**UNIVERSITI PUTRA MALAYSIA**

# *EFFECTS OF MIXTURES FROM SELECTED FUNCTIONAL FOODS IN HYPERCHOLESTEROLAEMIC RATS*

**NOOR SYAFIQA AQILA BINTI MOHD ROSMI**

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# EFFECTS OF MIXTURES FROM SELECTED FUNCTIONAL FOODS IN HYPERCHOLESTEROLAEMIC RATS

By

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**September 2020**

**Chairman : Nurul Husna Binti Shafie, PhD**
**Faculty : Medicine and Health Sciences**

The efficacy in cholesterol treatment by mixtures from selected functional foods (MSFF) including *nattokinase* (fermented soybean), red yeast rice extract, *Ginkgo biloba*, oat fiber, garlic, bee pollen and propolis in Sprague Dawley rats. This study was to determine the cholesterol-lowering effects in MSFF on the identification of bioactive compounds, enzymatic activities (HMGCoA reductase and ACAT2), lipid peroxidation (serum and tissue MDA), histopathological analysis of liver tissue, and biochemical profiles. The rats were divided into two groups (normal control (NC) and high cholesterol fed rats (HCD) for initial 4 weeks. After 4 weeks on high cholesterol diet, the group were divided into five groups: 1% HCD, 1% HCD + Simvastatin (10 mg/kg of body weight (BW)), 1% HCD + MSFF (50 mg/kg/BW), 1% HCD + MSFF (100 mg/kg/BW) and 1% HCD + MSFF (200 mg/kg /BW). LC-MS/MS analysis showed MSFF contained Monacolin K, naringin, tocopherol and glutamate. Changes of body weight and average feed intake/week were observed for all hypercholesterolaemic rats after four weeks of treatment compared to normal group. MSFF at 200 mg/kg/BW provide a significant ($p<0.05$) greatest inhibition activity of 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMGCoA reductase) (167.86 ± 5.54 pg/ml) and acetyl-Coenzyme A acetyltransferase 2 (ACAT2) (360.19 ± 44.11 pg/ml) than 1% HCD. Lipid peroxidation showed a significant decreased ($p<0.05$) in serum (3.82 ± 0.83 µmol/L) and liver tissues (15.24 ± 1.81 µmol/mg) of malondialdehyde (MDA) against hepatic steatosis. MSFF at 100 mg/kg/BW had significantly ($p<0.05$) decreased serum total cholesterol (TC) (1.35±0.09 mmol/L) whereby MSFF at 50 mg/kg/BW reduced low density lipoprotein (LDL) ($p<0.05$)at 0.52 ± 0.09 mmol/L. Serum liver profiles of aspartate aminotransferase (AST) (115.33 ± 8.69 U/L) and alanine aminotransferase (ALT) (61.00 ± 1.00 U/L) were decreased significantly ($p<0.05$) by MSFF at 200 mg/kg/BW. These combination of functional foods ingredients could provide health-promising effect for hypercholesterolaemia.

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**Pengerusi :Nurul Husna Binti Shafie, PhD**
**Fakulti :Perubatan dan Sains Kesihatan**

Keberkesanan campuran makanan berfungsi terpilih *(MSFF)* iaitu *nattokinase* (enzim fermentasi soya), ekstrak beras merah, *Ginkgo biloba,* bawang putih, debunga lebah dan propolis merawat kolesterol dalam tikus *Sprague Dawley*. Objektif kajian ini untuk menentukan kesan penurunan kadar kolesterol oleh *MSFF* menerusi pengenalpastian kandungan bioaktif, aktiviti enzim (*HMGCoA reductase* dan *ACAT2)*, peroksidasi lemak (serum dan tisu MDA), analisis histolopatologi tisu hati, dan analisis biokimia. Dua kumpulan tikus dibahagikan kepada (kawalan normal *(NC)* dan diet berkolesterol tinggi *(1% HCD)*) bagi empat minggu pertama. Selepas empat minggu induksi diet berkolesterol tinggi (1%), lima kumpulan berbeza dibahagikan: *1% HCD, 1% HCD* + Simvastatin (10 mg/kg/berat badan *(BW)*), *1% HCD + MSFF (50 mg/kg/BW*), *1% HCD + MSFF (100 mg/kg/BW)* dan *1% HCD + MSFF (200 mg/kg /BW*). Analisis LC-MS/MS mendapati MSFF mengandungi Monakolin K, naringin, tokoferol and glutamat. Perubahan berat badan dan purata pengambilan makanan telah dipantau kepada semua tikus hiperkolesterolemia selepas empat minggu dirawat dengan *MSFF.* Dos MSFF pada *200 mg/kg/BW* menurun secara signifikan ($p<0.05$) terhadap aktiviti enzim *HMGCoA reductase* (167.86 ± 5.54 pg/ml) dan *ACAT2* (360.19 ± 44.11 pg/ml). Peroksidasi lemak menurunkan kadar serum (3.82 ± 0.83 µmol/L) and tisu hati (15.24 ± 1.81 µmol/mg) secara signifikan ($p<0.05$) daripada hepatik steatosis. *MSFF* juga menurunkan profil serum lemak dengan signifikan ($p<0.05$) (jumlah kolesterol dan *LDL*) kepada 1.35±0.09 mmol/L pada dos *100 mg/kg/BW* dan 0.52 ± 0.09 mmol/L pada dos *50 mg/kg/BW*. Serum hati *aspartate aminotransferase (AST)* (115.33 ± 8.69 U/L) dan *alanine aminotransferase* (*ALT*) (61.00 ± 1.00 U/L) telah dikurangkan secara signifikan ($p<0.05$) pada dos *200 mg/kg/BW*. Oleh itu, makanan campuran berfungsi terpilih melalui gabungan bahan-bahan dalam MSFF dilihat berkesan bagi merawat keadaan hiperkolesterolemia.

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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 Sciences. The members of the Supervisory Committee were as follows:

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**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.

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## TABLE OF CONTENTS

# LIST OF TABLES

## LIST OF FIGURES

## LIST OF ABBREVIATIONS

| | |
|---|---|
| 1% HCD | 1 % high cholesterol diet |
| ACAT2 | Acyl-Coenzyme (coa) Cholesterol Acyl-Transferase 2 |
| ALT | Alanine aminotransferase |
| AST | Aspartate aminotransferase |
| CETP | Cholesteryl ester transfer protein |
| CV | Central vein |
| GABA | Gamma-aminobutyric acid |
| GSH | Glutathione |
| HDL | High-density lipoprotein |
| HMGCoA | 3-hydroxy-3 methylglutaryl coenzyme-A |
| IL-8 | Interleukin-8 |
| INSIG1 | Sterol sensing protein |
| LCAT | Lecithin cholesterol acyltransferase |
| LC-MS/MS | Liquid chromatography - mass spectrometry |
| LDL | Low-density lipoprotein |
| MDA | Malondialdehyde |
| MSFF | Mixtures from selected functional foods |
| NASH | Non-alcoholic steatohepatitis |
| ROS | Reactive oxygen species |
| SCAP | SREBP cleavage-activating protein |
| SOD | Superoxide dismutase |
| SVS | Simvastatin |
| SREBP | Sterol responsive element binding protein |
| TBARS | Thiobarbituric acid reactive substances |

| | |
|---|---|
| TC | Total cholesterol |
| TG | Triglyceride |
| TNF-α | Tumor necrosis factor–alpha |
| TGF-β | Transforming growth factor–beta |

# CHAPTER 1

# INTRODUCTION

This chapter represents research background, problem statement, significance of study, objectives and hypotheses of study.

## 1.1 Research background

Cardiovascular diseases (CVD) become main factor for an increasing rate of morbidity and mortality worldwide especially in most of developing countries (Berzou, Taleb-senouci, Guenzet, & Krouf, 2014). It is estimated about 2.6 million of deaths and 29.7 million disability-adjusted life years due to diseases related to high concentration of cholesterol in blood among the global population (World Health Organization, 2017). Nowadays, the frequent consumption of diet high in cholesterol, environmental, genetic factors and lack of physical activity are strongly correlated with hypercholesterolaemia (Cheong, Jessica Koh, Patrick, Tan, & Nyam, 2018).Hypercholesterolaemia is a metabolic disorder that mainly resulted in an elevated of plasma total cholesterol (TC) and low density lipoprotein (LDL) cholesterol (Mu et al., 2017; Adekiya, Shodehinde, & Aruleba, 2018).

The adverse effects of high level of total cholesterol level in body can link to several diseases such as obesity, hypercholesterolaemia, hyperlipidaemia, and cardiovascular diseases (atherosclerosis and myocardiac infarction) (Lee, Kim, Jang, Cho, & Choi, 2011; Adekiya et al., 2018). Hypercholesterolaemia is under oxidative stress can trigger the progression of atherosclerosis and abnormal lipid metabolism (Zulkhairi et al., 2010; Cheong et al., 2018). The production of reactive oxygen species (ROS) such as superoxide anions, hydrogen peroxide (H2O2) and hydroxyl radicals would react with unsaturated fatty acid chain stimulate lipid peroxidation that might decompose into malondialdehyde (MDA) that is considered as biological marker for lipid peroxidation (Janero, 1990).

