
1. INTRODUCTION

Cardiovascular diseases (CVDs) are the leading causes of death worldwide¹. Type 2 diabetes (T2D) however, is also on the rise and currently accounts for the majority of cases of diabetes worldwide². In addition, people with T2D are at higher risk of developing CVD³ making these two conditions highly associated. Low density lipoprotein cholesterol (LDL-C) concentration is considered a risk factor for CVD and thus a primary treatment target in the prevention of CVD³. In addition to increased LDL-C concentration, risk markers such as dyslipidemia (low high density lipoprotein cholesterol (HDL-C) and high fasting and postprandial triacylglycerol (TAG)), increased blood pressure (BP), increased fasting glucose, increased waist circumference and obesity, smoking and lack of physical activity all contribute to an increased risk of CVD and T2D^{3,4}. Today, there is strong evidence that diet may influence atherosclerosis and cardiovascular events, either due to dietary factors directly influencing atherogenesis or due to effects on risk markers such as blood lipids, BP or glucose levels³.

Dairy fat contains high amounts of saturated fatty acids (SFAs), especially the long chained SFAs myristic and palmitic acids, which are known to increase LDL-C concentrations in the blood⁵. Consequently, dietary guidelines recommend low-fat dairy products. However, meta-analyses of observational studies indicate that dairy is not associated with increased risk of CVD^{6,7} and instead point to an inverse association between dairy intake and T2D⁸⁻¹⁰. This discrepancy in evidence has given rise to studies examining the source of SFAs, which has shown differential associations to risk of CVD and T2D^{11,12}. In addition, the evidence for a dairy matrix effect was recently reviewed¹³ and suggested that different dairy product types are distinctly linked to various health effects and disease risk markers¹³. Still, only few studies have examined the effect of dairy products given as whole foods on risk of CVD and T2D. Therefore, dietary guidelines today are primarily based on expected effects of macronutrients and on that basis exclude or leave very little room for regular/high fat dairy products such as butter, whole milk and semi-skimmed milk. Taken together, there seems to be a knowledge gap when it comes to randomized controlled trials (RCT) studying the effects of specific dairy products and risk markers of CVD and T2D. Therefore, it has been stressed that there is a need for further studies examining health effects of whole dairy foods to accompany the more traditional studies on single nutrients¹³.

The overall aim of this PhD thesis was therefore to examine the effect of dairy products given as whole foods on risk markers of CVD and T2D. Butter in large amounts increases LDL-C concentration, but the effect of butter in moderate amounts in a normal diet has not been investigated. Moreover, a study comparing butter with cheese showed a modest increase in LDL-C after a rather high butter intake (13 E%). Dietary guidelines recommend intake of low-fat milk (<0.5 %), however the difference in effect on cholesterol between whole milk and skimmed milk in a normal diet is not examined in a human intervention study. Furthermore, the effects of milk intake on glucose tolerance and insulin sensitivity are examined in very few controlled studies with only one long-term study and results are inconclusive.

The objectives of this PhD thesis was therefore to investigate the effect of a moderate butter intake in a normal diet compared to olive oil (**Study I**), the effect of whole milk compared to skimmed milk (**Study II**), and the effect of a long-term high intake of semi-skimmed milk compared to other beverages (**Study III**) on risk markers of CVD and T2D.

1.1 Thesis delimitation

The chapters Background and Discussion of this PhD thesis are delimited to focusing on the research questions concerning dairy. Thus, the focus is on butter and milk and not on refined olive oil (**Study I**) or sugar-sweetened and non-caloric soft drinks and water (**Study III**). The background and the effect of these comparators are beyond the scope of this thesis and will only be briefly discussed when relevant in relation to butter and milk. In addition, the literature review done prior to the background section was not done according to the PRISMA guidelines, but the literature was however, thoroughly reviewed.