

# Theobromine

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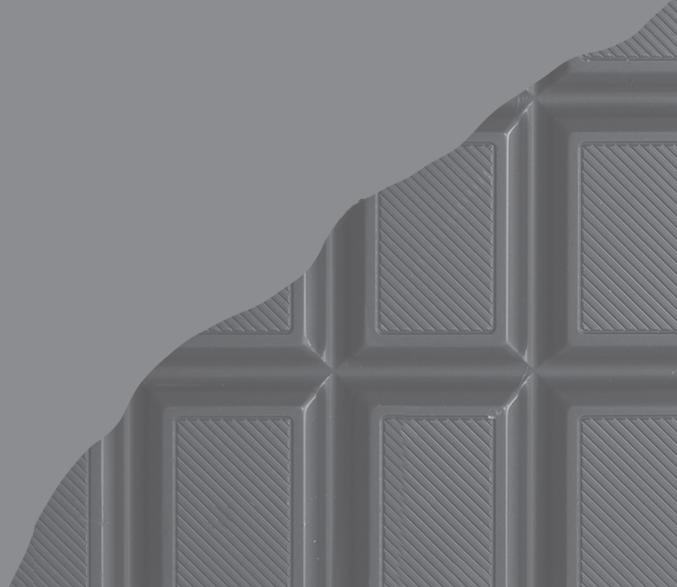
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# Valorisation



## Social relevance

Non-communicable diseases (NCDs) are chronic diseases, which are not transferred from person to person, but are caused by external factors such as an unhealthy lifestyle. These category of diseases are currently the leading cause of death worldwide, with cardiovascular diseases (CVD) accounting for the highest numbers.<sup>1</sup> Therefore, effective interventions or strategies to prevent or delay CVD development are needed. Since unhealthy diets and insufficient physical activity are key contributors to non-communicable diseases, these two characteristics are key targets in prevention. There are a growing number of foods that target health improvement, the so-called functional foods. The working definition of a functional food is: "a food that is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects, in a way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease. Functional foods must remain foods and they must demonstrate their effects in amounts that can normally be expected to be consumed in the diet: they are not pills or capsules, but part of a normal food pattern."<sup>2</sup> These functional foods can be consumed on a population level and can therefore easily be used in the prevention of CVD. The consumption of functional foods causes small effects on population level, but can have a big impact because many people can consume functional foods. With medicine however, the effects are bigger, but only in a small group of patients, which finally has a lower impact.

Over the years, the scientific interest for chocolate, a food that is extensively consumed in the Western World, has steadily increased. High chocolate consumption is inversely associated with cardiovascular diseases including, coronary heart disease (CHD) risk, stroke, cardiovascular events, and cardiovascular mortality.<sup>3</sup> It is therefore of interest to identify the compound(s) in cocoa that is/are responsible for these beneficial effects. Next, this compound could be isolated from cocoa or potentially other sources and subsequently added to other foods as functional ingredient. Therefore, the studies described in the present dissertation focused on one of the potentially healthy components of cocoa: theobromine. The two intervention studies performed were specifically designed to provide evidence that theobromine can improve cardiovascular health by causing beneficial effects on fasting and postprandial lipids, vascular endothelial function and arterial stiffness and to find the underlying mechanisms for these beneficial effects. Unfortunately, theobromine was found not to be the beneficial component from cocoa. It even had some unexpected negative effects on glucose metabolism and inflammation, and it is therefore not advised to use theobromine as a functional food ingredient for the prevention for CVD risk. It might of course still be possible that in a specific subpopulation theobromine, alone

or in combination with other compounds, has beneficial effects. However, to be used as functional food ingredient it is important that the enriched product can be used without undesirable effects in a wide population.

### **Economic relevance**

Identifying effective interventions to prevent or postpone CVD risk can have an enormous economic impact. CVD represents a major economic burden on health care systems, since it is one of the most costly diseases worldwide. Overall CVD is estimated to cost the Europe economy €210 billion a year.<sup>4</sup> The use of functional foods to prevent CVD can easily be achieved at low cost, which could scale down the medical cost.

### **Relevance of measurements**

The various measurements described in this dissertation may also function as markers to detect the presence of CVD at an early stage. In the Western world, the majority of the population spends a significant part of the day in the postprandial state. Furthermore, increasing evidence suggests that not only fasting lipid, lipoprotein and glucose concentrations, but also a disturbed postprandial lipid or glucose metabolism are important risk markers for CVD.<sup>5</sup> Postprandial measurements are therefore of clinical importance to consider when one studies CVD risk. Also, the vascular function measurements are of clinical importance in the prediction of CVD risk. Flow-mediated dilation is an accepted predictive biomarker for future CVD events.<sup>6</sup> Furthermore, the carotid-femoral pulse wave velocity has already been depicted as a promising future tool for CVD risk prediction in clinical practice.<sup>7</sup> However, more research is needed to determine the predictive value of these vascular function measurements in the postprandial state.

### **Translation into practice**

The finding that theobromine alone is not the compound from cocoa that is beneficial for human health is important for both the industry and science. In science we are a step closer to finding the beneficial compound(s) from cocoa. It is important to realize that with negative findings we also make important progress. Furthermore, for the industry it is clear that theobromine should not be used in functional foods.

The results described in this thesis have been presented at several national and international conferences to colleagues inside and outside the field. We hope to increase the awareness of the medical, societal and economical consequences of CVD and to highlight the potential impact of nutrition in CVD risk reduction. Furthermore, experts of the industrial partners within this project have contributed to the described

research projects through discussions at meetings. Moreover, all research findings have been submitted to international peer-reviewed scientific journals and are therefore accessible to scientists worldwide.

## References

1. World Health Organization. Noncommunicable diseases fact sheet No. 355 March 2017. Available from: <http://www.who.int/mediacentre/factsheets/fs355/en/>.
2. International Life Sciences Institute (ILSI) Europe. Scientific concepts of functional foods in Europe consensus document. *Br J Nutr.* 1999;81:S1-S27
3. Kwok CS, Boekholdt SM, Lentjes MA, et al. Habitual chocolate consumption and risk of cardiovascular disease among healthy men and women. *Heart.* 2015;101:1279-1287.
4. European Heart Network. European Cardiovascular Disease Statistics 2017. March 2017. Available from: <http://www.ehnheart.org/cvd-statistics.html>.
5. Cohn JS. Are we ready for a prospective study to investigate the role of chylomicrons in cardiovascular disease? *Atheroscler Suppl.* 2008;9:15-18.
6. Ras RT, Streppel MT, Draijer R, Zock PL. Flow-mediated dilation and cardiovascular risk prediction: a systematic review with meta-analysis. *Int J Cardiol.* 2013;168:344-351.
7. Holewijn S, den Heijer M, Stalenhoef AF, de Graaf J. Non-invasive measurements of atherosclerosis (NIMA): current evidence and future perspectives. *Neth J Med* 2010;68:388-99