BIOFUNCTIONAL CHARACTERISTICS OF DIETARY FIBER EXTRACTED FROM MALAYSIAN *ZIZIPHUS MAURITIANA* L. LEAVES AND ITS ASSOCIATION *IN VITRO* ANTIDIABETICS PROPERTIES

By

NUR SYUHADA BINTI ZAHARI

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

June 2021

FBSB 2021 40

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

BIOFUNCTIONAL CHARACTERISTICS OF DIETARY FIBER EXTRACTED FROM MALAYSIAN *ZIZIPHUS MAURITIANA* L. LEAVES AND ITS ASSOCIATION *IN VITRO* ANTIDIABETICS PROPERTIES

By

NUR SYUHADA BINTI ZAHARI

June 2021

Chair : Associate Professor Uswatun Hasanah Binti Zaidan, PhD
Faculty : Biotechnology and Biomolecular Sciences

Ziziphus mauritiana L. derived from Rhamnaceae family plant (known as Bidara tree in Malaysia) has been consumed by Malaysian through processing the fruit into pickles or eating it fresh, while the leaves are frequently used in traditional medicine, particularly in Islamic medicine. Although the *Z. mauritiana* L. plant rich in macronutrients, micronutrients, and phytochemicals that offer health benefits, yet, it is still considered underutilized in Malaysia due to a lack of scientific information about the health promoting effect of its fiber. In other countries, *Z. mauritiana* L. also used widely as traditional medicine and recently researchers start to study scientifically the health benefits of this plant especially in Asian country. The purpose of the study was therefore to explore the physicochemical properties relevant to the nutritional quality of one of the sources of dietary fiber (mucilage) necessary for the maintenance of population health in the community, especially in treating diabetes mellitus. Additionally, the potent phenolic content and α-amylase and α-glucosidase enzyme inhibitory activity were also investigated. The extraction yield of mucilage was investigated from *Z. mauritiana* L. fruit pulp and leaves where the preliminary screening has shown that the higher mucilage yield was obtained from the leaves with 1.24%, while the mucilage from the pulp yielded 0.34%. The mucilage of *Z. mauritiana* L. leaves with good hydration properties of swelling capacity (6.87 ± 0.23 mL/g), water holding capacity (3.960 ± 0.200 g/g), oil holding capacity (0.507 ± 0.083 g/g), and its emulsifying properties including emulsifying activity (56.0 ± 4.00%) and emulsifying stability (70.87 ± 2.31%) indicate that it may have the capability in regulating postprandial hyperglycemia. Fourier transform infrared spectroscopy (FTIR) demonstrated the band of functional group characteristics of dietary fiber while scanning electron microscopy (SEM) analysis revealed the structural characteristic of the extracted *Z. mauritiana* L. mucilage. Glucose dialysis retardation index (GDRI) analysis on *Z. mauritiana* L. leaves dietary fiber showed decreasing effect overtime at minutes 60 (from 70.94 to 62.57%). The phytochemical analysis has shown that the total phenolic content of the fiber

extract was 6.13 mg GAE/g dry sample extract while the total flavonoid content was 83.00 mg QE/g dry sample extract. In vitro studies exhibit excellent α-amylase and α-glucosidase inhibition activity with an IC50 of 138.3 µg/mL and 11.04 µg/mL, respectively as compared to one of synthetic drugs used for treating diabetes, acarbose. These features make the crude *Z. mauritiana* L. mucilaginous extract a remarkable candidate for functional food and nutraceutical dietary fiber especially in associated with antidiabetes.

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

CIRI-CIRI FUNGSIAN BIO SERAT DIET DARI DAUN *ZIZIPHUS MAURITIANA* L. MALAYSIA DAN PERKAITANNYA DENGAN SIFAT *IN VITRO* ANTIDIABETIK

Oleh

NUR SYUHADA BINTI ZAHARI

Jun 2021

Pengerusi : Prof Madya Uswatun Hasanah Binti Zaidan, PhD
Fakulti : Bioteknologi dan Sains Biomolekul

Ziziphus mauritiana L. yang berasal dari tumbuhan keluarga Rhamnaceae (dikenali sebagai pokok Bidara di Malaysia) telah digunakan oleh orang Malaysia dengan memproses buah menjadi jeruk atau memakannya segar, sementara daunnya biasa digunakan dalam perubatan tradisional terutama dalam perubatan Islam. Walaupun tumbuhan *Z. mauritiana* L. kaya dengan makronutrien, mikronutrien, dan fitokimia yang menawarkan faedah kesihatan, tetapi, tanaman *Z. mauritiana* L. masih dianggap kurang dimanfaatkan di Malaysia kerana kekurangan maklumat saintifik mengenai kesan kesihatan terhadap seratnya. Oleh itu, kajian ini bertujuan untuk mengkaji beberapa sifat fizikokimia yang berkaitan dengan kualiti pemakanannya dari sumber baru serat diet (lendir) yang diperlukan untuk menjaga kesihatan populasi dalam masyarakat, terutama dalam mengawal diabetes. Di negara lain, *Z. mauritiana* L. juga digunakan sebagai ubat tradisional dan baru-baru ini para penyelidik mula mengkaji secara saintifik faedah kesihatan tumbuhan ini terutama di negara Asia. Sebagai tambahan, potensi kandungan fenolik yang kuat dan aktiviti perencatan enzim α-amilase dan α-glukosidase juga diselidik. Hasil pengekstrakan lendir disiasat dari pulpa buah dan daun *Z. mauritiana* L. dimana pemeriksaan awal menunjukkan bahawa hasil lendir yang lebih tinggi diperoleh dari daun dengan 1.24%, sementara lendir dari pulpa menghasilkan 0.34%. Lendir daun *Z. mauritiana* L. dengan sifat penghidratan yang baik bagi kapasiti pengembangan (6.87 ± 0.23 mL/g), kapasiti mengikat air (3.960 ± 0.200 g/g), kapasiti mengikat minyak (0.507 ± 0.083 g/g) dan sifat pengemulsi termasuk aktiviti pengemulsi (56.0 ± 4.00%) dan kestabilan pengemulsi (70.87 ± 2.31%) menunjukkan bahawa ia mungkin mempunyai keupayaan dalam mengawal gula dalam darah. Spektroskopi infra merah (FTIR) menunjukkan kehadiran ciri khas kumpulan berfungsi serat diet sementara, analisis mikroskop elektron imbasan (SEM) membuktikan ciri struktur lendir *Z. mauritiana* L. yang diekstrak. Analisa indeks perencatan dialisis glukosa (GDRI) pada serat diet dari daun *Z. mauritiana* L. menunjukkan kesan penurunan pada minit ke 60 (dari 70.94 hingga 62.57%). Analisis fitokimia menunjukkan jumlah

kandungan fenolik untuk ekstrak serat ialah 6.13 mg ekstrak sampel kering GAE/g sementara jumlah kandungan flavonoid adalah 83.00 mg ekstrak sampel kering QE/g. Kajian *in vitro* menunjukkan aktiviti perencatan α-amilase dan α-glukosidase yang sangat baik dengan IC_{50} 138.3 µg/mL dan 11.04 µg/mL setiap satu dibandingkan dengan salah satu ubat sintetik yang digunakan untuk merawat diabetes, acarbose. Sifat-sifat ini menjadikan ekstrak lendir mentah dari daun *Z. mauritiana* L. sebagai calon yang baik dalam peranan serat makanan yang berpotensi untuk makanan berfungsi dan nutraseutikal terutama berkaitan dengan anti diabetes.

