SUMMARY

Cardiovascular diseases (CVD) are the main cause of death worldwide. Metabolic disturbances, such as high low density lipoprotein cholesterol (LDL-C), high triglyceride (TG), and low high density lipoprotein cholesterol (HDL-C) concentrations, as well as insulin resistance, cause increased risk of CVD. In several countries, the dietary guidelines for preventing CVD focus on reducing the intake of saturated fatty acids (SFAs), especially from the main sources, which are dairy products and meat. Observational data, although questionable, have shown that meat SFAs increase, but dairy SFAs reduce the CVD risk. Also, dairy products should not be considered similar regarding their effects on CVD risk. Cheese intake in particular may not be associated with CVD risk. This could be due to a lower fat digestibility caused by the calcium content of cheese. This may also explain the lack of increase in LDL-C concentration with cheese intake despite its high SFA content. Still, as a group of dairy products, cheese is very diverse with respect to fat, protein, and calcium content. Also, the ripening duration and methods used to manufacture different types of cheese vary considerably, and may influence how cheese intake affects cardiometabolic health.

The aim of this PhD thesis was to investigate how the fat content of the cheese-matrix and the cheese ripening duration affect cardiometabolic risk markers and fecal fat excretion. The thesis is based on three intervention studies, two in pigs (**study I** and **study II**) and one in humans (**study III**). **Study I** and **study II** were both designed as parallel-arm randomized, controlled intervention studies, and each included 36 crossbred female growing pigs. The objective of **study I** was to investigate how a diet with regular-fat cheese and reduced-fat cheese + butter affects fasting blood lipids, fecal fat and energy excretion, and gut microbiome. It was hypothesized that the diet with regular-fat cheese causes a lower LDL-C concentration and a higher fecal fat excretion compared to the diet with reduced-fat cheese + butter. In **study II**, the objective was to investigate how cheeses with different ripening durations affect fasting blood lipid concentrations, glucose, insulin, and fecal fat excretion. It was hypothesized that the intake of long-term ripened cheese causes a lower LDL-C, improves insulin sensitivity, and causes a higher fecal fat excretion compared to intake of short-term ripened cheese. **Study III** was a randomized, cross-over intervention study in 14 overweight, postmenopausal women. The objective was to investigate how diets with cheese and meat as sources of SFAs or iso-caloric replacement with carbohydrates affect blood lipids, apolipoproteins, and the fecal excretion of fat and bile acids. It was hypothesized that the diet with cheese favorably affects blood lipids and increases fecal fat excretion compared to the diets with meat as a source of SFAs or carbohydrates.

Study I showed higher concentrations of HDL-C and total cholesterol (TC) but not LDL-C in pigs consuming the diet with regular-fat cheese compared to those consuming the diet with butter. HDL-C and TC concentrations only tended to be higher in pigs consuming the diet with reduced-fat cheese + butter. HDL-C and TC did not differ significantly with the cheese-diets. Both cheese diets caused a higher fecal fat excretion compared to the diet with butter, however, the effect seemed to be highest for the diet with regular-fat cheese. These results do not support the previously observed lower LDL-C concentration after cheese intake compared to butter, but they do suggest that regular-fat cheese has a distinct effect, which may be linked to the cheese-matrix. In **study II**, no differences were found between pigs consuming short- or long-term ripened cheese regarding fecal fat excretion or concentrations of TC, LDL-C, HDL-C, or TG. However, a lower concentration of non-esterified fatty acids (NEFAs) was observed in pigs consuming the 14- and 24-month ripened cheese compared to the 4-month ripened cheese. Also, the insulin concentration and HOMA-IR were lower in pigs consuming the 24-month ripened cheese but not the 14-month ripened cheese compared to the 4-month ripened cheese. These results indicate improved insulin sensitivity and suggest that long-term ripened cheese is favorable over short-term ripened cheese. The content of bioactive peptides and amino acids produced during ripening may be important factors leading to these effects. In **study III**, it was found that diets with cheese and meat as sources of SFAs caused similar blood lipid responses and higher HDL-C and apoA-I concentrations compared to the low-fat carbohydrate diet. Furthermore, the cheese diet also caused a lower apoB: apoA-I ratio compared to the carbohydrate diet. No differences were found in the TC, LDL-C, apoB, or TG concentrations between the three diets. The fecal fat excretion was highest on the cheese diet, intermediate on the meat diet, and lowest on the carbohydrate diet. The fecal bile acid excretion did not differ with the cheese and meat diets but were higher on these diets compared to the carbohydrate diet. This may potentially explain the differences in the blood lipid response. Hence, the diets with cheese and meat as primary sources of SFAs appear to be less atherogenic than a low-fat carbohydrate diet.

In conclusion, in pigs, a diet with regular-fat cheese but not with reduced-fat cheese + butter caused higher concentrations of TC and HDL-C but not LDL-C compared to a diet with butter. In humans, higher HDL-C and apoA-I concentrations but not LDL-C concentration were caused by diets with cheese and meat as the sources of SFAs compared to a low-fat high-carbohydrate diet. Furthermore, in pigs, long-term ripened cheeses caused a lower NEFA concentration, and a 24-month ripened cheese also improved insulin sensitivity compared to short-term ripened cheese. Moreover, diets with cheese caused a higher fecal fat excretion compared to diets with meat as a source of SFAs, carbohydrates, and butter. Fecal fat excretion by cheese appears to be independent of the ripening duration and the fat content of the cheese-matrix. Finally, diets with cheese and meat as sources of SFAs caused a higher fecal bile acid excretion compared to a diet with carbohydrates.