An investigation into the effect of New Zealand green-lipped mussel (Perna *canaliculus*) on non-haem iron absorption

A thesis presented in partial fulfilment of

the requirements for the degree of

Doctor of Philosophy

in

Human Nutrition

at Massey University, Palmerston North, New Zealand

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2014

Abstract

The bioavailability of dietary non-haem iron can be influenced by the nutritional composition of a meal. Ascorbic acid and components within meat, fish and poultry, but particularly red meat and pork, all appear to enhance the absorption of non-haem iron when consumed together within a meal compared to other protein sources. However the promotion of red meat or pork is problematic due to their high saturated fatty acid content and alternative foods to red meat or pork that may enhance iron absorption such as oily fish or shellfish require further investigation. The aims of the present study were to investigate the effects of short-term and prolonged supplementation of New Zealand green-lipped mussel (Perna *canaliculus*) (NZGLM) on mucosal iron transport and iron retention. The mechanism(s) by which mucosal iron transport is affected during NZGLM supplementation was also investigated. When investigated *in vitro,* NZGLM and beef both enhanced iron absorption by a similar magnitude compared to egg albumin. The enhancing effect of NZGLM on iron absorption was repeatedly observed using two separate *in vitro* models; Caco-2 cells and mouse small intestine mounted on Ussing chambers. When investigated in iron-deficient mice, mucosal iron transport and extra-intestinal iron retention were significantly enhanced when an iron supplement was combined with NZGLM compared to egg albumin. Conversely, an inhibitory effect was observed when mice were supplemented with NZGLM for a prolonged period of time prior to consuming an iron supplement. The inhibitory effect of NZGLM was not associated with the dietary iron load. Prolonged NZGLM supplementation inhibits mucosal iron absorption by reducing brush border

iron transport. The inhibitory effect of prolonged NZGLM supplementation was observed to be associated with its high calcium content; however other competitive nutrients such as copper, manganese or zinc may also contribute to the inhibitory effect. The main inhibitory effect is proposed to be calcium-stimulated DMT1 internalisation into cytosolic vesicles. This occurs after prolonged or repeated NZGLM supplementation. The findings of this study suggest that NZGLM enhances mucosal iron transport and distribution to extra-intestinal tissues when consumed as a single dose with an iron supplement. For this reason NZGLM may be an alternative iron absorption enhancer to red meat or pork with additional cardio-protective properties. Repeated NZGLM supplementation may reduce mucosal transport; therefore repeated NZGLM supplementation should be moderated in order to ensure that mucosal iron transport is not compromised.

Acknowledgements

I am especially grateful to my main supervisor Associate Professor Kevin Pedley for his time, support, patience and guidance throughout the course of my doctoral studies. I am also sincerely grateful to my co-supervisors Associate Professor Jane Coad and Dr Gordon Reynolds for their encouragement, guidance and outstanding technical support. Collectively my supervisory team have made the course of my doctoral study an enjoyable and rewarding journey.

I would like to extend my gratitude to Dr David Simcock for his assistance and encouragement, both in the research and teaching laboratories. His commitment to helping students achieve their potential has been inspirational.

I would also like to thank the academic and technical staff of IFNHH and IFS for their support and encouragement. Specifically I would like to acknowledge Dr Wei-Hang Chua, Dr Chrissie Butts, Dr Gill Norris, Ms Anne Bloomfield and Mrs Vilma Rodriguez for their technical and intellectual assistance. I would like to extend this thanks to my fellow postgraduate students Ms Hannah Morton, Ms Rebecca Smith, Ms Anna Wawer and Mrs Merrin Quilter for their support and encouragement.

I am truly grateful to the Massey University Doctorial Scholarship for its financial assistance during the course of my doctoral studies. I am also grateful to the Nutrition Society of New Zealand for their financial support and assistance attending and presenting my research at national conferences. I would like to extend this gratitude to the Maurice & Phyllis Paykel Trust and the Jaycee Trust for their financial assistance.

Finally, I would like to thank my family and friends for their love and support, my partner Alice, flat mates and office colleagues for their understanding, support and encouragement, the Massey Surf, Snow and Skate Club, the Massey University Students Association for their support.

