RIPENED CHEDDAR CHEESE AS SOURCE OF BIOACTIVE PEPTIDES AND POTENTIAL ROLE IN THE PREVENTION OF CARDIOVASCULAR DISEASES

ABSTRACT

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Ripened cheese is a source of bioactive peptides with health beneficial properties. The aim of this study was to assess the effects of ripening of cheddar cheese produced with L. helveticus (Cougar Gold brand, CG) compared to a regular cheese without L. helveticus on production of peptides with antihypertensive and antioxidant activities. Furthermore, the identification of peptides in Cougar Gold cheese, their bioavailability, stability to gastric enzymes and anti-inflammatory activity were assessed in vitro.

Results demonstrated that 6 and 12 mo ripened CG peptides showed higher degree of proteolysis as compared to the regular cheddar cheese peptides. Further, the adjunct culture L. helveticus in cheddar cheese produces peptides with higher antioxidant and antihypertensive activities within 6 mo of ripening. Thus the use of L. helveticus would be economically beneficial for the cheese industry to shorten ripening time.

Ripening of CG beyond 6 mo did not enhance anti-hypertensive activity whereas bioavailability was similar at 6 and 12 mo. However, a higher stability to gastrointestinal in vitro digestion was found in 6 mo peptides. LC-MS/MS analysis confirmed the presence of various peptides in 0, 6 and 12 mo previously reported for their antihypertensive activities.

The CG peptides that were bioavailable, exerted protection against production of reactive oxygen
species (ROS) in human vein endothelial cells (HUVEC) and their potency increased by ripening. The underlying molecular mechanisms for this protection involves downregulation of the active phospho-NF-κB-p65 subunit of the pro-inflammatory transcription factor nuclear factor kappa B (NF-κB) and NF-κB-targets under basal and inflammatory conditions induced by *E. coli* lipopolysaccharides (LPS)-challenge. Further, the protection exerted by CG peptides against NF-κB upregulation was, at least in part, due to the induction of paraoxonase 2 (PON2) antioxidant enzyme. This was demonstrated when 6 and 12 mo cheese peptides upregulated PON2 in siRNA-PON2 silenced cells, which was accompanied by p-NF-κB-p65 downregulation.

Thus we can conclude that 6 mo ripened cheese peptides exerted antihypertensive and anti-inflammatory effects that help prevent expression of pro-atherogenic markers, in part mediated by upregulation of antioxidant activity. Further, these effects did not significantly increase by extended ripening up to 12 mo.