Nowadays, conventional synthetic lipid-lowering drugs such as fibrates, statins, and bile-acid sequestrants had been acknowledged for treatment of hypercholesterolaemia (Tiwari & Khokhar, 2014). However, these medications still have limited efficacy and severe side effects such as weakening muscle fibers, muscle injury, and damaging peripheral nerve (Moosmann & Behl, 2004). Hence, it is important to find an alternative for treatment of hypercholesterolaemia from natural sources due to their less side effects for long term consumption. Mixtures from selected functional foods (MSFF) utilized in this study consisted natural ingredients such as *nattokinase* (soybean), red yeast rice extract, *Ginkgo biloba*, oat fiber, garlic, bee pollen and propolis that have potential effects as anti-hypercholesteraemic agents.

*Nattokinase,* a product of fermentation from soybean is regarded as anti-atherosclerotic agent that demonstrated its ability to suppress intimal thickening in rats (Chen et al., 2018). Besides, red yeast rice extract can decrease blood cholesterol by reducing lipid peroxidation (Yeap et al., 2014). Ginkgo biloba, may provide hypocholesterolemic effect in regulation lipid in adipose tissue and increase HDL level (Kang, 2017). Oat fiber involves in lowering total cholesterol level due to its role in altering the metabolism of bile acids (Ban et al., 2015). Garlic also may reduce streaks formation of atherosclerosis whereby bee pollen also help to control the elevation of lipid profiles at normal level and prevent clumping of blood platelets (Vassev, et al., 2015; Lachhiramka & Patil, 2016). Propolis also has potential to decrease the level of triglyceride level in the rats (Albokhadaim, 2015).

Therefore, effects of mixtures from selected functional foods (MSFF) ingredients may provide strong health-promising effects compared to single ingredient consumption in management of hypercholesterolaemia. This study suggested that further comprehensive investigation should be conducted to provide an alternative to the synthetic drug and become a complementary natural treatment in the safest way to prevent the progression hypercholesterolaemia effectively.

## 1.2 Problem statement

On a global scale, a third of coronary heart disease was closely related to cholesterol. This scenario in line with the prevalence of hypercholesterolaemia that was found significantly higher in high-income countries compared to low-income countries (World Health Organization, 2017; Cheong et al., 2018). In Malaysia, the prevalence of diagnosed hypercholesterolaemia among adults was increasing about 40.3 % according to National Health and Morbidity Survey 2019 (NHMS 2019). Hypercholesterolaemia become a major concern for health professionals to tackle this issue since hypercholesterolaemia may result in various metabolic disorders including hypertension and diabetes mellitus.

This condition is regarded as one of the major socioeconomic problems and effect of sedentary modern lifestyle and lack of awareness about dietary habits. The elevation of total blood cholesterol (TC) and low-density lipoprotein (LDL) are deposited in the sub-endothelial region of arteries that lead to inflammation and formation of plaque that associated with development of hypertension and affect the function of liver and kidneys (Puttaswamy & Urooj, 2016). The continuous intake of diet high in cholesterol might directly related to hyperlipidemia in humans (Matos et al., 2005).

It also cannot be deniable that medications for the treatment of cholesterol has side effects. For example, statin functions through lowering total cholesterol (TC) and low density lipoprotein (LDL) cholesterol by inhibition of enzymatic activity by HMG-CoA reductase that involved in cholesterol biosynthesis but it frequently associated with side effects including abdominal pain, constipation, headache, fatigue, skin rashes, dizziness, blurred vision, muscle weakness and liver inflammation (Cheong et al., 2018). However, the unpleasant side effect of these medicines has been considerable to provide a further reference for complementary or alternative therapies which are marketed as "natural" treatment against hypercholesterolaemia.

Nutraceuticals and functional foods have attracted great interest as new possible treatments for lowering total cholesterol (Ajdari et al., 2014; Cheong et al., 2018). Meanwhile, the active substances in natural functional food become an interest as alternative due to their hypocholesterolemic properties, less side effects, easily absorbed by intestine (high bioavailability) and cost-effective (Al-Muzafar & Amin, 2017).The optimal physiological metabolism and cellular functions can be accomplished with the aid of functional foods that support the body in terms of its biochemical and physiological functions (Cencic & Chingwaru, 2010). The mechanisms of functional food are predicted to give positive impacts through improving the availability of several vitamins, minerals, essential fatty acids, amino acids, probiotics, and prebiotics as well (Yang et al., 2018). It is necessary to find an applicable source of natural ingredients as an alternative to synthetic drugs with minimal effects for the treatment of hypercholesterolaemia in the safest way.

This study is aimed to determine the potential of anti-hypercholesterolaemic activities of mixtures from selected functional foods in high cholesterol-fed rats. It constitutes several main ingredients that scientifically proven to reduce blood cholesterol levels such as *nattokinase* (fermented soybean), red yeast rice extract, *Ginkgo biloba,* oat fiber, garlic, bee pollen, and propolis.

## 1.3 Significance of study

In this study, the findings will contribute a reference for researcher and public about the potential of each ingredient in mixtures of selected functional foods such as *nattokinase* (fermented soybean), red yeast rice extract, *Ginkgo biloba*, oat fiber, garlic, bee pollen and propolis as natural alternative treatment of anti-hypercholesterolaemic compared to synthetic drugs. This study also will provide additional information for the public about the efficacy of functional foods as supplementary components in daily intake to provide adequate nutrients and good health outcomes in management of hypercholesterolaemia.

## 1.4 Objectives of study

### 1.4.1 General objectives

To determine anti-hypercholesterolaemic effects of mixtures from selected functional foods (MSFF) (*nattokinase* (fermented soybean), red yeast rice extract, *Ginkgo biloba*, oat fiber, garlic, bee pollen, and propolis) in hypercholesterolaemic rats.

### 1.4.2 Specific objectives

1. To identify the bioactive compounds of mixtures from selected functional foods (MSFF) identified by liquid chromatography with tandem mass spectrometry (LC-MS/ MS).

2. To determine the effects of mixtures from selected functional foods (MSFF) on enzymatic activities (HMGCoA reductase and ACAT2) in the liver of hypercholesterolaemic rats.

3. To determine the effects of mixtures from selected functional foods (MSFF) on lipid peroxidation using TBARS and histopathological analysis of liver tissues of hypercholesterolaemic rats.

4. To determine the effects of mixtures from selected functional foods (MSFF) on serum lipid profiles (TG, TC, LDL and HDL), kidney profiles (creatinine, urea, uric acid) and serum liver profile (ALT and AST) of hypercholesterolaemic rats.

## 1.5 Hypotheses

1. There are presence of bioactive compounds that have potential as anti-hypercholesterolaemic agents from the mixtures of selected functional foods (MSFF) identified by liquid chromatography with tandem mass spectrometry (LC-MS/ MS).

2. There are significant reduction in enzymatic activities (HMGCoA reductase and ACAT2) in the liver tissue hypercholesterolaemic rats fed with mixtures from selected functional foods (MSFF).

3. There are significant reduction on lipid peroxidation using TBARS assay and histopathological analysis of mixtures from selected functional foods (MSFF) in hypercholesterolaemic rats.

4. There are significant reduction in serum lipid profiles (TG, TC, LDL and HDL), serum kidney profiles (creatinine, urea, uric acid) and serum liver profiles (ALT and AST) of mixtures from selected functional foods (MSFF) in hypercholesterolaemic rats.

## REFERENCES


Abdel-Salam, A. M. (2010). Functional foods: Hopefulness to good health. *American Journal of Food Technology, 5*(2), 86-99.

Abuja, P. M., & Albertini, R. (2001). Methods for monitoring oxidative stress, lipid peroxidation and oxidation resistance of lipoproteins. *Clinica Chimica Acta*, *306*(1–2), 1–17.

Adekiya, T. A., Shodehinde, S. A., & Aruleba, R. T. (2018). Anti-hypercholesterolaemic effect of unripe *Musa paradisiaca* products on hypercholesterolaemia-induced rats. *Journal of Applied Pharmaceutical Science*, *8*(10), 90–97.

Adeneye, A. A., Adeyemi, O. O., & Agbaje, E. O. (2010). Anti-obesity and antihyperlipidaemic effect of Hunteria umbellata seed extract in experimental hyperlipidaemia. *Journal of Ethnopharmacology*, *130*(2), 307-314.

Adil, M., Kandhare, A. D., Ghosh, P., Venkata, S., Raygude, K. S., & Bodhankar, S. L. (2016). Ameliorative effect of naringin in acetaminophen-induced hepatic and renal toxicity in laboratory rats: role of FXR and KIM-1. *Renal Failure*, *38*(6), 1007-1020.

Ahmed, O. M., Fahim, H. I., Ahmed, H. Y., Al-Muzafar, H. M., Ahmed, R. R., Amin, K. A., ... & Abdelazeem, W. H. (2019). The preventive effects and the mechanisms of action of navel orange peel hydroethanolic extract, naringin, and naringenin in n-acetyl-p-aminophenol-induced liver injury in Wistar rats. *Oxidative Medicine and Cellular Longevity, 2019*, 1-19.

Ajdari, Z., Abd Ghani, M., Khan Ayob, M., Bayat, S., Mokhtar, M., Abbasiliasi, S., … Ariff, A. B. (2014). Hypocholesterolemic activity of Monascus fermented product in the absence of monacolins with partial purification for functional food applications. *The Scientific World Journal*, *2014*(2014), 1–12.

Alam, M. A., Subhan, N., Rahman, M. M., Uddin, S. J., Reza, H. M., & Sarker, S. D. (2014). Effect of citrus flavonoids, naringin and naringenin, on metabolic syndrome and their mechanisms of action. *Advances in Nutrition, 5*(4), 404-417.

