ABSTRACT

Introduction:
Dietary isothiocyanates (ITCs) found in cruciferous vegetables (Brassica spp.) has been reported to reduce cancer risk. ITCs act as anti-carcinogens by inducing phase II conjugating enzymes, in particular glutathione S-transferases (GSTs). These enzymes also metabolize ITCs, such that the protective effect of cruciferous vegetables may predicate on GST genotypes.

Objectives:
This case-control study aimed to determine the association between dietary ITCs, GSTs polymorphisms and ITCs-GSTs polymorphisms interaction with oral cancer risk.

Methods:
115 and 116 cases and controls respectively, were selected from within the Oral Cancer Research & Coordinating Centre (OCRCC), University of Malaya (UM) database between June 2006 and January 2007. Secondary data was used of which the information on dietary ITC intake from cruciferous vegetables was collected via a semi-quantitative food frequency questionnaire (FFQ). Peripheral blood lymphocytes were obtained for genotyping of GSTM1, GSTT1 and GSTP1 using PCR multiplex and PCR-RFLP respectively. Chi-square, logistic regression and stratified analysis was performed using the SPSS (ver 12.0) to investigate the role of ITC and GSTs polymorphism in modulating the risk of oral cancer.
**Results:**
When dietary ITC was categorized into high (greater than/equal to median) and low (less than median) intake, chi-square analysis revealed no significance difference in dietary ITC intake between cases and control group. Logistic regression yielding odd ratios resulted in no significant association observed between dietary ITC intake, GSTM1, GSTT1 or GSTP1 genotypes with oral cancer risk. Although not significant, stratified analysis, however, indicated a potential 20% risk reduction among GSTP1 polymorphism individuals that consumed high dietary ITC (OR 0.80, 95% CI 0.39 – 1.64).

**Conclusion:**
This study suggests that there was no association between dietary ITCs and GSTs polymorphisms with oral cancer risk. Further investigation, however, is strongly recommended to investigate the potential of higher dietary ITCs intake in reducing the risk of oral cancer among individuals with low GST activity.
ACKNOWLEDGEMENTS

First and foremost, I would like to thank God for His blessings and wisdom that has enabled me to complete this thesis successfully.

I would like to convey my most heartfelt gratitude to Prof Dr Rosnah Mohd Zain, for giving me the opportunity to learn and gain invaluable experiences in carrying out this research for the past two years. I am truly grateful for the opportunity to work part time as a research assistant with her. Her endless love, support and guidance during times of jubilation and melancholy have been a source of encouragement for me.

My deepest appreciation goes to Dr Marhazlinda Jamaludin, my second supervisor for who had assisted and supported me during the course of this research. Your tireless effort in providing valuable, professional guidance and constructive advice has made possible the achievement of this research. I truly appreciate your patience and encouragement throughout the time spent.

Special thanks to Dr Cheong Sok Ching and Sharifah Hamid from CARIF for allowing me to use the facility in CARIF to run laboratory experiments. Indeed, your invaluable comments and constructive advice had enriched my knowledge in the field of molecular biology.

Many thanks to my colleagues in OCRCC, Mr Koh Lam Seng, Wan Maria Nabillah, Zaki and Mak Su for their assistance and support throughout this research. I would also like to thank Mrs Khoo and Puan Latipah from the OPOM diagnostic
laboratory and clinic respectively for their help in the laboratory preparation. Thank you also to Dr Rahmi Amtha for her advice and fruitful discussions that we had when we faced problems during the course of the research.

Special appreciation also goes to my beloved fiancé, Dr Pong Loong Sean, for his love, patience and support in my research. His encouragement and moral support has been instrumental during challenging times.

Finally, I would like to thank my family for their patience throughout these years. My sincere appreciation is dedicated to all who had helped and supported me directly or indirectly in this research.