1. INTRODUCTION

The cardiovascular diseases (CVD) ischaemic heart disease (IHD) and stroke continue to be the leading causes of death in developed countries, and the incidence is rapidly increasing in developing countries[1]. Also, individuals with obesity related metabolic disturbances, such as insulin resistance (IR) or type 2 diabetes mellitus (T2DM), have a 2- to 6-fold greater risk of developing atherosclerosis compared to individuals with comparable risk factors but without these metabolic disturbances[2,3]. Prevention strategies, early intervention, and novel pharmaceutical treatment regimens have been successful and are important in terms of reducing the mortality rates of CVD. There is generally robust evidence that a healthier lifestyle in the population, which includes a healthy diet, could reduce future CVD incidences[4]. The official dietary recommendations in many countries, including Denmark, focus on reducing saturated fat (SF) intake, primarily from the main sources, which are dairy products and meat[5]. The long-chain saturated fatty acids (SFAs) myristic and palmitic acid in particular are known to increase the low density lipoprotein cholesterol (LDL-C) concentration, which is a strong CVD risk factor[6]. Despite this, recent observational studies have failed to find an association between SF intake and CVD[7,8]. It is becoming clear that SF should not be considered isolated but rather part of a food containing other compounds that may modify the effect of SF on blood lipid balance[9]. Also, SF should not be considered a homogenous group, as the intake of individual SFAs causes different changes in blood lipids[6]. Observational data suggest a distinct effect of the major dietary sources of SFAs, with SF from meat increasing and SF from dairy products reducing CVD risk[10]; however, this would not be expected by their SFA composition. In addition, dairy products should probably not be considered similar with respect to their effects on CVD risk[11,12]. Cheese, which is a fermented dairy product, is of particular interest, as it appears to have less of an effect on LDL-C concentration compared to other high-fat dairy products, such as butter[13]. Accordingly, some observational studies have found no association between cheese intake and CVD risk[14-17] or T2DM risk[12,18-22], while others even found cheese intake to be positively associated with cardiovascular health[23,24]. Cheese as a group of dairy products is also very diverse with respect to fat, protein, and calcium content, and the ripening duration and methods used in the production of different types of cheeses also vary considerably. These aspects may all influence how cheese intake affects cardiometabolic health and should therefore be investigated.

1.1 AIM OF THESIS

The overall aim of this PhD thesis was to examine how the fat content of the cheese-matrix (**study I** and **study III**), and cheese ripening duration (**study II**) affect cardiometabolic risk markers and fecal fat excretion.

1.2. THESIS DELIMITATIONS

Background

The background section of this PhD thesis is delimited to focusing on the background for the conducted research in particular. Hence, the chapters on cheese will focus on cheddar cheese (regular-fat type) and danbo cheese (regular-fat and reduced-fat types). The chapters on disease pathogenesis and the results from previous studies of cheese will focus only on the diseases of interest and the risk markers investigated in the conducted research (i.e., blood lipids, apolipoproteins, insulin, and glucose) knowing that other CVD risk markers, such as blood pressure and inflammation, exist. As numerous observational studies on cheese intake and CVD or T2DM are available, the results from prospective cohort studies are prioritized, as these are regarded as being superior to other observational studies. Thus, they do not introduce recall or selection bias to the same extent as retrospective cohort studies, case-control studies, and cross-sectional studies. Also, data on known or potential confounders or effect modifiers can be recorded in the prospective design, enabling later adjustments in the statistical analyses.

Results and discussion

The fecal microbiota, presented as part of the results in the manuscript for **study I**, was analyzed by colleagues at the Department of Biology, University of Copenhagen. Because gut microbiota is a very extensive and complex area of research and somewhat beyond the scope of this thesis, it will only be briefly discussed in relation to the other findings.