Alam, M., Kauter, K., & Brown, L. (2013). Naringin improves diet-induced cardiovascular dysfunction and obesity in high carbohydrate, high fat diet-fed rats. *Nutrients, 5*(3), 637-650.

Albokhadaim, I. (2015). Influence of dietary supplementation of propolis on hematology, biochemistry and lipid profile of rats fed high cholesterol diet. *Journal of Advanced Veterinary and Animal Research, 2*(1), 56, 56-63.

Ali, K. M., Wonnerth, A., Huber, K., & Wojta, J. (2012). Cardiovascular disease risk reduction by raising HDL cholesterol–current therapies and future opportunities. *British Journal of Pharmacology*, *167*(6), 1177-1194.

Alissa, E. M., & Ferns, G. A. (2012). Functional foods and nutraceuticals in the primary prevention of cardiovascular diseases. *Journal of Nutrition and Metabolism*, *2012*, 569486.

Al-Muzafar, H. M., & Amin, K. A. (2017). Efficacy of functional foods mixtures in improving hypercholesterolaemia, inflammatory and endothelial dysfunction biomarkers-induced by high cholesterol diet. *Lipids in Health and Disease, 16*(1), 194.

Almer, G., Mangge, H., Zimmer, A., & Prassl, R. (2015). Lipoprotein-related and apolipoprotein-mediated delivery systems for drug targeting and imaging. *Current Medicinal Chemistry, 22*(31), 3631-3651

Aly, N. H. (2012). Effect of Dietary Oat and Wheat Bran on Biochemical Changes in Rats Fed High Fat-. *Journal of Applied Sciences Research, 8*(1), 598–604.

Annamalay, S. D. (2018). Effects of anti-oxidants on oxidative stress: Assessing MDA in urine samples. *International Journal of Clinical Nutrition & Dietetics, 4*(35),135.

Arshade, A., Talebi, E., & Tahery, E. (2014). Effect of barley and oats on high-density lipoprotein cholesterol and triglycerides in rats. *Journal of Jahrom University of Medical Sciences*, *12*(2),29-34.

Ares, A. M., Valverde, S., Bernal, J. L., Nozal, M. J., & Bernal, J. (2018). Extraction and determination of bioactive compounds from bee pollen. *Journal of Pharmaceutical and Biomedical Analysis*, *147*, 110–124.

Arnedo, M., Latorre-Pellicer, A., Lucia-Campos, C., Gil-Salvador, M., Antoñanzas-Peréz, R., Gómez-Puertas, P., ... & Pié, J. (2019). more than one hmg-coa lyase: the classical mitochondrial enzyme plus the peroxisomal and the cytosolic ones. *International Journal of Molecular Sciences, 20*(24), 6124.

Axe, J. (2018). Ginkgo Biloba Benefits Energy, Mood & Memory. *Dr. Axe Food Is Medicine.* Retrieved on 15th July 2019 from https://draxe.com/ginkgo-biloba-benefits.

Ayala, A. (2014). Review article lipid peroxidation: production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal antonio. *Medical Technologies in Neurosurgery*, *2014*, 9–12.

Ban, Y., Qiu, J., Ren, C., & Li, Z. (2015). Effects of different cooking methods of oat on preventing the diet-induced increase of cholesterol level in hypercholesterolaemic rats. *Lipids in Health and Disease*, *14*(1), 1–8.

Banerjee, S. K., Maulik, M., & Manchanda, S. C. (2001). Garlic-induced alteration in rat liver and kidney morphology and associated changes in endogenous antioxidant status. *Food and Chemical Toxicology, 39*(8), 793–797.

Baskaran, G., Salvamani, S., Ahmad, S. A., Shaharuddin, N. A., Pattira, P. D., & Shukor, M. Y. (2015). HMG-CoA reductase inhibitory activity and phytocomponent investigation of Basella alba leaf extract as a treatment for hypercholesterolaemia. *Drug Design, Development and Therapy,9*(2015), 509–517.

Bate, C., Rumbold, L., & Williams, A. (2007). factor-induced neuronal damage. *Journal of Neuroinflammation*,*4*(1), 1–8.

Bellik, Y., Boukraâ, L., Alzahrani, H. A., Bakhotmah, B. A., Abdellah, F., Hammoudi, S. M., & Iguer-ouada, M. (2013). Molecular Mechanism Underlying Anti-Inflammatory and Anti-Allergic Activities of Phytochemicals: An Update. *Molecules*,*18*(1),324.

Berzou, S., Taleb-senouci, D., Guenzet, A., & Krouf, D. (2014). Zygophyllum gaetulum attenuates hypercholesterolaemia and protects against oxidative stress in rats fed a high-cholesterol diet. *Journal of Experimental and Integrative Medicine*, *4*(4), 255–260.

Bhagavan, N. V., & Ha, C.-E. (2015). Lipids II. *Essentials of Medical Biochemistry*, 299–320.

Bhagavan, N. V., & Ha, C.-E. (2011). Lipids III. *Essentials of Medical Biochemistry*, 225–239.

Bharti, U., Kumar, N. R., & Kaur, J. (2017). Modulatory Activity of Bee Pollen Against The Toxicity of Antitubersclerosis Drugs Rifampicin and Isonized in Testis of Sprague Dawley rats. *Asian Journal of Pharmaceutical and Clinical Research, 10*(9), 9–11.

Biwas, C., Bala, J., & Kharb, S. (2017). Effect of vitamin E supplementation on superoxide and malondialdehyde generation in acute celphos poisoning. *Archives of Medicine and Health Sciences, 5*(2), 200.

Bok, S. H., Shin, Y. W., Bae, K. H., Jeong, T. S., Kwon, Y. K., Park, Y. B., & Choi, M. S. (2000). Effects of naringin and lovastatin on plasma and hepatic lipids in high-fat and high-cholesterol fed rats. *Nutrition Research, 20*(7), 1007-1015.

Borradaile, N. M., Wilcox, L. J., Edwards, J. Y., & Murray, W. H. (2002). Soya phytoestrogens, genistein and daidzein, decrease apolipoprotein B secretion from HepG2 cells through multiple mechanisms. *Biochemical Journal, 366*(2), 531-539.

Boz, H. (2015). Phenolic Amides ( Avenanthramides ) in Oats – A review. Czech *Journal of Food Sciences, 33*(5), 399–404.

Brosnan, J. T., & Brosnan, M. E. (2013). Glutamate: a truly functional amino acid. *Amino acids, 45*(3), 413-418.

Brunt, E. M., Janney, C. G., Di Bisceglie, A. M., Neuschwander-Tetri, B. A., & Bacon, B. R. (1999). Nonalcoholic steatohepatitis: a proposal for grading and staging the histological lesions. *The American Journal of Gastroenterology, 94*(9), 2467.

Bunnoy, A., Saenphet, K., Lumyong, S., Saenphet, S., & Chomdej, S. (2015). Monascus purpureus -fermented Thai glutinous rice reduces blood and hepatic cholesterol and hepatic steatosis concentrations in diet-induced hypercholesterolaemic rats. *BMC Complementary and Alternative Medicin*e, *15*(88), 1–11.

Casares, D., Escribá, P. V., & Rosselló, C. A. (2019). Membrane lipid composition: effect on membrane and organelle structure, function and compartmentalization and therapeutic avenues. *International Journal of Molecular Sciences, 20*(9), 2167.

Cencic, A., & Chingwaru, W. (2010). The role of functional foods, nutraceuticals, and food supplements in intestinal health. *Nutrients,2*(6),611–625.

Chan, J., Karere, G. M., Cox, L. A., & VandeBerg, J. L. (2015). *Animal models of diet-induced hypercholesterolaemia.* Rijeka: IntechOpen.

Chang, T. Y., Li, B. L., Chang, C. C., & Urano, Y. (2009). Acyl-coenzyme A: cholesterol acyltransferases. *American Journal of Physiology-Endocrinology and Metabolism, 297*(1), E1-E9.

Charles, R. (1982). Baseline hematology and clinical chemistry values for Charles River Wistar rats (CRL (W) BR) as a function of sex and age. *Charles River Technical Bulletin, 1*(1), 1-4.

Chatterjee, C., Gleddie, S., & Xiao, C.-W. (2018). Soybean bioactive peptides and their functional properties. *Nutrients, 10*(9), 1211.

Chen, H., M McGowan, E., Ren, N., Lal, S., Nassif, N., Shad-Kaneez, F.,& Lin, Y. (2018). *Nattokinase:* A promising alternative in prevention and treatment of cardiovascular diseases. *Biomarker Insights*, *13*, 1–7.

Cheong, A. M., Jessica Koh, J. X., Patrick, N. O., Tan, C. P., & Nyam, K. L. (2018). Hypocholesterolemic effects of kenaf seed oil, macroemulsion, and nanoemulsion in high-cholesterol diet induced rats. *Journal of Food Science*, *83*(3), 854–863.

Cho, K. H., An, S., Lee, W. S., Paik, Y. K., Kim, Y. K., & Jeong, T. S. (2003). Mass-production of human ACAT-1 and ACAT-2 to screen isoform-specific inhibitor: A different substrate specificity and inhibitory regulation. *Biochemical and Biophysical Research Communications*, *309*(4), 864–872.

