IMPROVING FUNCTIONAL PROPERTIES OF *PUNICA GRANATUM* JUICE BY PROBIOTICATION USING *LACTOBACILLUS* SPECIES

SITI MARHAIDA BT MUSTAFA

A thesis submitted in fulfilment of the
requirements for the award of the degree of
Doctor of Philosophy (*Bioprocess Engineering*)

School of Chemical and Energy Engineering
Faculty of Engineering
Universiti Teknologi Malaysia

JULY 2019

DEDICATION

First and Foremost, thankful to Allah The Almighty

To my beloved husband Mohd Ramdan,
children Muhammad Zaid and Siti Sufiyyah, parents, family and friends,
thank you very much for the endless support

ACKNOWLEDGEMENT

First and foremost, thankful to Allah SWT for His blessing that strive me up to complete my thesis. All praises to Allah SWT, the Most Merciful, who is All Knower for all my words and prayers. I am deeply indebted to my beloved husband, Mohd Ramdan bin Mohd Rofi, the most supported person beside me throughout this PhD journey. Thank you very much for always being my side through my ups and downs, relieve my worries and comfort me with priceless words. By saying that Allah is everything to us is all enough. My children, Muhammad Zaid and Siti Sufiyyah, I would say that this thesis is yours too. Thank you for sharing this PhD journey with lots of patience.

I am really honored to appreciate my supervisor, Associate Professor Dr Chua Lee Suan, whose help, stimulating suggestions and encouragement helped me in all the time of research and writing of this thesis. Appreciation is also given to my co-supervisors, Professor Dr Hesham Ali El Enshasy, Professor Dr Fadzilah @ Adibah Abdul Majid and Dr Cheng Kiang Kai. They have generously allocated and shared their time to enable me to complete this study and have been in invaluable source of counsel and confidence throughout my research effort. I would also like to thank all the personnel and technicians in the Institute of Bioproduct Development for their assistance during the laboratory tasks. Finally, I am forever indebted and immensely grateful to my parents, Haji Mustafa Bin Che Harun and Hajah Minah Bt Mat Saman for their continuous support. My sincerest appreciation and gratitude also go to my siblings, family, in-laws and friends. To those who had contributed assistance and advices in this study, either directly or indirectly, yet their names are not cited here, they deserve my greatest gratitude. Million thanks to all.

ABSTRACT

Fruit juice enriched with probiotics is increasingly accepted nowadays, mainly due to its health benefits for digestive system and lactose intolerant problem. In the present study, the whole fruit of *Punica granatum* (pomegranate) was probioticated with selected strains of beneficial bacteria in order to improve the functionality of the juice. *Lactobacillus* species such as *L. plantarum, L. salivarius, L. casei and L. bulgaricus* were used for probiotication. Probiotication was optimized based on three parameters; temperature, agitation speed and fermentative pH. The growth profile of *Lactobacillu*s species was observed based on the biomass, pH and lactic acid content in the fermentation broth. The functionality of *L. casei* probioticated juice was further evaluated using samples from shake flasks and 5 L stirred tank bioreactor. The kinetic profile of *L. casei* in the pomegranate juice was also determined under the optimized conditions (37 °C, pH 4.0, 0 and 50 rpm). The results indicated that *L. casei* was the dominant species based on the high biomass, lactic acid and flavonoid content compared to other strains. The specific growth rate of *L. casei* in shake flasks and bioreactor were 0.083 h^{-1} and 0.111 h^{-1}, respectively. Probiotication of the juice with *L. casei* improved the concentration of quercetin-3-glucoside, as well as bioactivities of the juice. The radical scavenging and antidiabetic activities achieved more than 80 % inhibition during exponential phase, concurrently with the increase of biomass (13.0 %), lactic acid concentration (13.3 %) and quercetin-3-glucoside concentration (51.1 %) in the bioreactor samples. The ability of *L. casei* to rapidly utilize fermentable sugars of pomegranate for growth without further nutrient supplementation has proved the suitability of pomegranate juice as a growth medium for *L. casei.*

ABSTRAK

Jus buah diperkaya dengan probiotik semakin diterima pada masa kini, terutamanya disebabkan oleh manfaatnya pada kesihatan untuk sistem pencernaan dan masalah intoleransi laktosa. Dalam kajian ini, keseluruhan buah *Punica granatum* (delima) telah diprobiotikkan dengan bakteria terpilih yang bermanfaat untuk meningkatkan fungsi jus. Spesies *Lactobacillus* seperti *L. plantarum*, *L. salivarius*, *L. casei* dan *L. bulgaricus* digunakan untuk fermentasi menggunakan probiotik. Fermentasi dioptimumkan berdasarkan tiga parameter; suhu, kelajuan pengadukan dan pH fermentatif. Profil pertumbuhan spesies *Lactobacillus* diperhatikan berdasarkan kandungan biojisim, pH dan asid laktik di dalam *broth* fermentasi. Fungsi jus yang diprobiotikkan dengan *L. casei* dinilai menggunakan sampel dari kelalang goncang dan bioreaktor tangki teraduk 5 L. Profil kinetik *L. casei* dalam jus delima pada keadaan optimum (37 °C, pH 4.0, 0 dan 50 rpm) juga telah ditentukan. Keputusan menunjukkan bahawa *L. casei* merupakan spesies dominan berdasarkan kandungan biojisim, asid laktik dan flavonoid yang tinggi berbanding dengan bakteria lain. Kadar pertumbuhan spesifik *L. casei* dalam kelalang goncang dan bioreaktor masing-masing ialah 0.083 h^{-1} dan 0.111 h^{-1}. Jus yang diprobiotikkan dengan *L. casei* meningkatkan kepekatan quercetin-3-glukosida, serta bioaktiviti jus tersebut. Aktiviti antiradikal dan antidiabetik mencapai lebih daripada 80% perencatan semasa fasa eksponen dan pada masa yang sama berlaku peningkatan biojisim (13.0 %), kepekatan asid laktik (13.3 %) dan kepekatan quercetin-3-glukosida (51.1 %) di dalam sampel bioreaktor. Keupayaan *L. casei* untuk menggunakan gula yang boleh dieram dari buah delima untuk pertumbuhan telah membuktikan kesesuaian jus delima sebagai medium pertumbuhan untuk *L. casei*, walaupun tanpa penambahan nutrien dari sumber luar.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ANOVA	-	Analysis of Variance
MS	-	Mass Spectra
LCMS	-	Liquid Chromatography Mass Spectrometry
HPLC	-	High Performance Liquid Chromatography
NMR	-	Nuclear Magnetic Resonance
GCMS	-	Gas Chromatography Mass Spectrometry
HPTLC	-	High Performance Thin Layer Chromatography
UV	-	Ultraviolet
MRS medium	-	De Man, Rogosa and Sharpe
OD	-	Optical Density
GLP-1	-	Glucose-like Peptide – 1
DPP-IV	-	Dipeptidyl Peptidase IV (4)
PJ	-	Pomegranate Juice
BHA	-	Butylated hydroxyanisole
BHT	-	Butylated hydroxytoluene
ROS	-	Reactive oxygen species
RNS	-	Reactive nitrogen species
PON1	-	Paraoxonase-1
HDL	-	High density lipoprotein
LDL	-	Low density lipoprotein
ZOI	-	Zone of Inhibition
NAOH	-	Sodium Hydroxide
Q3G	-	Quercetin-3-glucoside
CE	-	Catechin equivalent
DPPH	-	1,1-diphenyl-2-picrylhydrazyl
DMSO	-	Dimethyl Sulfoxide

DMBA	-	7,12-dimethyl benz(a)anthracene
UPLC	-	Ultra Performance Liquid Chromatography
ESI	-	Electrospray ionization
µl	-	Microliter
ml	-	Mililiter
mg	-	Miligram
min	-	Minute
µm	-	Micrometer
g	-	Gram
m	-	Meter
mM	-	Milimeter
mg/g	-	Miligram per gram
cm	-	Centimeter
cfu/ml	-	Colony forming unit per milliliter
h	-	hour
rpm	-	Revolutions per minute
nm	-	Nanometer
RI	-	Refractive Index
%	-	Percentage
α	-	Alpha
β	-	Beta
°C	-	Degree Celsius

LIST OF APPENDICES

CHAPTER 1

INTRODUCTION

1.1 Research Background

Foods and beverages are important source of energy and nutrients for the survival of life. Fruits are nutrient-dense foods, rich in phytonutrients that offer good health benefits. Current processed foods and beverages are mostly fortified with synthetic preservatives, additives as well as adding excessive sugar. Poor nutrient-dense diet intake causes the explosion of various chronic-linked diseases that possibly lead to death. Oxidation linked diseases are caused by excessive reactive oxygen species (ROS) because of disruption in cellular antioxidant homeostasis. This could be due to overload of calories combined with stress, no exercise and diet low in antioxidants (Ankolekar, 2013). Increase consumption of fruits, vegetables and whole grains could be a possible solution (Hyson, 2011). Fruits present a healthy and colorful array of phytochemicals that have been shown to associate with lower risks of diseases.

The National Health and Morbidity Survey (NHMS), 2011 has shown that the prevalence of diabetes in Malaysia has increased within just 5 years, from 11.6% in 2006 to 15.2% in 2011. This means that there are about 2.6 million adults aged 18 years and above living with diabetes. Data from NHMS (2011) also shows that about 80% of patients diagnosed with diabetes are seeking treatment in public health care facilities, while the rest are treated by private practitioners, or taking complementary and alternative medicines (National Diabetes Registry 2009-2012). Even though the correlation of diet intake and disease is complex, various sources of functional foods are formulated to fulfil the demand of consumers for healthier foods recently (Mustafa and Chua, 2017). Functional foods are classified as foods comprising component(s) that able to avoid and/or treat diseases (Scheinbach, 1998). The formulation is based on the function of diet in the preclusion and dealing of particular illnesses (Viuda-Martos *et al.*, 2010).

The high prevalence of diabetes and its long-term complications has led to an ongoing search for hypoglycaemic agents. Fruit extracts have been used extensively in this context because they are natural, safe and readily available. Pomegranate has widely been investigated in recent years by scientists worldwide, as proven by hundreds of publications on their chemical composition, potential uses and health-promoting effects (Gumienna *et al.*, 2016). Its application against many ailments can be seen in folk medicine of the Near East (Langley, 2000; Jurenka, 2008). Currently, food-based phenolics are among the interest phytochemicals dealing with the occurrence of oxidation-linked diseases, most notably type 2 diabetes, cardiovascular disease and cancer. Products derived from pomegranate exhibit a broad spectrum of activity, improving human health, due to high contents of polyphenolics.

Fermentation is currently becoming the chosen method for preservation of fruit juices as the growing concern of consumers over artificial preservatives is continuously increased (Gumienna *et al.*, 2016). The fermentation process provides potential applications of whole fruit pomegranate juice with very attractive sensory attributes and health-promoting properties, which might become popular in the Eastern European market, and possibly in Asian countries (Mena *et al.*, 2012; Shubhada *et al.*, 2018). Probiotic product is the largest functional food market. This is because probiotication which is one of the food processing techniques that can preserve and enhance the functional and nutritional content of foods (Mustafa *et al.*, 2016). Probioticated products can be described as food containing live microorganisms that, when are ingested in adequate amount, confer a health benefit on the host. Meanwhile, probiotics are mostly lactic acid bacteria, which may provide antimicrobial, antiviral and antioxidant activities by the production of organic acids, hydrogen peroxide and bacteriocins. It is foreseen that food processing industry is going to develop the fruit-based probiotic product which shall have high resistance against the processing technology and gastrointestinal challenges, as well as meeting the requirement of medical application in the near future, particularly from the well-known “superfood”, namely pomegranate.

Concurrent with the increasing cost of health care, the human population is plagued by an epidemic of chronic diseases which has led consumers to adopt a "preventive" approach with a more careful and conscious selection of food for leading a healthy lifestyle (Ankolekar, 2013). Probiotic fermented foods with their low-cost and multi-faceted therapeutic potential is one of the top choices towards a healthier lifestyle. Fermentation has records on the history of food, eating habits and cultural exchange of food. Although fermentation provides a number of functional aspects, it primarily evolved as a process to preserve food safely or sometimes known as biopreservation. Fermentation may increase the shelf life of food by one to two orders of magnitude, by adding value to enrich it with nutrients, flavour, and in some cases, detoxifying substrate (Huynh *et al.*, 2014).

Owing to the benefit offers by fermentation, probiotic is inoculated into the food and beverage products. Lactic acid bacteria such as *Lactobacillus* sp. and *Bifidobacterium* sp. are the major class of probiotics, which are defined as living microorganisms which exert health benefits beyond basic nutrition (Ljungh and Wadstrom, 2006). Lactic acid bacteria have been shown to confer several benefits to the host including better absorption of nutrients from food, decrease in lactose intolerance in some individuals, control of diseases originating from intestinal infections, potential to control of some types of cancer and stimulation of host immune response (Perdigon *et al.*, 2001; Rafter, 2002). Moreover, lactic acid fermentation is used for commercial bulk storage of seasonal fruits to increase their availability and to obtain a desired sensory quality of the products (Thakur and Joshi, 2017).

The probiotic dairy products such as fermented milks, ice cream, various types of cheese, baby-food milk powder, frozen dairy desserts, whey-based beverages, sour cream, buttermilk, normal and flavoured liquid milk and concentrated milk are formerly well known (Mortazavian *et al.*, 2011). However, the increasing health concerns such as lactose intolerance, milk protein allergy, high cholesterol content and high amounts of saturated fatty acids of dairy based foods have promoted the growth of non-dairy foods such as probiotic fermented cereals, fruits and vegetables juices (Gupta and Abu-Ghannam, 2012; Peres *et al*. 2012;

Kumar *et al.* 2013, 2015). Hence, the non-dairy based probiotic foods and beverages have been gaining popularity.

Lately, various fruit juices have been investigated as a non-dairy probiotic drink after fermentation with selected probiotic lactic acid bacteria such as pear (Ankolekar *et al.*, 2012), watermelon (Fazeli *et al.*, 2007), cantaloupe (Fonteles *et al.*, 2012), orange (Escudero- Lopez *et al.*, 2013), as well as pomegranate fruit juice which is recommended to be as an appropriate substrate for cultivation of probiotic bacteria (Mousavi *et al.*, 2011, Fazeli *et al.*, 2011). The current trend is the use of fermentation to deliver fruit and juice products which are less “heavily” preserved, higher in quality, perceived as natural product containing fewer additives, and are nutritionally healthier (Mihiretie and Desta, 2015).