ACKNOWLEDGEMENTS

In The Name of ALLAH, The Most Merciful and Most Beneficent.

First and foremost, I would like to convey to Allah, the Lord of the universe, my deepest gratitude for His Mercy and Kindness in granting me the power to finish this thesis.

The heartiest appreciation goes to my supervisor, Assoc. Prof. Dr. Uswatun Hasanah binti Zaidan for her guidance, encouragement, persistence, patience, and trust from the beginning to the end of this study. My sincere appreciation also goes to my co-supervisors, Dr. Mohd Badrin Hanizam bin Abdul Rahim, Assoc. Prof. Dr. Siti Salwa Abd. Gani, and Dr. Mohd Izuan Effendi bin Halmi for their valuable time, comment and encouragement.

Heartfelt gratitude to the staff members of the Department of Biochemistry, Faculty of Biotechnology and Biomolecular Sciences, UPM, Institute of Advanced Technology (ITMA, UPM), Halal Products Research Institute (UPM), Institute of Bioscience (IBS, UPM) for their cooperation throughout the study.

My deepest love and gratitude is devoted to my beloved parents, Zahari Abdullah and Aidah Senin and not to be forgotten, my siblings for their continuous prayer and support in completing this study. Last but not least, my dedication to my lab mates and friends who always there for me through hardship and joy.

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:

Uswatun Hasanah binti Zaidan, PhD
Associate Professor
Faculty of Biotechnology and Biomolecular Sciences
Universiti Putra Malaysia
(Chairman)

Mohd Badrin Hanizam bin Abdul Rahim, PhD
Senior Lecturer
Faculty of Biotechnology and Biomolecular Science
Universiti Putra Malaysia
(Member)

Siti Salwa binti Abd Gani, PhD
Associate Professor
Faculty of Agriculture
Universiti Putra Malaysia
(Member)

Mohd Izuan Effendi bin Halmi, PhD
Associate Professor
Faculty of Agriculture
Universiti Putra Malaysia
(Member)

_____
ZALILAH MOHD SHARIFF, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

Date: 14 April 2022

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ACE	Angiotensin-converting enzyme
ALC	Absolute lymphocytes count
cm	Centimeters
Da	Dalton unit
DNSA	3,5- dinitrosalicylic acid
DPP-1	dipeptidyl peptidase-4
e.g	Example
FTIR	Fourier transform infrared
g	Gram
GAE	Gallic acid equivalent
GDRI	Glucose dialysis retardation index
GLP-1	Glucose like peptide-1
Hb1c	Hemoglobin 1Ac
IC_{50}	50% inhibitory concentration
IDF	International diabetes federation
KBr	Potassium bromide
mg	Miligrams
mins	Minutes
mL	Milliliters
mM	Micromolar
Mmol/L	Milimol per liter
NHMS	National Health and Morbidity Survey
nm	Nanometers
OHC	Oil holding capacity

PNPG	ρNitrophenyl-ρ-D-glucopyranosidase
ppm	Parts per million
QE	Quercetin equivalent
SC	Swelling capacity
SD	Standard deviation
Sdn. Bhd.	Sendirian Berhad
SEM	Scanning electron microscopy
SGLT-2	Sodium-glucose cotransporter 2
TFC	Total flavonoid content
TPC	Total phenolic content
TZDs	Thiazolidinediones
WHC	Water holding capacity
WHO	World Health Organization
ZMDF	*Ziziphus Mauritiana* Leaves Dietary Fiber
Z. mauritiana	*Ziziphus mauritiana*
µL	Microliters
µm	Micrometers

CHAPTER 1

INTRODUCTION

1.1 General Introduction

Diabetes mellitus or called diabetes is a chronic condition that happens when blood glucose levels increase because the body is not capable to efficiently generate or use sufficient insulin (DeFronzo *et al.*, 2015). Insulin is a pancreatic hormone that stimulates the body to consume sugar (glucose) from carbohydrates in foods that we ingest for energy or glucose storage for upcoming consumption. Insulin deficiency or failure of the cell to respond to insulin leads to elevated blood glucose levels or a diabetes condition called hyperglycemia (IDF, 2017).

Hyperglycemia is assessed by glycated hemoglobin A1C levels to reduce the long term diabetes-related complication (Bonora and Tuomilehto, 2011). The treatment is also considered a big global issue with the rise of diabetes mellitus, and effective therapy has yet to be identified. Although the first medication for diabetes mellitus is insulin therapy and oral hypoglycemic agents, they have certain side effects and may not improve the trend of diabetic cases substantially (Raman *et al.*, 2010). Besides, a large amount of medicinal plants has been formulated for diabetic treating purposes. However, several plants have been used as a dietary adjuvant and as a disease treatment even there was no specific knowledge on their proper functions and constituents (Patel *et al.*, 2011).

For the last few years, there is such a concern in finding alternative therapy especially using a natural product. Traditionally, as a complementary or alternative drug, antidiabetic plants or their active constituents are commonly used and more than 200 plant organisms have been found to possess antidiabetic properties (Cohen and Goedert, 2004). Scientists also discovered the development of a variety of bioactive molecules in plants that cope with diabetes mellitus problems over the last year (Zhao *et al.*, 2019). The extract dense in polyphenols decreases the function of enzymes that are involved in glucose formation derived from starch at the gastrointestinal tract for example αamylase also α-glucosidase, reported by McDougall *et al*. (2005). Phenols are naturally occurring compounds considered to have oxidative properties where their organic form is used in food to guard against oxidative rancidity (Cuvelier *et al.*, 1992). Data indicate a strong, consistent correlation between hyperglycemia mediated by oxidative stress and the progression of diabetic symptoms towards individuals who experience diabetes mellitus (Özkaya *et al.*, 2011).

Ziziphus mauritiana Lam. (*Z. mauritiana* L.) is one of the plants that has been discovered to associate with antidiabetic effects (Sangeethapriya & Siddhuraju;

2014). Since this plant is packed with minerals and vitamins (San *et al.,*2009), it is immense good health benefits. It gives benefits to the body organ, circulatory system, and skin and is also known for its preventive capacity against different diseases (Carol *et al.,* 2015). *Z. mauritiana* L. is defined as a good source of the important functional components such as polysaccharides, phenolics, flavonoids, and saponins that are beneficial for numerous biological behaviors, namely immune function regulation and blood triglyceride reduction (Dahiru and Obidoa, 2008; Li *et al*., 2011). Other than macronutrients, the nutritional value of *Z. mauritiana* L. also contains micronutrients and fiber. It was reported that *Z. mauritiana* L.'s fruit pulp contains one of the plant metabolites group that create cell signaling pathways and antioxidant effects known as flavonoids (Kerkar, 2017).

Stool weight is increased by fiber with high hydration properties and its viscosity characteristics hinder macronutrient intake, leading to higher susceptibility to insulin, elevated satiety, and decreased energy consumption (Sangeethapriya and Siddhuraju, 2014). The emulsifying capacity of fiber is very investigative in health possible advantages. The concentration of blood cholesterol in the small intestine tends to decrease when there is ingestion of biliary acids and excretion of the stool (Lopez *et al.*, 1996). The enriched fiber in *Z. mauritiana* L. can help reduce hypercholesterolemic effects, it is said to have many advantages in reducing diabetic effects too. Hence, further research on fiber contained in *Z. mauritiana* L. needed to explore the possible biological characteristic and antioxidant capacity related to the antidiabetic effect.

