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# *Short communication:* Is consumption of a cheese rich in angiotensin-converting enzyme-inhibiting peptides, such as the Norwegian cheese Gamalost, associated with reduced blood pressure?

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## ABSTRACT

Epidemiological and clinical studies have shown that angiotensin-converting enzyme (ACE)-inhibiting peptides derived from dairy products may decrease blood pressure. These peptides have been identified in many cheeses, and Gamalost, a traditional Norwegian cheese, is particularly rich in these peptides. The aim of this cross-sectional study was to examine whether frequency of Gamalost intake was associated with blood pressure in a Norwegian population sample. Blood pressure and other clinical measurements, including the factors of metabolic syndrome, were obtained from 168 participants (56% female, mean age = 51 yr) who completed a questionnaire about dietary habits and other health-related factors. Mean Gamalost intake was 2 servings per week. The prevalence of hypertension was 23.8% in the population, with mean systolic and diastolic blood pressures of 128 and 78 mmHg, respectively. Intake of Gamalost was inversely associated with systolic blood pressure. Each increase in frequency unit of Gamalost intake corresponded to a reduction in systolic blood pressure of 0.72 mmHg, after controlling for sex, age, education, waist circumference, physical activity, smoking status, and dairy food intake. Results from this study indicate that consumption of Gamalost (or other foods rich in ACE-inhibiting peptides) may reduce blood pressure.
**Key words:** cheese, angiotensin-converting enzyme (ACE)-inhibiting peptide, blood pressure, dairy product

## Short Communication

Milk proteins are considered one of the most important sources of bioactive peptides (Korhonen and Pihlanto, 2006) and studies have found that different cheeses contain several bioactive peptides in varying amounts. Angiotensin-converting enzyme (**ACE**) is an important enzyme in the renin-angiotensin system, which is one of the pathways that control blood pressure. The effect of ACE is to activate angiotensin II, a vasoconstrictor, and inactivate bradykinin, a vasodilator (Silva and Malcata, 2005; FitzGerald et al., 2004), resulting in an increase in blood pressure. Peptides with ACE-inhibiting or blood pressure (**BP**)-lowering activity have been identified in many cheeses (Sieber et al., 2010). Cheese and other dairy products are significant sources of saturated fat in the typical western diet (Sonestedt et al., 2011), a fat that may increase the amount of low density lipoprotein (**LDL**) cholesterol in the blood, which is a risk factor for cardiovascular disease (**CVD**). However, some studies have found that a higher intake of dairy products is associated with a reduced risk of CVD, and it was recently found that cheese intake is negatively associated with the metabolic syndrome (Høstmark and Tomten, 2011). Part of the reason why cheese may be protective against CVD could be the presence of bioactive peptides.

Gamalost is an autochthonous Norwegian cheese that is naturally low in fat (<1%), does not contain salt, and is high in protein (50%). Details on the production and ripening of Gamalost have been described elsewhere (Qureshi et al., 2012). The cheese was found to have a higher ACE-inhibitory potential than Norvegia, a Gouda-type cheese (Pripp et al., 2006; Qureshi et al., 2012, 2013), and it is one of the cheeses with the highest ACE-inhibitory potential (Sieber et al., 2010). Even though ACE-inhibiting peptides have been found in many cheeses, few studies describe their effect in humans.

The Global Burden of Disease Study 2010 identified high BP as the leading risk factor for global disease burden (Lim et al., 2012). Hypertension is a major risk factor for CVD, and systolic BP >130 mmHg or diastolic BP >85 mmHg are 2 of the diagnostic criteria for metabolic syndrome. Cardiovascular disease is the

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most common cause of death in Norway, accounting for about 35% of all deaths (Folkehelseinstituttet, 2010). The prevalence of hypertension in the adult population in the United States is about 30% (Yoon et al., 2010), and it has been estimated that a decrease in diastolic BP of just 5 mmHg can reduce the risk of CVD by 16% (FitzGerald et al., 2004). Pharmacological treatment of hypertension is often associated with undesirable side effects such as reduced kidney function and hypotension (Haque and Chand, 2008). Consequently, food-derived ACE-inhibitors would be of great interest, as these are not associated with side effects. A meta-analysis of randomized controlled trials on the effect of food-derived peptides on BP found a significant reduction in both systolic and diastolic BP, indicating a possible role for food in the management of mild hypertension (Pripp, 2008). We are not aware of any published observational studies with clinical tests regarding the association between cheese intake and BP. The aim of this epidemiological study was to assess whether the frequency of Gamalost intake was associated with blood pressure and other factors of the metabolic syndrome, in the population of Vik i Sogn, a small community on the Norwegian west coast.