Fermentation is a very effective method of food product biopreservation, as changes taking place during this process resulted in the extension of shelf life, modifying sensory attributes of the final product, in terms of its taste, aroma and texture (Gumienna *et al.*, 2016, Huynh *et al*, 2014). Chemical reactions may occur during this process, and thus contributing to the improvement of nutritive value by enhancing the bioavailability of compounds and improving their digestibility. Possibly, the process may also contribute to the formation of new compounds exhibiting many beneficial properties for human health.

Since pomegranate is rich with the therapeutic properties and the chronic diseases are becoming serious health concern, fermentation could play a significant role. During the last two decades, various parts of the plant had been subjected to extensive phytochemical, pharmacological and clinical investigations. Many interesting findings have been reported in various fields (Artik, 1998). Most of the previously probioticated pomegranate juice are utilizing the aril part of the fruit (Fazeli *et al.*, 2011) or simply the commercial concentrated fruit juice (Mousavi *et al.*, 2011). To date, fermentation of whole part of the pomegranate fruit is scarcely investigated. With respect to non-dairy food matrices, the information regarding the survival of microorganisms against the challenges, the criteria for fermentation, their use as starters and their relationship with other microorganisms are limited

(Schrezenmeir and de Vrese, 2001). The type of food matrix and the cell condition play a major role for the survivability of probiotics during long-term storage and processing (Endo *et al.,* 2014).

Therefore, different bioprocessing parameters such temperature, pH and agitation were tested in this study to investigate the quality of pomegranate juice with different cultivation conditions. The aim was to produce a successful culture, which is enriched with sustainable nutritive substances. Additionally, more research works should be implemented to obtain high yield of fermentation products with retention of functionality properties upon consumption. We sought more in-depth knowledge of the mechanisms of growth and survival in diverse and hostile fruit habitats with the aim of describing specific metabolic traits, which allows better design of fermentation strategies based on selected strains of lactic acid bacteria for targeted raw matrices.

1.2 Problem Statement

Reviews on scientific papers from the search engine Science Direct in 2010 revealed that 770 papers reported on the functional features of pomegranate like antioxidant, antimicrobial or anti-diabetes by its juice, seed oil, peel, flowers and other parts of the tree (Viuda-Martos *et al.,* 2010). From 2010 until 2017, research of pomegranate in the same search engine resulted 3274 accumulated manuscripts, which include 1957 research articles, 509 review articles, 459 book chapters and 61 encyclopaedias. Pomegranate flower extract, pomegranate pure juice and concentrates have been premeditated for their functions in treating diabetes through animal models like Zucker diabetic rats and in humans. Lansky and Newman (2007) indicated that further research in this field is crucial to evaluate the inclusive significance and safety of pomegranate as an intact fruit, extracts from the fruit or fermented pomegranate juice.

Fermentation of fruit juices by probiotic lactic acid bacteria was successfully investigated by several researchers (Klewicka *et al.,* 2004; Mousavi *et al.,* 2011;

Yoon *et al.*, 2004, 2005). As fruit juices encompass good sources of saccaharides, they are expected to be a proactive substrate in the cultivation of probiotic lactic acid bacteria, as well as to enrich the nutrient capacity of beverage products. With various phytochemicals in pomegranate juice, it is a good choice to initiate a functional drink to improve the health condition in a safe way. Most of the beverage products come with excessive sugar-added concept which would cause other diseases, mostly diabetes. The emergence of new food consumption patterns that lack of chemical preservatives yet preserved the food products naturally are the matter of interest. Process conditions play a critical role to lead the formation of desirable yield and product formation that serve benefits, as well as cost effectively. The health benefits of potential probiotic strains should be continuously assessed as the positive activity might be strain dependent and may be affected by the food matrix. Optimization of fermentation processes could be achieved through a selection of desirable trait of strain and process improvement. A successful culture with significant amount of probiotic upon ingestion into the human body is needed, at the same time with beneficial functionality properties.

The high prevalence of lactose intolerance and vegetarian people need an alternative as the carrier of probiotics. However, the largest probiotic food market share is dominated by dairy products (Mortazavian *et al*., 2011). Cultivation of probiotics with fruit juices is the possible alternative to fulfil the need of some people who require the probiotic products, but allergic to dairy-based medium. Fermentation using probiotic bacteria would produce a novel, non-dairy probiotic drink, which could be a good product for individuals with lactose intolerance (Gumienna *et al.*, 2016).

Chronic-linked diseases generate serious complication and reduce patients' quality of life and raise the cost of medical care. For example, the prevalence of diabetes is increasing steadily worldwide, and it is estimated that by 2025, 300 million people in the world will be affected by this illness (Rios *et al.*, 2015). Indeed, glycemic management in type 2 diabetes mellitus has become increasingly complex and, to some extent, controversial, with a widening array of pharmacological agents now available, mounting concerns about their potential adverse effects and new uncertainties regarding the benefits of intensive glycemic control on macrovascular complications (Inzucchi *et al.,* 2012). Hence, there is a strong need to look for effective and health-friendly antidiabetic agent with lesser adverse effects. Currently, plant source substances become possible therapeutic agent due to the safety and antioxidant activity (Qader, 2012). Thus, there is a need to establish an appropriate method, especially in quantifying phenolic compounds that are valuable for the bioactivities. Optimized fermentation process is crucial not only for having enough number of bacterial cells, but also retained phytonutrients upon ingestion.

Previous results showed that pomegranate juice is a good medium for the growth of probiotic bacteria, with their count being stable for 2-weeks of storage at 4 °C (Bialonska *et al.,* 2010; Plessas *et al.,* 2011; Mousavi *et al.,* 2011, Mousavi *et al.,* 2013). This process might yield pomegranate products exhibiting properties of functional food (Gumienna *et al.,* 2016). Only a few studies reported on the bioactivities after fermentation of fruit juice using *L. casei* (Wang *et al.,* 2009; Kumar *et al.,* 2013), some works focused on the growth and sensory properties (Pereira *et al.,* 2011; Yoon *et al.,* 2006; Costa *et al.,* 2013), metabolites components such as lactic acid (Silveira *et al*., 2012; Kaavessina *et al.,* 2017), enzyme (Matthews *et al.,* 2004), bacteriocin (Adebayo *et al.,* 2014), and exopolysaccharides (Mozzi *et al.,* 2003). Thus, the exploitation of whole pomegranate fruit as probiotic carrier, as well as characterization of specific growth potential and functional features is one of the interest scopes in this study.

1.3 Research Objective

This study was conducted to achieve the objectives below:

1. To optimize probiotication of pomegranate juice with *Lactobacillus* species in shake flasks based on the parameters of temperature, pH and agitation speed.
2. To determine the kinetic growth of *L. casei* probioticated pomegranate juice in shake flasks.

3. To determine the growth profile of *L. casei* probioticated pomegranate juice in shake flasks (30 ml) and scaled up stirred tank bioreactor (5L).
4. To characterize the functionality of *L. casei* probioticated pomegranate juice for high antioxidant and antidiabetic activity.

1.4 Scope of Research

Experimental works of this study was started with probiotication of pomegranate juice with several strains of *Lactobacillus* species; *L. plantarum*, *L. salivarius*, *L. casei* and *L. bulgaricus*. The whole fruit of pomegranate included the peel, seed and arils were used as the cultivation medium for the probiotic. The probioticated and fresh juice were compared in term of metabolite profile by using Liquid Chromatography integrated with Mass Spectrometry (LCMS/MS), specifically on flavonoid compounds; quercetin, quercetin-3-glucoside, kaempferol rutinoside, kaempferol glucoside, rutin, apigenin. The successful starter culture with higher growth rate and functionality was utilized in the following analysis.

The probioticated pomegranate juice was further evaluated based on three bioprocessing parameters; temperature (30, 35 and 37 °C), agitation speed (0, 50, 100, 150 rpm) and pH. (2.5, 4.0, 5.5). Optimization using One Factor at A Time was used to obtain the best processing condition for the cultured juice. There were several responses included growth of *Lactobacillus* species, lactic acid production, flavonoids and phenolic acids availability and antioxidant activity.

Growth kinetic studies in shake flasks and 5L stirred-tank bioreactor were carried out at optimized condition (Temperature 37 °C, without agitation 0 rpm, pH 4.0). Kinetic studies in shake flask at the same temperature and pH, but differed in agitation speed (50 rpm) was also added. The integration of growth profile in all conditions was based on the Monod equation, which is basically applied for the batch cultivation. The equation is useful in describing the microbial process in terms of growth (biomass), substrate consumption and product formation.

The correlation of growth profile of *L. casei* probioticated pomegranate juice was further evaluated with the kinetics of quercetin-3-glucoside, antidiabetic and antioxidant activities statistically during shake flask and bioreactor cultivation. Pearson's Correlation Coefficient was used to correlate the responses specifically for the bioreactor probioticated juice. It is estimated that the microbial growth is the influential factor towards the availability of the metabolite and bioactivities.

1.5 Significance of Research

This investigation offers several contributions in the bioprocessing technology using plant sources, mainly on the utilization of pomegranate juice as a probiotic carrier in the development of functional foods. This makes the research on this subject is not only timely, but also important for research and development of health promoting food and diseases prevention. Functional food is not the solely cure, but it could possibly assist our body system to be well-regulated and fight against various diseases.

To the best of our knowledge, the use of the whole part of pomegranate fruit is seldom studied by researchers. Most of the previous studies reported on the use of rind part of the fruit or fruit juice (rind) in the form of concentrate as the cultivation medium during probiotic action. Several researchers reported that pomegranate fruit is rich source of biologically active compounds in juice, peel and seed (Sreekumar *et al.,* 2014; Prakash and Prakash, 2011). After extensive literature survey on the medicinal properties of pomegranate, it is noted that Longtin (2003), referred pomegranate as “nature’s power fruit”. The utilization of the whole part of the fruit would possibly enhance phytonutrients accumulation in the medium during probiotic cultivation. With the improved fermentation condition, it is a good opportunity to evaluate the pomegranate's legacy and future as a powerful natural healing agent.

This study is intended to support the processing food and beverage industry for higher product quality. It can also be a method to improve a platform for phytoceutical or nutraceutical industries. Fermentation with selected probiotic bacteria provide not only supplementary health effect, but also promote a safe preservation method for fruit juices. Developing fruit juice beverages fortified with probiotics could be an improvement in drinks that usually contain large amount of synthetic flavor, coloring and additive. The presence of synthetic additives in the fruit-based beverages could inhibit natural benefits from fruits to be fully absorbed by human body. Furthermore, practicing healthy diet into our life will cut down the supply of supplements, indirectly reducing medical expenditure.

The advantages of fruit juices as substrates for probiotic cultivation have been reported (Mousavi *et al*.,2011; Kazakos *et al*., 2016; Thakur and Joshi, 2017) The low pH of fruit juices increases the acidity, thus making the incorporation of probiotics in this kind of matrix is challenging (Sheehan *et al*., 2007). Some strains of probiotics have low ability to withstand the acidic pH of medium. Somehow, probioticated fruit juices have the potential to be embarked into a new industrial option. Further studies need to be carried out to optimize the survival conditions for individual strain based on the physicochemical properties of fruit juices. This is because probioticated fruit juices are likely to be the priority choice of consumers because of good agreement with health benefits. However, the number of scientific works on fruit-based probiotic foods as a delivery vehicle for the activity of probiotic bacteria is relatively limited till to date. The phenolic compounds in the pomegranate juice which mostly presence as quercetin-3-glucoside, with the addition of probiotic is believed to contribute on the bioactivities of the juice. Antidiabetic and antioxidant activities of the probioticated juice offer alternative treatment for those group of people.

Furthermore, synthetic drugs for the treatment of diabetes have adverse effects on human body. Alternatively, plant source product has high phytonutrients contributed by the presence of phenolic content, less toxicity and safer for intake. Dipeptidyl peptidase-4 (DPP-4) is one of the widely explored methods for Type 2 diabetes mellitus (T2DM) evaluation. Research focused on the strategy to preserve the endogenous glucagon like peptide (GLP-1) activity by inhibiting the DPP-4 action. The DPP-4 inhibitors are weight neutral, well tolerated and giving better glycaemic control over longer duration of time compared to the existing conventional therapies (Patel and Ghate, 2014). The medical care of T2DM patients consumes between 5 and 10% of the budg*et al*located to the health system due to the higher frequency of consultations and hospitalizations, and longer rehospitalizations and more complex treatments (Gagliardino *et al.*, 2004). Several studies have shown that actions aimed at preventing these complications by good diet or functional food consumption like probioticated pomegranate juice are cost effective (CDC Diabetes Cost-effectiveness Group, 2002).

Through this study, *L. casei* was able to survive well in the whole fruit pomegranate juice even though without nutrient supplementation. Indeed, the combination of whole part of the fruit (peels, arils,seeds) as the cultivation medium supplied the required nutrients needed for probiotic survival, thus improving the juice functionality. Probioticated pomegranate juice was proved to have higher antidiabetic and antioxidant activities than non-fermented juice. This was shown through the kinetic growth profile of *L. casei* with the improvement in the content of quercetin-3-glucoside.

1.6 Thesis Structure and Organization

This thesis is divided into five chapters. Chapter 1 covers the overview of the research background, problem statement, objective with its related scopes and significance of the study.

Chapter 2 describes and introduces *Punica granatum* in terms of characteristics and phytochemicals. Its biological activities such as antioxidant and antidiabetic are critically reviewed. The chapter also highlights the application of fermentation technology with the mechanistic action of probiotics to enhance the functionality of fruit juice.

Chapter 3 presents the materials and methodologies in the fermentation of pomegranate juice, as well as related assays like antidiabetic activity by using DPPIV inhibition assay, antioxidant activity by DPPH assay, total phenolic content by Folin Ciocalteu assay, Liquid Chromatography tandem Mass Spectrometry (LCMS/MS) and High-Performance Liquid Chromatography (HPLC) for phytochemical compound identification and quantification. The process was also upscaled in 5L stirred-tank bioreactor for industrial platform basis.

