UNIVERSITI PUTRA MALAYSIA

ANTI-OBESITY STUDY OF Elateriospermun tapos BLUME HOT AQUEOUS EXTRACT IN HIGH-FAT DIET Sprague-Dawley RATS

NOR LIYANA BINTI JA'AFAR

FPSK(m) 2019 27

ANTI-OBESITY STUDY OF *Elateriospermun tapos* BLUME HOT AQUEOUS EXTRACT IN HIGH-FAT DIET *Sprague-Dawley* RATS

By

NOR LIYANA BINTI JA'AFAR

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Master of Science

April 2018

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfilment of the requirement for the degree of Master of Science

ANTI-OBESITY STUDY OF *Elateriospermun tapos* BLUME HOT AQUEOUS EXTRACT IN HIGH-FAT DIET *Sprague-Dawley* RATS

By

NOR LIYANA BINTI JA'AFAR

April 2018

Chair : Hasnah Bahari, PhD
Faculty : Medicine and Health Sciences

Obesity is a major public health burden and currently became a global pandemic. Current pharmacotherapy often accompanied with myriads of adverse side effects thus, the search for a safer novel cure is crucial. This study focus on the protective effects of *Elateriospermum tapos* extract on rats fed with high-fat diet and its potential as an anti-obesity agent through inhibition of lipoprotein lipase (LPL) and triglyceride (TG) absorption. Thirty-six male *Sprague-Dawley* rats were allocated to negative control group (NC) fed with normal diet, while positive control (PC), drug control (DC), and treatment groups (T10, T100 and T200) were fed with high-fat and cafeteria diet. The DC group was given orlistat of 10mg/kg bodyweight and treatment groups were supplemented with 10, 100 and 200mg/kg bodyweight of *E. tapos* shell extract respectively. The bodyweight and caloric intake were measured weekly. After 4 weeks, the rats were euthanized and the plasma, liver and retroperitoneal white adipose tissues (RpWAT) were collected for biological assays of TG, LPL and plasma lipid profiles. Liver and adipose tissues were stained with Haematoxylin & Eosin for histological analysis. The PC group had significantly (p<0.05) higher in bodyweight, caloric intake and weight of RpWAT compared to NC group. The extract significantly (p<0.05) lowered the bodyweight and the weight of fat depots in treatment groups as compared to PC group. Nonetheless, the *E. tapos* shell extract supplementation has no positive inhibiting effects on the tissues TG and LPL level. Further, only T100 group had significantly (p<0.05) lowered plasma TG level as compared to PC. The size of both hepatocytes and adipocytes of supplemented groups were significantly (p<0.05) smaller as compared to those in obese group. Based on the findings, this study suggests that supplementation of *E. tapos* shell extract exhibited preventive effects on high-fat and cafeteria diet-induced obesity in rats. The extract however has no potential in the inhibition of TG and LPL level.

Keyword: *Elateriospermum tapos,* obesity, cafeteria diet, triglycerides, lipoprotein lipase

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Sarjana Sains

KAJIAN ANTI-OBESITI DARIPADA EKSTRAK AIR-PANAS *Elateriospermum tapos* BLUME KEATAS TIKUS *Sprague-Dawley* YANG DIBERI MAKAN DIET TINGGI-LEMAK

Oleh

NOR LIYANA BINTI JA'AFAR

April 2018

Pengerusi : Hasnah Bahari, PhD
Fakulti : Perubatan dan Sains Kesihatan

Obesiti merupakan satu masalah kesihatan awam yang utama dan kini menjadi pandemik global. Farmakoterapi sering diiringi dengan pelbagai kesan sampingan, oleh yang demikian, kajian penyembuhan baharu yang lebih selamat adalah sangat penting bagi mengatasi masalah ini. Kajian ini menumpukan kepada kesan perlindungan ekstrak *Elateriospermum tapos* keatas tikus yang diberi makan diet tinggi-lemak dan potensinya sebagai agen anti-obesiti melalui perencatan penyerapan trigliserida (TG) dan lipoprotin lipase (LPL). Tiga puluh enam tikus *Sprague-Dawley* jantan dibahagikan kepada kumpulan kawalan negatif (NC) yang diberi makanan normal, manakala kawalan positif (PC), kawalan dadah (DC), dan kumpulan rawatan (T10, T100 dan T200) diberi makan diet tinggi-lemak dan diet kafeteria. Kumpulan DC diberikan Orlistat 10mg/kg berat badan dan kumpulan rawatan masing-masing diberikan ekstrak *E. tapos* 10, 100 dan 200mg /kg berat badan. Berat badan dan pengambilan kalori diukur setiap minggu. Selepas 4 minggu, tikus dimatikan dan plasma, organ hati, dan tisu adiposa putih (RpWAT) diambil untuk ujian biologi TG, LPL dan profil lipid plasma. Tisu hati dan adiposa putih diwarnakan dengan Haematoxylin & Eosin untuk analisis histologi. Kumpulan PC mempunyai berat badan, pengambilan kalori dan berat lemak yang tinggi yang ketara (p<0.05) berbanding dengan kumpulan NC. Pengambilan ekstrak menurunkan berat badan dan tisu lemak dengan ketara (p<0.05) dalam kumpulan rawatan berbanding dengan kumpulan PC. Walaupun begitu, pengambilan extrak kulit *E. tapos* tidak mempunyai kesan positif dalam pencegahan keatas paras TG and LPL dalm tisu. Selanjutnya, hany kumpulan T100 menunjukkan penurunan paars TG plasma yang ketara (p<0.05) berbanding dengan kumpulan PC. Saiz hepatosit dan adiposit dalam kumpulan rawatan lebih kecil (p<0.05) berbanding dengan kumpulan kawalan positif. Berdasarkan penemuan ini, kajian ini menunjukkan bahawa suplemen ekstrak *E.tapos* menunjukkan kesan pencegahan ke atas obesiti yang disebabkan oleh diet tinggi-lemak dan kafeteria pada tikus. Walau

bagaimanapun, ekstrak ini tidak mempunyai potensi dalam pencegahan paras TG dan LPL.

Kata kunci: *Elateriospermum tapos,* obesiti, diet kafeteria, trigliserida, lipoprotin lipase

ACKOWLEDGEMENTS

In The Name of Allah, the Most Gracious, the Most Merciful. Alhamdulillah, praised to Allah for His blessing and mercy, this thesis is completed with given strength and wisdom granted by Him.

First and foremost, I would like to express my heartfelt gratitude to my supervisor Dr. Hasnah Bahari for her constant guidance and valuable advice throughout my project. Her enthusiasm in scientific research really inspired me throughout this study. I also would like to express my deepest appreciation to my co-supervisor, Dr. Che Norma Mat Taib for her efforts to help me wholly throughout my project. I really do appreciate all their willingness to guide in order to let me understand, manage the lab operation systems and accomplish the understanding of the project.

A million thanks to all lab technicians and science officer for their kindness and help in providing me with a good environment and facilities to complete this study.

An honourable mention goes to my families and friends for their boundless understandings and supports. Without helps of the particular that mentioned above, I would face many difficulties in completing my master study.

Last but not least, I would like to thank all those who have involved directly and indirectly throughout my study. May the blessing of Allah be upon them.

This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Master of Science. The members of the Supervisory Committee were as follows:

Hasnah Bahari, PhD
Senior Lecturer
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Chairman)

Che Norma Mat Taib, PhD
Senior Lecturer
Faculty of Medicine and Health Sciences
Universiti Putra Malaysia
(Member)

ROBIAH BINTI YUNUS, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date:

Declaration by graduate student

I hereby confirm that:

- this thesis is my original work;
- quotations, illustrations and citations have been duly referenced;
- this thesis has not been submitted previously or concurrently for any other degree at any other institutions;
- intellectual property from the thesis and copyright of thesis are fully-owned by Universiti Putra Malaysia, as according to the Universiti Putra Malaysia (Research) Rules 2012;
- written permission must be obtained from supervisor and the office of Deputy Vice-Chancellor (Research and Innovation) before thesis is published (in the form of written, printed or in electronic form) including books, journals, modules, proceedings, popular writings, seminar papers, manuscripts, posters, reports, lecture notes, learning modules or any other materials as stated in the Universiti Putra Malaysia (Research) Rules 2012;
- there is no plagiarism or data falsification/fabrication in the thesis, and scholarly integrity is upheld as according to the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) and the Universiti Putra Malaysia (Research) Rules 2012. The thesis has undergone plagiarism detection software.

Signature: _____ Date: _____

Name and Matric No.: Nor Liyana Ja'afar (GS46260)

Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

Signature: _____
Name of Chairman of Supervisory Committee: Dr. Hasnah Bahari

Signature: _____
Name of Member of Supervisory Committee: Dr. Che Norma Mat Taib

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ºC	Degree Celsius
µg	Microgram
µl	Microliter
L	Litre
LC_{50}	Lethal concentration required to kill 50% of the population.
LDL	Low-density lipoprotein
HDL	High-density lipoprotein
TC	Total cholesterol
mL	Millilitre
SPSS	Statistical Package for Social Sciences
TG	Triglycerides
LPL	Lipoprotein Lipase
g	Gram
Kg	Kilogram
mg	Milligram
mmol/L	Milimole per Litre
RpWAT	Retroperitoneal white adipose tissue
BW	Bodyweight
PC	Positive control
NC	Negative control
DC	Drug control
T10	Group treated with *E. tapos* 10mg/kg of body weight
T100	Group treated with *E. tapos* 100mg/kg of body weight
T200	Group treated with *E. tapos* 200mg/kg of body weight
US	United States
UK	United Kingdom
USA	United States of America
WHO	World Health Organisation

CHAPTER 1

INTRODUCTION

1.1 Background of study

Obesity is an eminent global health challenge associated with a myriad of consequences to the society at large. Overweight and obesity prevalence has been increasing drastically over the last few decades. World Health Organization (2017) estimated that almost 2 billion adults worldwide aged above 18 years old were overweight and more than 600 million of those were considered obese. National Health and Morbidity Survey (2015) reported that almost 20% of Malaysian population were considered obese and those who categorized as overweight make up to 30 % of the population. The occurrence of obesity has multiplied drastically from 4.4% in 1996 to 17.7% in 2015 (Ghee, 2016).