Choi, M. S., Do, K. M., Park, Y. B., Jeon, S. M., Jeong, T. S., Lee, Y. K., ... & Bok, S. H. (2001). Effect of naringin supplementation on cholesterol metabolism and antioxidant status in rats fed high cholesterol with different levels of vitamin E. *Annals of Nutrition and Metabolism, 45*(5), 193-201.

Daemen, S., Kutmon, M., & Evelo, C. T. (2013). A pathway approach to investigate the function and regulation of SREBPs. *Genes & Nutrition, 8*(3), 289.

Denisow, B., & Denisow-Pietrzyk, M. (2016). Biological and therapeutic properties of bee pollen : a review. *Journal of the Science of Food and Agriculture*, 96, 4303–4309.

Dong, X. Y., Tang, S. Q., & Chen, J. D. (2012). Dual functions of INSIG proteins in cholesterol homeostasis. *Lipids in Health and Disease, 11*(1), 173.

Drzikova, B., Dongowski, G., Gebhardt, E., & Habel, A. (2005). The composition of dietary fibre-rich extrudates from oat affects bile acid binding and fermentation in vitro. *Food Chemistry*, *90*(1-2), 181-192.

Duraipandiyan, V., Al-dhabi, N. A., Stephen, S., & Sunil, C. (2016). Hypolipidemic activity of friedelin isolated from *Azima tetracantha* in hyperlipidemic rats. *Revista Brasileira de Farmacognosia, 26*(1), 89–93.

Ebada, M. E. (2018). Essential oils of green cumin and chamomile partially protect against acute acetaminophen hepatotoxicity in rats. *Anais da Academia Brasileira de Ciências*, *90*(2), 2347-2358.

Ebenezar, K. K., Sathish, V., & Devaki, T. (2003). Effect of oral administration of L-arginine and L-lysine on lipid metabolism against isoproterenol-induced myocardial infarction in rats. *Journal of Clinical Biochemistry and Nutrition*, *33*(1), 7-11.

El-Din, S. H. S., Sabra, A.-N. A., Hammam, O. A., Ebeid, F. A., & El-Lakkany, N. M. (2014). Pharmacological and antioxidant actions of garlic and.or onion in non-alcoholic fatty liver disease (NAFLD) in rats. *Journal of the Egyptian Society of Parasitology*, *44*(2), 295–308.

El Rabey, H. A., Al-Seeni, M. N., & Amer, H. M. (2013). Efficiency of barley bran and oat bran in ameliorating blood lipid profile and the adverse histological changes in hypercholesterolemic male rats. *Biomed Research International*, 2013.

Esterbauer, H., Eckl, P., & Ortner, A. (1990). Possible mutagens derived from lipids and lipid precursors. *Mutation Research/Reviews in Genetic Toxicology*, *238*(3), 223–233.

Esterbauer, H., & Cheeseman, K. H. (1990). [42] Determination of aldehydic lipid peroxidation products: malonaldehyde and 4-hydroxynonenal. In *Methods in Enzymology* (Vol. 186, pp. 407-421). Academic Press.

Fattepur, S., Nilugal, K. C., Rajendran, R., Asmani, F., & Yusuf, E. (2018). Anti-hyperlipidemic activity of methanolic extract of *Boesenbergia Pandurat*a ( finger root ) in experimental induced hypercholestrolemic Sprague Dawley rats. *Asian Journal of Pharmaceutical and Clinical Research, 11*(3), 9–12.

Feingold, K. R., & Grunfeld, C. (2018). *Introduction to lipids and lipoproteins.* In: De Groot LJ, Beck-Peccoz P, Chrousos G, et al, eds. *Endotext*.South Dartmouth (MA).

Fernando, D. H., Forbes, J. M., Angus, P. W., & Herath, C. B. (2019). Development and Progression of Non-Alcoholic Fatty Liver Disease: The Role of Advanced Glycation End Products. *International Journal Of Molecular Sciences, 20*(20), 5037.

Freeman, M. W., & Walford, G. A. (2016). Lipoprotein Metabolism and the Treatment of Lipid Disorders. Endocrinology: *Adult and Pediatric*, 715–736.

Fung, W. T., Subramaniam, G., Lee, J., Loh, H. M., & Leung, P. H. H. (2012). Assessment of extracts from red yeast rice for herb-drug interaction by in-vitro and in-vivo assays. *Scientific reports*, *2*(1), 1-6.

Gabriele, M., Parri, E., Felicioli, A., Sagona, S., Pozzo, L., Biondi, C., … Unit, T. (2015). Phytochemical Composition and Antioxidant Activity of Tuscan Bee Pollen of Different Botanic Origins. *Italian Journal of Food Science*, *27*(2015),120-131.

Gani, A., Wani, S. M., Masoodi, F. A., & Hameed, G. (2012). Whole-grain cereal bioactive compounds and their health benefits: a review. *Journal Food Processing & Technology*, *3*(3), 146-56.

Gao, X., Zeng, Y., Liu, S., & Wang, S. (2013). Acute stress show great influences on liver function and the expression of hepatic genes associated with lipid metabolism in rats. *Lipids in Health and disease, 12*(1), 118.

Gardana, C., Del Bo, C., Quicazán, M. C., Corrrea, A. R., & Simonetti, P. (2018). Nutrients, phytochemicals and botanical origin of commercial bee pollen from different geographical areas. *Journal of Food Composition and Analysis*, *73*, 29-38.

Gerards, M. C., Terlou, R. J., Yu, H., Koks, C. H. W., & Gerdes, V. E. A. (2015). Traditional Chinese lipid-lowering agent red yeast rice results in signi fi cant LDL reduction but safety is uncertain e A systematic review and meta-analysis. *Atherosclerosis*, *240*(2), 415–423.

Gerhardt, A. L., & Gallo, N. B. (1998). Full-fat rice bran and oat bran similarly reduce hypercholesterolaemia in humans. *The Journal of Nutrition*, *128*(5), 865-869.

Giera, M., Lingeman, H., & Niessen, W. M. A. (2012). Recent advancements in the LC- and GC-based analysis of malondialdehyde (MDA): A brief overview. *Chromatographia*, *75*(9–10), 433–440.

Gonen, A., Harats, D., Rabinkov, A., Miron, T., Mirelman, D., Wilchek, M., & Shaish, A. (2005). The antiatherogenic effect of allicin: possible mode of action. *Pathobiology*, *72*(6), 325-334.

Govindarajan, S., & Vellingiri, K. (2016). Effect of Red Yeast Rice and Coconut, Rice Bran or Sunflower Oil Combination in Rats on Hypercholesterolaemic Diet. *Journal of Clinical and Diagnostic Research* JCDR, 10(4), BF05–BF7.

Grimm, M., Regner, L., Mett, J., Stahlmann, C., Schorr, P., Nelke, C., ... & Thiel, A. (2016). Tocotrienol affects oxidative stress, cholesterol homeostasis and the amyloidogenic pathway in neuroblastoma cells: consequences for Alzheimer's disease. *International Journal of Molecular Sciences, 17*(11), 1809.

Gruhlke, M. C., Nicco, C., Batteux, F., & Slusarenko, A. J. (2017). The effects of allicin, a reactive sulfur species from garlic, on a selection of mammalian cell lines. *Antioxidants, 6*(1), 1.

Grgurevic, I., Podrug, K., Mikolasevic, I., Kukla, M., Madir, A., & Tsochatzis, E. A. (2020). Natural History of Nonalcoholic Fatty Liver Disease: Implications for Clinical Practice and an Individualized Approach. C*anadian Journal of Gastroenterology and Hepatology,* 2020,9181368.

Gulati, S., Misra, A., & Pandey, R. M. (2017). Effects of 3 g of soluble fiber from oats on lipid levels of Asian Indians-a randomized controlled, parallel arm study. *Lipids in Health and Disease*, *16*(1), 71.

Guo, L., Tong, L. T., Liu, L., Zhong, K., Qiu, J., & Zhou, S. (2014). The cholesterol-lowering effects of oat varieties based on their difference in the composition of proteins and lipids. *Lipids In Health And Disease, 13*(1), 182.

Hakkak, R., Gauss, C. H., Bell, A., & Korourian, S. (2018). Short-term soy protein isolate feeding prevents liver steatosis and reduces serum ALT and AST levels in obese female zucker rats. *Biomedicines, 6*(2), 55.

Harini, M., & Astirin, O. P. (2009). Blood cholesterol levels of hypercholesterolaemic rat (Rattus norvegicus) after VCO treatment. *Nusantara Bioscience*, *1*(2),53-58.

Hariri, N., Gougeon, R., & Thibault, L. (2010). A highly saturated fat-rich diet is more obesogenic than diets with lower saturated fat content. *Nutrition Research, 30*(9), 632–643.

Han, Q., Yeung, S. C., Ip, M. S., & Mak, J. C. (2018). Dysregulation of cardiac lipid parameters in high-fat high-cholesterol diet-induced rat model. *Lipids in health and disease*, *17*(1), 255.

Hassan, S., Hetta, M., & Mahmoud, B. (2011). Improvement of lipid profile and antioxidant of hypercholesterolaemic albino rats by polysaccharides extracted from the green alga Ulva lactuca Linnaeus. *Saudi Journal of Biological Sciences*, *18*(4), 333–340.

Hassan Abd E, E. R., Al-Yamani, M. A. S., & Sayrafi, M. A. (2017). Effect of Saudi Propolis on Hepatitis Male Rats. *Journal of Nutrition & Food Science*, *7*(619), 2.