1.2 Problem Statement

Plants and herbs that grow abundantly has been used in traditional way for treatment of diseases. Many plant and herbs species been using as an alternative for treatment of the chronic diseases upon their antioxidant potential. *Ziziphus mauritiana* Lam. is one of the plant species has been widely use traditionally in treating diseases not only in Malaysia but internationally. However, there are still lack of scientific study of the potential health benefits of *ZIziphus mauritiana* Lam. has been done in Malaysia.

Furthermore, in Malaysia, diabetes mellitus associated with elevated levels of blood glucose is a rising public health issue that presents a serious threat. There is a range of adverse effects among the conventional classes of drugs used to treat diabetes mellitus, for example biguanides, which has common adverse effect of gastrointestinal distress. Thus, more natural antidiabetic therapies that are better and more reliable need to be relied on. Further studies are needed upon functional characteristics and antioxidant potential of dietary fiber from *Ziziphus mauritiana* L. (Malaysia) in controlling hyperglycemia.

1.3 Research Objectives

The key objectives of this present study were to evaluate the biofunctional and phytochemical properties of dietary fiber extracted from the leaves of *Ziziphus mauritiana* L. and its associated inhibitory activity. Therefore, the research was conducted according to the following specific objectives:

1. To study the biofunctional characteristics of *Ziziphus mauritiana* L. leaves dietary fiber through swelling capacity, water, and oil holding capacity, and emulsifying properties.

2. To determine the characteristic of the *Ziziphus mauritiana* L. leaves dietary fiber (Fourier transform infrared and Scanning electron microscopy) and its phytochemical content through total phenolic content (TPC) and total flavonoid content (TFC) assays

3. To evaluate the *in vitro* α-amylase and α-glucosidase inhibitory activities of *Ziziphus mauritiana* L. leaves dietary fiber.

REFERENCES

Abdel-Fattah, Y.R. and Gaballa, A.A. (2008). Identification and over-expression of a thermostable lipase from *Geobacillus Thermoleovorans* Toshki in *Escherichia coli*. *Microbiological Research*. 163(1): 13–20.

Abdallah, E. M., Elsharkawy, E. R., and Ed-dra, A. (2016). *Biological activities of methanolic leaf extract of Ziziphus mauritiana*. *Bioscience Biotechnology Research Communication.* 9(4): 605-614.

Abirami, A., Nagarani, G., and Siddhuraju, P. (2014). Measurement of functional properties and health promoting aspects-glucose retardation index of peel, pulp and peel fiber from *Citrus hystrix* and *Citrus maxima. Bioactive Carbohydrates and Dietary Fibre*. 4(1): 16-26.

Adeyemo, S. O. (2011). Studies on in-vitro antioxidant and free radical scavenging potential and phytochemical screening of leaves of *Ziziphus mauritiana* L and *Ziziphus spina- christi* L. compared with ascorbic acid. *Journal of Medical Genetics*. 3(2): 28–34.

Ahmad, K. 2012. A study on sorcery therapy methods at islamic therapeutic centres in Malaysia. *Perspektif Journal*. 4(1):82–111

Ahmed, F., Sairam, S., and Urooj, A. (2011). In vitro hypoglycemic effects of selected dietary fiber sources. *Journal of Food Science and Technology*. 48(3): 285-289.

Ajila, C. M., and Rao, U. P. (2013). Mango peel dietary fibre: Composition and associated bound phenolics. *Journal of Functional Foods*. 5(1): 444-450.

Ali Asgar, M. D. (2013). Anti-diabetic potential of phenolic compounds: A review. *International Journal of Food Properties.* 16(1): 91-103.

Al-Sayed, H. M. A., Rasmy, N. M. H., Rizk, I. R. S., and Yousef, E. E. I. (2012). Functional properties of some fat-replacers and their uses in preparation of reduced-fat mayonnaise. *World Journal of Dairy and Food Sciences.* 7(1): 109-119.

American Diabetes Association. (2004). Gestational diabetes mellitus. *Diabetes care*. 27 (1): 88-90.

Antonella Tromba. (2019, July 3). Food emulsifiers: what they are and how they can be multi-functional. Retrieved from https://foodensity.com/lecithinin-chocolate/

Apostolidis, E., and Lee, C. M. (2010). In vitro potential of *Ascophyllum nodosum* phenolic antioxidant-mediated α-glucosidase and α-amylase inhibition. *Journal of Food Science.* 75(3): 97-102.

Aqilah, S., Yusof, M., and Saat, R. (2017). Phytochemical analysis and bioactivity studies of *Ziziphus mauritiana* (twigs and leaves). *Journal of Academia UiTM Negeri Sembilan.* 5: 17–26.

Ariaratnam, S., Rodzlan Hasani, W. S., Krishnapillai, A. D., Abd Hamid, H. A., Jane Ling, M. Y., Ho, B. K., and Mohd Yusoff, M. F. (2020). Prevalence of obesity and its associated risk factors among the elderly in Malaysia: Findings from The National Health and Morbidity Survey (NHMS) 2015. *Plos One*, 15(9), e0238566.

Asmat, U., Abad, K., and Ismail, K. (2016). Diabetes mellitus and oxidative stress—A concise review. *Saudi Pharmaceutical Journal*. 24(5): 547553.

Atlas, D. (2015). *International diabetes federation*. IDF Diabetes Atlas, 7th edetion. Brussels, Belgium: International Diabetes Federation.

Azam, S. S., Uddin, R., and Wadood, A. (2012). Structure and dynamics of αglucosidase through molecular dynamics simulation studies. *Journal of Molecular Liquids*. 174: 58-62.

Bai, L., Huan, S., Li, Z., and McClements, D. J. (2017). Comparison of emulsifying properties of food-grade polysaccharides in oil-in-water emulsions: Gum arabic, beet pectin, and corn fiber gum. *Food Hydrocolloids.* 66: 144-153.

Balakumar, P., Maung-U, K., and Jagadeesh, G. (2016). Prevalence and prevention of cardiovascular disease and diabetes mellitus. *Pharmacological Research*. 113: 600-609.

Balfour, J. A., & McTavish, D. (1993). Acarbose. An update of its pharmacology and therapeutic use in diabetes mellitus. *Drugs*, 46(6), 1025–1054.

Barrett, M. L., and Udani, J. K. (2011). A proprietary α-amylase inhibitor from white bean (*Phaseolus vulgaris*): a review of clinical studies on weight loss and glycemic control. *Nutrition Journal*. 10(1): 24.

Biswas, A. K., Kumar, V., Bhosle, S., Sahoo, J., and Chatli, M. K. (2011). Dietary fibers as functional ingredients in meat products and their role in human health. International *Journal of Livestock Production.* 2(4): 45-54.

Bonora, E., and Tuomilehto, J. (2011). The pros and cons of diagnosing diabetes with A1C. *Diabetes care, 34 (Supplement 2).* 184-190.

Boulton, A. J. (1998). Guidelines for diagnosis and outpatient management of diabetic peripheral neuropathy. *European Association for the Study of Diabetes, Neurodiabetic Diabetes and Metabolism.* 24: 55.

Brás, N. F., Santos-Martins, D., Fernandes, P. A., and Ramos, M. J. (2018). Mechanistic pathway on human α-glucosidase maltase-glucoamylase unveiled by QM/MM calculations. *The Journal of Physical Chemistry B.* 122(14): 3889-3899.

Brayer, G. D., Luo, Y., and Withers, S. G. (1995). The structure of human pancreatic α-amylase at 1.8 Å resolution and comparisons with related enzymes. *Protein Science*. 4(9): 1730-1742.

Burrows, T. (1992). Review articles: Drug therapy (Metformin). *Australian Academic and Research Libraries.* 23(4): 217–220.