Chapter 4 denotes the comprehensive results and discussion on the fermentation of pomegranate juice with the chosen probiotic lactic acid bacteria. Functionality of the probioticated fruit juice was determined by using the aforementioned analysis and thoroughly discussed and correlated.

Chapter 5 summarizes and concludes the research findings and suggests relevant recommendations for future works.

REFERENCES

Achraf, A., Hamdi, C., Turki, M., Abdelkarim, O., Ayadi, F., Hoekelmann, A., ... and Souissi, N. (2018). Natural pomegranate juice reduces inflammation, muscle damage and increase platelets blood levels in active healthy Tunisian aged men. *Alexandria Journal of Medicine*, *54*(1), 45-48.

Adams, L. S., Seeram, N. P., Aggarwal, B. B., Takada, Y., Sand, D., and Heber, D. (2006). Pomegranate juice, total pomegranate ellagitannins, and punicalagin suppress inflammatory cell signaling in colon cancer cells. *Journal of Agricultural and Food Chemistry*, *54*(3), 980-985.

Adams, M. R. (1990). Topical aspects of fermented foods. *Trends in Food Science & Technology*, *1*, 140-144.

Adebayo, F. A., Afolabi, O. R., and Akintokun, A. K. (2014). Antimicrobial Properties of Purified Bacteriocins Produced from *Lactobacillus casei* and *Lactobacillus fermentum* against Selected Pathogenic Microorganisms.

Afaq, F., Saleem, M., Krueger, C. G., Reed, J. D., and Mukhtar, H. (2005). Anthocyanin-and hydrolyzable tannin-rich pomegranate fruit extract modulates MAPK and NF-κB pathways and inhibits skin tumorigenesis in CD-1 mice. *International Journal of Cancer*, *113*(3), 423-433.

Aherne, S. A., and O'Brien, N. M. (2002). Dietary flavonols: chemistry, food content, and metabolism. *Nutrition*, *18*(1), 75-81.

Ahmed, O. M., Moneim, A. A., Yazid, I. A., and Mahmoud, A. M. (2010). Antihyperglycemic, antihyperlipidemic and antioxidant effects and the probable mechanisms of action of *Ruta graveolens* infusion and rutin in nicotinamide-streptozotocin-induced diabetic rats. *Diabetologia Croatica*, *39*(1), 15-35.

Aissaoui, A., Zizi, S., Israili, Z. H., and Lyoussi, B. (2011). Hypoglycemic and hypolipidemic effects of *Coriandrum sativum* L. in *Meriones shawi* rats. *Journal of ethnopharmacology*, *137*(1), 652-661.

Almeida, C. C., Lorena, S. L. S., Pavan, C. R., Akasaka, H. M. I., and Mesquita, M. A. (2012). Beneficial effects of long-term consumption of a probiotic combination of *Lactobacillus casei* Shirota and *Bifidobacterium breve* Yakult may persist after suspension of therapy in lactose-intolerant patients. *Nutrition in Clinical Practice*, *27*(2), 247-251.

Alonso, S., Herrero, M., Rendueles, M., and Díaz, M. (2010). Residual yoghurt whey for lactic acid production. *Biomass and Bioenergy*, *34*(7), 931-938.

Alper, N., Bahçeci, K. S., and Acar, J. (2005). Influence of processing and pasteurization on color values and total phenolic compounds of pomegranate juice. *Journal of food processing and preservation*, 29(5-6), 357-368.

Altiok, D., Tokatlı, F., and Harsa, Ş. (2006). Kinetic modelling of lactic acid production from whey by Lactobacillus casei (NRRL B-441). *Journal of Chemical Technology & Biotechnology: International Research in Process, Environmental & Clean Technology*, *81*(7), 1190-1197.

Anhe, F. F., Desjardins, Y., Pilon, G., Dudonne, S., Genovese, M. I., Lajolo, F. M., and Marette, A. (2013). Polyphenols and type 2 diabetes: A prospective review. *PharmaNutrition*, *1*(4), 105-114.

Ankolekar, C. (2013). *Lactic acid bacteria mediated phenolic bioactive modulation from fruit systems for health benefits.* Doctor Philosophy, University of Massachusetts Amherst.

Ankolekar, C., and Shetty, K. (2011). Fermentation-Based Processing of Food Botanicals for Mobilization of Phenolic Phytochemicals for Type 2 Diabetes Management. *Functional Foods, Nutraceuticals, and Degenerative Disease Prevention*, 341-355.

Ankolekar, C., Johnson, K., Pinto, M., Johnson, D., Labbe, R. G., Greene, D., and Shetty, K. (2012). Fermentation of whole apple juice using *Lactobacillus acidophilus* for potential dietary management of hyperglycemia, hypertension, and modulation of beneficial bacterial responses. *Journal of Food Biochemistry*, *36*(6), 718-738.

Ankolekar, C., Pinto, M., Greene, D., and Shetty, K. (2012). *In vitro* bioassay based screening of antihyperglycemia and antihypertensive activities of *Lactobacillus acidophilus* fermented pear juice. *Innovative food science & emerging technologies*, 13, 221-230.

Artik, N. (1998). Determination of phenolic compounds in pomegranate juice by using HPLC. *Fruit Processing*, *8*, 492-499.

Arts, I. C., Sesink, A. L., Faassen-Peters, M., and Hollman, P. C. (2004). The type of sugar moiety is a major determinant of the small intestinal uptake and subsequent biliary excretion of dietary quercetin glycosides. *British Journal of Nutrition*, *91*(6), 841-847.

Ávila, M., Hidalgo, M., Sánchez-Moreno, C., Pelaez, C., Requena, T., and de Pascual-Teresa, S. (2009). Bioconversion of anthocyanin glycosides by *Bifidobacteria* and *Lactobacillus*. *Food Research International*, *42*(10), 1453-1461.

Aviram, M., and Dornfeld, L. (2001). Pomegranate juice consumption inhibits serum angiotensin converting enzyme activity and reduces systolic blood pressure. *Atherosclerosis*, *158*(1), 195-198.

Aviram, M., Rosenblat, M., Gaitini, D., Nitecki, S., Hoffman, A., Dornfeld, L., ... and Hayek, T. (2004). Pomegranate juice consumption for 3 years by patients with carotid artery stenosis reduces common carotid intima-media thickness, blood pressure and LDL oxidation. *Clinical Nutrition*, *23*(3), 423-433.

Aviram, M., Volkova, N., Coleman, R., Dreher, M., Reddy, M. K., Ferreira, D., and Rosenblat, M. (2008). Pomegranate phenolics from the peels, arils, and flowers are antiatherogenic: studies in vivo in atherosclerotic apolipoprotein E-deficient (E0) mice and in vitro in cultured macrophages and lipoproteins. *Journal of Agricultural and Food Chemistry*, *56*(3), 1148-1157.

Axelsson, L. (2004). Lactic acid bacteria: classification and physiology. In:Salminen S, von Wright A, Ouwehand A, editors. Lactic acid bacteria: microbiological and functional aspects. 1-66.

Azadzoi, K. M., Schulman, R. N., Aviram, M., and Siroky, M. B. (2005). Oxidative stress in arteriogenic erectile dysfunction: prophylactic role of antioxidants. *The Journal of urology*, *174*(1), 386-393.

Bagri, P., Ali, M., Sultana, S., and Aeri, V. (2010). New flavonoids from *Punica granatum* flowers. *Chemistry of natural compounds*, *46*(2), 201-204.

Bahadoran, Z., Mirmiran, P., and Azizi, F. (2013). Dietary polyphenols as potential nutraceuticals in management of diabetes: a review. *Journal of Diabetes & Metabolic Disorders*, *12*(1), 43.

Bakri, Y., Mekaeel, A., and Koreih, A. (2011). Influence of agitation speeds and aeration rates on the xylanase activity of *Aspergillus niger* SS7. *Brazilian Archives of Biology and Technology*, *54*(4), 659-664.

Baliga, M. S., Shivashankara, A. R., Shetty, C. B., Thilakchand, K. R., Periera, N., and Palatty, P. L. (2013). Antidiabetic effects of *Punica granatum* L (Pomegranate): a review. In *Bioactive food as dietary interventions for diabetes* (pp. 355-369).

Bandaiphet, C., and Prasertsan, P. (2006). Effect of aeration and agitation rates and scale-up on oxygen transfer coefficient, kLa in exopolysaccharide production from *Enterobacter cloacae* WD7. *Carbohydrate Polymers*, *66*(2), 216-228.

Banihani, S., Swedan, S., and Alguraan, Z. (2013). Pomegranate and type 2 diabetes. *Nutrition research*, *33*(5), 341-348.

Bansal, P., Paul, P., Mudgal, J., Nayak, P. G., Pannakal, S. T., Priyadarsini, K. I., and Unnikrishnan, M. K. (2012). Antidiabetic, antihyperlipidemic and antioxidant effects of the flavonoid rich fraction of *Pilea microphylla* (L.) in high fat diet/streptozotocin-induced diabetes in mice. *Experimental and Toxicologic Pathology*, *64*(6), 651-658.

Basu, A., and Lyons, T. J. (2011). Strawberries, blueberries, and cranberries in the metabolic syndrome: clinical perspectives. *Journal of agricultural and food chemistry*, *60*(23), 5687-5692.

Basu, A., and Penugonda, K. (2009). Pomegranate juice: a heart-healthy fruit juice. *Nutrition reviews*, *67*(1), 49-56.

Basu, A., Fu, D. X., Wilkinson, M., Simmons, B., Wu, M., Betts, N. M., and Lyons, T. J. (2010). Strawberries decrease atherosclerotic markers in subjects with metabolic syndrome. *Nutrition research*, *30*(7), 462-469.

Batt, C. A., and Tortorello, M. O. (2014). Encyclopaedia of Food Microbiology. Elsevier Academic Press (2nd ed.). Oxford, UK. pp.14-1000.

Baumgarten, S. C., and Frasor, J. (2012). Minireview: inflammation: an instigator of more aggressive estrogen receptor (ER) positive breast cancers. *Molecular Endocrinology*, *26*(3), 360-371.

Bergqvist, S. W., Sandberg, A. S., Carlsson, N. G., and Andlid, T. (2005). Improved iron solubility in carrot juice fermented by homo-and hetero-fermentative lactic acid bacteria. *Food microbiology*, *22*(1), 53-61.

Bertrand, A., Morel, S., Lefoulon, F., Rolland, Y., Monsan, P., and Remaud-Simeon, M. (2006). *Leuconostoc mesenteroides* glucansucrase synthesis of flavonoid glucosides by acceptor reactions in aqueous-organic solvents. *Carbohydrate research*, *341*(7), 855-863.

Bialonska, D., Ramnani, P., Kasimsetty, S. G., Muntha, K. R., Gibson, G. R., and Ferreira, D. (2010). The influence of pomegranate by-product and punicalagins on selected groups of human intestinal microbiota. *International journal of food microbiology*, *140*(2-3), 175-18

Bierhaus, A., Chevion, S., Chevion, M., Hofmann, M., Quehenberger, P., Illmer, T., and Wahl, P. (1997). Advanced glycation end product-induced activation of NF-κB is suppressed by α-lipoic acid in cultured endothelial cells. *Diabetes*, *46*(9), 1481-1490.

Bishayee, A., Mandal, A., Bhattacharyya, P., and Bhatia, D. (2016). Pomegranate exerts chemoprevention of experimentally induced mammary tumorigenesis by suppression of cell proliferation and induction of apoptosis. *Nutrition and cancer*, *68*(1), 120-130.

Blumberg, J. B., Camesano, T. A., Cassidy, A., Kris-Etherton, P., Howell, A., Manach, C., and Vita, J. A. (2013). Cranberries and their bioactive constituents in human health. *Advances in Nutrition*, *4*(6), 618-632.

Bnouham, M., Ziyyat, A., Mekhfi, H., Tahri, A., and Legssyer, A. (2006). Medicinal plants with potential antidiabetic activity-A review of ten years of herbal medicine research (1990-2000). *International Journal of Diabetes and Metabolism*, *14*(1), 1.

Bolling, B. W., Chen, Y. Y., and Chen, C. Y. O. (2013). Contributions of phenolics and added vitamin C to the antioxidant capacity of pomegranate and grape juices: synergism and antagonism among constituents. *International journal of food science & technology*, *48*(12), 2650-2658.

Bolling, B. W., Chen, Y. Y., Kamil, A. G., and Oliver Chen, C. Y. (2012). Assay Dilution Factors Confound Measures of Total Antioxidant Capacity in Polyphenol-Rich Juices. *Journal of food science*, *77*(2).

Bolton, R. P., Heaton, K. W., and Burroughs, L. F. (1981). The role of dietary fiber in satiety, glucose, and insulin: studies with fruit and fruit juice. *The American journal of clinical nutrition*, *34*(2), 211-217.

Borges, G., and Crozier, A. (2012). HPLC–PDA–MS fingerprinting to assess the authenticity of pomegranate beverages. *Food chemistry*, *135*(3), 1863-1867.

Borges, G., Mullen, W., and Crozier, A. (2010). Comparison of the polyphenolic composition and antioxidant activity of European commercial fruit juices. *Food & function*, *1*(1), 73-83.

Borresen, E., J Henderson, A., Kumar, A., L Weir, T., and P Ryan, E. (2012). Fermented foods: patented approaches and formulations for nutritional supplementation and health promotion. *Recent patents on food, nutrition & agriculture*, *4*(2), 134-140.

Bouguettoucha, A., Balannec, B., and Amrane, A. (2011). Unstructured models for lactic acid fermentation–a review. *Food Technology and Biotechnology*, *49*(1), 3-12.

Brasnyó, P., Molnár, G. A., Mohás, M., Markó, L., Laczy, B., Cseh, J., ... and Mészáros, L. G. (2011). Resveratrol improves insulin sensitivity, reduces oxidative stress and activates the Akt pathway in type 2 diabetic patients. *British Journal of Nutrition*, *106*(3), 383-389.

Broadbent, J. R., Larsen, R. L., Deibel, V., and Steele, J. L. (2010). Physiological and transcriptional response of *Lactobacillus casei* ATCC 334 to acid stress. *Journal of bacteriology*, 192(9), 2445-2458.

Bruneton J. (1999). Pharmacognosie: phytochimie, plantes medicinales; Editions Tec & Doc: Paris, France.