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%	*Percent*
Δ	*Change*
°C	*Degrees Celsius*
µg	*Micrograms*
µL	*Microliter*
µM	*Micromole/Litre*
β-CPP	*β-casein phosphopeptide*
Ω	*Ohms*
Ω/cm^2	*Ohms per centimetre squared*
AA	*Ascorbic acid*
AHA	*American Heart Association*
ANOVA	*Analysis of variance*
AP	*Alkaline phosphatase*
Asc	*Ascorbate*
ATCC	*American Type Culture Collection*
ATP	*Adenosine triphosphate*
BMP (2,4,6)	*Bone morphogenetic proteins (2,4,6)*
$CaCl_2$	*Calcium chloride*
Caco-2	*Colorectal carcinoma cell line*
cm	*Centimetre*
cm^2	*Square centimetre*
CO_2	*Carbon dioxide*
cpm	*Counts per minute*
CS	*Chondroitin sulfate*
DcytB	*Duodenal cytochrome B*
DHA	*Dehydroascorbic acid*
DMEM	*Dulbecco's modified eagle medium*
DMSO	*Dimethyl sulfoxide*
DMT1	*Divalent metal transporter 1*
EDTA	*Ethylenediaminetetraacetic acid*
ELISA	*Enzyme-linked immunosorbent assay*
ERT	*Extrinsic radionuclide tracer*
FAK	*Focal Adhesion Kinase*
FBS	*Foetal bovine serum*
Fe	*Iron*
Fe^{2+}	*Ferrous iron*
Fe^{3+}	*Ferric iron*
$FeCl_3$	*Ferric chloride*
$FeSO_4$	*Ferrous sulphate*
FLVCR	*Feline leukemia virus subgroup C receptor-related protein*
FOS	*Fructooligosaccharide*

g	*Grams*
g/L	*Grams per litre*
GAG	*Glycosaminoglycan*
GLUT (1,2,3)	*Glucose transporter (1,2,3)*
H^+	*Hydrogen*
HA	*Hyaluronic acid*
HBSS	*Hanks balanced salt solution*
HCl	*Hydrochloric acid*
HFE	*High iron gene*
HHC	*Hereditary hemochromatosis*
HJV	*Hemojuvelin*
HO (1,2)	*Haem oxidase (1,2)*
ID	*Iron deficiency*
IDA	*Iron deficiency anaemia*
IL-6	*Interleuken-6*
IMP	*Integrin mobilferrin paraferritin*
IRE	*Iron response element*
IREG1	*Iron regulating protein 1*
IRP	*Iron response protein*
IRT	*Intrinsic radionuclide tracer*
K^+	*Potassium*
KCl	*Potassium chloride*
Kg	*Kilogram*
LIP	*Labile iron pool*
LPS	*Lipopolysaccharide*
LSD	*Least square difference*
L-α	*L-a-Glycerophosphocholine*
M	*Mole/litre*
MAPK	*Mitogen-activated protein kinase*
mg	*Milligram*
mg/L	*milligrams per litre*
min	*Minute*
mL	*Millilitre*
mm	*Millimetre*
mM	*Millimole/litre*
mOsm	*Milliosmole/kg*
MPF	*Meat poultry fish*
MPF factor	*Meat poultry fish factor*
mRNA	*Messenger ribonucleic acid*
MUFA	*Monounsaturated fatty acid*
mV	*Millivolts*
n	*Number*
n-3 PUFA	*Omega three polyunsaturated fatty acid*
NA	*Nitric acid*
Na^+	*Sodium*
Na^+/K^+ATPase	*Sodium/potassium ATPase pump*
NaCl	*Sodium chloride*

$NaHCO_3$	*Sodium bicarbonate*
NHE	*Sodium hydrogen exchanger*
nM	*Nanometres*
NRAMP	*Natural resistance-associated macrophage protein*
NZBS	*New Zealand blood service*
NZGLM	*New Zealand green-lipped mussel*
O_2	*Oxygen*
OH	*Hydroxide*
P	*Probability*
PBS	*Phosphate buffered saline*
PC	*Polycarbonate*
PCFT/HCP1	*Haem carrier protein 1*
PE	*Polyethylene*
PET	*Polyethylene terephthalate*
ppm	*parts per million*
PUFA	*Polyunsaturated fatty acid*
RBC	*Red blood cell*
rpm	*Revolutions per minute*
SCFA	*Short chain fatty acids*
SEM	*Standard error of the mean*
SFA	*Saturated fatty acid*
SGLT (1,2)	*Sodium-dependent glucose co-transporter (1,2)*
SI	*Sucrose isomaltase*
SS	*Semi-synthetic*
STAT	*Signal Transducer and Activator of Transcription*
STEAP3	*STEAP family member 3*
TCA	*Trichloroacetic acid*
TEER	*Trans-epithelial electrical resistance*
TfR (1,2)	*Transferrin receptor (1,2)*
UTR	*Un-translated region*
w/w	*Weight for weight*
WBC	*White blood cell*
WHO	*World Health Organization*
ZIP (8, 14)	*Zrt- and Irt-like protein (8, 14)*
Zn	*Zinc*