Herbet, M., Izdebska, M., Piątkowska-Chmiel, I., Gawrońska-Grzywacz, M., Natorska-Chomicka, D., Pawłowski, K., ... & Dudka, J. (2018). α-Tocopherol ameliorates redox equilibrium and reduces inflammatory response caused by chronic variable stress. *Biomed Research International, 2018*,1-12.

Hori, M., Satoh, M., Furukawa, K., Sakamoto, Y. I., Hakamata, H., Komohara, Y., … Horiuchi, S. (2004). Acyl-coenzyme A:cholesterol acyltransferase-2 (ACAT-2) is responsible for elevated intestinal ACAT activity in diabetic rats. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *24*(9), 1689–1695.

Hochwald, L. (2016). What is natto?. Mother Nature Network. Retrieved on 15th ,July 2019 from https://www.mnn.com/food/healthy-eating/stories/what-natto.

Hsu, A., Bray, T. M., Helferich, W. G., Doerge, D. R., & Ho, E. (2010). Differential effects of whole soy extract and soy isoflavones on apoptosis in prostate cancer cells. *Experimental Biology and Medicine, 235*(1), 90-97.

Hofmann, A. F., & Hagey, L. R. (2008). Review Bile Acids : Chemistry , Pathochemistry , Biology , Pathobiology , and Therapeutics. *Cellular and Molecular Life Sciences, 65*, 2461–2483.

Institute for Public Health 2020*. National Health and Morbidity Survey (NHMS) 2019:* Non-communicable diseases, healthcare demand, and health literacy—Key Findings.

Ito, F., Sono, Y., & Ito, T. (2019). Measurement and clinical significance of lipid peroxidation as a biomarker of oxidative stress: Oxidative stress in diabetes, atherosclerosis, and chronic inflammation. *Antioxidants, 8*(3), 72.

Iwai, K., Nakaya, N., Kawasaki, Y., & Matsue, H. (2002). Antioxidative functions of natto, a kind of fermented soybeans: effect on LDL oxidation and lipid metabolism in cholesterol-fed rats. *Journal of Agricultural and Food Chemistry*, *50*(12), 3597-3601.

Jadoon, S., & Malik, A. (2017). A review article on the formation, mechanism and biochemistry of MDA and MDA as a biomarker of oxidative stress. *International Journal of Advanced Research*, *5*(12), 811–818.

Jahala, O. A. M., Izzeldin, O. M., & Abdalla, R. E. (2014). Effect of Fagonia cretica linn ethanolic extract on different hematological parameters in albino rats in Sudan. *Journal of Biological and Medical Sciences,1*(4),100-104.

Janero, D. R. (1990). Malondialdehyde and thiobarbituric acid-reactivity as diagnostic indices of lipid peroxidation and peroxidative tissue injury. *Free Radical Biology & Medicine*, *9*(6), 515–540.

Jayusman, P. A., Budin, S. B., Taib, I. S., & Ghazali, A. R. (2017). The effect of tocotrienol-rich fraction on oxidative liver damage induced by fenitrothion. *Sains Malaysiana, 46*(9), 1603-1609.

Joles, J. A., Kunter, U. T. A., Janssen, U. L. F., Kriz, W., Rabelink, T. J., Koomans, H. A., & Floege, J. (2000). Early mechanisms of renal injury in hypercholesterolaemic or hypertriglyceridemic rats. *Journal of the American Society of Nephrology, 11*(4), 669-683.

Jonas, A. (2002). Lipoprotein structure. In *New Comprehensive Biochemistry* (Vol. 36, pp. 483-504). Elsevier.

Kai, N. S., Nee, T. A., Lai, E., Ling, C., Ping, T. C., Kamariah, L., & Kar, N. (2015). Anti-hypercholesterolaemic effect of kenaf ( *Hibiscus cannabinus L* .) seed on high-fat diet Sprague dawley rats. *Asian Pacific Journal of Tropical Medicine*, *8*(1), 6–13.

Kamesh, V., & Sumathi, T. (2012). Antihypercholesterolaemic effect of *Bacopa monniera linn* . on high cholesterol diet induced hypercholesterolaemia in rats. *Asian Pacific Journal of Tropical Medicine, 5*(12), 949–955.

Kang, H. (2017). Hypocholesterolemic Effect of Ginkgo Biloba Seeds Extract from High Fat Diet Mice. *Biomedical Science Letters*, *23*(2), 2–7.

Karanjia, R. N., Crossey, M. M., Cox, I. J., Fye, H. K., Njie, R., Goldin, R. D., & Taylor-Robinson, S. D. (2016). Hepatic steatosis and fibrosis: Non-invasive assessment. *World Journal of Gastroenterology, 22(*45), 9880.

Kaya, E., Yılmaz, S., & Ceribasi, S. (2019). Protective role of propolis on low and high dose furan-induced hepatotoxicity and oxidative stress in rats. *Journal of Veterinary Research, 63,* 423–431.

Mohd Adzim Khalili, R., Norhayati, A. H., Rokiah, M. Y., Asmah, R., Siti Muskinah, M., & Abdul Manaf, A. (2009). Hypocholesterolemic effect of red pitaya (Hylocereus sp.) on hypercholesterolaemia induced rats. *International Food Research Journal*, *16*(3),431-440.

Mourad, A. M., de Carvalho Pincinato, E., Mazzola, P. G., Sabha, M., & Moriel, P. (2010). Influence of soy lecithin administration on hypercholesterolaemia. Cholesterol, 2010,1-4.

Kim, J., Choi, J. N., Kang, D., Son, G. H., Kim, Y., Choi, H., & Lee, C. H. (2011). Correlation between antioxidative activities and metabolite changes during cheonggukjang fermentation. *Bioscience Biotechnology and Biochemistry, 75*(4), 732–739.

Kocot, J., Kiełczykowska, M., Luchowska-kocot, D., Kurzepa, J., & Musik, I. (2018). Review article antioxidant potential of propolis , bee pollen , and royal jelly : possible medical application. *Oxidative Medicine and Cellular Longevity, 2018,* 1–29.

Komosinska-Vassev, K., Olczyk, P., Kazmierczak, J., Mencner, L., & Olczyk, K. (2015). Bee pollen: chemical composition and therapeutic application. *Evidence-Based Complementary and AlternativeMedicine*, *2015* (2015), 1–6.

Kongbuntad, W., & Saenphet, S. (2016). Effects of red mold rice produced from *Monascus purpureu*s CMU002U on growth performances and antioxidant activity of japanese quail. *International Journal of Poultry Science*, *15*(1), 9–12.

Kopaei, M.R., Setorki, M., Doudi, M., Baradaran, A., & Nasri, H. (2014). Atherosclerosis: process, indicators, risk factors and new hopes. *International Journal of Preventive Medicine, 5*(8), 927–946.

Kourounakis, A. P., Rekka, E. A., & Kourounakis, P. N. (1997). Antioxidant activity of guaiazulene and protection against paracetamol hepatotoxicity in rats. *Journal of Pharmacy and Pharmacology, 49*(9), 938-942.

Kurosawa, Y., Nirengi, S., Homma, T., Esaki, K., Ohta, M., Clark, J. F., & Hamaoka, T. (2015). A single-dose of oral nattokinase potentiates thrombolysis and anti-coagulation profiles. *Scientific Reports*, *5*, 11601.

Kumar, M. S., Pandita, N. S., & Pal, A. K. (2012). LC-MS / MS as a tool for identifi cation of bioactive compounds in marine sponge *Spongosorites halichondriodes* ( Dendy 1905).*Toxicon*, *60*(6),1135–1147.

Kwan, M. (2018). Bee pollen can treat autism says research. Health Journal. Retrieved on 15th July 2019 from https://tophealthjournal.com/2768/bee-pollen-can-treat-autism-says-research.

Lachhiramka, P., & Patil, S. (2016). Cholesterol lowering property of garlic (Allium sativum) on patients with hypercholesterolaemia. *International Journal of Medical Science and Public Health*, *5*(11), 2249.

Lecumberri, E., Goya, L., Mateos, R., Alía, M., Ramos, S., Izquierdo-pulido, M., & Bravo, L. (2007). A diet rich in dietary fiber from cocoa improves lipid profile and reduces malondialdehyde in hypercholesterolaemic rats. *Nutrition, 23*(2007), 332–341.

Lee, M. T., Lin, W. C., Yu, B., & Lee, T. T. (2017). Antioxidant capacity of phytochemicals and their potential effects on oxidative status in animals — A review. *Asian-Australasian Journal of Animal Sciences*, *30*(3), 299–308.

Lee, S., Kim, C., Jang, H., Cho, S., & Choi, J. (2011). Anti-hyperlipidemia and Anti-arteriosclerosis Effects of *Laminaria japonica* in Sprague-Dawley Rats. *Fisheries and Aquatic Sciences*, *14*(4), 235–241.

Lee, M., Moon, S., Lee, S., Bok, S., Jeong, T., Bok, Y., & Choi, M. (2003). Naringenin 7- O -cetyl Ether as Inhibitor of HMG-CoA Reductase and Modulator of Plasma and Hepatic Lipids in High Cholesterol-Fed Rats. *Bioorganic & Medicinal Chemistry, 11*(2003), 393–398.

Li, X., Ji, L., Fu, Y., Ying, Y., & Hu, Y. (2012, May). Effects of Ginkgo Biloba Extract on Cellular Cholesterol Content and CD36 Expression of Macrophages from Diabetic Rats. In *2012 International Conference on Biomedical Engineering and Biotechnology* (pp. 221-223).