The prevalence of obesity and overweight are escalating in most developing countries including Malaysia due to swift growth of socio- economic in recent years (Jan et al., 2015). Major shift of dietary practices from healthy balanced to popular "Westernized" diets that are energy-rich, nutrient-deprived and small in fibre is one of the predisposing factors of obesity (Popkin, 2003). The parallel of obese patient with the expansion of fast food restaurant is no coincidence. Sustained sedentary behaviour among the population also contribute to the incidence of obesity (Maguire & Haslam, 2010). Individuals with less physical activity more prone to gain weight (Hurt et al., 2010). Prevention of obesity nowadays is very demanding as the disease is influenced by many elements.

Literatures have reported a clear causal correlation between surplus body weight and high risk of morbidity and mortality (Ferguson et al., 2013). By estimation, obesity alone may contribute for almost 3 million deaths and $2 trillion in medical expenses and lost productivity every year (Dobbs et al., 2014). Obesity is often associated with several chromic disorder like dyslipidaemia and coronary atherosclerosis which are predisposing elements for cardiovascular disease (Boden, 2011). The typical dyslipidaemia of obesity marked by high level of triglycerides (TG) and free fatty acid, low level of high-density lipoprotein (HDL) and high level of low-density lipoprotein (LDL) (Franssen et al., 2011).

Lipoprotein lipase (LPL) and triglyceride (TG) are two primary aspects in obesity study. The LPL is a fundamental enzyme in lipids and lipoprotein metabolism in the body (Kusunoki et al., 2012). The LPL hydrolysed the TG-rich lipoproteins, then taken up in peripheral tissues for metabolic energy. The unused TG are stored in adipose tissue. Disparity of LPL level may change the

balance of plasma TG between muscle and adipose tissue, thus can lead to obesity. Mode of action of LPL has been intensively examined *in vitro* and *in vivo* (Wang and Eckel, 2009).

Lifestyle and pharmacotherapy interventions has resulted in limited efficacy as yet, thus the debate over treatment is currently raging. Orlistat, current drug treatment for obesity has been approved by Federal Drug and Administration in 2007 as an over-the-counter weight loss aid can result in adverse side effects like faecal incontinence, flatulence and steatorrhea (Birari and Bhutani, 2007; Kaya et al., 2004). Orlistat, act primarily in the interior of stomach and small intestine is a reversible lipases inhibitor that which form a stable bond with serine residue (Cudrey et al., 1993). The bonding then lead to the inactivation of lipase thus hydrolysis of dietary lipid in triglycerides form become unavailable which then excreted out (Hadvary et al., 1988). Caloric deficit may occurred causes by the undigested triglycerides, subsequently lead to weight reduction. At the suggested therapeutic dose of 120 mg three times a day, orlistat is able to inhibit dietary fat absorption by approximately 30% (Hadvary et al., 1998; Apovian et al., 2015).

In addition, Meridia a sibutramine drug was retracted from the U.S. market after strong associations between the drug and several acute disorders like heart failure and stroke was found (Felix and West, 2013). Due to very little efficacy in terms of current drug intervention, a novel alternative should be offered that directly target obesity. Supplementation from the natural sources is one of the initiative program that yet to be further studied. The significant progress of the development of anti-obesity from medicinal plants has provided potential therapeutic measure for obesity (Abdul Rahman et al., 2017). Numerous studies have reported natural sources from plants and other organisms are effective to reduce bodyweight that targeting pancreatic lipase activities (Birari and Bhutani, 2007; Lunagaria et al., 2014). Malaysia has over 6000 plants of medicinal values. It is an opportunity to utilise our natural resources in promoting naturopath approach in health which eventually lead to economic enhancement.

In current study, we proposed that *Elateriospermum tapos* is able to replicate the effect of orlistat as an inhibitor of lipase. *E. tapos* is widely distributed in Southeast Asian tropical rain forest. In Malaysia, this species is widely distributed in Jengka Forest Reserve, Peninsular Malaysia. The *E. tapos* seed has a great potential for commercial development in the pharmacological industry due to its nutritive seed oil contents. Several known phytochemicals were found in *E. tapos* including flavonoid, tannins and alkaloid which hold therapeutic properties against many diseases (Ling et al., 2006). Study by Ooi and Salimon, (2006) showed that *E. tapos* seed oil contain α-linolenic acid (ALA.18:3n-3), the parent of omega-3 polyunsaturated fatty acids (PUFAs). Omega 3 is one of the essential PUFAs that carry a potential value to combat obesity.

The natives from Sarawak or Pahang often consumed the *E. tapos* seed in raw or in fermented forms and the shell would be thrown away. However, despite often considered as waste material, *E. tapos* shell carries abundant of beneficial properties according to recent studies (Chang et al., 2017; Bakhtiar et al., 2017). In fact, several studies mentioned that peeling fruits or vegetables will reduce the nutritional contents (Slavin & Lloyd, 2012; Vinha et al., 2014). Therefore, in present study we sought out the anti-obesity potential of the *E. tapos* shell extract as well as to sustain the development of novel therapeutic from natural product.

Study has revealed that the flavonoid has significant effect in reducing body weight through the inhibition of the triglycerides level in obese model (Yamamoto and Que, 2006). Further, the flavonoids also play a focal role in the pathway of lipid hyrolysis in adipose tissue (Frayn et al., 2003). As of today, no study has highlight the potential role of *E. tapos* shell against obesity, hence deeper understanding on the mechanisms are necessary. Here, this study aims to explore the protective effects of *E. tapos* shell on body weight gain, caloric intake, triglyceride, lipoprotein lipase and plasma lipid profiles in high-fat diet *Sprague-Dawley* rats.

1.2 Hypothesis

Elateriospermum tapos shell extract is able to exert anti-obesity effect in rats fed with high fat diet through inhibition of triglyceride absorption and lipoprotein lipase.

1.3 Objective

1.3.1 General objectives:

To assess the effects of *E. tapos* shell extract on rats fed with high fat diet and to evaluate its potential as an anti-obesity agent.

1.3.2 Specific objectives:

(1) To investigate the effects of *E. tapos* shell extract supplementation on body weight gain and caloric intake in rats fed with high-fat diet.
(2) To determine the effects *E. tapos* shell extract supplementation on triglyceride and lipoprotein lipase level in liver and adipose tissue of rats fed with high-fat diet.
(3) To determine the effects of *E. tapos* shell extract supplementation on plasma lipid profiles (total cholesterol, low-density lipoprotein, high-

density lipoprotein, and triglyceride) and lipoprotein lipase in rats fed with high-fat diet.

(4) To study the effects *E. tapos* supplementation on the size of the liver and adipose tissue of rats fed with high-fat diet.

REFERENCES

Abdul Rahman, H., Saari, N., Abas, F., Ismail, A., Mumtaz, M. W. and Abdul Hamid, A. (2017). Anti-obesity and antioxidant activities of selected medicinal plants and phytochemical profiling of bioactive compounds. *International Journal of Food Properties*, 20(11): 2616-2629.

Ahn, J., Lee, H., Chung, C. H. and Ha, T. (2011). Biochemical and Biophysical Research Communications High fat diet induced downregulation of microRNA-467b increased lipoprotein lipase in hepatic steatosis. *Biochemical and Biophysical Research Communications*, *414*(4): 664–669.

Albaugh, V. L., Flynn, C. R., Tamboli, R. A. and Abumrad, N. N. (2016). Recent advances in metabolic and bariatric surgery. *F1000Research*, *5*: 978.

Albracht-Schulte, K., Kalupahana, N., Ramalingam, L., Rosairo, S., Wijetunge, S., Kotakadeniya, H. M. S. R. B., Ratnayake, R. M. C. J. and Moustaid-Moussa, N. (2016). Metabolic changes underlying interactions between obesity and non-alcoholic fatty liver disease in South Asian adults. *The FASEB Journal*, *30*(1): 667-2.

Alexander, C. M., Landsman, P. B., Teutsch, S. M. and Haffner, S. M. (2003). NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. *Diabetes*, *52*(5): 1210-1214.

Amin, F., Fatima, S. S., Islam, N. and Gilani, A. H. (2015a). Prevalence of obesity and overweight, its clinical markers and associated factors in a high risk South-Asian population. *BMC Obesity*, *2*(1): 16.

Amin, H. M., Tawfek, N. S., Hussein, B. K. A., & El-ghany, M. S. A. (2015b). Anti-obesity potential of orlistat and amphetamine in rats fed on high fat diet. *Sciences*, 5(02): 453–461.

Amengual-Cladera, E., Lladó, I., Gianotti, M. and Proenza, A. M. (2012). Sex differences in the effect of high-fat diet feeding on rat white adipose tissue mitochondrial function and insulin sensitivity. *Metabolism-Clinical and Experimental*, 61(8): 1108-1117.

Apovian, C. M., Aronne, L. J., Bessesen, D. H., McDonnell, M. E., Murad, M. H., Pagotto, U., Ryan, D. H. and Still, C. D. (2015). Pharmacological management of obesity: an Endocrine Society clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*, 100(2): 342-362.

Arçari, D. P., Bartchewsky, W., Santos, T. W., Oliveira, K. A., Funck, A., Pedrazzoli, J., de Souza, M. F. F. Saad, M. J., Bastos, D. H. M., Gambero, A., Carvalho, P. D. O. and Ribeiro, M. L. (2009). Antiobesity effects of Yerba Maté extract (*Ilex paraguariensis*) in high-fat diet–induced obese mice. *Obesity*, *17*(12): 2127-2133.

Asterholm, I. W., Tao, C., Morley, T. S., Wang, Q. A., Delgado-Lopez, F., Wang, Z. V. and Scherer, P. E. (2014). Adipocyte inflammation is essential for healthy adipose tissue expansion and remodeling. *Cell Metabolism*, *20*(1): 103-118.

Astrup, A., Raben, A. and Geiker, N. (2015). The role of higher protein diets in weight control and obesity-related comorbidities. *International Journal of Obesity*, *39*(5): 721.

Aucouturier, J., Baker, J. S. and Duché, P. (2008). Fat and carbohydrate metabolism during submaximal exercise in children. *Sports Medicine*, *38*(3): 213-238.

Bakhtiar, N. S. M., Shafie, N. H. Ishak, A. H. and Bahari, H (2017). Proceeding from 31st Scientific Conference: Better Nutrition Healthier Malaysians. Screening for total phenolic content, total flavonoid content and antioxidant activity of *Elateriospermum tapos* in aqueous and ethanol extracts.

Ballinger, A. and Peikin, S. R. (2002). Orlistat: its current status as an anti-obesity drug. *European Journal of Pharmacology*, 440(2-3): 109-117.

Baltzell, J. K., Wooten, J. T. and Otto, D. A. (1991). Lipoprotein lipase in rats fed fish oil: apparent relationship to plasma insulin levels. *Lipids*, 26(4), 289-294.