Campos-Vega, R., Oomah, B. D., & Vergara-Castañeda, H. A. (2016). *In vivo* and *in vitro* studies on dietary fiber and gut health. dietary fibre functionality in food and nutraceuticals: *From Plant to Gut*, 123–177

Carracher, A. M., Marathe, P. H., and Close, K. L. (2018). International diabetes federation 2017. *Journal of Diabetes*, 10(5), 353-356.

Carvalho, A. F. U., Portela, M. C. C., Sousa, M. B., Martins, F. S., Rocha, F. C., Farias, D. F., and Feitosa, J. P. A. (2009). Physiological and physicochemical characterization of dietary fibre from the green seaweed *Ulva fasciata Delile. Brazilian Journal of Bi*ology. 69(3): 969-977.

Cavalot, F. (2013). Do data in the literature indicate that glycaemic variability is a clinical problem? Glycaemic variability and vascular complications of diabetes*. Diabetes, Obesity and Metabolism*. 15(2): 3-8.

Chau, C. F., Chen, C. H., and Lin, C. Y. (2004). Insoluble fiber-rich fractions derived from *Averrhoa carambola*: hypoglycemic effects determined by in vitro methods. *LWT-Food Science and Technology*. 37(3): 331-335.

Chau, C. F., Wang, Y. T., and Wen, Y. L. (2007). Different micronization methods significantly improve the functionality of carrot insoluble fibre*. Food Chemistry*. 100(4): 1402-1408.

Chebouat, E., Dadamoussa, B., Kabouche, A., Allaoui, M., Gouamid, M., and Gherraf, N. (2013). Gas chromatography-mass spectrometry (GC-MS) analysis of the crude alkaloid extract of *Ziziphus mauritiana Lam*., grown in Algerian. *Journal of Medicinal Plants Research*. 7(20): 1511-1514.

Chen, M., Hu, C., and Jia, W. (2015). Pharmacogenomics of glinides. *Pharmacogenomics*. 16(1): 45-60.

Cho, N., Shaw, J. E., Karuranga, S., Huang, Y., da Rocha Fernandes, J. D., Ohlrogge, A. W., and Malanda, B. (2018). IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Research and Clinical Practice*.138: 271-281.

Choudhury, H., Gorain, B., Pandey, M., Chatterjee, L. A., Sengupta, P., Das, A., and Kesharwani, P. (2017). Recent update on nanoemulgel as topical drug delivery system. *Journal of Pharmaceutical Sciences.* 106(7): 1736-1751.

Choudhury, H., Pandey, M., Hua, C. K., Mun, C. S., Jing, J. K., Kong, L., and Pichika, M. R. (2018). An update on natural compounds in the remedy of diabetes mellitus: A systematic review. *Journal of Traditional and Complementary Medicine.* 8(3): 361-376.

Clifford, S. C., Arndt, S. K., Popp, M., and Jones, H. G. (2002). Mucilages and polysaccharides in *Ziziphus species* (Rhamnaceae): localization, composition and physiological roles during drought-stress. *Journal of Experimental Botany.* 53(366): 131-138.

Cohen, P., and Goedert, M. (2004). GSK3 inhibitors: development and therapeutic potential. *Nature reviews Drug discovery*. 3(6): 479-487.

Cos, P., Vlietinck, A. J., Berghe, D. V., and Maes, L. (2006). Anti-infective potential of natural products: how to develop a stronger in vitro 'proof-ofconcept'. *Journal of Ethnopharmacology*. 106(3): 290-302.

Cuvelier, M. E., Richard, H., and Berset, C. (1992). Comparison of the antioxidative activity of some acid-phenols: structure-activity relationship. *Bioscience, Biotechnology, and Biochemistry*. 56(2): 324325.

Dahiru, D., and Obidoa, O. (2008). Evaluation of the antioxidant effects of *Ziziphus mauritiana* lam. leaf extracts against chronic ethanol-induced hepatotoxicity in rat liver. *African Journal of Traditional, Complementary and Alternative Medicines.* 5(1): 39-45.

Dahiru, D., William, E. T., and Nadro, M. S. (2005). Protective effect of *Ziziphus mauritiana* leaf extract on carbon tetrachloride-induced liver injury. *African Journal of Biotechnology.* 4(10).

Daoub, R. M., Elmubarak, A. H., Misran, M., Hassan, E. A., and Osman, M. E. (2018). Characterization and functional properties of some natural Acacia gums. *Journal of the Saudi Society of Agricultural Sciences*. 17(3): 241-249.

DeFronzo, R. A. (1988). The triumvirate: β-cell, muscle, liver: a collusion responsible for NIDDM. *Diabetes*. 37(6): 667-687.

DeFronzo, R. A., Ferrannini, E., Groop, L., Henry, R. R., Herman, W. H., Holst, J. J., and Simonson, D. C. (2015). Type 2 diabetes mellitus. *Nature Reviews Disease Primers*. 1(1): 1-22.

Diabetes Control and Complications Trial Research Group. (1993).The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *New England Journal of Medicine*. 329(14): 977-986.

Dinicolantonio, J. J., Bhutani, J., & O'keefe, J. H. (2015). Acarbose: safe and effective for lowering postprandial hyperglycaemia and improving cardiovascular outcomes. *Open Heart*, 2, 327.

Eastwood, M. A. (1992). The physiological effect of dietary fiber: an update. *Annual Review of Nutrition.* 12(1): 19-35.

Ekor, M. (2014). The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in Pharmacology*. 4: 177.

Elleuch, M., Bedigian, D., Roiseux, O., Besbes, S., Blecker, C., and Attia, H. (2011). Dietary fibre and fibre-rich by-products of food processing: Characterisation, technological functionality and commercial applications: A review. *Food Chemistry.* 124(2): 411-421.

Emeje, M., Isimi, C., Byrn, S., Fortunak, J., Kunle, O., and Ofoefule, S. (2011). Extraction and physicochemical characterization of a new polysaccharide obtained from the fresh fruits of *Abelmoschus esculentus*. *Iranian Journal of Pharmaceutical Research*. 10(2): 237.

Feisul (2017, July 29) Diabetes Support Group. Retrieved from https://www.slideshare.net/feisul/diabetes-support-group-fibm-ndc2017

Fleury, N., and Lahaye, M. (1991). Chemical and physico-chemical characterisation of fibres from *Laminaria digitata* (Kombu breton): A physiological approach. *Journal of the Science of Food and Agriculture.* 55(3): 389-400.

Fonseca, V. A., and Haggar, M. A. (2014). Achieving glycaemic targets with basal insulin in T2DM by individualizing treatment. *Nature Reviews Endocrinology*. 10(5): 276.

Gardner, T. W., Antonetti, D. A., Barber, A. J., LaNoue, K. F., Levison, S. W., and Penn State Retina Research Group. (2002). Diabetic retinopathy: more than meets the eye. *Survey of Ophthalmology.* 47: 253-262.

Glovaci, D., Fan, W., and Wong, N. D. (2019). Epidemiology of diabetes mellitus and cardiovascular disease. *Current Cardiology Reports*. 21(4): 21.

Gourgue, C. M., Champ, M. M., Lozano, Y., and Delort-Laval, J. (1992). Dietary fiber from mango byproducts: Characterization and hypoglycemic effects determined by *in vitro* methods. *Journal of Agricultural and Food Chemistry.* 40(10): 1864-1868.

Graf, B. A., Milbury, P. E., & Blumberg, J. B. (2005). Flavonols, flavones, flavanones, and human health: epidemiological evidence. *Journal of Medicinal Food*, 8(3), 281–290.