Li, Y., Luo, Y., Chen, G., Xiao, Z., Wang, Q., Zhao, L., & Ji, B. (2011). Comparison of protective effects between oat β-Glucan and phenol-rich extracts in hyperlipidemic ICR mice. *Journal of Food and Drug Analysis, 19*(1), 49–57.

Limantara, L., Indrawati, R., Wijaya, D. E., Sulistiawati, E., Suparto, H., Dumilah, R., Panintingjati, T. H. (2017). Hypercholesterolaemic effect and pigments composition of herbal medicine containing higher and lower plants. *International Journal of Pharmacy and Pharmaceutical Sciences, 9(*11), 97-103.

Lin, Chao-zhan, Zhang, R., Yao, Y., Huang, X., Zheng, R., Wu, B.-J., & Zhu, C.-C. (2018). Qualitative and quantitative analysis of the major constituents in WLJ Herbal Tea Using Multiple Chromatographic Techniques. *Molecules, 23,* 1–12.

Lin, C., Tsai, C., & Lin, S. (2005). Effects of soy components on blood and liver lipids in rats fed high-cholesterol diets. *World Journal of Gastroenterology, 11*(35), 5549–5552.

Liu, S., He, L., & Yao, K. (2018). The antioxidative function of alpha-ketoglutarate and its applications. *Biomed Research International,* 2018,1-6.

Liu, Y., An, W., & Gao, A. (2016). Protective effects of naringenin in cardiorenal syndrome. *Journal of Surgical Research*, *203*(2), 416–423.

Liu, H., Pathak, P., Boehme, S., & Chiang, J. Y. (2016). Cholesterol 7α-hydroxylase protects the liver from inflammation and fibrosis by maintaining cholesterol homeostasis. Journal of Lipid Research, *57*(10), 1831-1844.

Liu, Y., Yang, J., Lei, L., Wang, L., Wang, X., Ma, K. Y., ... & Chen, Z. Y. (2019). Isoflavones enhance the plasma cholesterol-lowering activity of 7S protein in hypercholesterolaemic hamsters. *Food & Function, 10*(11), 7378-7386.

Lu, C., Hou, M., Lin, L., & Tsai, T. (2013). Chemical and physical methods to analyze a multicomponent traditional chinese herbal prescription using lc-ms / ms , electron microscope , and congo red staining. *Evidence-Based Complementary and Alternative Medicine, 2013*, 1–10.

Lobo, V., Patil, A., Phatak, A., & Chandra, N. (2010). Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacognosy Reviews, 4*(8), 118.

Madani, S., Prost, J., Narce, M., & Belleville, J. (2003). VLDL metabolism in rats is affected by the concentration and source of dietary protein. *The Journal of Nutrition*, *133*(12), 4102-4106.

Majewski, M. (2014). *Allium sativum* : Facts and myths regarding human health. *National Institute of Public Health - National Institute of Hygiene*, *65*(1), 1–8.

Marcucci, M. C. (1995). Propolis: chemical composition, biological properties and therapeutic activity. *Apidologie*, *26*(2), 83–99.

Matei, A. O., Gatea, F., & Radu, G. L. (2015). Analysis of phenolic compounds in some medicinal herbs by LC–MS. *Journal of Chromatographic Science*, *53*(7), 1147-1154.

Matos, S. L., Paula, H. De, Pedrosa, M. L., Cardoso, R., Oliveira, E. L. De, Alves, D., … Silva, E. (2005). Dietary models for inducing hypercholesterolaemia in rats. *Brazilian Archives of Biology and Technology, 48*(2), 203–209.

McGill, M. R. (2016). The past and present of serum aminotransferases and the future of liver injury biomarkers. *EXCLI Journal*, *15*, 817.

Mehta, V., & Bhatt, K. (2017). Lipids and its metabolism. *Journal of Cardiology & Cardiovascular Therapy*, *4*(2),555635.

Millar, C. L., Duclos, Q., & Blesso, C. N. (2017). Effects of dietary flavonoids on reverse cholesterol transport , HDL metabolism and HDL function. *Advanced Nutrition, 8,* 226–229.

Miranda-Velasquez, L., Oranday-Cardenas, A., Lozano-Garza, H., Rivas-Morales, C., Chamorro-Cevallos, G., & Cruz-Vega, D. E. (2010). Hypocholesterolemic activity from the leaf extracts of *Cnidoscolus chayamansa*. *Plant Foods For Human Nutrition, 65*(4), 392-395.

Mohdaly, A. A., Roby, M., Smetanska, I., Fawzy, M., & Hassanien, R. (2015). Phenolic Extract from Propolis and Bee Pollen : Composition , Antioxidant and Antibacterial Activities. *Journal of Food Biochemistry, 39*(2015), 538–547.

Moosmann, B., & Behl, C. (2004). Selenoprotein synthesis and side-effects of statins. *Hypothesis*, *363*(9412*)*, 892–894.

Morgano, M. A., Milani, R. F., Martins, M. C. T., & Rodriguez-Amaya, D. B. (2011). Determination of water content in Brazilian honeybee-collected pollen by Karl Fischer titration. *Food Control*, *22*(10), 1604–1608.

Mu, F., Rich-edwards, J., Rimm, E. B., Spiegelman, D., Forman, J. P., & Missmer, S. A. (2017). Association between endometriosis and hypercholesterolaemia or hypertension. *Epidemiology/ Population*, (7), 59–65.

Mujica, V., Orrego, R., Pérez, J., Romero, P., Ovalle, P., Zúñiga-Hernández, J., … Leiva, E. (2017). The role of propolis in oxidative stress and lipid metabolism: a randomized controlled trial. *Evidence-Based Complementary and Alternative Medicine*, *2017*, 1–11.

Nakamura, T., Ohta, Y., Ohashi, K., Ikeno, K., Watanabe, R., Tokunaga, K., & Harada, N. (2013). Protective Effect of Brazilian Propolis against Liver Damage with Cholestasis in Rats Treated with-Naphthylisothiocyanate. *Evidence-Based Complementary And Alternative Medicine*, *2013*.

Nagy, G., Farkas, A., Csernetics, Á., Bencsik, O., Szekeres, A., Nyilasi, I., ... & Papp, T. (2014). Transcription of the three HMG-CoA reductase genes of Mucor circinelloides. *BMC Microbiology, 1*4(1), 93.

Nascimbeni, F., Pellegrini, E., Lugari, S., Mondelli, A., Bursi, S., Onfiani, G., & Lonardo, A. (2019). Statins and nonalcoholic fatty liver disease in the era of precision medicine: More friends than foes. *Atherosclerosis*, *284*(2019), 66-74.

Nassir, F., Rector, R. S., Hammoud, G. M., & Ibdah, J. A. (2015). Pathogenesis and prevention of hepatic steatosis. *Gastroenterology & Hepatology, 11*(3), 167.

National Institute of Health Office of Dietary Supplements. (1994). Dietary Supplement Health and Education Act of 1994 Public Law 103-417 103rd Congress. Retrieved on February, 5th, 2020 from https://ods.od.nih.gov/About/DSHEA_Wording.aspx.

Nelson, R. H. (2013). Hyperlipidemia as a risk factor for cardiovascular disease. *Primary Care: Clinics in Office Practice*, *40*(1), 195-211.

Nguyen, H. T. L., Panyoyai, N., Kasapis, S., Pang, E., & Mantri, N. (2019). Honey and its role in relieving multiple facets of atherosclerosis. *Nutrients, 17*(167), 1–22.

Nguyen, T., Karl, M., & Santini, A. (2017). Red Yeast Rice. *Foods*, *6*(19), 13–16.

Nurhidajah, Astuti, R., & Nurrahman. (2019). Black rice potential in HDL and LDL profile in Sprague Dawley Rat with high cholesterol diet. In *International Conference on Food Science & Technology* (pp. 2–7).

Nurmasitoh, T., & Pramaningtyas, M. D. (2016). Honey improves lipid profile of diet-induced hypercholesterolaemic rats Correspondence : *Universa Medicina*, *34*(3), 177–186.

Olorunnisola, O., Bradley, G., & Afolayan, A. J. (2012). Anti-hyperlipidemic and biochemical effect of extract of T*ulbaghia violacea rhizome*s on high cholesterol diet fed rats. *African Journal of Biotechnology, 11*(70), 13498–13505.

Orekhov, A. N., & Tertov, V. V. (1997). In Vitro effect of garlic powder extract on lipid content in normal and atherosclerotic human aortic cells. *Lipids in Health and Disease, 32*(10), 1057–1059.

Orth, M., & Bellosta, S. (2012). Cholesterol: Its regulation and role in central nervous system disorders. *Cholesterol*, *2012*, 1-19.

Palani, S., Joseph, N. M., Tegene, Y., & Zacharia, A. (2014). Medicinal Properties of Garlic – A concise review. *Current Research in Pharmaceutical Sciences*, *04*(04), 92–98.

Park, Y., Park, E., Kim, E., & Chung, I. (2014). Hypocholesterolemic metabolism of dietary red pericarp glutinous rice rich in phenolic compounds in mice fed a high cholesterol diet. *Nutrition Research and Practice, 8*(6), 632–637.

Park, K., Kang, J. Il, Kim, T., & Yeo, I. (2012). The antithrombotic and fibrinolytic effect of natto in hypercholesterolaemia rats. *Preview Nutrition Food Science*, *17*(1), 78–82.