This cross-sectional study was conducted in Vik, Norway, in May 2012. The adult population of Vik comprised the study sample. Participants were recruited through the 4 largest work places in Vik, and one person worked specifically to reach the elderly population. Furthermore, a short article was published in the local newspaper inviting people to participate in the study. One hundred eighty-six people completed the questionnaire. Of those, 5 did not show up for clinical assessment. Pregnant women and participants lacking information on cheese and dairy intake were excluded from the analyses, resulting in a final study sample of 168. Subjects who lacked information on the factors included in the ANOVA or who reported taking BP-lowering medications were further excluded from this analysis, resulting in a sample size of 153. This study was conducted according to the guidelines in the Declaration of Helsinki, and all procedures involving human subjects were approved by Regional Committees for Medical and Health Research Ethics (Oslo, Norway) on April 24, 2012. Written informed consent was obtained from all subjects. The participants were offered breakfast and one Gamalost cheese as compensation for participation.

A questionnaire was developed specifically for this study, based on the previously used food frequency questionnaire from the Oslo Health Study (Mostøl, 2004). In addition to questions about health and physical activity, the questionnaire included a short section on dietary habits, emphasizing dairy intake. Four questions inquired about the intake of cheese, including all cheese, regular (mostly Gouda type) cheeses, brown whey cheese, and Gamalost. Five questions inquired about the intake of other dairy products; for example, milk and yogurt. The variables concerning cheese intake were categorized into rarely or never, 1 to 3 times per month, 1 to 3 times per week, 4 to 6 times per week, 1 to 2 times per day, and 3 times or more per day. For statistical analyses, the midpoint in each category was recalculated into frequency in times per week; that is, 0, 0.5, 2.0, 5.0, 10.5, and 21.0 servings per week, respectively. Total dairy product intake was calculated by summarizing the frequency of intake of all cheese, all milk, and fermented milk.

Height was measured to the nearest 0.1 cm using a portable stadiometer (Seca 217, Seca, Hamburg, Germany). Weight was measured to the nearest 0.1 kg using digital scales (TBF-300A Body Composition Analyzer, Tanita, Tokyo, Japan). Waist circumference was measured in accordance with World Health Organization recommendations, at the midpoint between the iliac crest and the lowest rib margin, to the nearest 0.1 cm (WHO, 2011) using a measuring tape (Seca 201 Circumference measuring tape, Seca). Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m).

Blood pressure was measured according to recommendations from the American Heart Association (Pickering et al., 2005). Participants rested for approximately 10 min before BP was measured using a Microlife BP A200 BP meter (Microlife, Widnau, Switzerland). Three consecutive measurements were taken, and the average of the second and third measurements was used for analysis (automatically calculated by the blood pressure device). In some cases, the device used 4 measurements to get a more accurate reading. Venous blood samples were drawn in the morning after an overnight fast (approximately 10–12 h), using the Vacutainer system (Becton Dickinson Co., Franklin Lakes, NJ). The samples were centrifuged at 833 × *g* for 10 min at room temperature, and the serum was separated 1 to 2 h after the blood was drawn. The serum was frozen to −20°C within 5 h. Fürst Medical Laboratories (Oslo, Norway) conducted the lipid analyses. The measured biochemical markers were total cholesterol, high density lipoprotein (**HDL**) cholesterol, LDL cholesterol, and triglycerides. Blood glucose was measured in capillary blood by the finger stick method.

Daily physical activity was assessed by 2 questions in the questionnaire; one question regarding amount of leisure time physical activity and one regarding type of physical activity. For statistical analyses, participants were classified into 3 groups of physical activity: sedentary, light physical activity, and moderate to hard