Miguel, G.N., and Belloso, M. O. (1998). Characterization of dietary fiber from orange juice extraction. *Food Research International*. 31(5): 355-361.

Gupta, P., and Premavalli, K. S. (2011). In-vitro studies on functional properties of selected natural dietary fibers. *International Journal of Food Properties.* 14(2): 397-410.

Gupta, R., Gigras, P., Mohapatra, H., Goswami, V. K., and Chauhan, B. (2003). Microbial α-amylases: a biotechnological perspective. *Process Biochemistry*. 38(11): 1599-1616.

Heuzé V., Tran G., Boval M., Lebas F., 2019. Indian jujube (*Ziziphus mauritiana*). Feedipedia, a programme by INRAE, CIRAD, AFZ and FAO. Retrieved from https://www.feedipedia.org/node/80

Hinterstoisser, B., and Salmén, L. (2000). Application of dynamic 2D FTIR to cellulose. *Vibrational Spectroscopy*. 22(1-2): 111-118.

Holt, R. I. (2004). Diagnosis, epidemiology and pathogenesis of diabetes mellitus: an update for psychiatrists. *The British Journal of Psychiatry*. 184(S47): 55-63.

Home, P. D., Pocock, S. J., Beck-Nielsen, H., Gomis, R., Hanefeld, M., Jones, N. P., McMurray, J. J. V. (2009). Rosiglitazone evaluated for cardiovascular outcomes — an interim analysis. 357(1), 28–38.

Hu, C., and Jia, W. (2019). Therapeutic medications against diabetes: What we have and what we expect. *Advanced Drug Delivery Reviews*. 139: 3-15.

Huang, J. Y., Liao, J. S., Qi, J. R., Jiang, W. X., and Yang, X. Q. (2020). Structural and physicochemical properties of pectin-rich dietary fiber prepared from citrus peel. *Food Hydrocolloids*. 110: 106-140.

Stoilova, I., Trifonova, D., Marchev, A., Stanchev, V., Angelova, G., and Krastanov, A. (2017). Phytochemical constituents and in vitro antidiabetic properties of *Ziziphus jujuba* (Rhamnaceae) fruits. *International Journal of Pharmacognosy and Phytochemical Research*. 9(2): 150– 158

Iulek, J., Franco, O. L., Silva, M., Slivinski, C. T., Bloch Jr, C., Rigden, D. J., and de Sá, M. F. G. (2000). Purification, biochemical characterisation and partial primary structure of a new α-amylase inhibitor from *Secale cereale* (rye). *The International Journal of Biochemistry and Cell Biology.* 32(11-12): 1195-1204.

Izydorczyk, M. S., Chornick, T. L., Paulley, F. G., Edwards, N. M., and Dexter, J. E. (2008). Physicochemical properties of hull-less barley fibre-rich fractions varying in particle size and their potential as functional ingredients in two-layer flat bread. *Food Chemistry.* 108(2): 561-570.

Jafari, S. M., Assadpoor, E., He, Y., and Bhandari, B. (2008). Re-coalescence of emulsion droplets during high-energy emulsification. *Food Hydrocolloids*. 22(7): 1191-1202.

Jantaramanant, P., Sermwittayawong, D., Noipha, K., Hutadilok-Towatana, N., and Wititsuwannakul, R. (2014). [Beta]-glucan-containing polysaccharide extract from the grey oyster mushroom [*Pleurotus sajorcaju (Fr.) Sing*.] stimulates glucose uptake by the L6 myotubes. *International Food Research Journal*. 21(2): 779.

Jenkins, A. L., Jenkins, D. J., Wolever, T. M., Rogovik, A. L., Jovanovski, E., Božikov, V., and Vuksan, V. (2008). Comparable postprandial glucose reductions with viscous fiber blend enriched biscuits in healthy subjects and patients with diabetes mellitus: acute randomized controlled clinical trial. *Croatian Medical Journal.* 49(6): 772.

Joshi, S. R., Parikh, R. M., and Das, A. K. (2007). Insulin-history, biochemistry, physiology and pharmacology. *Journal Association of Physicians of India.* 55(L): 19.

Kalegowda, P., Chauhan, A. S., and Urs, S. M. N. (2017). *Opuntia dillenii* (KerGawl) Haw cladode mucilage: Physico-chemical, rheological and functional behavior. *Carbohydrate Polymers.* 157: 1057-1064.

Kamtekar, S., Keer, V., and Patil, V. (2014). Estimation of phenolic content, flavonoid content, antioxidant and α amylase inhibitory activity of marketed polyherbal formulation. *Journal of Applied Pharmaceutical Science*. 4(9): 61.

Kandra, L. (2003). α-Amylases of medical and industrial importance. *Journal of Molecular Structure: THEOCHEM*. 666: 487-498.

Kangralkar, V. A., Patil, S. D., and Bandivadekar, R. M. (2010). Oxidative stress and diabetes: a review. *International Journal of Pharmaceutical Applications.* 1(1): 38-45.

Karaman, E., Yılmaz, E., and Tuncel, N. B. (2017). Physicochemical, microstructural and functional characterization of dietary fibers extracted from lemon, orange and grapefruit seeds press meals. *Bioactive Carbohydrates and Dietary Fibre*. 11: 9-17.

Khaleel, S. M., Jaran, A. S., and Haddadin, M. S. (2016). Evaluation of total phenolic content and antioxidant activity of three leaf extracts of Ziziphus spina-christi (Sedr) grown in Jordan. *Journal of Advances in Medicine and Medical Research*. 1-8.

Khatiwora, E., Adsul, V. B., Kulkarni, M. M., Deshpande, N. R., and Kashalkar, R. V. (2010). Spectroscopic determination of total phenol and flavonoid contents of *Ipomoea carnea*. *International Journal of ChemTech Research.* 2(3): 1698-1701.

Khatun, M. A., Harun-Or-Rashid, M., and Rahmatullah, M. (2011). Scientific validation of eight medicinal plants used in traditional medicinal systems of Malaysia: a review. *American-Eurasian Journal of Sustainable Agriculture*. 5(1): 67-75.

Khullar, P., Khar, R. K., and Agarwal, S. P. (1998). Evaluation of guar gum in the preparation of sustained-release matrix tablets. *Drug Development and Industrial Pharmacy*. 24(11): 1095-1099.

Koh, L. W., Wong, L. L., Loo, Y. Y., Kasapis, S., and Huang, D. (2010). Evaluation of different teas against starch digestibility by mammalian glycosidases. *Journal of Agricultural and Food Chemistry.* 58(1): 148154.

Kohei, K. A. K. U. (2010). Pathophysiology of type 2 diabetes and its treatment policy. J*ournal of the Japan Medical Association.* 53(1): 41-46.

Kralova, I., and Sjöblom, J. (2009). Surfactants used in food industry: a review. *Journal of Dispersion Science and Technology*. 30(9): 1363-1383.

Kumar, P., and Kulkarni, G. T. (2013). Characterization of mucilage from artocarpus heterophyllus as pharmaceutical excipient. *Journal of Chronotherapy and Drug Delivery*. 4(1): 31-43.

L'heveder, R., & Nolan, T. (2013). International diabetes federation. *Diabetes Research and Clinical Practice*. 101(3): 349-351.

Larger, E. Dubois-Laforgue, D., and Timsit, J. (1999). Type 1 diabetes mellitus. *Presse Medicale (Paris, France: 1983).* (34): 1895-1903.