Buchta, K. (1983). Lactic acid. *Biotechnology*, *3*, 409-412.

Busairi, A. M. (2002). *Lactic Acid Fermentation of Pineapple Wastes Fermentation Using Lactobacillus Delbrueckii*. PhD Thesis, Universiti Technologi Malaysia.

Çam, M., Hışıl, Y., and Durmaz, G. (2009). Classification of eight pomegranate juices based on antioxidant capacity measured by four methods. *Food chemistry*, *112*(3), 721-726.

CDC Diabetes Cost-effectiveness Group (2002). Cost-effectiveness of intensive glycemic control, intensified hypertension control, and serum cholesterol level reduction for type 2 diabetes, JAMA 287, 2542–2551.

Cevallos-Cevallos, J. M., Reyes-De-Corcuera, J. I., Etxeberria, E., Danyluk, M. D., and Rodrick, G. E. (2009). Metabolomic analysis in food science: a review. *Trends in Food Science & Technology*, *20*(11-12), 557-566.

Chakrabarti, R., Bhavtaran, S., Narendra, P., Varghese, N., Vanchhawng, L., Mohamed Sham Shihabudeen, H., and Thirumurgan, I. V. K. (2011).

Dipeptidyl peptidase-IV inhibitory activity of *Berberis aristata*. *J Nat Prod*, *4*, 158-163.

Champagne, C. P., Gardner, N. J., and Roy, D. (2005). Challenges in the addition of probiotic cultures to foods. *Critical reviews in food science and nutrition*, *45*(1), 61-84.

Chan, H. T., Yiu, K. H., Wong, C. Y., Li, S. W., Tam, S., and Tse, H. F. (2013). Increased dietary fruit intake was associated with lower burden of carotid atherosclerosis in Chinese patients with Type 2 diabetes mellitus. *Diabetic Medicine*, *30*(1), 100-108.

Chen, S., Xing, X. H., Huang, J. J., and Xu, M. S. (2011). Enzyme-assisted extraction of flavonoids from Ginkgo biloba leaves: improvement effect of flavonol transglycosylation catalyzed by *Penicillium decumbens* cellulase. *Enzyme and microbial technology*, *48*(1), 100-105.

Chidambara Murthy, K. N., Jayaprakasha, G. K., and Singh, R. P. (2002). Studies on antioxidant activity of pomegranate (*Punica granatum*) peel extract using *in vivo* models. *Journal of agricultural and food chemistry*, *50*(17), 4791-4795.

Chien, H. L., Huang, H. Y., and Chou, C. C. (2006). Transformation of isoflavone phytoestrogens during the fermentation of soymilk with lactic acid bacteria and bifidobacteria. *Food microbiology*, *23*(8), 772-778.

Cho, K. M., Hong, S. Y., Math, R. K., Lee, J. H., Kambiranda, D. M., Kim, J. M., ... and Yun, H. D. (2009). Biotransformation of phenolics (isoflavones, flavanols and phenolic acids) during the fermentation of cheonggukjang by *Bacillus pumilus* HY1. *Food Chemistry*, *114*(2), 413-419.

Chua, L. S., Latiff, N. A., Lee, S. Y., Lee, C. T., Sarmidi, M. R., and Aziz, R. A. (2011). Flavonoids and phenolic acids from *Labisia pumila* (Kacip Fatimah). *Food Chemistry*, 127(3), 1186–1192.

Chung, S. S., Ho, E. C., Lam, K. S., and Chung, S. K. (2003). Contribution of polyol pathway to diabetes-induced oxidative stress. *Journal of the American Society of Nephrology*, *14*(suppl 3), S233-S236.

Colombo, E., Sangiovanni, E., and Dell'Agli, M. (2013). A review on the anti-inflammatory activity of pomegranate in the gastrointestinal tract. *Evidence-Based Complementary and Alternative Medicine*, *2013*.

Coman, C., Rugina, O. D., and Socaciu, C. (2012). Plants and natural compounds with antidiabetic action. *Notulae Botanicae Horti Agrobotanici Cluj-Napoca*, *40*(1), 314-325.

Corcionivoschi, N., Drinceanu, D., Stef, L., Luca, I., and Julean, C. (2010). Probiotics-identification and ways of action. *Innovative Romanian Food Biotechnology*, *6*, 1.

Corcoran, B. M., Stanton, C., Fitzgerald, G. F., and Ross, R. P. (2005). Survival of probiotic lactobacilli in acidic environments is enhanced in the presence of metabolizable sugars. *Applied and environmental microbiology*, *71*(6), 3060-3067.

Costa, M. G. M., Fonteles, T. V., de Jesus, A. L. T., and Rodrigues, S. (2013). Sonicated pineapple juice as substrate for L. casei cultivation for probiotic beverage development: process optimisation and product stability. *Food chemistry*, *139*(1-4), 261-266.

Coulon, S., Chemardin, P., Gueguen, Y., Arnaud, A., and Galzy, P. (1998). Purification and characterization of an intracellular β-glucosidase from *Lactobacillus casei* ATCC 393. *Applied biochemistry and biotechnology*, *74*(2), 105-114.

Craddy, P., Palin, H. J., and Johnson, K. I. (2014). Comparative effectiveness of dipeptidylpeptidase-4 inhibitors in type 2 diabetes: a systematic review and mixed treatment comparison. *Diabetes Therapy*, *5*(1), 1-41.

Cristofori, V., Caruso, D., Latini, G., Dell'Agli, M., Cammilli, C., Rugini, E., ... and Muleo, R. (2011). Fruit quality of Italian pomegranate (*Punica granatum* L.) autochthonous varieties. *European Food Research and Technology*, *232*(3), 397-403.

Crozier, A., Jaganath, I. B., and Clifford, M. N. (2009). Dietary phenolics: chemistry, bioavailability and effects on health. *Natural product reports*, *26*(8), 1001-1043.

Curiel, J. A., Pinto, D., Marzani, B., Filannino, P., Farris, G. A., Gobbetti, M., and Rizzello, C. G. (2015). Lactic acid fermentation as a tool to enhance the antioxidant properties of *Myrtus communis* berries. *Microbial cell factories*, *14*(1), 67.

da Silva, C. M. G., Contesini, F. J., Sawaya, A. C. F., Cabral, E. C., da Silva Cunha, I. B., Eberlin, M. N., and de Oliveira Carvalho, P. (2013). Enhancement of the antioxidant activity of orange and lime juices by flavonoid enzymatic de-glycosylation. *Food research international*, *52*(1), 308-314.

da Silva, J. A. T., Rana, T. S., Narzary, D., Verma, N., Meshram, D. T., and Ranade, S. A. (2013). Pomegranate biology and biotechnology: a review. *Scientia Horticulturae*, *160*, 85-107.

Dave, R. I., and Shah, N. P. (1997). Viability of yoghurt and probiotic bacteria in yoghurts made from commercial starter cultures. *International Dairy Journal*, *7*(1), 31-41.

Davidson, B. E., Llanos, R. M., Cancilla, M. R., Redman, N. C., and Hillier, A. J. (1995). Current research on the genetics of lactic acid production in lactic acid bacteria. *International Dairy Journal*, *5*(8), 763-784.

de Araújo, M. E. M. B., Franco, Y. E. M., Alberto, T. G., Sobreiro, M. A., Conrado, M. A., Priolli, D. G. and de Oliveira Carvalho, P. (2013). Enzymatic de-glycosylation of rutin improves its antioxidant and antiproliferative activities. *Food chemistry*, *141*(1), 266-273.

Dehkharghanian, M., Adenier, H., and Vijayalakshmi, M. A. (2010). Study of flavonoids in aqueous spinach extract using positive electrospray ionisation tandem quadrupole mass spectrometry. *Food chemistry*, *121*(3), 863-870.

Dembinska-Kiec, A., Mykkänen, O., Kiec-Wilk, B., and Mykkänen, H. (2008). Antioxidant phytochemicals against type 2 diabetes. *British Journal of Nutrition*, *99*.

Demir, N., BAHÇECİ, K. S., and Acar, J. (2006). The effects of different initial *Lactobacillus plantarum* concentrations on some properties of fermented carrot juice. *Journal of Food Processing and Preservation*, *30*(3), 352-363.

Devalaraja, S., Jain, S., and Yadav, H. (2011). Exotic fruits as therapeutic complements for diabetes, obesity and metabolic syndrome. *Food Research International*, *44*(7), 1856-1865.

Dey, D., Debnath, S., Hazra, S., Ghosh, S., Ray, R., and Hazra, B. (2012). Pomegranate pericarp extract enhances the antibacterial activity of ciprofloxacin against extended-spectrum β-lactamase (ESBL) and metallo-β-lactamase (MBL) producing Gram-negative bacilli. *Food and chemical toxicology*, *50*(12), 4302-4309.

Di Cagno, R., Coda, R., De Angelis, M., and Gobbetti, M. (2013). Exploitation of vegetables and fruits through lactic acid fermentation. *Food Microbiology*, *33*(1), 1-10.

Di Maio, I., Esposto, S., Taticchi, A., Selvaggini, R., Veneziani, G., Urbani, S., and Servili, M. (2011). HPLC–ESI-MS investigation of tyrosol and hydroxytyrosol oxidation products in virgin olive oil. *Food chemistry*, *125*(1), 21-28.

Dickerman, J. M., and Liberman, S. (1952). Studies on The Chemical Nature of An Antibiotic Present in Water Exteacts Of Cabbage a. *Journal of Food Science*, *17*(1-6), 438-441.

Doblado, R., Zielinski, H., Piskula, M., Kozlowska, H., Muñoz, R., Frías, J., and Vidal-Valverde, C. (2005). Effect of processing on the antioxidant vitamins and antioxidant capacity of *Vigna sinensis* Var. *carilla*. *Journal of agricultural and food chemistry*, *53*(4), 1215-1222.

Dogahe, M. K., Khosravi-Darani, K., Tofighi, A., Dadgar, M., and Mortazavian, A. M. (2015). Effect of process variables on survival of bacteria in probiotics enriched pomegranate juice. *British Biotechnology Journal*, *5*(1), 37.

Elfalleh, W., Hannachi, H., Tlili, N., Yahia, Y., Nasri, N., and Ferchichi, A. (2012). Total phenolic contents and antioxidant activities of pomegranate peel, seed, leaf and flower. *Journal of Medicinal Plants Research*, *6*(32), 4724-4730.

El-Nemr, S. E., Ismail, I. A., and Ragab, M. (1990). Chemical composition of juice and seeds of pomegranate fruit. *Food/Nahrung*, *34*(7), 601-606.

Ercolini, D., Moschetti, G., Blaiotta, G., and Coppola, S. (2001). Behavior of variable V3 region from 16S rDNA of lactic acid bacteria in denaturing gradient gel electrophoresis. *Current Microbiology*, *42*(3), 199-202.

Escudero-López, B., Cerrillo, I., Herrero-Martín, G., Hornero-Méndez, D., Gil-Izquierdo, A., Medina, S., and Fernández-Pachón, M. S. (2013). Fermented orange juice: Source of higher carotenoid and flavanone contents. *Journal of agricultural and food chemistry*, *61*(37), 8773-8782.

Esmaillzadeh, A., Tahbaz, F., Gaieni, I., Alavi-Majd, H., and Azadbakht, L. (2006). Cholesterol-lowering effect of concentrated pomegranate juice consumption in type II diabetic patients with hyperlipidemia. *International journal for vitamin and nutrition research*, *76*(3), 147-151.

Fadavi, A., Barzegar, M., and Azizi, M. H. (2006). Determination of fatty acids and total lipid content in oilseed of 25 pomegranates varieties grown in Iran. *Journal of Food Composition and Analysis*, *19*(6-7), 676-680.

Fahey, J. W., Zalcmann, A. T., and Talalay, P. (2001). The chemical diversity and distribution of glucosinolates and isothiocyanates among plants. *Phytochemistry*, *56*(1), 5-51.

Fan, J., Johnson, M. H., Lila, M. A., Yousef, G., and de Mejia, E. G. (2013). Berry and citrus phenolic compounds inhibit dipeptidyl peptidase IV: Implications in diabetes management. *Evidence-Based Complementary and Alternative Medicine*, *2013*.

Fang, Z., Hu, Y., Liu, D., Chen, J., and Ye, X. (2008). Changes of phenolic acids and antioxidant activities during potherb mustard (*Brassica juncea*, Coss.) pickling. *Food chemistry*, *108*(3), 811-817.

FAO/WHO working group. (2001). Report of a joint FAO/WHO expert consultation on evaluation of health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria. *Córdoba, Argentina (October 1–4, 2001)*.

Faria, A., and Calhau, C. (2010). Pomegranate in human health: An overview. In *Bioactive Foods in Promoting Health* (pp. 551-563). USA: Academic Press

Faria, A., and Calhau, C. (2011). The bioactivity of pomegranate: impact on health and disease. *Critical reviews in food science and nutrition*, *51*(7), 626-634.

Farr, S. B., and Kogoma, T. (1991). Oxidative stress responses in *Escherichia coli* and *Salmonella typhimurium*. *Microbiological reviews*, *55*(4), 561-585.

Fazeli, M. R., Amirmozafari, N., and Jamalifar, H. (2007). Antagonistic action of watermelon juice probioticated using different strains of *Lactobacilli* against *Salmonella typhimurium*. *Iranian Journal of Public Health*, *36*(4), 70-73.

Fazeli, M. R., Bahmani, S., Jamalifar, H., and Samadi, N. (2011). Effect of probiotication on antioxidant and antibacterial activities of pomegranate juices from sour and sweet cultivars. *Natural product research*, *25*(3), 288-297.

Feldman, M., and Schiller, L. R. (1983). Disorders of gastrointestinal motility associated with diabetes mellitus. *Annals of Internal Medicine*, *98*(3), 378-384.

Felse, P. A., and Panda, T. (2000). Submerged culture production of chitinase by *Trichoderma harzianum* in stirred tank bioreactors–the influence of agitator speed. *Biochemical engineering journal*, *4*(2), 115-120.

Feng, P., Weagant, S. D., Grant, M. A., Burkhardt, W., Shellfish, M. and Water, B. (2002). BAM: Enumeration of *Escherichia coli* and the Coliform Bacteria. *Bacteriological analytical manual*, 13-19.