Bergö, M., Olivecrona, G. and Olivecrona, T. (1996). Forms of lipoprotein lipase in rat tissues: in adipose tissue the proportion of inactive lipase increases on fasting. *Biochemical Journal*, 313(3): 893-898.

Berthoud, H.R. and Unzberg, H.M. (2011). The lateral hypothalamus as integrator of metabolic and environmental needs: from electrical self-stimulation to opto-genetics. *Physiology and Behavior*, 104(1): 29–39.

Bhatti, M. S., Akbri, M. Z. and Shakoor, M. (2001). Lipid profile in obesity. *Journal of Ayub Medical College, Abbottabad: JAMC*, 13(1): 31-33.

Bhurosy, T., & Jeewon, R. (2013). Pitfalls of using body mass index (BMI) in assessment of obesity risk. *Current Research in Nutrition and Food Science Journal*, 1(1): 71-76.

Bjermo, H., Iggman, D., Kullberg, J., Dahlman, I., Johansson, L., Persson, L., Berglund, J., Pulkki, K., Basu, S., Rudling, M. U. M., Arner, P., Cederholm, T., Ahlstrom, H. and Riserus, U. (2012). Effects of n-6 PUFAs compared with SFAs on liver fat, lipoproteins, and inflammation in abdominal obesity: a randomized controlled trial. *The American Journal of Clinical Nutrition*, 95(5): 1003-1012.

Birari, R. B. and Bhutani, K. K. (2007). Pancreatic lipase inhibitors from natural sources: unexplored potential. *Drug Discovery Today*, 12(19): 879-889.

Blackburn, G. L. and Waltman, B. A. (2005). Pharmacotherapy to reduce visceral fat. *Clinical Cornerstone*, 7: 52-60.

Boden, G. (2011). 45Obesity, insulin resistance and free fatty acids. *Current Opinion in Endocrinology, Diabetes, and Obesity*, 18(2): 139.

Bolkent, S., Yanardag, R., Bolkent, S. and Döger, M. M. (2004). Beneficial effects of combined treatment with niacin and chromium on the liver of hyperlipemic rats. *Biological Trace Element Research*, 101(3): 219-229.

Boon, M. R., Kooijman, S., van Dam, A. D., Pelgrom, L. R., Berbée, J. F., Visseren, C. A., Aggele, R. C. V., van den Hoek, A. M., Sips, H. C. M., Lombes, M., Havekes, L. M., Tamsma, J. T., Guigas, B., Meijer, L. M., Jukema, J. W. and Rensen, C. N. (2014). Peripheral cannabinoid 1 receptor blockade activates brown adipose tissue and diminishes dyslipidemia and obesity. *The FASEB Journal*, 28(12): 5361-5375.

Bozza, P. T. and Viola, J. P. (2010). Lipid droplets in inflammation and cancer. *Prostaglandins, Leukotrienes and Essential Fatty Acids (PLEFA)*, 82(4-6): 243-250.

Braun, J. E. and Severson, D. L. (1992). Regulation of the synthesis, processing and translocation of lipoprotein lipase. *Biochemical Journal*, 287(2): 337-347.

Bray, G. A. (1993). Use and abuse of appetite-suppressant drugs in the treatment of obesity. *Annals of Internal Medicine*, *119*(7_Part_2): 707-713.

Bray, G. A. (2000). A concise review on the therapeutics of obesity. *Nutrition*, 16(10): 953-960.

Brown, R. M., Kupchik, Y. M., Spencer, S., Garcia-Keller, C., Spanswick, D. C., Lawrence, A. J., Simonds, S. E., Schwarts, D. J., Jordan, K. A., Jhou, T. C. and Kalivas, P. W. (2017). Addiction-like synaptic impairments in diet-induced obesity. *Biological Psychiatry*, 81(9): 797-806.

Brown, M. S. and Goldstein, J. L. (1997). The SREBP pathway: regulation of cholesterol metabolism by proteolysis of a membrane-bound transcription factor. *Cell*, 89(3): 331-340.

Browning, J. D. and Horton, J. D. (2004). Molecular mediators of hepatic steatosis and liver injury. *The Journal of Clinical Investigation*, 114(2): 147-152.

Brunt, E. M. (2007). Pathology of fatty liver disease. *Modern Pathology*, 20(1s): S40.

Cani, P. D., Possemiers, S., Van de Wiele, T., Guiot, Y., Everard, A., Rottier, O., Geurts, L., Naslain, D. Neyrinck, A., Lambert, D. M., Muccioli, G. G. and Delzenne, N. M. (2009). Changes in gut microbiota control inflammation in obese mice through a mechanism involving GLP-2-driven improvement of gut permeability. *Gut*, 58(8): 1091-1103.

Chai, P. P., Lee, B. M., & Ismawi, O. (1989). *Native medicinal plants of Sarawak*. Sarawak Forest Botany Unit, Forest Department, 1989.

Chan, R. S. and Woo, J. (2010). Prevention of overweight and obesity: how effective is the current public health approach. *International Journal of Environmental Research and Public Health*, 7(3): 765-783.

Chang, W. L., Shafie, N. H. and Bahari, H. (2017). Proceeding from 31st Scientific Conference: Better Nutrition Healthier Malaysians. Anti-obesity and anti-diabetic effects of *Elateriospermum tapos* crude extracts *in vitro.*

Chaput, J. P., St-Pierre, S. and Tremblay, A. (2007). Currently available drugs for the treatment of obesity: sibutramine and orlistat. *Mini Reviews in Medicinal Chemistry*, 7(1): 3-10.

Chen, H. C. and Farese, R. V. (2005). Inhibition of triglyceride synthesis as a treatment strategy for obesity: Lessons from DGAT1-deficient mice. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 25(3): 482–486.

Chen, W. L., Lu, H. C. and Huang, H. Y. (2010). Sesame lignans significantly alleviate liver damage of rats caused by carbon tetrachloride in combination with kava. *Journal of Food and Drug Analysis*, 18(4): 249-255.

Chen, I. J., Liu, C. Y., Chiu, J. P., & Hsu, C. H. (2016). Therapeutic effect of high-dose green tea extract on weight reduction: A randomized, double-blind, placebo-controlled clinical trial. *Clinical Nutrition*, 35(3): 592-599.

Cheurfa, M. and Allem, R. (2015). Study of hypocholesterolemic activity of Algerian *Pistacia lentiscus* leaves extracts in vivo. *Revista Brasileira de Farmacognosia*, 25(2): 142-144.

Choonhahirun, A. (2010). Proximate composition and functional properties of pra (Elateriospermun tapos Blume) seed flour. *African Journal of Biotechnology*, 9(36): 5946-5949.

Chris. (2014, April 16). LPL – An important key of the metabolic equation of fat. Retrieved from http://cristivlad.com/lpl-lipoprotein-lipase-key-metabolic-equation-fat/

Colas, R., Sassolas, A., Guichardant, M., Cugnet-Anceau, C., Moret, M., Moulin, P. Lagarde, M. and Calzada, C. (2011). LDL from obese patients with the metabolic syndrome show increased lipid peroxidation and activate platelets. *Diabetologia*, 54(11): 2931.

Connolly, H.M., Crary, J.L., McGoon, M.D., Hensrud, D.D., Edwards, B.S., Edwards, W.D. and Schaff, H.V. (1997). Valvular heart disease associated with fenfluramine-phentermine. *The New England Journal of Medicine*, 337: 581–588.

Cudrey, C., Van Tilbeurgh, H., Gargouri, Y. and Verger, R. (1993). Inactivation of pancreatic lipases by amphiphilic reagents 5-(dodecyldithio)-2-nitrobenzoic acid and tetrahydrolipstatin. Dependence upon partitioning between micellar and oil phases. *Biochemistry*, 32(50): 13800-13808.

Cullen, P. (2000). Evidence that triglycerides are an independent coronary heart disease risk factor. *American Journal of Cardiology*, 86(9): 943-949.

Cummins, S., Flint, E. and Matthews, S. A. (2014). New neighborhood grocery store increased awareness of food access but did not alter dietary habits or obesity. *Health Affairs*, 33(2), 283-291.

Davey, T. M., Allotey, P. and Reidpath, D. D. (2013). Is obesity an ineluctable consequence of development? A case study of Malaysia. *Public Health*, 127(12): 1057–1062.

Del Parigi A. (2010). Endocrinology Book. *Definitions and Classification of Obesity*. South Dartmouth, Massachusetts.

de La Serre, C. B., Ellis, C. L., Lee, J., Hartman, A. L., Rutledge, J. C. and Raybould, H. E. (2010). Propensity to high-fat diet-induced obesity in rats is associated with changes in the gut microbiota and gut inflammation. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, *299*(2): G440-G448.

Deurenberg-Yap, M., Chew, S. K., Lin, V. F., Tan, B. Y., van Staveren, W. A. and Deurenberg, P. (2001). Relationships between indices of obesity and its co-morbidities in multi-ethnic Singapore. *International Journal Of Obesity And Related Metabolic Disorders: Journal of the International Association for the Study of Obesity*, 25(10): 1554–1562.

Divella, R., De Luca, R., Abbate, I., Naglieri, E. and Daniele, A. (2016). Obesity and cancer: the role of adipose tissue and adipo-cytokines-induced chronic inflammation. *Journal of Cancer*, 7(15): 2346-2359.

Dobbs, R., Sawers, C., Thompson, F., Manyika, J., Woetzel, J. R., Child, P., McKenna, S. and Spatharou, A. (2014). *Overcoming obesity: an initial economic analysis*. McKinsey global institute.

Donnelly, J.E., Blair, S.N., Jakicic, J.M., Manore, M.M., Rankin, J.W. and Smith, B.K. (2009). Appropriate Physical Activity Intervention Strategies for Weight Loss and Prevention of Weight Regain for Adults. *Medicine & Science in Sports & Exercise*, 41(7): 459–471.

D'souza, A. M., Beaudry, J. L., Szigiato, A. A., Trumble, S. J., Snook, L. A., Bonen, A., Giaca, A. and Riddell, M. C. (2012). Consumption of a high-fat diet rapidly exacerbates the development of fatty liver disease that occurs with chronically elevated glucocorticoids. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, *302*(8), G850-G863.

Edens, N. K., Fried, S. K., Kral, J. G., Hirsch, J. U. L. E. S. and Leibel, R. L. (1993). In vitro lipid synthesis in human adipose tissue from three abdominal sites. *American Journal of Physiology-Endocrinology and Metabolism*, 265(3): E374-E379.