Lattimer, J. M., and Haub, M. D. (2010). Effects of dietary fiber and its components on metabolic health. *Nutrients*. 2(12): 1266-1289.

Lazaridou, A., Biliaderis, C. G., and Izydorczyk, M. S. (2007). Cereal betaglucans: structures, physical properties, and physiological functions. *Functional Food Carbohydrates.*1-72.

Lee, S. Y., Mediani, A., Nur Ashikin, A. H., Azliana, A. B. S., and Abas, F. (2014).

Antioxidant and α-glucosidase inhibitory activities of the leaf and stem of selected traditional medicinal plants. *International Food Research Journal*. 21(1).

Lebovitz H. E. (2019). Thiazolidinediones: the Forgotten Diabetes Medications. *Current Diabetes Reports*, 19(12), 151

Li, J. W., Ding, S. D., and Ding, X. L. (2005). Comparison of antioxidant capacities of extracts from five cultivars of Chinese jujube. *Process Biochemistry*. 40(11): 3607-3613.

Li, J., Fan, L., and Ding, S. (2011). Isolation, purification and structure of a new water-soluble polysaccharide from *Zizyphus jujuba* cv. *Jinsixiaozao. Carbohydrate Polymers*. 83(2): 477-482.

Lim, T. K. (2013): Edible Medicinal and Non-Medicinal Plants: Fruits, Springer Science+Business Media Dordrecht. 605-613.

López, G., Ros, G., Rincón, F., Periago, M. J., Martinez, M. C., and Ortuno, J. (1996). Relationship between physical and hydration properties of soluble and insoluble fiber of artichoke. *Journal of Agricultural and Food Chemistry.* 44(9): 2773-2778.

López-Vargas, J. H., Fernández-López, J., Pérez-Álvarez, J. A., and ViudaMartos, M. (2013). Chemical, physico-chemical, technological, antibacterial and antioxidant properties of dietary fiber powder obtained from yellow passion fruit (*Passiflora edulis var. flavicarpa*) co-products. *Food Research International*. 51(2): 756-763.

Mafauzy, M. (2006). Diabetes mellitus in Malaysia. *The Medical journal of Malaysia*. 61(4): 397.

Marikkar, J. M. N., Tan, S. J., Salleh, A., Azrina, A., and Shukri, M. A. M. (2016). Evaluation of banana (*Musa sp*.) flowers of selected varieties for their antioxidative and anti-hyperglycemic potentials. *International Food Research Journal*. 23(5).

Mathieu, C., Gillard, P., and Benhalima, K. (2017). Insulin analogues in type 1 diabetes mellitus: getting better all the time. *Nature Reviews Endocrinology.* 13(7): 385.

Mbahi, M. A., Mbahi, A. M., Umar, I. A., Ameh, D. A., and Joseph, I. (2018). Phytochemical Screening and Antimicrobial Activity of the Pulp Extract and Fractions of *Ziziphus mauritiana. Biochemistry and Analytical Biochemistry.* 7: 352.

Mcdougall, G. J., and Stewart, D. (2005). The inhibitory effects of berry polyphenols on digestive enzymes. *Biofactors*. 23(4): 189-195.

Melo, K. F., Bahia, L. R., Pasinato, B., Porfirio, G. J., Martimbianco, A. L., Riera, R., and Schaan, B. D. (2019). Short-acting insulin analogues versus regular human insulin on postprandial glucose and hypoglycemia in type 1 diabetes mellitus: a systematic review and meta-analysis. *Diabetology and Metabolic Syndrome*. 11(1): 2.

Memon, A., Memon, N., Luthria, D., Pitafi, A., and Bhanger, M. (2012). Phenolic compounds and seed oil composition of *Ziziphus mauritiana L*. fruit. *Polish Journal of Food and Nutrition Sciences*. 62(1): 15-21.

Meyer, K. A., Kushi, L. H., Jacobs Jr, D. R., Slavin, J., Sellers, T. A., and Folsom, A. R. (2000). Carbohydrates, dietary fiber, and incident type 2 diabetes in older women. *The American Journal of Clinical Nutrition*. 71(4): 921930.

Mohamud, W. N. W., Ismail, A. A. S., Sharifuddin, A., Ismail, I. S., Musa, K. I., Kadir, K. A., and Harnida, S. (2011). Prevalence of metabolic syndrome and its risk factors in adult Malaysians: results of a nationwide survey. *Diabetes Research and Clinical Practice*. 91(2): 239-245.

Mohd Jailani, F. N. A., Zaidan, U. H., Hanizam Abdul Rahim, M. B., Abd Gani, S. S., and Halmi, M. I. E. (2020). Evaluation of constituents and physicochemical properties of Malaysian underutilized *Ziziphus mauritiana* (bidara) for nutraceutical potential. *International Journal of Fruit Science*. *20*(3): 394-402.

Morton, J. F. (1987). Fruits of warm climates (pp 446-483). *CAB International.*

Musman, M., Zakia, M., Rahmayani, R. F. I., Erlidawati, E., & Safrida, S. (2019). Pharmaceutical hit of anti type 2 Diabetes mellitus on the phenolic extract of Malaka (*Phyllanthus emblica* L.) flesh. *Clinical Phytoscience*, 5(1)

Nakamura, A., Takahashi, T., Yoshida, R., Maeda, H., and Corredig, M. (2004). Emulsifying properties of soybean soluble polysaccharide. *Food Hydrocolloids*. 18(5): 795-803.

Navarro-González, I., García-Valverde, V., García-Alonso, J., and Periago, M. J. (2011). Chemical profile, functional and antioxidant properties of tomato peel fiber. *Food Research International*. 44(5): 1528-1535.

Neto, V. Q., Narain, N., Silva, J. B., and Bora, P. S. (2001). Functional properties of raw and heat processed cashew nut (*Anacardium occidentale,* L.) kernel protein isolates. *Food/Nahrung*. 45(4): 258-262.

Nishimune, T., Yakushiji, T., Sumimoto, T., Taguchi, S., Konishi, Y., Nakahara, S. and Kunita, N. (1991). Glycemic response and fiber content of some foods. *The American Journal of Clinical Nutrition*. 54(2): 414-419.

Oboh, G., Ademiluyi, A. O., Akinyemi, A. J., Henle, T., Saliu, J. A., and

Schwarzenbolz, U. (2012). Inhibitory effect of polyphenol-rich extracts of jute leaf (*Corchorus olitorius*) on key enzyme linked to type 2 diabetes (α-amylase and α-glucosidase) and hypertension (angiotensin I converting) in vitro. *Journal of Functional Foods*. 4(2): 450-458.

Ogurtsova, K., da Rocha Fernandes, J. D., Huang, Y., Linnenkamp, U., Guariguata, L., Cho, N. H., and Makaroff, L. E. (2017). IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. *Diabetes Research and Clinical Practice*. 128: 40-50.

Olajuyigbe, O. O., and Afolayan, A. J. (2011). Phenolic content and antioxidant property of the bark extracts of *Ziziphus mucronata Willd*. Sub sp. *mucronata* Willd*. BMC Complementary and Alternative Medicine*. 11(1): 130.

Orchard, T. J., Nathan, D. M., Zinman, B., Cleary, P., Brillon, D., Backlund, J. Y. C., and Lachin, J. M. (2015). Association between 7 years of intensive treatment of type 1 diabetes and long-term mortality. *Jama*. 313(1): 4553.