Fernandez-Orozco, R., Frias, J., Muñoz, R., Zielinski, H., Piskula, M. K., Kozlowska, H., and Vidal-Valverde, C. (2007). Fermentation as a bioprocess to obtain functional soybean flours. *Journal of agricultural and food chemistry*, *55*(22), 8972-8979.

Ferreira, O., and Pinho, S. P. (2012). Solubility of flavonoids in pure solvents. *Industrial & Engineering Chemistry Research*, *51*(18), 6586-6590.

Filannino, P., Azzi, L., Cavoski, I., Vincentini, O., Rizzello, C. G., Gobbetti, M., and Di Cagno, R. (2013). Exploitation of the health-promoting and sensory properties of organic pomegranate (*Punica granatum* L.) juice through lactic acid fermentation. *International journal of food microbiology*, *163*(2-3), 184-192.

Filannino, P., Bai, Y., Di Cagno, R., Gobbetti, M., and Gänzle, M. G. (2015). Metabolism of phenolic compounds by *Lactobacillus* spp. during fermentation of cherry juice and broccoli puree. *Food microbiology*, *46*, 272-279.

Filannino, P., Cardinali, G., Rizzello, C. G., Buchin, S., De Angelis, M., Gobbetti, M., and Di Cagno, R. (2014). Metabolic responses of *Lactobacillus plantarum* strains during fermentation and storage of vegetable and fruit juices. *Applied and environmental microbiology*, AEM-03885.

Fischer, U. A., Carle, R., and Kammerer, D. R. (2011). Identification and quantification of phenolic compounds from pomegranate (*Punica granatum* L.) peel, mesocarp, aril and differently produced juices by HPLC-DAD–ESI/MSn. *Food chemistry*, *127*(2), 807-821.

Fonteles, T. V., Costa, M. G. M., de Jesus, A. L. T., and Rodrigues, S. (2012). Optimization of the fermentation of cantaloupe juice by *Lactobacillus casei* NRRL B-442. *Food and Bioprocess Technology*, *5*(7), 2819-2826.

Friedman, M., and Jurgens, H. S. (2000). Effect of pH on the stability of plant phenolic compounds. *Journal of agricultural and food chemistry*, *48*(6), 2101-2110.

Fu, W., and Mathews, A. P. (1999). Lactic acid production from lactose by *Lactobacillus plantarum*: kinetic model and effects of pH, substrate, and oxygen. *Biochemical engineering journal*, *3*(3), 163-170.

Fu, Z., Gilbert, E. R., Pfeiffer, L., Zhang, Y., Fu, Y., and Liu, D. (2012). Genistein ameliorates hyperglycemia in a mouse model of nongenetic type 2 diabetes. *Applied Physiology, Nutrition, and Metabolism*, *37*(3), 480-488.

Fuhrman, B., Volkova, N., and Aviram, M. (2010). Pomegranate juice polyphenols increase recombinant paraoxonase-1 binding to high-density lipoprotein: studies *in vitro* and in diabetic patients. *Nutrition*, *26*(4), 359-366.

Fukuda, S., Nakanishi, Y., Chikayama, E., Ohno, H., Hino, T., and Kikuchi, J. (2009). Evaluation and characterization of bacterial metabolic dynamics with a novel profiling technique, real-time metabolotyping. *PLoS One*, *4*(3), e4893.

Furrie, E., Macfarlane, S., Kennedy, A., Cummings, J. H., Walsh, S. V., O'neil, D. A., and Macfarlane, G. T. (2005). Synbiotic therapy (*Bifidobacterium longum*/Synergy 1) initiates resolution of inflammation in patients with active ulcerative colitis: a randomised controlled pilot trial. *Gut*, *54*(2), 242-249.

Gagliardino, J. J., Martella, A., Etchegoyen, G. S., Caporale, J. E., Guidi, M. L., Olivera, E. M., and González, C. (2004). Hospitalization and re-hospitalization of people with and without diabetes in La Plata, Argentina: comparison of their clinical characteristics and costs. *Diabetes research and clinical practice*, *65*(1), 51-59.

Ganugapati, J., Baldwa, A., and Lalani, S. (2012). Molecular docking studies of banana flower flavonoids as insulin receptor tyrosine kinase activators as a cure for diabetes mellitus. *Bioinformation, 8*(5), 216.

Gao, C., Mayon, P., MacManus, D. A., and Vulfson, E. N. (2000). Novel enzymatic approach to the synthesis of flavonoid glycosides and their esters. *Biotechnology and bioengineering*, *71*(3), 235-243.

Gardner, N. J., Savard, T., Obermeier, P., Caldwell, G., and Champagne, C. P. (2001). Selection and characterization of mixed starter cultures for lactic acid fermentation of carrot, cabbage, beet and onion vegetable mixtures. *International journal of food microbiology*, *64*(3), 261-275.

Gebremariam, M. M., Hassani, A., Zarnkow, M., and Becker, T. (2015). Investigation of fermentation conditions for teff (Eragrostis tef) malt-wort by *Lactobacillus amylolyticus*. *LWT-Food Science and Technology*, *61*(1), 164-171.

Ghosh, S., Chakraborty, R., Chatterjee, G., and Raychaudhuri, U. (2012). Study on fermentation conditions of palm juice vinegar by response surface methodology and development of a kinetic model. *Brazilian Journal of Chemical Engineering*, *29*(3), 461-472.

Giavasis, I., Harvey, L. M., and McNeil, B. (2006). The effect of agitation and aeration on the synthesis and molecular weight of gellan in batch cultures of *Sphingomonas paucimobilis*. *Enzyme and microbial technology*, *38*(1-2), 101-108.

Gil, M. I., Tomás-Barberán, F. A., Hess-Pierce, B., Holcroft, D. M., and Kader, A. A. (2000). Antioxidant activity of pomegranate juice and its relationship with phenolic composition and processing. *Journal of Agricultural and Food chemistry*, *48*(10), 4581-4589.

Gliszczyńska-Świgło, A., and Muzolf, M. (2007). pH-Dependent radical scavenging activity of folates. *Journal of agricultural and food chemistry*, *55*(20), 8237-8242.

Gözlekçi, Ş., Saraçoğlu, O., Onursal, E., & Özgen, M. (2011). Total phenolic distribution of juice, peel, and seed extracts of four pomegranate cultivars. *Pharmacognosy Magazine*, 7(26), 161.

Guerin, D., Vuillemard, J. C., and Subirade, M. (2003). Protection of *Bifidobacteria* encapsulated in polysaccharide-protein gel beads against gastric juice and bile. *Journal of food protection*, *66*(11), 2076-2084.

Gugliucci, A. (2010). Beyond the antioxidant properties: pomegranate juice polyphenols increase hepatocyte paraoxonase 1 secretion. *Atherosclerosis*, *208*(1), 28-29.

Guillarme, D., Casetta, C., Bicchi, C., and Veuthey, J. L. (2010). High throughput qualitative analysis of polyphenols in tea samples by ultra-high pressure liquid chromatography coupled to UV and mass spectrometry detectors. *Journal of Chromatography A*, *1217*(44), 6882-6890.

Gumienna, M., Szwengiel, A., and Górna, B. (2016). Bioactive components of pomegranate fruit and their transformation by fermentation processes. *European Food Research and Technology*, 242(5), 631-640.

Guo, C., Wei, J., Yang, J., Xu, J., Pang, W., and Jiang, Y. (2008). Pomegranate juice is potentially better than apple juice in improving antioxidant function in elderly subjects. *Nutrition Research*, *28*(2), 72-77.

Guo, C., Yang, J., Wei, J., Li, Y., Xu, J., and Jiang, Y. (2003). Antioxidant activities of peel, pulp and seed fractions of common fruits as determined by FRAP assay. *Nutrition research*, *23*(12), 1719-1726.

Guo, S., Deng, Q., Xiao, J., Xie, B., and Sun, Z. (2007). Evaluation of antioxidant activity and preventing DNA damage effect of pomegranate extracts by chemiluminescence method. *Journal of agricultural and food chemistry*, *55*(8), 3134-3140.

Gupta, S., Abu-Ghannam, N., and Scannell, A. G. (2011). Growth and kinetics of *Lactobacillus plantarum* in the fermentation of edible Irish brown seaweeds. *Food and Bioproducts Processing*, *89*(4), 346-355.

Gupta, S., and Abu-Ghannam, N. (2012). Probiotic fermentation of plant based products: possibilities and opportunities. *Critical reviews in food science and nutrition*, *52*(2), 183-199.

Ha, M. Y., Kim, S. W., Lee, Y. W., Kim, M. J., and Kim, S. J. (2003). Kinetics analysis of growth and lactic acid production in pH-controlled batch cultures of *Lactobacillus casei* KH-1 using yeast extract/corn steep liquor/glucose medium. *Journal of Bioscience and Bioengineering*, *96*(2), 134-140.

Hajimahmoodi, M., Oveisi, M. R., Sadeghi, N., Jannat, B., Hadjibabaie, M., Farahani, E., ... and Namdar, R. (2008). Antioxidant properties of peel and pulp hydro extract in ten Persian pomegranate cultivars. *Pak J Biol Sci*, *11*(12), 1600-4.

Hal, P. H., Bille, P. G., Verkerk, R., and Dekker, M. (2013). The effect of temperature and time on the quality of naturally fermented marula (*Sclerocarya birrea* subsp. caffra) juice. *LWT-Food Science and Technology*, *53*(1), 70-75.

Halberstein, R. A. (2005). Medicinal plants: historical and cross-cultural usage patterns. *Annals of epidemiology*, *15*(9), 686-699.

Hansen, H. B., Andreasen, M., Nielsen, M., Larsen, L., Knudsen, B. K., Meyer, A., and Christensen, L. (2002). Changes in dietary fibre, phenolic acids and activity of endogenous enzymes during rye bread-making. *European Food Research and Technology*, *214*(1), 33-42.

Hassani, A., Procopio, S., and Becker, T. (2016). Influence of malting and lactic acid fermentation on functional bioactive components in cereal-based raw materials: a review paper. *International journal of food science & technology*, *51*(1), 14-22.

He, Q., Lv, Y., and Yao, K. (2007). Effects of tea polyphenols on the activities of α-amylase, pepsin, trypsin and lipase. *Food Chemistry*, *101*(3), 1178-1182.

He, X., Zou, Y., Yoon, W. B., Park, S. J., Park, D. S., and Ahn, J. (2011). Effects of probiotic fermentation on the enhancement of biological and pharmacological activities of *Codonopsis lanceolata* extracted by high pressure treatment. *Journal of bioscience and bioengineering*, *112*(2), 188-193.

Heber, D. (2011). Pomegranate ellagitannins. Herbal Medicine: Biomolecular and Clinical Aspects. 2nd edition. Benzie IFF, Wachtel-Galor S, editors.

Herrera-Arellano, A., Aguilar-Santamaria, L., Garcia-Hernandez, B., Nicasio-Torres, P., and Tortoriello, J. (2004). Clinical trial of *Cecropia obtusifolia* and *Marrubium vulgare* leaf extracts on blood glucose and serum lipids in type 2 diabetics. *Phytomedicine*, *11*(7-8), 561-566.

Hii, C. S. T., and Howell, S. L. (1985). Effects of flavonoids on insulin secretion and $45Ca^{2+}$ handling in rat islets of Langerhans. *Journal of Endocrinology*, *107*(1), 1-8.

Hofvendahl, K., and Hahn-Hägerdal, B. (1997). L-lactic acid production from whole wheat flour hydrolysate using strains of *Lactobacilli* and *Lactococci*. *Enzyme and Microbial Technology*, *20*(4), 301-307.

Holst, J. J. (2007). The physiology of glucagon-like peptide 1. *Physiological reviews*, *87*(4), 1409-1439.

Holst, J. J., and Deacon, C. F. (1998). Inhibition of the activity of dipeptidyl-peptidase IV as a treatment for type 2 diabetes. *Diabetes*, *47*(11), 1663-1670.

Holzapfel, W. H. (2002). Appropriate starter culture technologies for small-scale fermentation in developing countries. *International journal of food microbiology*, *75*(3), 197-212.

Holzapfel, W. H., and Schillinger, U. (2002). Introduction to pre-and probiotics. *Food Research International*, *35*(2-3), 109-116.

Holzapfel, W. H., Haberer, P., Geisen, R., Björkroth, J., and Schillinger, U. (2001). Taxonomy and important features of probiotic microorganisms in food and nutrition–. *The American journal of clinical nutrition*, *73*(2), 365s-373s.

Holzapfel, W. H., Haberer, P., Snel, J., and Schillinger, U. (1998). Overview of gut flora and probiotics. *International journal of food microbiology*, *41*(2), 85-101.

Hood, S. K., and Zoitola, E. A. (1988). Effect of low pH on the ability of *Lactobacillus acidophilus* to survive and adhere to human intestinal cells. *Journal of Food Science*, *53*(5), 1514-1516.

Houseknecht, K. L., Cole, B. M., and Steele, P. J. (2002). Peroxisome proliferator-activated receptor gamma (PPARγ) and its ligands: a review. *Domestic animal endocrinology*, *22*(1), 1-23.

Hsieh, P. C., Huang, G. J., Ho, Y. L., Lin, Y. H., Huang, S. S., Chiang, Y. C., ... and Chang, Y. S. (2010). Activities of antioxidants, α-Glucosidase inhibitors and aldose reductase inhibitors of the aqueous extracts of four Flemingia species in Taiwan. *Botanical Studies*, *51*(293), 302.

Huang, T. H., Yang, Q., Harada, M., Li, G. Q., Yamahara, J., Roufogalis, B. D., and Li, Y. (2005). Pomegranate flower extract diminishes cardiac fibrosis in Zucker diabetic fatty rats: modulation of cardiac endothelin-1 and nuclear factor-kappaB pathways. *Journal of cardiovascular pharmacology*, *46*(6), 856-862.

Hunaefi, D., Gruda, N., Riedel, H., Akumo, D. N., Saw, N. M. M. T., and Smetanska, I. (2013). Improvement of antioxidant activities in red cabbage sprouts by lactic acid bacterial fermentation. *Food biotechnology*, *27*(4), 279-302.

Hunt, J. V., Smith, C. C., and Wolff, S. P. (1990). Autoxidative glycosylation and possible involvement of peroxides and free radicals in LDL modification by glucose. *Diabetes*, *39*(11), 1420-1424.