Esposito, K., Kastorini, C. M., Panagiotakos, D. B. and Giugliano, D. (2013). Mediterranean diet and metabolic syndrome: an updated systematic review. *Reviews in Endocrine and Metabolic Disorders*, 14(3): 255-263.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). (2001). JAMA, 285:2486–2497.

Fabbarini, E., Sullivan, S. and Klein, S. (2010). Obesity and nonalcoholic fatty liver disease: biochemical, metabolic, and clinical implications. *Hepatology*, *51*(2): 679-689.

Farnier, C., Krief, S., Blache, M., Diot-Dupuy, F., Mory, G., Ferre, P. and Bazin, R. (2003). Adipocyte functions are modulated by cell size change: potential involvement of an integrin/ERK signalling pathway. *International Journal of Obesity*, 27(10): 1178.

Felix, H. C. and West, D. S. (2013). Effectiveness of weight loss interventions for obese older adults. *American Journal of Health Promotion*, 27(3): 191-199.

Ferretti, G., Bacchetti, T., Masciangelo, S. and Bicchiega, V. (2010). HDL-paraoxonase and membrane lipid peroxidation: a comparison between healthy and obese subjects. *Obesity*, 18(6): 1079-1084.

Ferguson, R. D., Gallagher, E. J., Scheinman, E. J., Damouni, R. and LeRoith, D. (2013). The epidemiology and molecular mechanisms linking obesity, diabetes, and cancer. In *Vitamins & Hormones*, (Vol. 93, pp. 51-98). Academic Press.

Fiori, C. Z., Martinez, D. and Carissimi, A. (2018). Obesity and Comorbidities. In *Mechanical Ventilation in the Critically Ill Obese Patient* (pp. 43-49). Springer, Cham.

Franssen, R., Monajemi, H., Stroes, E. S. G. and Kastelein, J. J. P. (2011). Obesity and Dyslipidemia. *Medical Clinics of North America*, *95*(5): 893–902.

Frayn, K. N., Karpe, F., Fielding, B. A., Macdonald, I. A. and Coppack, S. W. (2003). Integrative physiology of human adipose tissue. *International Journal of Obesity*, *27*(8): 875.

Frey, L., Riva, M., Grosshans, M. and Mutschler, J. (2016). Food addiction as a possible risk factor for obesity. *Praxis*, *105*(7), 397-404.

Fried, S. K., Tittelbach, T., Blumenthal, J., Sreenivasan, U., Robey, L., Yi, J., Khan, S., Hollender, C., Ryan, A. S. and Goldberg, A. P. (2010). Resistance to the antilipolytic effect of insulin in adipocytes of African-American compared to Caucasian postmenopausal women. *Journal of Lipid Research*, 51(5): 1193-1200.

Fung, T. T., Rimm, E. B., Spiegelman, D., Rifai, N., Tofler, G. H., Willett, W. C. and Hu, F. B. (2001). Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk. *The American Journal of Clinical Nutrition*, 73(1): 61-67.

Fungwe, T. V., Aldawood, F., Ngwa, J. S. and Hatahet, W. (2015). Stimulation of adipose tissue lipoprotein lipase activity improves glucose metabolism and increases high density lipoprotein cholesterol in the spontaneously hypertensive stroke-prone rat. *Current Research in Nutrition and Food Science Journal*, 3(3): 177-186.

Galarraga, M., Campión, J., Muñoz-barrutia, A., Boqué, N., Moreno, H., Martínez, J. A., Milagro, F. and Ortiz-de-solórzano, C. (2012). Adiposoft : automated software for the analysis of white adipose tissue

cellularity in histological sections.*Journal of Lipid Research*, 53(12): 2791–2796.

Ghee, L. K. (2016). A review of adult obesity research in Malaysia. *Medical Journal of Malaysia*, 71(1): 1-19.

Goldberg, I. J. and Merkel, M. (2001). Lipoprotein lipase: Physiology, biochemistry, and molecular biology. *Frontiers in Bioscience: A Journal and Virtual Library*, 6: D388–405.

Goto, T., Teraminami, A., Lee, J. Y., Ohyama, K., Funakoshi, K., Kim, Y. I., Hirai, S., Uemura, T., Yu, R., Takahashi, N. and Kawada, T. (2012). Tiliroside, a glycosidic flavonoid, ameliorates obesity-induced metabolic disorders via activation of adiponectin signaling followed by enhancement of fatty acid oxidation in liver and skeletal muscle in obese–diabetic mice. *The Journal of Nutritional Biochemistry*, 23(7): 768-776.

Grefhorst, A., Hoekstra, J., Derks, T. G., Ouwens, D. M., Baller, J. F., Havinga, R., Havakes, L. M., Romijin, J. A. and Kuipers, F. (2005). Acute hepatic steatosis in mice by blocking β-oxidation does not reduce insulin sensitivity of very-low-density lipoprotein production. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, 289(3): G592-G598.

Gregor, M. F. and Hotamisligil, G. S. (2011). Inflammatory Mechanisms in Obesity. *Annual Review of Immunology*, 29(1): 415–445.

Grundy, S. M. (2002). National Cholesterol Education Program (NCEP)-The National Cholesterol Guidelines in 2001, Adult Treatment Panel (ATP) III. Approach to lipoprotein management in 2001 National Cholesterol Guidelines. *American Journal of Cardiology*, 90(8A): 11i-21i.

Gugusheff, J. R., Ong, Z. Y. and Muhlhausler, B. S. (2015). The early origins of food preferences : targeting the critical windows of development. *The FASEB Journal*, 29(2): 365–373.

Guo, H., Li, D., Ling, W., Feng, X. and Xia, M. (2011). Anthocyanin inhibits high glucose-induced hepatic mtGPAT1 activation and prevents fatty acid synthesis through PKCζ. *Journal of Lipid Research*, 52(5): 908-922.

Guilherme, A., Virbasius, J. V., Puri, V. and Czech, M. P. (2008). Adipocyte dysfunctions linking obesity to insulin resistance and type 2 diabetes. *Nature Reviews Molecular Cell Biology*, 9(5): 367-377.

Hadvary, P., Lengsfeld, H. and Wolfer, H. (1988). Inhibition of pancreatic lipase in vitro by the covalent inhibitor tetrahydrolipstatin. *Biochemical Journal*, 256(2): 357-361.

Hainer, V., Toplak, H. and Mitrakou, A. (2008). Treatment modalities of obesity: what fits whom?. *Diabetes Care*, 31(2): S269-S277.

Hainer, V. and Aldhoon-Hainerová, I. (2014). Tolerability and safety of the new anti-obesity medications. *Drug Safety*, 37(9): 693-702.

Hansson, G. K. (2005). Inflammation, atherosclerosis, and coronary artery disease. *New England Journal of Medicine*, 352(16): 1685-1695.

Heck, A. M., Yanovski, J. A. and Calis, K. A. (2000). Orlistat, a new lipase inhibitor for the management of obesity. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, 20(3): 270-279.

Hill, J. O., Wyatt, H. R. and Peters, J. C. (2012). Energy balance and obesity. *Circulation*, 126(1): 126-132.

Hoang, V. S., & Van Welzen, P. C. (2004). Revision of Annesijoa, Elateriospermum and the Introduced Species of Hevea in Malesia (Euphorbiaceae). *Blumea: Journal of Plant Taxonomy and Plant Geography*, 49(2–3), 425–440.

Hoefle, G., Saely, C.H., Aczel, S., Benzer, W., Marte, T., Langer, P. and Drexel, H. (2005). Impact of total and central obesity on vascular mortality in patients undergoing coronary angiography. *International Journal of Obesity and Related Metabolic Disorders,* 29(7): 785-791.

Holsen, L. M., Savage, C. R., Martin, L. E., Bruce, A. S., Lepping, R. J., Ko, E., Brooks, W. M., Butler, M. G. and Goldstein, J. M. (2012). Importance of reward and prefrontal circuitry in hunger and satiety: Prader–Willi syndrome vs simple obesity. *International Journal of Obesity*, 36(5): 638-647.

Hooper, L., Abdelhamid, A., Moore, H. J., Douthwaite, W., Skeaff, C. M. and Summerbell, C. D. (2012). Effect of reducing total fat intake on body weight: systematic review and meta-analysis of randomised controlled trials and cohort studies. *BMJ*, 345: e7666.

Hossain, K M., Abdal Dayem, A., Han, J., Yin, Y., Kim, K., Kumar Saha, S., Yang, G. M., Choi, H. Y. and Cho, S. G. (2016). Molecular mechanisms of the anti-obesity and anti-diabetic properties of flavonoids. *International Journal of Molecular Sciences*, 17(4): 569.

Hotamisligil, G. S. (2006). Inflammation and metabolic disorders. *Nature*, 444(7121): 860.

Huang, P. L. (2009). A comprehensive definition for metabolic syndrome. *Disease Models & Mechanisms*, *2*(5-6): 231-237.

Hurt, R. T., Kulisek, C., Buchanan, L. A. and McClave, S. A. (2010). The obesity epidemic: Challenges, health initiatives, and implications for gastroenterologists. *Gastroenterology and Hepatology*, 6(12): 780–792.

Husin, N., Tan, N. A. H., Muhammad, I. I. And Nawi, N. M. (2013). Physicochemical and biochemical characteristics of the underutilized *Elateriospermum tapos*. *Jurnal Teknologi,* 64: 57–61.

Institute for Public Health (IPH). National Health and Morbidity Survey 2011 (NHMS 2011) Vol II, Non-communicable Diseases; 2011

Institute for Public Health (IPH) (2015). National Health and Morbidity Survey 2015 (NHMS 2015). Vol. II: Non-Communicable Diseases, Risk Factors

Islam, M. S., Islam, M. K. and Das, S. K. (2014). Effects of butter and estrogen on lipid profile and histotexure of liver and skin in reference to the development of obesity in Swiss albino MICE. *International Journal of Innovation and Applied Studies*, *8*(1): 71.

Iwasaki, Y., Maejima, Y., Suyama, S., Yoshida, M., Arai, T., Katsurada, K., Kumari, P., Nkabayashi, H., Kakei, M. and Yada, T. (2015). Peripheral oxytocin activates vagal afferent neurons to suppress feeding in normal and leptin-resistant mice: a route for ameliorating hyperphagia and obesity. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, *308*(5): R360-R369.