Orqueda, M. E., Zampini, I. C., Torres, S., Alberto, M. R., Ramos, L. L. P., Schmeda-Hirschmann, G., and Isla, M. I. (2017). Chemical and functional characterization of skin, pulp and seed powder from the Argentine native fruit mistol (*Ziziphus mistol*). Effects of phenolic fractions on key enzymes involved in metabolic syndrome and oxidative stress. *Journal of Functional Foods*. 37: 531-540.

Ou, S., Kwok, K. C., Li, Y., and Fu, L. (2001). In vitro study of possible role of dietary fiber in lowering postprandial serum glucose. *Journal of Agricultural and Food Chemistry*. 49(2): 1026-1029.

Özkaya, D., Nazıroğlu, M., Armağan, A., Demirel, A., Köroglu, B. K., Çolakoğlu, N and Sönmez, T. T. (2011). Dietary vitamin C and E modulates oxidative stress induced-kidney and lens injury in diabetic aged male rats through modulating glucose homeostasis and antioxidant systems. *Cell Biochemistry and Function.* 29(4): 287-293.

Ozougwu, J. C., Obimba, K. C., Belonwu, C. D., and Unakalamba, C. B. (2013). The pathogenesis and pathophysiology of type 1 and type 2 diabetes mellitus. *Journal of Physiology and Pathophysiology*. 4(4): 46-57.

Pant, G., Kumar, G., Karthik, L., Prasuna, R. G., and Rao, K. B. (2011). Antioxidant activity of methanolic extract of blue green algae *Anabaena* sp. (Nostocaceae). *European Journal of Experimental Biology.* 1(1): 156-162.

Pareek, S. (2013). Nutritional composition of jujube fruit. *Emirates Journal of Food and Agriculture.* 463-470.

Park, Y., Brinton, L. A., Subar, A. F., Hollenbeck, A., and Schatzkin, A. (2009). Dietary fiber intake and risk of breast cancer in postmenopausal women: the National Institutes of Health–AARP Diet and Health Study. *The American Journal of Clinical Nutrition*. 90(3): 664-671.

Parmar, P., Bhatt, S., Dhyani, S., and Jain, A. (2012). Phytochemical studies of the secondary metabolites of *Ziziphus mauritiana Lam*. Leaves. *International Journal of Current Pharmaceutical Research*. 4(3): 153155.

Patel, D. K., Kumar, R., Prasad, S. K., Sairam, K., and Hemalatha, S. (2011). Antidiabetic and in vitro antioxidant potential of *Hybanthus enneaspermus (Linn) F. Muell* in streptozotocin–induced diabetic rats. *Asian Pacific Journal of Tropical Biomedicine*, 1(4): 316-322.

Patterson, C. C., Karuranga, S., Salpea, P., Saeedi, P., Dahlquist, G., Soltesz, G., and Ogle, G. D. (2019). Worldwide estimates of incidence, prevalence and mortality of type 1 diabetes in children and adolescents: Results from the International Diabetes Federation Diabetes Atlas. *Diabetes Research and Clinical Practice*. 157: 107-842.

Payan, F. (2004). Structural basis for the inhibition of mammalian and insect αamylases by plant protein inhibitors. *Biochimica et Biophysica Acta (BBA)-Proteins and Proteomics*. 1696(2): 171-180.

Picot, C., Subratty, A. H., and Mahomoodally, M. F. (2014). Inhibitory potential of five traditionally used native antidiabetic medicinal plants on αamylase, α-glucosidase, glucose entrapment, and amylolysis kinetics in vitro. *Advances in Pharmacological Sciences.* 2014.

Pop-Busui, R. (2010). Cardiac autonomic neuropathy in diabetes: a clinical perspective. *Diabetes Care*. 33(2): 434-441.

Quirós-Sauceda, A. E., Palafox-Carlos, H., Sáyago-Ayerdi, S. G., Ayala-Zavala, J. F., Bello-Perez, L. A., Alvarez-Parrilla, E., and González-Aguilar, G. A. (2014). Dietary fiber and phenolic compounds as functional ingredients: interaction and possible effect after ingestion. *Food and Function*. 5(6): 1063-1072.

Rajagopalan, G., and Krishnan, C. (2008). α-Amylase production from catabolite derepressed Bacillus subtilis KCC103 utilizing sugarcane bagasse hydrolysate. *Bioresource Technology*. 99(8): 3044-3050.

Raman, R., Gupta, A., Pal, S. S., Ganesan, S., Venkatesh, K., Kulothungan, V., and Sharma, T. (2010). Prevalence of metabolic syndrome and its influence on microvascular complications in the Indian population with type 2 diabetes mellitus. Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetic Study (SN-DREAMS, report 14). *Diabetology & Metabolic Syndrome*. 2(1): 67.

Rashid, Z. M., Nasir, N. A. M., and Aziz, N. (2018). Biochemical analysis and αglucosidase inhibition of *Ziziphus mauritiana* (bidara) immature leaves extracts. *Journal of Agrobiotechnology*. 9(1): 43-53.

Reddy, N. V. L. S., Anarthe, S. J., and Raghavendra, N. M. (2010). In vitro antioxidant and antidiabetic activity of *Asystasia gangetica* (Chinese Violet) *Linn*.(Acanthaceae). *International Journal of Research in Pharmaceutical and Biomedical Sciences*. 1(2): 72-75.

Robertson, J. A., de Monredon, F. D., Dysseler, P., Guillon, F., Amado, R., and Thibault, J. F. (2000). Hydration properties of dietary fibre and resistant starch: a European collaborative study. *LWT-Food Science and Technology*. 33(2): 72-79.

Rothman, K. J. (2012). Analyzing simple epidemiologic data. *Epidemiology: An Introduction*: 164-175.

Saini, V. (2010). Molecular mechanisms of insulin resistance in type 2 diabetes mellitus. *World Journal of Diabetes.* 1(3): 68.

Sangeethapriya, M., and Siddhuraju, P. (2014). Health related functional characteristics and antioxidant potential of mucilage (dietary fiber) from *Zizyphus mauritiana* fruits. *Food Science and Human Wellness*. 3(2): 7988.

Sasidharan, S., Chen, Y., Saravanan, D., Sundram, K. M., and Latha, L. Y. (2011). Extraction, isolation and characterization of bioactive compounds from plants' extracts. *African Journal of Traditional, Complementary and Alternative Medicines*. 8(1).

Saura-Calixto, F. (2011). Dietary fiber as a carrier of dietary antioxidants: an essential physiological function. *Journal of Agricultural and Food Chemistry*. 59(1): 43-49.

Schneeman, B. O. (1999). Fiber, inulin and oligofructose: similarities and differences. *The Journal of Nutrition.* 129(7): 1424-1427. Ševčík, J., Hostinová, E., Solovicová, A., Gašperík, J., Dauter, Z., & Wilson, K. S. (2006). Structure of the complex of a yeast glucoamylase with acarbose reveals the presence of a raw starch binding site on the catalytic domain. *The FEBS Journal*. 273(10): 2161-2171.

Shevkani, K., Singh, N., Rana, J. C., and Kaur, A. (2014). Relationship between physicochemical and functional properties of amaranth (*A maranthus hypochondriacus*) protein isolates. *International Journal of Food Science and Technology*. 49(2): 541-550.

Silverstein, R. M., Bassler, G. C., and Morrill, T. C. (1980). *Identificación espectrométrica de compuestos orgánicos* (No. 547 S586i). México, MX: Diana.

Sim, L., Willemsma, C., Mohan, S., Naim, H. Y., Pinto, B. M., and Rose, D. R. (2010). Structural basis for substrate selectivity in human maltaseglucoamylase and sucrase-isomaltase N-terminal domains. *Journal of Biological Chemistry*. 285(23): 17763-17770.