Pastori, D., Polimeni, L., Baratta, F., Pani, A., Del Ben, M., & Angelico, F. (2015). The efficacy and safety of statins for the treatment of non-alcoholic fatty liver disease. *Digestive and Liver Disease, 47*(1), 4-11.

Pavadhgul, P., Bumrungpert, A., & Harjani, Y. (2019). Oat porridge consumption alleviates markers of inflammation and oxidative stress in hypercholesterolaemic adults. *Asia Pacific Journal of Clinical Nutrition, 28*(2), 260–265.

Peng, J., Luo, F., Ruan, G., Peng, R., & Li, X. (2017). Hypertriglyceridemia and atherosclerosis. *Lipids in Health and Disease, 16*(1), 233.

Pengnet, S., Prommaouan, S., Sumarithum, P., & Malakul, W. (2019). Naringin reverses high-cholesterol diet-induced vascular dysfunction and oxidative stress in rats via regulating LOX-1 and NADPH oxidase subunit expression. *Biomed Research International,* 2019,1-11.

Phaniendra, A., Jestadi, D. B., & Periyasamy, L. (2015). Free radicals: properties, sources, targets, and their implication in various diseases. *Indian Journal of Clinical Biochemistry, 30*(1), 11-26.

Podrez, E. A. (2010). Anti-oxidant properties of high-density lipoprotein and atherosclerosis. *Clinical and Experimental Pharmacology and Physiology*, *37*(7), 719-725.

Pramfalk, C., Eriksson, M., & Parini, P. (2012). Cholesteryl esters and ACAT. *European Journal of Lipid Science and Technology*, *114*(6), 624–633.

Presa, N., Clugston, R. D., Lingrell, S., Kelly, S. E., Merrill Jr, A. H., Jana, S., ... & van der Veen, J. N. (2019). Vitamin E alleviates non-alcoholic fatty liver disease in phosphatidylethanolamine N-methyltransferase deficient mice. *Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease, 1865*(1), 14-25.

Puttaswamy, N. Y., & Urooj, A. (2016). In Vivo Antihypercholesterolaemic Potential of Swietenia mahagoni Leaf Extract. *Cholesterol*, *2016,* 1–6.

Püschel, G. P., & Henkel, J. (2018). Dietary cholesterol does not break your heart but kills your liver. *Porto Biomedical Journal, 3*(1), 1–7.

Pyo, Y. H., & Seong, K. S. (2009). Hypolipidemic effects of Monascus-fermented soybean extracts in rats fed a high-fat and-cholesterol diet. *Journal of Agricultural and Food Chemistry,* 57(18), 8617-8622.

Qiu, J., Chen, X., Netrusov, A.I., Zhou, Q., Guo, D., Liu, X., He, H.,Xin, X., Wang, Y., & Chen, L . (2017) Screening and identifying antioxidative components in *Ginkgo Biloba* pollen by DPPH-HPLC-PAD Coupled with HPLC-ESI-MS2. *PLoS ONE 12*(1),1-12.

Rasane, P., Jha, A., Sabikhi, L., Kumar, A., & Unnikrishnan, V. S. (2015). Nutritional advantages of oats and opportunities for its processing as value added foods-a review. *Journal of Food Science and Technology, 52*(2), 662-675.

Rebello, C. J., O'Neil, C. E., & Greenway, F. L. (2016). Dietary fiber and satiety: the effects of oats on satiety. *Nutrition Reviews, 74*(2), 131-147.

Repetto, M., Semprine, J., & Boveris, A. (2012). Lipid Peroxidation: Chemical Mechanism, Biological Implications and Analytical Determination. *InTech, 1*(2012), 3–30.

Rajeswari, R., Divya, J., Jayasudha, E., Thellamudhu, G., Suresh, M., Raman, T. K., ... & Kalaiselvi, P. (2017). Impact of high cholesterol diet in mediating inflammation provoked calcinosis in renal tissue of experimental rats. *Indian Journal of Biochemistry & Biophysics, 54,* 71-81.

Rudel, L. L., Lee, R. G., & Cockman, T. L. (2001). Acyl coenzyme A : cholesterol acyltransferase types 1 and 2 : structure and function in atherosclerosis. *Current Opinion in Lipidology*, *12*(121–127), 121–127.

Rudel, L. L, Lee, R. G., & Parini, P. (2005). ACAT2 Is a target for treatment of coronary heart disease associated with hypercholesterolaemia. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *25*(6), 1112–1118.

Rzepecka-Stojko, A.., Stojko, J., Jasik, K., & Buszman, E. (2017). Anti-atherogenic activity of polyphenol-rich extract from bee pollen. *Nutrients*, *9*(12),1369.

Rzepecka-stojko, A., Stojko, J., & Kubina, R. (2015). Polyphenols from Bee Pollen : Structure , Absorption , Metabolism and Biological Activity. *Molecules, 20*, 21732–21749.

Sakashita, N., Miyazaki, A., Takeya, M., Horiuchi, S., Chang, C. C., Chang, T. Y., & Takahashi, K. (2000). Localization of human acyl-coenzyme A: cholesterol acyltransferase-1 (ACAT-1) in macrophages and in various tissues. *The American Journal of Pathology, 156*(1), 227-236.

Samout, N., Bouzenna, H., Ettaya, A., Elfeki, A., & Hfaiedh, N. (2015). Antihypercholesterolaemic effect of *Cleome Arabica L* on high cholesterol diet induced damaged in rats. *EXCLI Journal, 14*, 791–800.

Santini, A., & Novellino, E. (2017). Nutraceuticals in hypercholesterolaemia: an overview. *British Journal of Pharmacology*, *174*(11), 1450–1463.

Sarega, N., Imam, M. U., Ooi, D., Chan, K. W., Esa, N., Zawawi, N., & Ismail, M. (2016). Phenolic Rich Extract from Clinacanthus nutans Attenuates Hyperlipidemia- Associated Oxidative Stress in Rats. *Oxidative Medicine and Cellular Longevity*, 2016, 1–16.

Sayeed, B., S., M., Karim, S. M. R., Sharmin, T., & Morshed, M. M. (2016). Critical analysis on characterization, systemic effect, and therapeutic potential of beta-sitosterol: a plant-derived orphan phytosterol. *Medicines, 3*(4), 29.

Sellmann, C.S., Baumann, A., Brandt, A., Jin, C. J., Nier, A., & Bergheim, I. (2017). Oral supplementation of glutamine attenuates the progression of nonalcoholic steatohepatitis in c57bl/6j mice. *The Journal of Nutrition, 147*(11), 2041-2049.

Selamoglu, Z. S., Ozdemir, I., Ciftci, O., Gulhan, M. F., & Savci, A. (2015). Antioxidant effect of ethanolic extract of propolis in liver of L-name treated rats. *Advances in Clinical and Experimental Medicine*, *24*(2), 227-232.

Sen, C. K., Khanna, S., & Roy, S. (2007). Tocotrienols in health and disease: the other half of the natural vitamin E family. *Molecular Aspects of Medicine*, *28*(5-6), 692-728.

Schemitt, E. G., Hartmann, R. M., Colares, J. R., Licks, F., Salvi, J. O., Marroni, C. A., & Marroni, N. P. (2019). Protective action of glutamine in rats with severe acute liver failure. *World Journal of Hepatology, 11*(3), 273.

Sforcin, J. M. (2007). Propolis and the immune system: a review. *Journal of Ethnopharmacology*, *113*(1), 1–14.

Sharma, A.K.; Bharti, S.; Ojha, S.; Bhatia, J.; Kumar, N.; Ray, R.; Kumari, S.; Arya, D.S.(2011). Up-regulation of PPARγ, heat shock protein-27 and -72 by naringin attenuates insulin resistance, β-cell dysfunction, hepatic steatosis and kidney damage in a rat model of type 2 diabetes. *British Journal of Nutrition, 106*, 1713–172.

Sharpe, L. J., & Brown, A. J. (2013). Controlling cholesterol synthesis beyond 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR). *Journal of Biological Chemistry, 288*(26), 18707-18715.

Simmons, M. (2018). The sweet cure: Brazilian propolis can prevent metabolic disorders such as Type 2 diabetes and arteriosclerosis. *Health News.* Retreived on 15th July 2019 from https://health.news/2018-07-10-the-sweet-cure-brazilian-propolis-can-prevent-metabolic-disorders.html.

Sobral, F., Calhelha, R., Barros, L., Dueñas, M., Tomás, A., Santos-Buelga, C., ... & Ferreira, I. (2017). Flavonoid composition and antitumor activity of bee bread collected in northeast Portugal. *Molecules, 22*(2), 248.

Soliman A. Ghada. (2018). Dietary Cholesterol and the Lack of Evidence in Cardiovascular Disease. *Nutrients*, *10*(780), 1–14.

Suzuki, J., Eduardo, K., Ribeiro, C., Rezende, G., Carlos, A., César, Á., & Penoni, D. O. (2018). Effects of simvastatin associated with exercise on the mechanical resistance of muscle and bone in rats. *Revista Brasileira de Ortopedia, 53*(3), 287–292.

Takahashi, Y., & Fukusato, T. (2014). Histopathology of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. *World Journal of Gastroenterology: WJG*, *20*(42), 15539.