Jan, H. J. M., Yap, R. W. K., Loy, S. L., Norris, S. A., Biesma, R. and Aagaard-Hansen, J. (2015). Prevalence and determinants of overweight, obesity, and type 2 diabetes mellitus in adults in Malaysia. *Asia Pacific Journal of Public Health*, 27(2): 123-135.

Janssen, I., Katzmarzyk, P.T. and Ross, R. (2004). Waist circumference and not body mass index explains obesity-related health risk. *American Journal of Clinical Nutrition*, 79(3): 379-84.

Jin, T. and Teng, X. (2014). Update on lipid metabolism and thyroid disorders. *J Endocrinol Diabetes Obesity*, *2*(3): 1043.

Johari, S. M. and Shahar, S. (2014). Metabolic syndrome: The association of obesity and unhealthy lifestyle among Malaysian elderly people. *Archives of Gerontology and Geriatrics*, 59(2): 360-366.

Jung, C., Gerdes, N., Fritzenwanger, M. and Figulla, H. R. (2010). Circulating levels of interleukin-1 family cytokines in overweight adolescents. *Mediators of Inflammation*, *2010*(II): 1–7.

Jurado-Ruiz, E., Varela, L. M., Luque, A., Berná, G., Cahuana, G., Martinez-Force, E., Gallego-Duran, R., Soria, B., de Roos, B. and Martín, F. (2017). An extra virgin olive oil rich diet intervention ameliorates the nonalcoholic steatohepatitis induced by a high-fat "Western-type" diet in mice. *Molecular Nutrition & Food Research*, 61(3): 1600549.

Kadir, N. A. A. A., Rahmat, A. and Jaafar, H. Z. E. (2015). Protective effects of tamarillo (*Cyphomandra betacea*) extract against high fat diet induced obesity in Sprague-Dawley rats. *Journal of Obesity*, 2015:1-8.

Kaya, A., Aydın, N., Topsever, P., Filiz, M., Öztürk, A., Dağar, A. Ebru, K. and Ekmekcioglu, C. (2004). Efficacy of sibutramine, orlistat and combination therapy on short-term weight management in obese patients. *Biomedicine and Pharmacotherapy*, 58(10): 582-587.

Kinzl, J.F., Schrattenecker, M., Traweger, C., Mattesich, M., Fiala, M. and Biebl, W. (2006). Psychosocial predictors of weight loss after bariatric surgery. *Obesity Surgery*, 16: 1609-1614.

Karimi, G., Sabran, M. R., Jamaluddin, R., Parvaneh, K., Mohtarrudin, N., Ahmad, Z. Khazaai, H. and Khodavandi, A. (2015). The anti-obesity effects of *Lactobacillus casei* strain Shirota versus Orlistat on high fat diet-induced obese rats. *Food and Nutrition Research*, 59(1): 1–9.

Kawano, Y. and Cohen, D. E. (2013). Mechanisms of hepatic triglyceride accumulation in non-alcoholic fatty liver disease. *Journal of Gastroenterology*, *48*(4): 434–441.

Kern, P. a. (1997). Potential Role of TNF a and Lipoprotein Lipase as Candidate Genes for Obesity. *Journal of Nutrition*, *127*: 1917S–1922S.

Kersten, S. (2014). Physiological regulation of lipoprotein lipase. *Biochimica Et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids*, 1841(7): 919-933.

Kim, S., Jin, Y., Choi, Y. and Park, T. (2011). Resveratrol exerts anti-obesity effects via mechanisms involving down-regulation of adipogenic and inflammatory processes in mice. *Biochemical Pharmacology*, 81(11): 1343-1351.

Knuth, N. D., Johannsen, D. L., Tamboli, R. A., MarksShulman, P. A., Huizenga, R., and Chen, K. Y. (2015). Metabolic adaptation following massive weight loss is related to the degree of energy imbalance and changes in circulating leptin. Obesity. *Journal of Clinical Endocrinology Metabolism*, 100: E443-E452.

Klop, B., Elte, J. W. F. and Cabezas, M. C. (2013). Dyslipidemia in Obesity: Mechanisms and Potential Targets. *Nutrients*, 5(4): 1218–1240.

Kotsis, V., Antza, C., Doundoulakis, G. and Stabouli, S. (2017). Obesity, Hypertension, and Dyslipidemia. *Obesity: Pathogenesis, Diagnosis, and Treatment*, 1-15.

Kumon, Y., Suehiro, T., Ikeda, Y. and Hashimoto, K. (2003). Human paraoxonase-1 gene expression by HepG2 cells is downregulated by interleukin-1beta and tumor necrosis factor-alpha, but is upregulated by interleukin-6. *Life Science*, 73: 2807–2815.

Kusunoki, M., Tsutsumi, K., Sato, D. and Nakamura, T. (2012). Lipoprotein lipase and obesity, *4*(12): 1405–1412.

Laaksonen, D.E., Lakka, H.M., Salonen, J.T., Niskanen, L.K., Rauramaa, R., Lakka, T.A. (2002). Low levels of leisure-time physical activity and cardiorespiratory fitness predict development of the metabolic syndrome. *Diabetes Care*, 25(9):1612–1618.

Lafontan, M. (2009). Advances in adipose tissue metabolism. *International journal of Obesity*, 32(S7): S39.

Laforest, S., Jennifer, L., Andréanne, M., Katherine, C. and André, T. (2015). Adipocyte size as a determinant of metabolic disease and adipose tissue dysfunction. *Critical Reviews in Clinical Laboratory Sciences,* 52(6): 301-313.

Lanaspa, M. A., Ishimoto, T., Li, N., Cicerchi, C., Orlicky, D. J., Ruzycki, P., Rivaed, C., Inaba, S., Roncal-Jimenez, C. A., Sanchez-Lozada, L. G., MnManaman, J. L., Bonthron, D. T., Sautin, M. and Diggle, C. P. (2013). Endogenous fructose production and metabolism in the liver contributes to the development of metabolic syndrome. *Nature Communications*, 4: 2434.

Lee, Y. S., Kim, W. S., Kim, K. H., Yoon, M. J., Cho, H. J., Shen, Y., ye, J. M. and Hohnen-Behrens, C. (2006). Berberine, a natural plant product, activates AMP-activated protein kinase with beneficial metabolic effects in diabetic and insulin-resistant states. *Diabetes*, *55*(8): 2256-2264.

Lee, H. M., Yang, G., Ahn, T. G., Kim, M. D., Nugroho, A., Park, H. J., Lee, K. T., Park, W. and An, H. J. (2013). Antiadipogenic effects of Aster glehni extract: in vivo and in vitro effects. *Evidence-Based Complementary and Alternative Medicine*, 2013:1-10.

Levin, B. E. and Dunn-Meynell, A. A. (2002). Defence of body weight depends on dietary composition and palatability in rats with diet-induced obesity. *The American Journal of Physiology— Regulatory Integrative and Comparative Physiology*, 282(1): R46–R54.

Li, Q., Liu, Z., Huang, J., Luo, G., Liang, Q., Wang, D., Ye, X., Wu, C., Wang, L. and Hu, J. (2013). Anti-obesity and hypolipidemic effects of Fuzhuan brick tea water extract in high-fat diet-induced obese rats. *Journal of the Science of Food and Agriculture*, 93(6): 1310-1316.

Li, X., Wang, T., Zhou, B., Gao, W., Cao, J. and Huang, L. (2014). Chemical composition and antioxidant and anti-inflammatory potential of peels and flesh from 10 different pear varieties (Pyrus spp.). *Food Chemistry*, 152: 531-538.

Lim, K. G. (2015). Asia Pacific Conference on Public Health. *The Medical Journal of Malaysia*.

Lima, S. C., Arrais, R. F., Almeida, M. G., Souza, Z. M. and Pedrosa, L. F. (2004). Plasma lipid profile and lipid peroxidation in overweight or obese children and adolescents. *Jornal de Pediatria*, 80(1): 23-28.

Linehan, C., Gupta, S., Samali, A. and O'Connor, L. (2012). Bisphenol A-mediated suppression of LPL gene expression inhibits triglyceride accumulation during adipogenic differentiation of human adult stem cells. *PLoS One*, 7(5): e36109.

Ling, S. K., Fukumori, S., Tomii, K., Tanaka, T. and Kouno, I. (2006). Isolation, purification and identification of chemical constituents from Elateriospermum tapos. *Journal of Tropical Forest Science*, 18(1): 81-85.

Liu, X., Zhu, Z., Kalyani, M., Janik, J. M. and Shi, H. (2014). Effects of energy status and diet on Bdnf expression in the ventromedial hypothalamus of male and female rats. *Physiology and Behaviour*, 130: 99-107.

Liu, Y. and Ding, Z. (2017). Obesity, a serious etiologic factor for male subfertility in modern society. *Reproduction*, 154(4): R123-R131.

Lunagariya, N. A., Patel, N. K., Jagtap, S. C. and Bhutani, K. K. (2014). Inhibitors of pancreatic lipase: state of the art and clinical perspectives. *EXCLI Journal*, 13, 897.

Lustig, R. H. (2006). Childhood obesity: behavioral aberration or biochemical drive? Reinterpreting the First Law of Thermodynamics. *Nature Reviews Endocrinology*, 2(8): 447.

Madura, J. A. and DiBaise, J. K. (2012). Quick fix or long-term cure? Pros and cons of bariatric surgery. *F1000 Medicine Reports,* 4: 19.

Maguire, T. and Haslam, D. W. (2010). *The Obesity Epidemic and its Management*. Pharmaceutical Press, 281.

Magkos, F., Fraterrigo, G., Yoshino, J., Luecking, C., Kirbach, K., Kelly, S. C., de las Fuentes, L., He, S. B., Okunade, A. L., Patterson, B. W. and Klein, S. (2016). Effects of moderate and subsequent progressive weight loss on metabolic function and adipose tissue biology in humans with obesity. *Cell Metabolism*, *23*(4): 591-601.

Marques, C., Meireles, M., Norberto, S., Leite, J., Freitas, J., Pestana, D., Faria, A. and Calhau, C. (2016). High-fat diet-induced obesity Rat model: a comparison between Wistar and Sprague-Dawley Rat. *Adipocyte*, *5*(1): 11-21.

Marchesini, G., Bugianesi, E., Forlani, G., Cerrelli, F., Lenzi, M., Manini, R., Natale, S., Vanni, E., Villanova, N., Melchionda, N. and Rizzetto, M. (2003). Nonalcoholic fatty liver, steatohepatitis, and the metabolic syndrome. *Hepatology*, *37*(4): 917-923.