Singleton, V. L., and Rossi, J. A. (1965). Colorimetry of total phenolics with phosphomolybdic-phosphotungstic acid reagents. *American journal of Enology and Viticulture.* 16(3): 144-158.

Souid, S., Brahmi, D., Lepesant, J. A., and Zourgui, L. (2011). Cactus (*Opuntia ficus indica*) extract improves endoplasmic reticulum stress in Drosophila melanogaster. *African Journal of Biotechnology.* 10(66): 14699-14705.

Streppel, M. T., Ocké, M. C., Boshuizen, H. C., Kok, F. J., and Kromhout, D. (2008). Dietary fiber intake in relation to coronary heart disease and allcause mortality over 40 y: the Zutphen Study. *The American Journal of Clinical Nutrition*. 88(4): 1119-1125

.Tangphatsornruang, S., Naconsie, M., Thammarongtham, C., and Narangajavana, J. (2005). Isolation and characterization of an αamylase gene in cassava (*Manihot esculenta*). *Plant Physiology and Biochemistry.* 43(9): 821-827.

Tee, E. S., and Yap, R. W. K. (2017). Type 2 diabetes mellitus in Malaysia: current trends and risk factors. *European Journal of Clinical Nutrition*. 71(7): 844-849.

Thanatcha, R., and Pranee, A. J. I. F. R. J. (2011). Extraction and characterization of mucilage in *Ziziphus mauritiana Lam*. *International Food Research Journal*. 18(1).

Thebaudin, J. Y., Lefebvre, A. C., Harrington, M., and Bourgeois, C. M. (1997). Dietary fibres: nutritional and technological interest. *Trends in Food Science and Technology.* 8(2): 41-48.

Thibault, J. F., Lahaye, M., and Guillon, F. (1992). Physico-chemical properties of food plant cell walls. *In Dietary Fibre - A Component of Food* (pp. 2139). Springer, London.

Thomas, M. C., Groop, P. H., and Tryggvason, K. (2012). Towards understanding the inherited susceptibility for nephropathy in diabetes. *Current Opinion in Nephrology and Hypertension*. 21(2): 195-202.

Thompson, L. U. (1993). Potential health benefits and problems associated with antinutrients in foods. *Food Research International*. 26(2): 131-149.

Tran, N., Pham, B., & Le, L. (2020). Bioactive compounds in anti-diabetic plants: from herbal medicine to modern drug. *Discovery. Biology* 2020, Vol. 9, Page 252, 9(9), 252.

Tucker, L. A., and Thomas, K. S. (2009). Increasing total fiber intake reduces risk of weight and fat gains in women. *The Journal of Nutrition.* 139(3): 576581.

Type 1 Diabetes Mellitus and Its Aetiology (November 15, 2012). Retrieved from http://edusanjalbiochemist.blogspot.com/2012/11/type-1-diabetesmellitus-and-its.html.

Type of Diabetes. (n.d) Retrieved from https://www.gluxus.com/diabetesresources/about-diabetes/diabetes-types/

Valdez-Solana, M. A., Mejía-García, V. Y., Téllez-Valencia, A., García-Arenas, G., Salas-Pacheco, J., Alba-Romero, J. J., and Sierra-Campos, E. (2015). Nutritional content and elemental and phytochemical analyses of *Moringa oleifera* grown in Mexico. *Journal of Chemistry*. 2015.

Verrotti, A., Prezioso, G., Scattoni, R., and Chiarelli, F. (2014). Autonomic neuropathy in diabetes mellitus. *Frontiers in Endocrinology.* 5: 205.

Vinayagam, R., & Xu, B. (2015). Antidiabetic properties of dietary flavonoids: a cellular mechanism review. *Nutrition & Metabolism,* 12, 60

Wang, C. H., Ma, Y. L., Zhu, D. Y., Wang, H., Ren, Y. F., Zhang, J. G., and Wei, Z. J. (2017). Physicochemical and functional properties of dietary fiber from bamboo shoots (*Phyllostachys praecox*). *Emirates Journal of Food and Agriculture.* 509-517.

Watanabe, J., Kawabata, J., Kurihara, H., and Niki, R. (1997). Isolation and identification of α-glucosidase inhibitors from tochu-cha (*Eucommia ulmoides*). *Bioscience, Biotechnology, and Biochemistry*. 61(1): 177178.

Weng, J., Li, Y., Xu, W., Shi, L., Zhang, Q., Zhu, D. and Ran, X. (2008). Effect of intensive insulin therapy on β-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: a multicentre randomised parallel-group trial. *The Lancet*. 371(9626): 1753-1760.

Whiting, D. R., Guariguata, L., Weil, C., & Shaw, J. (2011). IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. *Diabetes Research and Clinical Practice*. 94(3): 311-321.

World Health Organization. (2010). *World health statistics 2010*. World Health Organization. (Pp155-168).

Yusof, M. Y., Salleh, R. A. A. R., Yahaya, F., Hassan, P., Abd Munir Mohamed Noh, M. Z., and Abidin, H. Z. (2017). Funeral management in the Malay world: local knowledge and practices. *Journal of Applied Environmental and Biological Sciences*. 7(1): 72-77.

Zaidan, U. H., Zen, N. I. M., Amran, N. A., Shamsi, S., & Abd Gani, S. S. (2019). Biochemical evaluation of phenolic compounds and steviol glycoside from *Stevia rebaudiana* extracts associated with in vitro antidiabetic potential. *Biocatalysis and Agricultural Biotechnology*, 18, 101049.

Zaki, M., Robaayah, Z., Chan, S. P., Vadivale, M., and Lim, T. O. (2010). Malaysia Shape of the Nation (MySoN): a primary care based study of abdominal obesity in Malaysia. *Medicine Journal Malaysia.*, 65 (A): 143149.

Zhao, C., Yang, C., Wai, S. T. C., Zhang, Y., P. Portillo, M., Paoli, P., & Xiao, J. (2019). Regulation of glucose metabolism by bioactive phytochemicals for the management of type 2 diabetes mellitus. *Critical Reviews in Food Science and Nutrition*, 59(6): 830-847.

Zheng, Y., Wang, Q., Huang, J., Fang, D., Zhuang, W., Luo, X. and Cao, H. (2019). Hypoglycemic effect of dietary fibers from bamboo shoot shell: An in vitro and in vivo study. *Food and Chemical Toxicology.* 127: 120126.

Zhishen, J., Mengcheng, T., and Jianming, W. (1999). The determination of flavonoid contents in mulberry and their scavenging effects on superoxide radicals. *Food Chemistry*. 64(4): 555-559.

Zhou, B., Bentham, J., Di Cesare, M., Bixby, H., Danaei, G., Cowan, M. J., and Taddei, C. (2017). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19· 1 million participants. *The Lancet.* 389(10064): 37-55.

Zhu, Y., Chu, J., Lu, Z., Lv, F., Bie, X., Zhang, C., and Zhao, H. (2018). Physicochemical and functional properties of dietary fiber from foxtail millet (*Setaria italic*) bran. *Journal of Cereal Science*. 79: 456-461.

Zidane. Z., (2020, August 14). *Ziziphus mauritiana* leaves. Retrieved from https://lamosea.com/manfaat-daun-bidara/

Zi-qin, F., Bao-chang, C., and Chang-xia, B. (2008). Comparison of the effect of polysaccharides from crude and processed *Rhizoma Dioscoreae* on gastrointestinal function in mice of splenic asthenia. *Pharmacology and Clinical Research.* 181-183.