Hur, S. J., Lee, S. Y., Kim, Y. C., Choi, I., and Kim, G. B. (2014). Effect of fermentation on the antioxidant activity in plant-based foods. *Food chemistry*, *160*, 346-356.

Hussain, S. A., Ahmed, Z. A., Mahwi, T. O., and Aziz, T. A. (2012a). Effect of quercetin on postprandial glucose excursion after mono-and disaccharides challenge in normal and diabetic rats. *Journal of Diabetes Mellitus*, *2*(01), 82.

Hussain, S. A., and Marouf, B. H. (2013). Flavonoids as alternatives in treatment of type 2 diabetes mellitus. *Academia journal of medicinal plants*, *1*(2), 031-036.

Hussain, S. A., Mahwi, T. O., and Aziz, T. A. (2012b). Quercetin dampens postprandial hyperglycemia in type 2 diabetic patients challenged with carbohydrates load. *International Journal of Diabetes Research*, *1*(3), 32-35.

Huynh, N. T., Van Camp, J., Smagghe, G., and Raes, K. (2014). Improved release and metabolism of flavonoids by steered fermentation processes: a review. *International journal of molecular sciences*, 15(11), 19369-19388.

Hyson, A. (2011). Comprehensive Review of Apples and Apple Components and Their Relationship to Human Health. *Advances in Nutrition*, 2, 408–420.

Ibrahim, D., Weloosamy, H., and Lim, S. H. (2015). Effect of agitation speed on the morphology of *Aspergillus niger* HFD5A-1 hyphae and its pectinase production in submerged fermentation. *World journal of biological chemistry*, *6*(3), 265.

Inzucchi, S. E., Bergenstal, R. M., Buse, J. B., Diamant, M., Ferrannini, E., Nauck, M. and Matthews, D. R. (2012). Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetologia*, *55*(6), 1577-1596.

Ismail, T., Sestili, P., and Akhtar, S. (2012). Pomegranate peel and fruit extracts: a review of potential anti-inflammatory and anti-infective effects. *Journal of ethnopharmacology*, *143*(2), 397-405.

Ivanova, D., Gerova, D., Chervenkov, T., and Yankova, T. (2005). Polyphenols and antioxidant capacity of Bulgarian medicinal plants. *Journal of ethnopharmacology*, *96*(1-2), 145-150.

Jackman, R. L., Yada, R. Y., TUNG, M. A., and SPEERS, R. A. (1987). Anthocyanins as food colorants—a review. *Journal of food biochemistry*, 11(3), 201-247.

Jadhav, R., and Puchchakayala, G. (2012). Hypoglycemic and antidiabetic activity of flavonoids: boswellic acid, ellagic acid, quercetin, rutin on streptozotocin-nicotinamide induced type 2 diabetic rats. *Group*, *1*, 100g. *International Journal of Pharmacy and Pharmaceutical Sciences*, 4 (2), 251-256.

Jafari, A. R., Sarrafzadeh, M. H., Alemzadeh, I., and Vosoughi, M. (2007). Effect of stirrer speed and aeration rate on the production of glucose oxidase by *Aspergillus niger*. *Journal of Biological Sciences*, *7*(2), 270-275.

Jain, S., Rai, R., Upadhyaya, A. R., and Malhotra, G. (2014). *Punica granatum*: a natural and recent approach towards dental problem. *International Journal of Pharmaceutical Sciences and Research*, *2*(1), 1-6.

Jain, V., Viswanatha, G. L., Manohar, D., and Shivaprasad, H. N. (2012). Isolation of antidiabetic principle from fruit rinds of *Punica granatum*. *Evidence-Based Complementary and Alternative Medicine*, *2012*.

Jamal, P., Idris, Z. M., and Alam, M. Z. (2011). Effects of physicochemical parameters on the production of phenolic acids from palm oil mill effluent under liquid-state fermentation by *Aspergillus niger* IBS-103ZA. *Food chemistry*, *124*(4), 1595-1602.

Jay, J. M. (2000). Fermentation and fermented dairy products. Modern food microbiology. 6th edition. Gaithersburg, USA: An Aspen Publication, Aspen Publishers, Inc.113-30.

Jayaprakasha, G. K., Singh, R. P., and Sakariah, K. K. (2001). Antioxidant activity of grape seed (*Vitis vinifera*) extracts on peroxidation models in vitro. *Food chemistry*, *73*(3), 285-290.

Jayashree, B., Bibin, Y. S., Prabhu, D., Shanthirani, C. S., Gokulakrishnan, K., Lakshmi, B. S., ... and Balasubramanyam, M. (2014). Increased circulatory levels of lipopolysaccharide (LPS) and zonulin signify novel biomarkers of proinflammation in patients with type 2 diabetes. *Molecular and cellular biochemistry*, *388*(1-2), 203-210.

Jayawardena, M. H. S., De Alwis, N. M. W., Hettigoda, V., and Fernando, D. J. S. (2005). A double blind randomised placebo controlled cross over study of a herbal preparation containing *Salacia reticulata* in the treatment of type 2 diabetes. *Journal of ethnopharmacology*, *97*(2), 215-218.

Johnston, K. L., Clifford, M. N., and Morgan, L. M. (2003). Coffee acutely modifies gastrointestinal hormone secretion and glucose tolerance in humans: glycemic effects of chlorogenic acid and caffeine. *The American journal of clinical nutrition*, *78*(4), 728-733.

Ju, H. K., Cho, E. J., Jang, M. H., Lee, Y. Y., Hong, S. S., Park, J. H., and Kwon, S. W. (2009). Characterization of increased phenolic compounds from fermented Bokbunja (*Rubus coreanus* Miq.) and related antioxidant activity. *Journal of Pharmaceutical and biomedical analysis*, *49*(3), 820-827.

Juan, M. Y., and Chou, C. C. (2010). Enhancement of antioxidant activity, total phenolic and flavonoid content of black soybeans by solid state fermentation with *Bacillus subtilis* BCRC 14715. *Food microbiology*, *27*(5), 586-591.

Jung, M., Park, M., Lee, H. C., Kang, Y. H., Kang, E. S., and Kim, S. K. (2006). Antidiabetic agents from medicinal plants. *Current medicinal chemistry*, *13*(10), 1203-1218.

Jurenka, J. (2008). Therapeutic applications of pomegranate (*Punica granatum* L.): a review. *Alternative medicine review*, 13(2), 128.

Justen, P., Paul, G. C., Nienow, A. W., and Thomas, C. R. (1996). Dependence of mycelial morphology on impeller type and agitation intensity. *Biotechnology and Bioengineering*, *52*(6), 672-684.

Jyothsna, K. (2017). The Study of Effect of Pomegranate Juice on Type 2 Diabetes Mellitus. *IOSR Journal of Dental and Medical Sciences*, 16 (4), 28-30.

Kaavessina, M., Khanifatun, F., and Alzahrani, S. M. (2017). Lactic acid production from date juice using *Lactobacillus casei* ATCC 393 in batch fermentation. In *MATEC Web of Conferences* (Vol. 101, p. 02002). EDP Sciences.

Kachouri, F., Ksontini, H., Kraiem, M., Setti, K., Mechmeche, M., and Hamdi, M. (2015). Involvement of antioxidant activity of *Lactobacillus plantarum* on functional properties of olive phenolic compounds. *Journal of food science and technology*, *52*(12), 7924-7933.

Kador, P. F., Kinoshita, J. H., and Sharpless, N. E. (1985b). Aldose reductase inhibitors: a potential new class of agents for the pharmacological control of certain diabetic complications. *Journal of medicinal chemistry*, *28*(7), 841-849.

Kador, P. F., Robison Jr, W. G., and Kinoshita, J. H. (1985a). The pharmacology of aldose reductase inhibitors. *Annual review of pharmacology and toxicology*, *25*(1), 691-714.

Kailasapathy, K. (2006). Survival of free and encapsulated probiotic bacteria and their effect on the sensory properties of yoghurt. *LWT-Food Science and Technology*, *39*(10), 1221-1227.

Kanwar, S. S. and Keshani (2016). Fermentation of Apple Juice with a Selected Yeast Strain Isolated from the Fermented Foods of Himalayan Regions and Its Organoleptic Properties. *Frontiers in microbiology*, *7*, 1012.

Karasu, Ç., Cumaoğlu, A., Gúrpinar, A., Kartal, M., Kovacikova, L., Milackova, I., and Stefek, M. (2012). Aldose reductase inhibitory activity and antioxidant capacity of pomegranate extracts. *Interdisciplinary toxicology*, *5*(1), 15-20.

Karovičová, J., and Kohajdová, Z. (2003). Lactic acid fermented vegetable juices. *Horticultural Science*, *30*(4), 152-158.

Katina, K., Liukkonen, K. H., Kaukovirta-Norja, A., Adlercreutz, H., Heinonen, S. M., Lampi, A. M., ... and Poutanen, K. (2007b). Fermentation-induced changes in the nutritional value of native or germinated rye. *Journal of Cereal Science*, *46*(3), 348-355.

Kaufman, M., and Wiesman, Z. (2007). Pomegranate oil analysis with emphasis on MALDI-TOF/MS triacylglycerol fingerprinting. *Journal of agricultural and food chemistry*, *55*(25), 10405-10413.

Kaur, S., Kaur, H. P., and Grover, J. (2016). Fermentation of tomato juice by probiotic lactic acid bacteria. *International Journal of Advances in Pharmacy, Biology and Chemistry*, 5(2), 212-219.

Kazakos, S., Mantzourani, I., Nouska, C., Alexopoulos, A., Bezirtzoglou, E., and Bekatorou, A. (2016). Production of low-alcohol fruit beverages through fermentation of pomegranate and orange juices with kefir grains. *Current Research in Nutrition and Food Science Journal*, *4*(1), 19-26.

Kemertelidze, E., Sagareishvili, T., Syrov, V., Khushbaktova, Z., Tsutskiridze, L., and Kurashvili, R. (2012). Saturin-effective vegetative remedy in treatment of type 2 diabetes mellitus. *Georgian medical news*, (203), 47-52.

Kesari, A. N., Gupta, R. K., Singh, S. K., Diwakar, S., and Watal, G. (2006). Hypoglycemic and antihyperglycemic activity of *Aegle marmelos* seed extract in normal and diabetic rats. *Journal of ethnopharmacology*, *107*(3), 374-379.

Khoddami, A., Wilkes, M. A., and Roberts, T. H. (2013). Techniques for analysis of plant phenolic compounds. *Molecules*, *18*(2), 2328-2375.

Kilari, E. K., Mullapudi, B., Moka, P. V., Silakabattini, K., and Nelli IV, G. (2014). Inhibition of DPP-IV Activity and Enhancement of GLP-1 Expression by Aqueous Peel Extract of *Punica granatum* in Albino Wistarrats. *Journal of Global Trends in Pharmaceutical Sciences*, *5*, 1528-1541.

Kim, D. O., Jeong, S. W., and Lee, C. Y. (2003). Antioxidant capacity of phenolic phytochemicals from various cultivars of plums. *Food chemistry*, *81*(3), 321-326.

Kim, H. S., Chae, H. S., Jeong, S. G., Ham, J. S., Im, S. K., Ahn, C. N., and Lee, J. M. (2005). Antioxidant activity of some yogurt starter cultures. *Asian-Aust. J. Anim. Sci*, *18*(2), 255-258.

Kim, N. D., Mehta, R., Yu, W., Neeman, I., Livney, T., Amichay, A., ... and Mansel, R. (2002). Chemopreventive and adjuvant therapeutic potential of pomegranate (*Punica granatum*) for human breast cancer. *Breast cancer research and treatment*, *71*(3), 203-217.

Kim, Y., Goodner, K. L., Park, J. D., Choi, J., and Talcott, S. T. (2011). Changes in antioxidant phytochemicals and volatile composition of *Camellia sinensis* by oxidation during tea fermentation. *Food Chemistry*, *129*(4), 1331-1342.

Klewicka, E., Motyl, I., and Libudzisz, Z. (2004). Fermentation of beet juice by bacteria of genus *Lactobacillus* sp. *European Food Research and Technology*, *218*(2), 178-183.

Kobayashi, H., Mitsui, T., Nomura, S., Ohno, Y., Kadomatsu, K., Muramatsu, T., ... and Mizutani, S. (2004). Expression of glucose transporter 4 in the human pancreatic islet of Langerhans. *Biochemical and biophysical research communications*, *314*(4), 1121-1125.

Kohajdová, Z., Karovičová, J. and Greifová, M. (2006). Lactic acid fermentation of some vegetable juices. *Journal of Food and Nutrition Research*, *45*(3), 115-119.

Kohno, H., Suzuki, R., Yasui, Y., Hosokawa, M., Miyashita, K., and Tanaka, T. (2004). Pomegranate seed oil rich in conjugated linolenic acid suppresses chemically induced colon carcinogenesis in rats. *Cancer science*, *95*(6), 481-486.

Kok, F. S. (2014). *Bioprocess Strategy for the Production of Lactobacillus Rhamnosus NRRL B442 with High Cell-B-Glucosidase Activity*. PhD Thesis. Universiti Teknologi Malaysia.

Kourkoutas, Y., Xolias, V., Kallis, M., Bezirtzoglou, E., and Kanellaki, M. (2005). *Lactobacillus casei* cell immobilization on fruit pieces for probiotic additive, fermented milk and lactic acid production. *Process Biochemistry*, *40*(1), 411-416.

Krentz, A. J., Patel, M. B., and Bailey, C. J. (2008). New drugs for type 2 diabetes mellitus. *Drugs*, *68*(15), 2131-2162.

Krischke, W., Schröder, M., and Trösch, W. (1991). Continuous production of l-lactic acid from whey permeate by immobilized *Lactobacillus casei* subsp. *casei*. *Applied microbiology and biotechnology*, *34*(5), 573-578.

Kumar, B. V., Sreedharamurthy, M., and Reddy, O. V. S. (2013). Physico-Chemical Analysis of Fresh and Fermented Fruit Juices Probioticated with *Lactobacillus casei*. *International Journal of Applied Sciences and Biotechnology*, 1(3), 127-131.

Kumar, B. V., Vijayendra, S. V. N., and Reddy, O. V. S. (2015). Trends in dairy and non-dairy probiotic products-a review. Journal of food science and technology, 52(10), 6112-6124.