Meydani, M. and Hasan, S. T. (2010). Dietary polyphenols and obesity. *Nutrients*, 2(7): 737-751.

Mead, J. R., Irvine, S. A. and Ramji, D. P. (2002). Lipoprotein lipase: structure, function, regulation, and role in disease. *Journal of Molecular Medicine*, 80(12): 753-769.

Merkel, M., Eckel, R. H. and Goldberg, I. J. (2002). Lipoprotein lipase: Genetics, lipid uptake, and regulation. *Journal of Lipid Research*, 43(12): 1997–2006.

Meyer, B. N., Ferrigni, N. R., Putnam, J .E., Jacobsen, L. B., Nichols, D. E., and McLaughlin, J. L. (1982). Brine shrimp: A convenient general bioassay for active plant constituents. *Plant Medicine,* 45: 31-34.

Minehira, K., Young, S. G., Villanueva, C. J., Yetukuri, L., Oresic, M., Hellerstein, M. K., Farese Jr, R. V., Horton, J. D. Preitner, F., Thorens, B. and Tappy, L. (2008). Blocking VLDL secretion causes hepatic steatosis but does not affect peripheral lipid stores or insulin sensitivity in mice. *Journal of Lipid Research*, 49(9): 2038-2044.

Minnich, A., Nordestgaard, B. G. and Zilversmit, D. B. (1989). A novel explanation for the reduced LDL cholesterol in severe hypertriglyceridemia. *Journal of Lipid Research*, 30(3): 347-355.

Miwa, Y., Mitsuzumi, H., Sunayama, T., Yamada, M., Okada, K., Kubota, M., Chean, H., Mishima, Y. and Kibata, M. (2005). Glucosyl hesperidin lowers serum triglyceride level in hypertriglyceridemic subjects through the improvement of very low-density lipoprotein metabolic abnormality. *Journal of Nutritional Science and Vitaminology*, *51*(6): 460-470.

Mohamed, G. A., Ibrahim, S. R., Elkhayat, E. S. and El Dine, R. S. (2014). Natural anti-obesity agents. *Bulletin of Faculty of Pharmacy, Cairo*

University, 52(2): 269-284.

Mohamud, W. N. W., Musa, K. I., Khir, A. S. M., Ismail, A. A. S., Ismail, I. S., Kadir, K. A., Kamaruddin, N. A., Yaacob, N. A., Mustafa, N., Ali, O., Isa, S. H. M. and Bebakar, W. M. W. (2011). Prevalence of overweight and obesity among adult Malaysians: an update. *Asia Pacific Journal of Clinical Nutrition*, 20(1): 35-41.

Monetti, M., Levin, M. C., Watt, M. J., Sajan, M. P., Marmor, S., Hubbard, B. K., Stevens, R. D., Bain, J. R., Newgard, C. B., Farese, R. V., Hevener, A. L., and Farese Jr, R. V. (2007). Dissociation of hepatic steatosis and insulin resistance in mice overexpressing DGAT in the liver. *Cell Metabolism*, 6(1), 69-78.

Morris, M. J., Beilharz, J. E., Maniam, J., Reichelt, A. C. and Westbrook, R. F. (2015). Why is obesity such a problem in the 21st century? The intersection of palatable food, cues and reward pathways, stress, and cognition. *Neuroscience and Biobehavioral Reviews*, 58: 36-45.

Muntzel, M. S., Al-Naimi, O. A. S., Barclay, A. and Ajasin, D. (2012). Cafeteria diet increases fat mass and chronically elevates lumbar sympathetic nerve activity in rats novelty and significance. *Hypertension*, 60(6): 1498-1502.

Murphy, E. A., Velazquez, K. T., & Herbert, K. M. (2015). Influence of high-fat-diet on gut microbiota: a driving force for chronic disease risk. *Current Opinion in Clinical Nutrition and Metabolic Care*, 18(5), 515.

Narasimhan, S., Nagarajan, L., Vaidya, R., Gunasekaran, G., Rajagopal, G., Parthasarathy, V., Unnikrishnan, R., Anjana, R. M., Mohan, V. and Sudha, V. (2016). Dietary fat intake and its association with risk of selected components of the metabolic syndrome among rural South Indians. *Indian Journal of Endocrinology and Metabolism*, 20(1): 47.

Nascimento, C. M. O. Do, Ribeiro, E. B. and Oyama, L. M. (2009). Metabolism and secretory function of white adipose tissue: effect of dietary fat. *Anais Da Academia Brasileira de Ciências*, 81(3): 453–466.

National Health and Morbidity Survey (NHMS) (1996). Institute for Public Health, Kuala Lumpur. Ministry of Health, Malaysia.

National Health and Morbidity Survey (NHMS) (2006), Nutritional Status. Institute for Public Health, Ministry of Health, Malaysia.

National Health and Morbidity Survey (NHMS) (2011): Volumn II Non-Communicable Disease. Kuala Lumpur, Malaysia: Malaysia Institute for Public Health, Ministry of Health.

National health and morbidity survey (2015). Volume II: Non- communicable disease, risk factors and other health problems. Institute for Public Health, National Institutes of Health, Ministry of Health Malaysia, Kuala Lumpur.

National Institute of Health (1998). Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. The evidence report. *NIH Publication* No. 98-4083; 1998 September.

Neff, K.J., Olbers, T. and le Roux, C.W. (2013). Bariatric surgery: the challenges with candidate selection, individualizing treatment and clinical outcomes. *BMC Medicine*, 11(8): 1-17.

Neuschwander-Tetri, B. A. (2010). Hepatic lipotoxicity and the pathogenesis of nonalcoholic steatohepatitis: the central role of nontriglyceride fatty acid metabolites. *Hepatology (Baltimore, Md)*, 52: 774–788.

Ng, M., Fleming, T., Robinson, M., Thomson, B. and Graetz, N. (2014). Global, regional and national prevalence of overweight and obesity in children and adults 1980-2013: A systematic analysis. *Lancet*, *384*(9945): 766–781.

Ngamriabsakul, C. and Kommen, H. (2011). The preliminary detection of cyanogenic glycosides in pra (Elateriospermum tapos Blume) by HPLC. *Walailak Journal of Science and Technology (WJST)*, *6*(1): 141-147.

Nisoli, E. and Carruba, M. O. (2000). An assessment of the safety and efficacy of sibutramine, an anti-obesity drug with a novel mechanism of action. *Obesity Reviews*, 1(2): 127-139.

Norris, L. E., Collene, A. L., Asp, M. L., Hsu, J. C., Liu, L. F., Richardson, J. R., Li, D., Bell, D., Osei, K., Belury, R. J. M. A. (2009). Comparison of dietary conjugated linoleic acid with safflower oil on body composition in obese postmenopausal women with type 2 diabetes mellitus. *The American Journal of Clinical Nutrition*, 90(3): 468-476.

Novelli, E. L. B., Diniz, Y. S., Galhardi, C. M., Ebaid, G. M. X., Rodrigues, H. G., Mani, F., Fernandes, A. A. H., Cicogna, A. C. and Novelli Filho, J. L. V. B. (2007). Anthropometrical parameters and markers of obesity in rats. *Laboratory Animals*, 41(1): 111-119.

Ochoa, M., Lallès, J. P., Malbert, C. H. and Val-Laillet, D. (2015). Dietary sugars: their detection by the gut-brain axis and their peripheral and central effects in health and diseases. *European Journal of Nutrition*, 54(1): 1–24.

Olivecrona, G. (2016). Role of lipoprotein lipase in lipid metabolism. *Current*

Opinion in Lipidology, 27(3): 233-241.

Olivecrona, T. and Olivecrona, G. (2009). The ins and outs of adipose tissue. In Cellular lipid metabolism (pp. 315-369). Springer Berlin Heidelberg.

Ong, Z. Y., Wanasuria, A. F., Lin, M. Z., Hiscock, J. and Muhlhausler, B. S. (2013). Chronic intake of a cafeteria diet and subsequent abstinence. Sex-specific effects on gene expression in the mesolimbic reward system. *Appetite*, *65*: 189-199.

Ong, J. M. and Kern, P. A. (1989). Effect of feeding and obesity on lipoprotein lipase activity, immunoreactive protein, and messenger RNA levels in human adipose tissue. *The Journal of Clinical Investigation*, 84(1): 305-311.

Ong, S. L., Paneerchelvan, S., Lai, H. Y. and Rao, N. K. (2014). In vitro lipase inhibitory effect of thirty two selected plants in Malaysia. *Asian Journal of Pharmaceutical and Clinical Research*, 7(2): 19-24.

Ooi, Y. Y. and Salimon, J. (2006). Characteristics of *Elateriospermum tapos* seed oil as a new source of oilseed. *Industrial Crops and Products*, 24(2): 146-151.

Pardina, E., Baena-Fustegueras, J. A., Llamas, R., Catalán, R., Galard, R., Lecube, A., Fort, J. M., Llobera, M., Allende, H., Vargas, V. and Peinado-Onsurbe, J. (2009). Lipoprotein lipase expression in livers of morbidly obese patients could be responsible for liver steatosis. *Obesity Surgery*, 19(5): 608-616.

Park, H. J., Jung, U. J., Cho, S. J., Jung, H. K., Shim, S. and Choi, M. S. (2013). Citrus unshiu peel extract ameliorates hyperglycemia and hepatic steatosis by altering inflammation and hepatic glucose-and lipid-regulating enzymes in db/db mice. *The Journal of Nutritional Biochemistry*, 24(2): 419-427.

Parks, E. J. and Hellerstein, M. K. (2000). Carbohydrate-induced hypertriacylglycerolemia: historical perspective and review of biological mechanisms. *The American Journal of Clinical Nutrition*, 71(2): 412-433.

Park, H. J., Yun, J., Jang, S. H., Kang, S. N., Jeon, B. S., Ko, Y. G., Kim, H. D., Won, C. K., Kim, G. S. and Cho, J. H. (2014). *Coprinus comatus* cap inhibits adipocyte differentiation via regulation of PPARγ and Akt signaling pathway. *PloS one*, 9(9): e105809.

Pattamadilok, D. and Suttisri, R. (2008). Seco-terpenoids and other constituents from Elateriospermum tapos. *Journal of Natural Products*, 71(2): 292-294.

Poulliot, M. C., Després, J. P., Lemieux, S., Moorjani, S., Bouchard, C., Tremblay, A., Nadeau, A. and Lupien, P. J. (1994). Waist circumference and abdominal sagittal diameter: best simple anthropometric indexes of abdominal visceral adipose tissue accumulation and related cardiovascular risk in men and women. *American Journal of Cardiology*, *73*(7): 460-468.