Tapiero, H., Mathe, G., Couvreur, P., & Tew, K. D. (2002). II. Glutamine and glutamate. Biomedicine & pharmacotherapy, 56(9), 446-457.abas, I., García-Cardeña, G., & Owens, G. K. (2015). Recent insights into the cellular biology of atherosclerosis. *Journal of Cell Biology*, *209*(1), 13–22.

Tzanetakou, I. P., Doulamis, I. P., Korou, L. M., Agrogiannis, G., Vlachos, I. S., Pantopoulou, A., ... & Perrea, D. N. (2012). Water soluble vitamin E administration in Wistar rats with non-alcoholic fatty liver disease. *The Open Cardiovascular Medicine Journal, 6*, 88.

The Heart Foundation of Malaysia. (2019).Inherited cholesterol disorder. Retrieved March 15th, 2019, from http://www.yjm.org.my/index.cfm?&menuid=35

Tiwari, V., & Khokhar, M. (2014). Mechanism of action of anti-hypercholesterolaemia drugs and their resistance. *European Journal of Pharmacology*, *741*(2014), 156–170.

Tiwari, R., & Pathak, K. (2011). Statins therapy: a review on conventional and novel formulation approaches. *Journal of Pharmacy and Pharmacology*, *63*(8), 983-998.

Tong, L., Zhong, K., Liu, L., Qiu, J., Guo, L., Zhou, X., … Zhou, S. (2014). Effects of dietary wheat bran arabinoxylans on cholesterol metabolism of hypercholesterolaemic hamsters. *Carbohydrate Polymers*, *112*, 1–5.

Usman, U. Z., Bakar, A. B. A., Zin, A. A. M., & Mohamed, M. (2017). LC-MS analysis and effects of Malaysian propolis on insulin, glucagon, pancreas and oxidative stress status in streptozotocin-induced diabetic rats. *Journal of Medicine and Biomedical Research*, *16*(1), 15-27.

Venero, J. L., Revuelta, M., Atiki, L., Santiago, M., Tomás-Camardiel, M. C., Cano, J., & Machado, A. (2003). Evidence for dopamine-derived hydroxyl radical formation in the nigrostriatal system in response to axotomy. *Free Radical Biology and Medicine*, *34*(1), 111–123.

Verhoeven, V., Lopez Hartmann, M., Remmen, R., Wens, J., Apers, S., & Van Royen, P. (2013). Red yeast rice lowers cholesterol in physicians - a double blind, placebo controlled randomized trial. *BMC Complementary and Alternative Medicine*, *13*(1), 2–7.

Vlase, L., Parvu, M., Parvu, E. A., & Toiu, A. (2013). Phytochemical Analysis of *Allium Fistulosum L*. and *A. Ursinum L. Digest Journal of Nanomaterials & Biostructures (DJNB)*, *8*(1), 457-467.

Vučić, V., & Cvetković, Z. (2016). Cholesterol: Absorption, Function and Metabolism. *Encyclopedia of Food and Health*, *2016*, 47–52.

Wan Saidatul Syida, W. K., Noriham, A., Normah, I., & Mohd Yusuf, M. (2018). Changes in chemical composition and amino acid content of soy protein isolate (SPI) from tempeh. *International Food Research Journal, 25*(4),1-6.

Wang, Y. M., Zhang, B., Xue, Y., Li, Z. J., Wang, J. F., Xue, C. H., & Yanagita, T. (2010). The mechanism of dietary cholesterol effects on lipids metabolism in rats. *Lipids in Health and Disease, 9*(1), 4.

Wani, S. A., Shah, T. R., Bazaria, B., Nayik, G. A., Gull, A., Muzaffar, K., & Kumar, P. (2014). Oats as a functional food : A review. *Universal Journal of Pharmacy, 3*(1), 14–20.

Weng, Y., Yao, J., Sparks, S., & Wang, K. Y. (2017). Nattokinase: An oral antithrombotic agent for the prevention of cardiovascular disease. *International Journal of Molecular Sciences*, *18*(3), 1-13.

Wilcox, L. J., Borradaile, N. M., & Huff, M. W. (1999). Antiatherogenic properties of naringenin, a citrus flavonoid. *Cardiovascular Drug Reviews, 17*(2), 160-178.

Whitehead, A., Beck, E. J., Tosh, S., & Wolever, T. M. S. (2014). Cholesterol-lowering effects of oat b -glucan : a meta-analysis of randomized controlled trials 1 – 4. *The American Journal Of Clinical Nutrition, 100*(6), 1413–1421.

Wollam, J., & Antebi, A. (2011). Sterol Regulation of Metabolism , Homeostasis , and Development. *Annual Review of Biochemistry I*,80(2011), *885–907*.

Wong, C. (2019). The Health Benefits of Allicin; Garlic's Heart-Health Booster.*Very Well Health.* Retrieved on 15th July 2019 from https://www.verywellhealth.com/the-benefits-of-allicin-88606

World Health Organization (WHO). Raised cholesterol, situation and trends. (2017). Retrieved on January, 2nd 2019, from https://www.who.int/gho/ncd/risk_factors/cholesterol_text/en

Xie, Y., Liang, X., Wei, M., Zhao, W., He, B., Lu, Q., ... & Ma, C. (2012). Optimization of glutamine peptide production from soybean meal and analysis of molecular weight distribution of hydrolysates. *International Journal of Molecular Sciences, 13*(6), 7483-7495.

Yan, Z., Fan, R., Yin, S., Zhao, X., Liu, J., Li, L., … Ge, L. (2015). Protective effects of *Ginkgo biloba leaf* polysaccharide on nonalcoholic fatty liver disease and its mechanisms. *International Journal of Biological Macromolecules*, *80*, 573–580.

Yang, C., Li, L., Yang, L., Hui, L., Wang, S., & Sun, G. (2018). Anti-obesity and Hypolipidemic effects of garlic oil and onion oil in rats fed a high-fat diet. *Nutrition & Metabolism, 15*(43), 4–11.

Yao, Z. X., Han, Z., Drieu, K., & Papadopoulos, V. (2004). *Ginkgo biloba* extract (Egb 761) inhibits β-amyloid production by lowering free cholesterol levels. *Journal of Nutritional Biochemistry*, *15*(12), 749–756.

Yeap, S. K., Beh, B. K., Kong, J., Ho, W. Y., Mohd Yusof, H., Mohamad, N. E., & Long, K. (2014). In vivo hypocholesterolemic effect of MARDI fermented red yeast rice water extract in high cholesterol diet fed mice. *Evidence-Based Complementary and Alternative Medicine*, 2014,707829.

Yeap, S. K., Beh, B. K., Ho, W. Y., Mohd Yusof, H., Mohamad, N. E., Ali, N. M., &Long, K. (2015). In vivo antioxidant and hypolipidemic effects of fermented mung bean on hypercholesterolaemic mice. *Evidence-Based Complementary and Alternative Medicine,* 2015.

Yeh, Y., Lee, Y., Hsieh, H., & Hwang, D. (2010). Dietary cholestin ( red yeast extract ) reduces toxicity of oxidized cholesterol in rats. *Journal of Food and Drug Analysis, 18*(3), 211–220.

Yeh, Y. Y., & Liu, L. (2001). Cholesterol-lowering effect of garlic extracts and organosulfur compounds: human and animal studies. *The Journal of Nutrition*, *131*(3), 989S-993S.

Zakerkish, M., Jenabi, M., Zaeemzadeh, N., & Hemmati, A. A. (2019). The effect of iranian propolis on glucose metabolism , lipid profile , insulin resistance , renal function and inflammatory biomarkers in patients with type 2 diabetes mellitus : a randomized double- blind clinical trial. *Scientific Reports,* 9, 1–11.

Zeb, A., & Khan, A. A. (2019). Improvement of serum biochemical parameters and hematological indices through α -tocopherol administration in dietary oxidized olive oil induced toxicity in rats. *Frontiers in Nutrition, 5*(1), 1–8.

Zeka, K., Ruparelia, K., Arroo, R. R. J., Budriesi, R., & Micucci, M. (2017). Flavonoids and their metabolites : *Prevention in Cardiovascular Diseases and Diabetes. Diseases, 5*(19), 1–18.

Zhang, J., & Liu, Q. (2015). Cholesterol metabolism and homeostasis in the brain. *Protein and Cell*, *6*(4), 254–264.

Zhu, W., Chen, M., Shou, Q., Li, Y., & Hu, F. (2011). Biological activities of Chinese propolis and Brazilian propolis on streptozotocin-induced type 1 diabetes mellitus in rats. *Evidence-Based Complementary and Alternative Medicine*, *2011*.

Zou, X., Huang, Y., Li, H., Fan, Y., Li, J., Deng, Z., & Xu, T. (2018). Effects of Chinese dietary pattern of fat content , n-6 / n-3 polyunsaturated fatty acid ratio , and cholesterol content on lipid profile in rats. *BioMed Research International*, *2018*, 1–13.

Zulkhairi, H. A., Khairunnuur, A. F., Hafipah, M. R. N., Azrina, A., Rasadah, M. A., Kamilah, K. A. K., & Shahidan, M. A. (2010). An aqueous extract of *Citrus mitis* possesses antioxidative properties and improves plasma lipid profiles in rat induced with high cholesterol diet. *Journal of Medicinal Plants Research, 4*(1), 049-057.

Zwer, P. (2017). Oats: Grain-quality characteristics and management of quality requirements. In *Cereal Grains* (pp. 235-256). Woodhead Publishing.