Effects of Exercise and Cocoa Flavanol Supplementation on Cardiometabolic Function

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Declaration

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Kade Davison (candidate)

The following works are published or in press as they appear in this thesis:

Chapter 4 – Published

Davison, K, Coates A, Buckley J, Howe P., *Effect of cocoa flavanols and exercise on cardiometabolic risk factors in overweight and obese subjects.* International Journal of Obesity, 2008. **32**(8): p. 1289-96.

Chapter 5 – In Press

Berry N, **Davison K**, Misan G, Coates A, Buckley J, Howe P., *Impact of cocoa flavanol consumption on blood pressure responsiveness to exercise.* British Journal of Nutrition (in press).

Chapter 6 – In Press

Davison K, Berry N, Misan G, Coates, A, Buckley J, Howe P. *Dose-related effects of flavanol-rich cocoa on blood pressure*. Journal of Human Hypertension (in press).

The following peer reviewed conference presentations have come from the work within this thesis:

K Davison, AM Coates, JD Buckley, PRC Howe. Selective effects of cocoa flavanols and exercise on cardio-metabolic risk factors in overweight/obese individuals. *29th Annual Scientific Meeting of the High Blood Pressure Research Council of Australia*. Dec 2007

Davison K, Bircher S, Hill A, Howe P, Buckley J. Fitness vs Fatness: Differential effects on blood vessel health. in *Australian Association for Exercise and Sports Science biennial conference*. 2006 Sydney, NSW 2006

K Davison, AM Coates, JD Buckley, PRC Howe. *Dose-related effects of flavanol-rich cocoa on blood pressure in borderline/mild hypertension*. *30th Annual Scientific Meeting of the High Blood Pressure Research Council of Australia*. Dec 2008 (poster presentation).

NM Berry, **K Davison**, JD Buckley, AM Coates, PRC Howe. Flavanol-rich cocoa attenuates blood pressure response to exercise, *International Society for Hypertension*, Berlin, June 2008.

K Davison, NM Berry, AM Coates, JD Buckley, PRC Howe. Resting blood pressure does not predict the blood pressure response to exercise in borderline hypertensives. *Australian Association for Exercise and Sports Science biennial conference*. 2008

Howe PRC, **Davison K**, Berry N, Coates A, Buckley J. Cocoa flavanols – circulatory and heart health benefits. *Asia Pacific Journal of Clinical Nutrition* 2007; 16(Suppl 3):s32.

Acknowledgements

Dedication

This thesis is dedicated to the memory of my grandfather, Francis William Davison (AM) and the enormous contribution he made to my life and the lives of so many others. His inspiration lives within me always.

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Abstract

The link between excess adipose tissue and an increased risk of developing various pathologies, including cardiovascular (CV) diseases and type 2 diabetes, is now well accepted. There is increasing evidence supporting impaired arterial function (AF) as a causal link in this process. It can therefore be postulated that interventions aimed at improving AF may attenuate or prevent this progression from overweight/obesity to CV and metabolic disease.

Exercise has been shown to improve AF in various pathologies. A limitation in the evidence for exercise or increased fitness in an obese population is the differentiation of effects of obesity and fitness or exercise on CV function and risk. To investigate this, a cross sectional study was done to compare cardiorespiratory fitness (CRF; predicted VO_2max) and markers of AF (brachial flow mediated dilatation (FMD), arterial compliance (AC) and blood pressure (BP)) in sedentary obese (N=27) and sedentary lean (N=26) volunteers. The obese group had more whole body fat and abdominal fat (43.5 ± 1.2% vs. 27.2 ± 1.6%; $p<0.001$ and 48.6 ± 0.9% vs. 28.9 ± 1.8%; $p<0.001$ respectively) and lower FMD (3.2 ± 0.4% vs. 5.7 ± 0.7%; $p<0.01$) than the lean subjects but there was no difference in AC. FMD correlated with whole body fat ($R = 0.28$; $p<0.05$) and abdominal fat ($R = 0.34$; $p<0.05$) but not with CRF. By comparison AC in large arteries was positively associated with CRF ($R = 0.5$; $p<0.01$) but not with fatness. These results suggest a differential influence of fitness and fatness on AF.

Flavanols from cocoa have been shown to positively influence AF in a variety of CV risk groups, however this effect has not been investigated in obese subjects or in long term studies. This question was addressed by conducting a 2x2 factorial, randomised controlled trial comparing a high flavanol (HF; 902mg/day) and low flavanol (LF;

36mg/day) cocoa drink, with or without a moderate exercise program for 12 weeks in 49 overweight/obese volunteers. Compared with LF, HF increased FMD acutely (2 hrs post dose) by 2.42% ($p < 0.01$) and chronically (over 12 weeks; $p < 0.01$) by 1.63% and reduced insulin resistance by 0.31 ($p < 0.05$), diastolic BP by 1.57mmHg and mean BP by 1.17mmHg ($p < 0.05$), independent of exercise. Regular exercise increased fat oxidation during exercise by 0.10g.m^{-1} ($p < 0.01$) and reduced abdominal fat by 0.92% ($p < 0.05$), independent of cocoa consumption. This study provides the first evidence for a sustained improvement in CV and metabolic function with HF cocoa in an overweight/obese population. To expand upon these potential benefits of cocoa in overweight/obesity a further study was conducted to compare the acute effects of HF (701mg) to LF (22mg) cocoa on BP during exercise in 21 overweight/obese volunteers. Results of this study showed a significant attenuation of the exercise induced rise in BP with the HF compared to LF cocoa.

The antihypertensive effects of cocoa flavanols were further examined by 24 hour ambulatory monitoring in 52 untreated hypertensive volunteers consuming 1 of 4 doses (state doses) of cocoa flavanols for 6 weeks. There were significant reductions in 24-hour systolic (5.3 ± 0.8 mmHg; $p = 0.001$), diastolic (3 ± 0.7 mmHg; $p = 0.002$) and mean arterial blood pressure (3.8 ± 0.8 mmHg; $p = 0.0004$) at the highest dose only (1052 mg/d). No reduction in BP was seen at any other dose. These results support the previous evidence for a BP lowering effect of HF cocoa but indicate that the effective dose may be higher than previously indicated. Collectively these results provide considerable support for the potential use of cocoa flavanols to resist the progressive decline in AF leading from obesity to metabolic syndrome.