Kumar, D., Gupta, N., Ghosh, R., Gaonkar, R. H., and Pal, B. C. (2013). α-Glucosidase and α-amylase inhibitory constituent of *Carex baccans*: Bio-assay guided isolation and quantification by validated RP-HPLC–DAD. *Journal of Functional Foods*, *5*(1), 211-218.

Kun, S., Rezessy-Szabó, J. M., Nguyen, Q. D., and Hoschke, Á. (2008). Changes of microbial population and some components in carrot juice during fermentation with selected *Bifidobacterium* strains. *Process Biochemistry*, *43*(8), 816-821.

Kwon, Y. I., Apostolidis, E., and Shetty, K. (2006). Anti-diabetes functionality of Kefir culture-mediated fermented soymilk supplemented with Rhodiola extracts. *Food Biotechnology*, *20*(1), 13-29.

Kyung, K. H., and Fleming, H. P. (1994). Antibacterial activity of cabbage juice against lactic acid bacteria. *Journal of food Science*, *59*(1), 125-129.

Lai, B., Plan, M. R., Hodson, M. P., and Krömer, J. O. (2016). Simultaneous determination of sugars, carboxylates, alcohols and aldehydes from fermentations by high performance liquid chromatography. *Fermentation*, *2*(1), 6.

Lambert, M., Meudec, E., Verbaere, A., Mazerolles, G., Wirth, J., Masson, G. and Sommerer, N. (2015). A high-throughput UHPLC-QqQ-MS method for polyphenol profiling in rosé wines. *Molecules*, *20*(5), 7890-7914.

Langley, P. (2000). Why a pomegranate? *BMJ: British Medical Journal*, *321*(7269).

Lansky, E. P., and Newman, R. A. (2007). *Punica granatum* (pomegranate) and its potential for prevention and treatment of inflammation and cancer. *Journal of ethnopharmacology*, *109*(2), 177-206.

Lansky, E. P., Harrison, G., Froom, P., and Jiang, W. G. (2005). Pomegranate (*Punica granatum*) pure chemicals show possible synergistic inhibition of human PC-3 prostate cancer cell invasion across Matrigel™. *Investigational new drugs*, *23*(2), 121-122.

Lansky, E. P., Jiang, W., Mo, H., Bravo, L., Froom, P., Yu, W., ... and Campbell, M. J. (2005). Possible synergistic prostate cancer suppression by anatomically discrete pomegranate fractions. *Investigational new drugs*, *23*(1), 11-20.

Larrosa, M., González-Sarrías, A., Yáñez-Gascón, M. J., Selma, M. V., Azorín-Ortuño, M., Toti, S., ... and Espín, J. C. (2010). Anti-inflammatory properties of a pomegranate extract and its metabolite urolithin-A in a colitis rat model and the effect of colon inflammation on phenolic metabolism. *The Journal of nutritional biochemistry*, *21*(8), 717-725.

Lee, S. Y., Park, S. L., Hwang, J. T., Yi, S. H., Nam, Y. D., and Lim, S. I. (2012). Antidiabetic effect of *Morinda citrifolia* (Noni) fermented by Cheonggukjang in KK-Ay diabetic mice. *Evidence-Based Complementary and Alternative Medicine*, *2012*.

Legua, P., Melgarejo, P., Martínez, J. J., Martínez, R., and Hernández, F. (2012). Evaluation of Spanish pomegranate juices: organic acids, sugars, and anthocyanins. *International journal of food properties*, *15*(3), 481-494.

Lemanska, K., Szymusiak, H., Tyrakowska, B., Zieliński, R., Soffers, A. E., and Rietjens, I. M. (2001). The influence of pH on antioxidant properties and the mechanism of antioxidant action of hydroxyflavones. *Free Radical Biology and Medicine*, *31*(7), 869-881.

Li, E., and Mira de Orduna, R. (2010). A rapid method for the determination of microbial biomass by dry weight using a moisture analyser with an infrared heating source and an analytical balance. *Letters in applied microbiology*, *50*(3), 283-288.

Li, Y., Guo, C., Yang, J., Wei, J., Xu, J., and Cheng, S. (2006). Evaluation of antioxidant properties of pomegranate peel extract in comparison with pomegranate pulp extract. *Food chemistry*, *96*(2), 254-260.

Li, Z., Jiang, H., Xu, C., and Gu, L. (2015). A review: Using nanoparticles to enhance absorption and bioavailability of phenolic phytochemicals. *Food Hydrocolloids*, *43*, 153-164.

Lindgren, S. E., and Dobrogosz, W. J. (1990). Antagonistic activities of lactic acid bacteria in food and feed fermentations. *FEMS Microbiology Letters*, *87*(1-2), 149-164.

Liu, S. N., Han, Y., and Zhou, Z. J. (2011). Lactic acid bacteria in traditional fermented Chinese foods. *Food Research International*, *44*(3), 643-651.

Ljungh, A., and Wadstrom, T. (2006). Lactic acid bacteria as probiotics. *Current issues in intestinal microbiology*, 7(2), 73-90.

Lobas, D., Schumpe, S., and Deckwer, W. D. (1992). The production of gellan exopolysaccharide with Sphingomonas paucimobilis E2 (DSM 6314). *Applied microbiology and biotechnology*, *37*(4), 411-415.

Loncar, E., Djuric, M., Malbasa, R., Kolarov, L. J., and Klasnja, M. (2006). Influence of working conditions upon kombucha conducted fermentation of black tea. *Food and Bioproducts Processing*, *84*(3), 186-192.

Longtin, R. (2003). The pomegranate: nature's power fruit?. *CancerSpectrum Knowledge Environment*, *95*(5), 346-348.

Lu, Y., Hu, F., Miyakawa, T., and Tanokura, M. (2016). Complex mixture analysis of organic compounds in yogurt by NMR spectroscopy. *Metabolites*, *6*(2), 19.

Luckow, T., and Delahunty, C. (2004). Which juice is ‘healthier’? A consumer study of probiotic non-dairy juice drinks. *Food Quality and Preference*, *15*(7-8), 751-759.

Luckow, T., Sheehan, V., Fitzgerald, G., and Delahunty, C. (2006). Exposure, health information and flavour-masking strategies for improving the sensory quality of probiotic juice. *Appetite*, *47*(3), 315-323.

Maccio, A., and Madeddu, C. (2011). Obesity, inflammation, and postmenopausal breast cancer: therapeutic implications. *The Scientific World Journal*, *11*, 2020-2036.

Magnusson, J., and Schnürer, J. (2001). *Lactobacillus coryniformis* subsp. coryniformis strain Si3 produces a broad-spectrum proteinaceous antifungal compound. *Applied and Environmental Microbiology*, *67*(1), 1-5.

Mandal, A., Bhatia, D., and Bishayee, A. (2017). Anti-inflammatory mechanism involved in pomegranate-mediated prevention of breast cancer: The role of NF-κB and Nrf2 signaling pathways. *Nutrients*, *9*(5), 436.

Mantzouridou, F., Roukas, T., and Kotzekidou, P. (2002). Effect of the aeration rate and agitation speed on β-carotene production and morphology of *Blakeslea trispora* in a stirred tank reactor: mathematical modeling. *Biochemical Engineering Journal*, *10*(2), 123-135.

Martin, F. P. J., Wang, Y., Sprenger, N., Holmes, E., Lindon, J. C., Kochhar, S., and Nicholson, J. K. (2007). Effects of probiotic *Lactobacillus paracasei* treatment on the host gut tissue metabolic profiles probed via magic-angle-spinning NMR spectroscopy. *Journal of proteome research*, *6*(4), 1471-1481.

Matthews, A., Grimaldi, A., Walker, M., Bartowsky, E., Grbin, P., and Jiranek, V. (2004). Lactic acid bacteria as a potential source of enzymes for use in vinification. *Applied and environmental microbiology*, *70*(10), 5715-5731.

Mattila-Sandholm, T., Myllärinen, P., Crittenden, R., Mogensen, G., Fondén, R., and Saarela, M. (2002). Technological challenges for future probiotic foods. *International Dairy Journal*, *12*(2-3), 173-182.

Mauro, C. S. I., Guergoletto, K. B., and Garcia, S. (2016). Development of blueberry and carrot juice blend fermented by *Lactobacillus reuteri* LR92. *Beverages*, *2*(4), 37.

Mazlan, F. A., Annuar, M. S. M., and Sharifuddin, Y. (2015). Biotransformation of *Momordica charantia* fresh juice by *Lactobacillus plantarum* BET003 and its putative anti-diabetic potential. *PeerJ*, *3*, e1376.

Mccue, P., Kwon, Y. I., and Shetty, K. (2005). Anti-amylase, anti-glucosidase and anti-angiotensin i-converting enzyme potential of selected foods. *Journal of food biochemistry*, *29*(3), 278-294.

McGovern, P. E., Zhang, J., Tang, J., Zhang, Z., Hall, G. R., Moreau, R. A., ... and Cheng, G. (2004). Fermented beverages of pre-and proto-historic China. *Proceedings of the National Academy of Sciences*, *101*(51), 17593-17598.

McIntosh, C. H. (2008). Incretin-based therapies for type 2 diabetes. *Canadian Journal of Diabetes*, *32*(2), 131-139.

McNeil, B. and Harvey, L. (Eds.). (2008). *Practical fermentation technology*. John Wiley & Sons.

Mehta, R., and Lansky, E. P. (2004). Breast cancer chemopreventive properties of pomegranate (*Punica granatum*) fruit extracts in a mouse mammary organ culture. *European Journal of Cancer Prevention*, *13*(4), 345-348.

Melgarejo, P., Salazar, D. M., and Artes, F. (2000). Organic acids and sugars composition of harvested pomegranate fruits. *European Food Research and Technology*, *211*(3), 185-190.

Mena, P., Calani, L., Dall'Asta, C., Galaverna, G., García-Viguera, C., Bruni. R., Alan, C., and Del Rio, D. (2012). Rapid and Comprehensive Evaluation of (Poly) phenolic Compounds in Pomegranate (*Punica granatum* L.) Juice by UHPLC-MSn. *Molecules*, 17, 14821-14840.

Mena, P., García-Viguera, C., Navarro-Rico, J., Moreno, D. A., Bartual, J., Saura, D., and Martí, N. (2011). Phytochemical characterisation for industrial use of pomegranate (*Punica granatum* L.) cultivars grown in Spain. *Journal of the Science of Food and Agriculture*, *91*(10), 1893-1906.

Miguel, M. G., Neves, M. A., and Antunes, M. D. (2010). Pomegranate (*Punica granatum* L.): A medicinal plant with myriad biological properties-A short review. *Journal of Medicinal Plants Research*, *4*(25), 2836-2847.

Mihiretie, H., and Desta, K. (2015). Microbiological Criteria and Quality of Fruits and Fruit Juices in Ethiopia and International Experience. *Journal of Medical Microbiology and Diagnosis*, *4*(207), 2.

Mirdehghan, S. H., and Rahemi, M. (2007). Seasonal changes of mineral nutrients and phenolics in pomegranate (*Punica granatum* L.) fruit. *Scientia Horticulturae*, *111*(2), 120-127.

Mirmiran, P., Bahadoran, Z., and Azizi, F. (2014). Functional foods-based diet as a novel dietary approach for management of type 2 diabetes and its complications: A review. *World journal of diabetes*, *5*(3), 267.

Mishra, K., Ojha, H., and Chaudhury, N. K. (2012). Estimation of antiradical properties of antioxidants using DPPH assay: A critical review and results. *Food chemistry*, *130*(4), 1036-1043.

Mogensen, G., Salminen, S., O'brien, J., Ouwenhand, A., Holzapfel, W., Shortt, C., ... and Crittenden, R. G. (2002). Inventory of microorganisms with a documented history of use in food, *Bulletin of the IDF* 10-19.

Mohamadshahi, M., Veissi, M., Haidari, F., Javid, A. Z., Mohammadi, F., and Shirbeigi, E. (2014). Effects of probiotic yogurt consumption on lipid profile in type 2 diabetic patients: A randomized controlled clinical trial. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences*, *19*(6), 531.

Mohammadi, R., Mortazavian, A. M., Khosrokhavar, R., and da Cruz, A. G. (2011). Probiotic ice cream: viability of probiotic bacteria and sensory properties. *Annals of microbiology*, *61*(3), 411-424.

Mortazavian, A. M., Ehsani, M. R., Mousavi, S. M., Reinheimer, J. A., Emamdjomeh, Z., Sohrabvandi, S., and Rezaei, K. (2006). Preliminary investigation of the combined effect of heat treatment and incubation temperature on the viability of the probiotic micro-organisms in freshly made yogurt. *International journal of dairy technology*, *59*(1), 8-11.

Mortazavian, A. M., Mohammadi. R., Cruz, A.G., Faria, J. A. F (2011) Technology and stability of probiotics in dairy desserts. In: Shah NP, Cruz AG, Faria JAF (eds). *Probiotic and Prebiotic Foods: Technology, Stability and Benefits to human health* (pp. 233-252). New York: Nova Science Publishing Ltd.

Mousavi, Z. E., Mousavi, S. M., Razavi, S. H., Emam-Djomeh, Z., and Kiani, H. (2011). Fermentation of pomegranate juice by probiotic lactic acid bacteria. *World Journal of Microbiology and Biotechnology*, *27*(1), 123-128.

Mousavi, Z. E., Mousavi, S. M., Razavi, S. H., Hadinejad, M., Emam-Djomeh, Z., and Mirzapour, M. (2013). Effect of fermentation of pomegranate juice by *Lactobacillus plantarum* and *Lactobacillus acidophilus* on the antioxidant activity and metabolism of sugars, organic acids and phenolic compounds. *Food biotechnology*, *27*(1), 1-13.

Mozzi, F., Ortiz, M. E., Bleckwedel, J., De Vuyst, L., and Pescuma, M. (2013). Metabolomics as a tool for the comprehensive understanding of fermented and functional foods with lactic acid bacteria. *Food research international*, *54*(1), 1152-1161.

Mozzi, F., Savoy de Giori, G., and Font de Valdez, G. (2003). UDP-galactose 4-epimerase: a key enzyme in exopolysaccharide formation by *Lactobacillus casei* CRL 87 in controlled pH batch cultures. *Journal of applied microbiology*, *94*(2), 175-183.