Pelkman, C. L., Fishell, V. K., Maddox, D. H., Pearson, T. A., Mauger, D. T. and Kris-Etherton, P. M. (2004). Effects of moderate-fat (from monounsaturated fat) and low-fat weight-loss diets on the serum lipid profile in overweight and obese men and women. *American Journal of Clinical Nutrition*, 79(2): 204-212.

Pereira-Lancha, L. O., Campos-Ferraz, P. L. and Lancha, A. H. (2012). Obesity: considerations about etiology, metabolism, and the use of experimental models. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, *5*: 75.

Petersson, U., Östgren, C. J., Brudin, L., Brismar, K. and Nilsson, P. M. (2009). Low levels of insulin-like growth-factor-binding protein-1 (IGFBP-1) are prospectively associated with the incidence of type 2 diabetes and impaired glucose tolerance (IGT): the Söderåkra Cardiovascular Risk Factor Study. *Diabetes and Metabolism*, 35(3): 198-205.

Pham, S., Gancel, A., Scotte, M., Houivet, E., Huet, E., Lefebvre, H., Kuhn, J. M. and Prevost, G. (2014). Comparison of the effectiveness of four bariatric surgery procedures in obese patients with type 2 diabetes: a retrospective study. *Journal of Obesity*, *2014:* 1-7.

Pirgon, Ö., & Aslan, N. (2015). The role of urbanization in childhood obesity. *Journal of Clinical Research in Pediatric Endocrinology*, 7(3): 163.

Popkin, B. M (2003). The nutrition transition in the developing world. *Development Policy Review*, 21(5-6): 581-597.

Rada, P., Bocarsly, M. E., Barson, J. R., Hoebel, B. G. and Leibowitz, S. F. (2010). Reduced accumbens dopamine in Sprague–Dawley rats prone to overeating a fat-rich diet. *Physiology and Behaviour*, 101(3): 394-400.

Ramli, N. S., Brown, L., Ismail, P. and Rahmat, A. (2014). Effects of red pitaya juice supplementation on cardiovascular and hepatic changes in high-carbohydrate, high-fat diet-induced metabolic syndrome rats. *BMC Complementary and Alternative Medicine*, 14(1): 189.

Roberts, C. K., Hevener, A. L., & Barnard, R. J. (2013). Metabolic syndrome and insulin resistance: underlying causes and modification by exercise training. *Comprehensive Physiology,* 3:1-58.

Rosen, E. D. and Spiegelman, B. M. (2014). What we talk about when we talk about fat. *Cell*, 156(1-2): 20-44.

Ruge, T., Svensson, M., Eriksson, J. W. and Olivecrona, G. (2005). Tissue-specific regulation of lipoprotein lipase in humans: Effects of fasting. *European Journal of Clinical Investigation*, 35(3): 194–200.

Ryden, K. and Torgersen, A. (2006). The Swedish obese subjects study—what has been accomplished to date?. *Surgery for Obesity and Related Diseases*. 2(5): 549–556.

Salma, I., Mohd. Nor, A., Masrom, H., & Raziah, M. L. (2006). Diversity and use of traditional fruit species in selected home gardens or fruit orchards in Malaysia. *Journal of Tropical Agricalture and Food Science*, 34(1), 149-164.

Sampey, B. P., Vanhoose, A. M., Winfield, H. M., Freemerman, A. J., Muehlbauer, M. J., Fueger, P. T., Newgard, C. B. and Makowski, L. (2011). Cafeteria diet is a robust model of human metabolic syndrome with liver and adipose inflammation: comparison to high-fat diet. *Obesity*, 19(6): 1109-1117.

Saris, W.H., Blair, S.N., Van Baak, M.A., Eaton, S.B., Di Pietro, L., Fogelholm, M., Rissanen, A., Schoeller, D., Swinburn, B., Tremblay, A., Westerterp, K.R. and Wyatt, H. (2003). How much physical activity is enough to prevent unhealthy weight gain? Outcome of the IASO 1st stock conference and consensus statement. *Obesity Review*, 4(2): 101–114.

Savastano, D. M. and Covasa, M. (2005). Adaptation to a high-fat diet leads to hyperphagia and diminished sensitivity to cholecystokinin in rats. *The Journal of Nutrition*, *135*(8): 1953-1959.

Seip, R. L., Angelopoulos, T. J. and Semenkovich, C. F. (1995). Exercise induces human lipoprotein lipase gene expression in skeletal muscle but not adipose tissue. *American Journal of Physiology-Endocrinology and Metabolism*, 268(2): E229-E236.

Sarjeant, K. and Stephens, J. M. (2012). Adipogenesis. *Cold Spring Harbor Perspectives in Biology*, 4(9): a008417.

Seo, J. B., Moon, H. M., Kim, W. S., Lee, Y. S., Jeong, H. W., Yoo, E. J., Ham, J., Kang, H., Park, M. G., Steffensen, K. R., Stulnig, T. M., Gustafsson, J. A., Park, S. D. and Kim, J. B. (2004). Activated liver X receptors stimulate adipocyte differentiation through induction of peroxisome proliferator-activated receptor γ expression. *Molecular and Cellular Biology*, 24(8): 3430-3444.

Serra, M. C., Ryan, A. S., Sorkin, J. D., Favor, K. H. and Goldberg, A. P. (2015). High adipose LPL activity and adipocyte hypertrophy reduce visceral fat and metabolic risk in obese, older women. *Obesity*, 23(3): 602-607.

Schwartz, M.W., Woods, S.C., Porte, D. Jr., Seeley, R.J. and Baskin, D.G. (2000). Central nervous system control of food intake. *Nature*, 404: 661–71.

Sclafani, A. and Springer, D. (1976). Dietary obesity in adult rats: similarities to hypothalamic and human obesity syndromes. *Physiology and Behaviour*, *17*(3): 461-471.

Shafat, A., Murray, B. and Rumsey, D. (2009). Energy density in cafeteria diet induced hyperphagia in the rat. *Appetite*, *52*(1): 34-38.

Shehab, A., Abdulle, A., El Issa, A., Al Suwaidi, J. and Nagelkerke, N. (2012). Favorable changes in lipid profile: the effects of fasting after Ramadan. *PloS One*, *7*(10): e47615.

Shook, R.P., Hand, G.A., Drenowatz, C., Hebert, J.R., Paluch, A.E., Blundell J.E., Hill, J.O., Katzmarzyk., P.T., Church, T.S. and Blair, S. N. (2015). Low levels of physical activity are associated with dysregulation of energy intake and fat mass gain over 1 year. *American Journal of Clinical Nutrition*, 102: 1332–1338.

Sjøgaard, G., Christensen, J. R., Justesen, J. B., Murray, M., Dalager, T., Fredslund, G. H. and Søgaard, K. (2016). Exercise is more than medicine: The working age population's well-being and productivity. *Journal of Sport and Health Science*, *5*(2): 159-165.

Sjogren, P., Basu, S., Rosell, M., Silveira, A., de Faire, U., Vessby, B., Hamsten, A., Hellenius, M. L. and Fisher, R. M. (2005). Measures of oxidized low-density lipoprotein and oxidative stress are not related and not elevated in otherwise healthy men with the metabolic syndrome. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *25*(12): 2580-2586.

Sjöström, L., Lindroos, A.K., Peltonen, M., Torgerson, J., Bouchard, C., Carlsson, B., Dahlgren, S., Larsson, B., Narbro, K., Sjöström, C.D., Sullivan, M., Wedel, H; Swedish Obese Subjects Study Scientific Group (2004). Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *The New England Journal of Medicine*, 351(26): 2683-2693.

Singer, P., Shapiro, H., Theilla, M., Anbar, R., Singer, J. and Cohen, J. (2008). Anti-inflammatory properties of omega-3 fatty acids in critical illness: novel mechanisms and an integrative perspective. *Intensive Care Medicine*, *34*(9): 1580.

Slavin, J. L. and Lloyd, B. (2012). Health benefits of fruits and vegetables. *Advances in Nutrition*, *3*(4): 506-516.

Stahl, A. (2004). A current review of fatty acid transport proteins (SLC27). *Pflügers Archive*, 447(5): 722-727.

Stenman, L. K., Waget, A., Garret, C., Klopp, P., Burcelin, R. and Lahtinen, S. (2014). Potential probiotic Bifidobacterium animalis ssp. lactis 420 prevents weight gain and glucose intolerance in diet-induced obese mice. *Beneficial Microbes*, *5*(4): 437-445.

Sugano, M., Yamato, H., Hayashi, T., Ochiai, H., Kakuchi, J., Goto, S., Nishijima, F., Lino, N., Kazama, J. J., Takeuuchi, T., Mokuda, O., Ishikawa, T. and Okazaki, R. (2006). High-fat diet in low-dose-streptozotocin-treated heminephrectomized rats induces all features of human type 2 diabetic nephropathy: a new rat model of diabetic nephropathy. *Nutrition, Metabolism and Cardiovascular Diseases*, *16*(7): 477-484.

Summers, L. K. M., Fielding, B. A., Bradshaw, H. A., Ilic, V., Beysen, C., Clark, M. L., Moore, N. R. and Frayn, K. N. (2002). Substituting dietary saturated fat with polyunsaturated fat changes abdominal fat distribution and improves insulin sensitivity. *Diabetologia*, *45*(3): 369-377.

Sun, K., Kusminski, C. M., & Scherer, P. E. (2011). Adipose tissue remodeling and obesity. *The Journal of clinical investigation*, 121(6), 2094-2101.

Swift, D. L., Johannsen, N. M., Lavie, C. J., Earnest, C. P. and Church, T. S. (2014). The role of exercise and physical activity in weight loss and maintenance. *Progress in Cardiovascular Diseases*, 56(4): 441-447.

Szczygielska, A., Widomska, S., Jaraszkiewicz, M., Knera, P. and Muc, K. (2003). Blood lipids profile in obese or overweight patients. *Annales Universitatis Mariae Curie-Sklodowska. Sectio D: Medicina*, 58(2): 343-349.

Talukdar, S., Zhou, Y., Li, D., Rossulek, M., Dong, J., Somayaji, V. and Brenner, M. B. (2016). A long-acting FGF21 molecule, PF-05231023, decreases body weight and improves lipid profile in non-human primates and type 2 diabetic subjects. *Cell Metabolism*, 23(3), 427-440.

