the characteristic flavour of each variety. The ripening process of different cheese varieties of Swiss origin, such as Emmental [7, 8], Gruyère [120], Sbrinz [119], Appenzell [121], Tilsit [122] and Raclette [108], has been investigated in detail. Proteolysis is the principal event of cheese ripening and starts with the initial breakdown of the caseins through the action of coagulants and indigenous proteinases in milk. Through the action of bacterial proteases and peptidases during secondary proteolysis, a large number of peptides of variable chain length are released from the protein [99]. In Emmental, for example, in a Swiss study [14] more than 100 and in a French study [28] 91 water-soluble peptides were found in cheeses aged 4, 13, 36 and 50 d; similarly, a total of 107 peptides were identified in protein fractions of artisanal or industrial Manchego cheese after 4 and 8 months of ripening [34].

Recently, it has been recognized that various specific peptides that are released by digestive enzymes or that are present in fermented foods may exert beneficial effects in vivo. Cheese and milk products have been found to be a rich source of so-called bioactive peptides [36, 75]. Depending on their functionality, bioactive peptides are divided into various groups, such as casomorphins, angiotensin-converting enzyme (ACE = dipeptidyl carboxypeptidase; EC 3.4.15.1)-inhibiting peptides, phosphopeptides, immunopeptides, casoplatin (with antithrombotic effects) and antimicrobial and cytmodulating peptides [9, 50]. Due to their hypotensive effect, ACE-inhibitory peptides are of special interest, as hypertension is a major risk factor for both coronary heart disease and stroke, and represents an increasing health problem in Western countries. Different medical drugs, including ACE inhibitors, antagonists of angiotensin II type 1 receptors, beta-blockers, calcium antagonists and diuretics, have been developed for the treatment of hypertension. According to Nussberger [83], more than 40 million patients are treated worldwide with ACE-inhibiting drugs, such as Captopril or Enalapril, that are structurally related to the ACE-inhibiting peptides present in snake venom [18, 29]. Smaller reductions in average blood pressure may be obtained by nutritional measures, such as reducing sodium intake or increasing daily consumption of ACE-inhibitory peptides. The results of a large meta-analysis indicate that even a 2 mm Hg-lower usual SBP would involve about 10% lower stroke mortality and about 7% lower mortality from ischaemic heart disease in middle age [96].

ACE is part of the rennin-angiotensin system that regulates peripheral blood pressure. It catalyses the conversion of angiotensin I into the potent vasoconstrictor angiotensin II and, simultaneously, the degradation of bradykinin, a vasodilatory nonapeptide. These two reactions cause a contraction of the blood vessels and