Tanaka, H., Zaima, N., Ito, H., Hattori, K., Yamamoto, N., Konno, H., Setau, M. and Unno, N. (2013). Cilostazol inhibits accumulation of triglycerides in a rat model of carotid artery ligation. *Journal of Vascular Surgery*, 58(5): 1366-1374.

Thaler, J. P., Guyenet, S. J., Dorfman, M. D., Wisse, B. E. and Schwartz, M. W. (2013). Hypothalamic inflammation: marker or mechanism of obesity pathogenesis?. *Diabetes*, 62(8): 2629-2634.

Tiikkainen, M., Bergholm, R., Rissanen, A., Aro, A., Salminen, I., Tamminen, M., Teramo, K. and Yki-Järvinen, H. (2004). Effects of equal weight loss with orlistat and placebo on body fat and serum fatty acid composition and insulin resistance in obese women. *The American Journal of Clinical Nutrition*, *79*(1): 22-30.

Tontonoz, P., Hu, E. and Spiegelman, B. M. (1995). Regulation of adipocyte gene expression and differentiation by peroxisome proliferator activated receptor γ. *Current Opinion in Genetics and Development*, *5*(5): 571-576.

Traifler, H., Wille, H. J. and Studer, A. (1988). Fractionation of blackcurrant seed oil. *Journal of the American Oil Chemists Society*, *65*(5): 755-760.

Tucci, S. A., Boyland, E. J. and Halford, J. C. (2010). The role of lipid and carbohydrate digestive enzyme inhibitors in the management of obesity: a review of current and emerging therapeutic agents. *Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy*, *3*: 125.

Van Welzen, P. C. and Chayamarit, K. (2007). Flora of Thailand 8. *The forest herbarium, National Park, Wildlife and Plant Conservation Department, Bangkok*, 305-479.

Vázquez-Vela, M. E. F., Torres, N. and Tovar, A. R. (2008). White adipose tissue as endocrine organ and its role in obesity. *Archives of Medical Research*, *39*(8): 715-728.

Vilchis-Gil, J., Galván-Portillo, M., Klünder-Klünder, M., Cruz, M. and Flores-Huerta, S. (2015). Food habits, physical activities and sedentary lifestyles of eutrophic and obese school children: a case–control study. *BMC Public Health*, *15*(1): 124.

Vincent, H. K. and Taylor, A. G. (2006). Biomarkers and potential mechanisms of obesity-induced oxidant stress in humans. *International Journal of Obesity*, *30*(3): 400.

Vinha, A. F., Alves, R. C., Barreira, S. V., Castro, A., Costa, A. S. and Oliveira, M. B. P. (2014). Effect of peel and seed removal on the nutritional value and antioxidant activity of tomato (*Lycopersicon esculentum* L.) fruits. *LWT-Food Science and Technology*, *55*(1): 197-202.

Vrablik, M., Dobiasova, M., Zlatohlavek, L., Urbanová, Z. and Ceska, R. (2014). Biomarkers of cardiometabolic risk in obese/overweight children: effect of lifestyle intervention. *Physiological Research*, *63*(6): 743.

Wang, H. and Eckel, R. H. (2009). Lipoprotein lipase: from gene to obesity. *American Journal of Physiology-Endocrinology and Metabolism*, 297(2): E271-E288.

Wang, S., Moustaid-Moussa, N., Chen, L., Mo, H., Shastri, A., Su, R., Bapat, P., Kwun, I. and Shen, C. L. (2014). Novel insights of dietary polyphenols and obesity. *The Journal of Nutritional Biochemistry*, *25*(1): 1-18.

Wang, G. J., Volkow, N. D., Logan, J., Pappas, N. R., Wong, C. T., Zhu, W., Netusil, N. and Fowler, J. S. (2001). Brain dopamine and obesity. *The Lancet*, 357(9253): 354-357.

Wang, Y. and Lim, H. (2012). The global childhood obesity epidemic and the association between socio-economic status and childhood obesity. *International Review of Psychiatry (Abingdon, England)*, *24*(3): 176–88.

Wensveen, F. M., Valentić, S., Šestan, M., Turk Wensveen, T. and Polić, B. (2015). The "Big Bang" in obese fat: Events initiating obesity-induced adipose tissue inflammation. *European Journal of Immunology*, *45*(9): 2446-2456.

WHO/FAO (2003). Expert Consultation. Diet, nutrition and the prevention of chronic diseases. WHO technical report series. World Health Organisation (WHO), Geneva, Switzerland. Retrieved from http://www.who.int/dietphysicalactivity/publications/trs916/download/en/, 31st January 2018.

Whigham, L. D., Watras, A. C. and Schoeller, D. A. (2007). Efficacy of conjugated linoleic acid for reducing fat mass: a meta-analysis in humans. *The American Journal of Clinical Nutrition*, 85(5): 1203-1211.

White, U. A. and Stephens, J. M. (2010). Transcriptional factors that promote formation of white adipose tissue. *Molecular and Cellular Endocrinology*, 318(1-2): 10-14.

Wiklund, P. (2016). The role of physical activity and exercise in obesity and weight management: Time for critical appraisal. *Journal of Sport and Health Science*, *5*(2): 151–154.

Withrow, D. and Alter, D. A. (2011). The economic burden of obesity worldwide: a systematic review of the direct costs of obesity. *Obesity Reviews*, *12*(2): 131-141.

World Health Organisation (WHO) (2004). The World Health Report 2004: Changing History, World Health Organisation, Geneva, Switzerland. Retrieved from http://www.who.int/iris/handle/10665/42891, 31st January 2018.

World Health Organisation (WHO) (2017). Factsheet: Obesity and Overweight, Geneva, Switzerland. Retrieved from http://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight, 31st January 2018.

Wree, A., Kahraman, A., Gerken, G. and Canbay, A. (2011). Obesity affects the liver–the link between adipocytes and hepatocytes. *Digestion*, *83*(1-2): 124-133.

Wu, O., Leng, J. H., Yang, F. F., Yang, H. M., Zhang, H., Li, Z. F., Zhang, X. Y., Yuan, C. D., Li, J. J., Pan, Q., Liu, W., Ren, Y. J., Liu, B., Liu, W. and Cao, C. J. (2017). A comparative research on obesity hypertension by the comparisons and associations between waist circumference, body mass index with systolic and diastolic blood pressure, and the clinical laboratory data between four special Chinese adult groups. *Clinical and Experimental Hypertension*, 40(1): 1-6.

Yamamoto, Y. and Oue, E. (2006). Antihypertensive effect of quercetin in rats fed with a high-fat high-sucrose diet. *Bioscience, Biotechnology, and Biochemistry*, *70*(4), 933-939.

Yoshikawa, T., Shimano, H., Yahagi, N., Ide, T., Amemiya-Kudo, M., Matsuzaka, T., Nakakuki, M., Tomita, S., Okazaki, H., Takamura, Y., Iizuka, Y., Ohashi, K., Takahashi, A., Sone, H., Osuga, J. I., Gotoda, T., Ishibashi, S. and Yamada, N. (2002). Polyunsaturated fatty acids suppress sterol regulatory element-binding protein 1c promoter activity by inhibition of liver X receptor (LXR) binding to LXR response elements. *Journal of Biological Chemistry*, 277(3): 1705-1711.

Yu, Y. H. and Ginsberg, H. N. (2005). Adipocyte signaling and lipid homeostasis: Sequelae of insulin-resistant adipose tissue. *Circulation Research*, 96(10): 1042–1052.

Yun, J. W. (2010). Possible anti-obesity therapeutics from nature–A review. *Phytochemistry*, 71(14-15): 1625-1641.

Zechner, R., Strauss, J., Frank, S., Wagner, E., Hofmann, W., Kratky, D., Hiden, M. and Levak-Frank, S. (2000). The role of lipoprotein lipase in adipose tissue development and metabolism. *International Journal of Obesity*, *24*(S4): S53.

Zhang, Y., Wu, L., Ma, Z., Cheng, J. and Liu, J. (2015). Anti-diabetic, anti-oxidant and anti-hyperlipidemic activities of flavonoids from corn silk on STZ-induced diabetic mice. *Molecules*, *21*(1): 7.

Zoair, A. M., Muhammad, K. T., Abu-Ammo, D. E. and Motawea, M. M. (2013). Lipid profile and some cardiac functions in children with obesity. *Egyptian Pediatric Association Gazette*, *61*(1): 15–22.

BIODATA OF STUDENT

My name is Nor Liyana Ja'afar. I was born as raised in Besut, Terengganu. I started school at 5 years old then I went to Sekolah Kebangsaan Jabi for primary school. I managed to do well in UPSR which gave me the opportunity to study in Sekolah Menengah Ugama Arab Maahad Muhammadi (P) for secondary school. I did quite well in SPM and I have been offered to enter Foundation Centre of IIUM in 2009. I completed my matriculation study in 2 years then I was accepted to further my first degree in Biomedical Science at International Islamic University Malaysia. Now, I'm a final year student in Master Science of Human Physiology.

UNIVERSITI PUTRA MALAYSIA

STATUS CONFIRMATION FOR THESIS / PROJECT REPORT AND COPYRIGHT

ACADEMIC SESSION : _____

TITLE OF THESIS / PROJECT REPORT :

ANTI-OBESITY STUDY OF *Elateriospermun tapos* BLUME HOT AQUEOUS EXTRACT IN HIGH-FAT DIET *Sprague-Dawley* RATS

NAME OF STUDENT: NOR LIYANA BINTI JA'AFAR

I acknowledge that the copyright and other intellectual property in the thesis/project report belonged to Universiti Putra Malaysia and I agree to allow this thesis/project report to be placed at the library under the following terms:

1. This thesis/project report is the property of Universiti Putra Malaysia.
2. The library of Universiti Putra Malaysia has the right to make copies for educational purposes only.
3. The library of Universiti Putra Malaysia is allowed to make copies of this thesis for academic exchange.

I declare that this thesis is classified as :

*Please tick (√)

☐	**CONFIDENTIAL**	(Contain confidential information under Official Secret Act 1972).
☐	**RESTRICTED**	(Contains restricted information as specified by the organization/institution where research was done).
☐	**OPEN ACCESS**	I agree that my thesis/project report to be published as hard copy or online open access.

This thesis is submitted for :

☐	**PATENT**	Embargo from_____ until _____ (date) (date)

Approved by:

_____	_____
(Signature of Student)	(Signature of Chairman of Supervisory Committee)
New IC No/ Passport No.:	Name:
Date :	Date :

[Note : If the thesis is CONFIDENTIAL or RESTRICTED, please attach with the letter from the organization/institution with period and reasons for confidentially or restricted.]