Murphy, M. G., and Condon, S. (1984). Comparison of aerobic and anaerobic growth of *Lactobacillus plantarum* in a glucose medium. *Archives of microbiology*, *138*(1), 49-53.

Mustafa, S. M. and Chua, L.S. (2017). Critical Review of Fruit Juices as Nutrient-Dense Foods for Health Enhancement. In Fleming, D. L. (Ed.) *Fruit Juices Bioactive Properties, Consumption and Role in Disease Prevention* (pp. 25-50). New York: Nova Science Publishers, Inc.

Mustafa, S.M., Chua, L.S., El-Enshasy, H.A, AA Majid, F., and Malek, R. A. (2016). A Review on Fruit Juice Probiotication: Pomegranate. *Current Nutrition & Food Science*, *12*(1), 4-11.

Muzolf, M., Szymusiak, H., Gliszczyńska-Świgło, A., Rietjens, I. M., and Tyrakowska, B. E. (2008). pH-dependent radical scavenging capacity of green tea catechins. *Journal of agricultural and food chemistry*, *56*(3), 816-823.

Nabi, B., Gh, R. and Baniardalan, P. (2004). Batch and continuous production of lactic acid from whey by immobilized *Lactobacillus*. *J. Environ. Studies*, 30, 47-53.

Naczk, M., and Shahidi, F. (2006). Phenolics in cereals, fruits and vegetables: Occurrence, extraction and analysis. *Journal of pharmaceutical and biomedical analysis*, *41*(5), 1523-1542.

Najafzadeh, H., Aghel, N., Hemmati, A. A., and Oulapour, S. (2011). Effect of hydro alcoholic extract of peel of *Punica granatum* on experimental diabetes mellitus by streptozotocin in rats. *J Pharm Sci*, *16*(4), 239-48.

Nancib, A., Nancib, N., Meziane-Cherif, D., Boubendir, A., Fick, M., and Boudrant, J. (2005). Joint effect of nitrogen sources and B vitamin supplementation of date juice on lactic acid production by *Lactobacillus casei* subsp. rhamnosus. *Bioresource Technology*, *96*(1), 63-67.

Nancib, N., Nancib, A., Boudjelal, A., Benslimane, C., Blanchard, F., and Boudrant, J. (2001). The effect of supplementation by different nitrogen sources on the production of lactic acid from date juice by *Lactobacillus casei* subsp. rhamnosus. *Bioresource Technology*, *78*(2), 149-153.

Naqvi, S., Khan, M. S. Y., and Vohora, S. B. (1991). Anti-bacterial, anti-fungal and anthelmintic investigations on Indian medicinal plants. *Fitoterapia*, *62*, 221-228.

Natarajan, K., and Rajendran, A. (2009). Effect of fermentation parameters on extra cellular tannase production by *Lactobacillus plantarum* MTCC 1407. *Journal of Chemistry*, *6*(4), 979-984.

National Diabetes Registry Report, Volume 1, 2009-2012, Ministry of Health Malaysia.

Nawwar, M. A., Hussein, S. A., and Merfort, I. (1994). Leaf phenolics of *Punica granatum*. *Phytochemistry*, *37*(4), 1175-1177.

Nayak, B. S., Isitor, G. N., Maxwell, A., Bhogadi, V., and Ramdath, D. D. (2007). Wound-healing activity of *Morinda citrifolia* fruit juice on diabetes-induced rats. *Journal of wound care*, *16*(2), 83-86.

Nayak, B. S., Marshall, J. R., Isitor, G., and Adogwa, A. (2011). Hypoglycemic and hepatoprotective activity of fermented fruit juice of *Morinda citrifolia* (Noni) in diabetic rats. *Evidence-Based Complementary and Alternative Medicine*, *2011*.

Negi, P. S., and Jayaprakasha, G. K. (2003). Antioxidant and antibacterial activities of *Punica granatum* peel extracts. *Journal of Food Science*, *68*(4), 1473-1477.

Nematollahi, A., Sohrabvandi, S., Mortazavian, A. M., and Jazaeri, S. (2016). Viability of probiotic bacteria and some chemical and sensory characteristics in cornelian cherry juice during cold storage. *Electronic Journal of Biotechnology*, *21*, 49-53.

Neto, C. C. (2007a). Cranberry and blueberry: evidence for protective effects against cancer and vascular diseases. *Molecular nutrition & food research*, *51*(6), 652-664.

Nezhad, M. H., Stenzel, D. J., and Britz, M. L. (2010). Effect of growth at low pH on the cell surface properties of a typical strain of *Lactobacillus casei* group. *Iranian journal of microbiology*, *2*(3), 147.

Ng, C. C., Wang, C. Y., Wang, Y. P., Tzeng, W. S., and Shyu, Y. T. (2011). Lactic acid bacterial fermentation on the production of functional antioxidant herbal *Anoectochilus formosanus Hayata*. *Journal of bioscience and bioengineering*, *111*(3), 289-293.

Niku-Paavola, M. L., Laitila, A., Mattila-Sandholm, T., and Haikara, A. (1999). New types of antimicrobial compounds produced by *Lactobacillus plantarum*. *Journal of Applied Microbiology*, *86*(1), 29-35.

Nout, M. J. R. (1994). Fermented foods and food safety. *Food Research International*, *27*(3), 291-298.

Nout, M. J. R., and Ngoddy, P. O. (1997). Technological aspects of preparing affordable fermented complementary foods. *Food Control*, *8*(5/6), 279.

Nualkaekul, S., Lenton, D., Cook, M. T., Khutoryanskiy, V. V., and Charalampopoulos, D. (2012). Chitosan coated alginate beads for the survival of microencapsulated *Lactobacillus plantarum* in pomegranate juice. *Carbohydrate Polymers*, *90*(3), 1281-1287.

O'Sullivan, L., Ross, R. P., and Hill, C. (2002). Potential of bacteriocin-producing lactic acid bacteria for improvements in food safety and quality. *Biochimie*, *84*(5-6), 593-604.

Oboh, G., Alabi, K. B., and Akindahunsi, A. A. (2008). Fermentation changes the nutritive value, polyphenol distribution, and antioxidant properties of *Parkia biglobosa* seeds (African locust beans). *Food biotechnology*, *22*(4), 363-376.

Ochi, H., Naito, H., Iwatsuki, K., Bamba, T., and Fukusaki, E. (2012). Metabolomics-based component profiling of hard and semi-hard natural cheeses with gas chromatography/time-of-flight-mass spectrometry, and its application to sensory predictive modeling. *Journal of bioscience and bioengineering*, *113*(6), 751-758.

Ohland, C. L., and MacNaughton, W. K. (2010). Probiotic bacteria and intestinal epithelial barrier function. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, *298*(6), G807-G819.

Ortega, N., Romero, M. P., Macià, A., Reguant, J., Anglès, N., Morelló, J. R., and Motilva, M. J. (2010). Comparative study of UPLC–MS/MS and HPLC–MS/MS to determine procyanidins and alkaloids in cocoa samples. *Journal of food composition and analysis*, *23*(3), 298-305.

Othman, N. B., Roblain, D., Chammen, N., Thonart, P., and Hamdi, M. (2009). Antioxidant phenolic compounds loss during the fermentation of Chétoui olives. *Food Chemistry*, *116*(3), 662-669.

Ozcan, T., Akpinar-Bayizit, A., Yilmaz-Ersan, L., and Delikanli, B. (2014). Phenolics in human health. *International Journal of chemical engineering and applications*, *5*(5), 393.

Ozgul-Yucel, S. (2005). Determination of conjugated linolenic acid content of selected oil seeds grown in Turkey. *Journal of the American Oil Chemists' Society*, *82*(12), 893-897.

Oziyci, H. R., Karhan, M., Tetik, N., and Turhan, I. (2013). Effects of processing method and storage temperature on clear pomegranate juice turbidity and color. *Journal of Food Processing and Preservation*, *37*(5), 899-906.

Palama, T. L., Canard, I., Rautureau, G. J., Mirande, C., Chatellier, S., and Elena-Herrmann, B. (2016). Identification of bacterial species by untargeted NMR spectroscopy of the exo-metabolome. *Analyst*, *141*(15), 4558-4561.

Paliyath, G., Bakovic, M., and Shetty, K. (Eds.). (2011). *Functional foods, nutraceuticals, and degenerative disease prevention*. John Wiley & Sons.

Pande, G., and Akoh, C. C. (2009). Antioxidant capacity and lipid characterization of six Georgia-grown pomegranate cultivars. *Journal of agricultural and food chemistry*, *57*(20), 9427-9436.

Pandey, K. B., and Rizvi, S. I. (2009). Plant polyphenols as dietary antioxidants in human health and disease. *Oxidative medicine and cellular longevity*, *2*(5), 270-278.

Panesar, P. S., Kennedy, J. F., Knill, C. J., and Kosseva, M. (2010). Production of L (+) lactic acid using *Lactobacillus casei* from whey. *Brazilian archives of Biology and Technology*, *53*(1), 219-226.

Panwar, H., Calderwood, D., Grant, I. R., Grover, S., and Green, B. D. (2016). Lactobacilli possess inhibitory activity against dipeptidyl peptidase-4 (DPP-4). *Annals of microbiology*, *66*(1), 505-509.

Parish, M. E., Sadler, G. D., and Wicker, L. (1990). Viability of *Lactobacillus plantarum* in orange juice under low pH and temperature conditions. *Journal of Food Science*, *55*(4), 1023-1025.

Park, J. S., Rho, H. S., Kim, D. H., and Chang, I. S. (2006). Enzymatic preparation of kaempferol from green tea seed and its antioxidant activity. *Journal of agricultural and food chemistry*, *54*(8), 2951-2956.

Patel, B. D., and Ghate, M. D. (2014). Recent approaches to medicinal chemistry and therapeutic potential of dipeptidyl peptidase-4 (DPP-4) inhibitors. *European journal of medicinal chemistry*, *74*, 574-605.

Patel, D. K., Prasad, S. K., Kumar, R., and Hemalatha, S. (2012). An overview on antidiabetic medicinal plants having insulin mimetic property. *Asian Pacific journal of tropical biomedicine*, *2*(4), 320.

Pederson, C.S., and Albury, M.N., (1969). The sauerkraut fermentation. In: N.Y. State Agricultural Exp. Sta. Bull., vol. 824, Geneva, NY.

Perdigon, G., Fuller, R. and Raya, R. (2001). Lactic Acid Bacteria and their Effect on the Immune System. *Current issues in intestinal microbiology*. 2. 27-42.

Pereira, A. L. F., Maciel, T. C., and Rodrigues, S. (2011). Probiotic beverage from cashew apple juice fermented with *Lactobacillus casei*. *Food Research International*, *44*(5), 1276-1283.

Pereira, D. M., Valentao, P., Pereira, J. A., and Andrade, P. B. (2009). Phenolics: From chemistry to biology. *Molecules*, *14*(6), 2202-221.

Peres, C. M., Peres, C., Hernández-Mendoza, A., and Malcata, F. X. (2012). Review on fermented plant materials as carriers and sources of potentially probiotic lactic acid bacteria–with an emphasis on table olives. *Trends in Food Science & Technology*, *26*(1), 31-42.

Petersen, K. F. and Shulman, G.I. (2006). *Etiology of insulin resistance*. *Am J Med*, *119*, S10-S16.

Petti, S., and Scully, C. (2009). Polyphenols, oral health and disease: A review. *Journal of dentistry*, *37*(6), 413-423.

Phung, O. J., Scholle, J. M., Talwar, M., and Coleman, C. I. (2010). Effect of noninsulin antidiabetic drugs added to metformin therapy on glycemic control, weight gain, and hypoglycemia in type 2 diabetes. *Jama*, *303*(14), 1410-1418.

Pinent, M., Castell, A., Baiges, I., Montagut, G., Arola, L., and Ardévol, A. (2008). Bioactivity of flavonoids on insulin-secreting cells. *Comprehensive Reviews in Food Science and Food Safety*, *7*(4), 299-308.

Plaza, M., Pozzo, T., Liu, J., Gulshan Ara, K. Z., Turner, C., and Nordberg Karlsson, E. (2014). Substituent effects on in vitro antioxidizing properties, stability, and solubility in flavonoids. *Journal of agricultural and food chemistry*, *62*(15), 3321-3333.

Plessas, S., Koulis, M., Alexopoulos, A., and Bezirtzoglou, E. (2011). Functional drink production through pomegranate juice fermentation. In *11th International Congress on Engineering and Food. ICEF11* (pp. 2029-2030).

Plumb, G. W., de Pascual-Teresa, S., Santos-Buelga, C., Rivas-Gonzalo, J. C., and Williamson, G. (2002). Antioxidant properties of gallocatechin and prodelphinidins from pomegranate peel. *Redox Report*, *7*(1), 41-46.

Post, R. C. (1996). Regulatory perspective of the USDA on the use of antimicrobials and inhibitors in foods. *Journal of food protection*, *59*(13), 78-81.

Prakash, C. V. S., and Prakash, I. (2011). Bioactive chemical constituents from pomegranate (*Punica granatum*) juice, seed and peel-a review. *IJRCE*, *1*.

Prema, P., Smila, D., Palavesam, A., and Immanuel, G. (2010). Production and characterization of an antifungal compound (3-phenyllactic acid) produced by *Lactobacillus plantarum* strain. *Food and Bioprocess Technology*, *3*(3), 379-386.

Pucel, N. W. (2013). *Improvement of Functional Bioactivity in Pear: Blackberry Synergies with Lactic Acid Fermentation for Type 2 Diabetes and Hypertension Management.* Masters Theses, University of Massachusetts Amherst.

Pyo, Y. H., Lee, T. C., and Lee, Y. C. (2005). Effect of lactic acid fermentation on enrichment of antioxidant properties and bioactive isoflavones in soybean. *Journal of Food Science, 70*(3), S215-S220.

Qader, S. W., Abdulla, M. A., Chua, L. S., Sirat, H. M., and Hamdan, S. (2012). Pharmacological mechanisms underlying gastroprotective activities of the fractions obtained from *Polygonum minus* in Sprague Dawley rats. *International journal of molecular sciences*, *13*(2), 1481-1496.

Qiu, Z., Zhou, B., Jin, L., Yu, H., Liu, L., Liu, Y., ... and Zhu, F. (2013). In vitro antioxidant and antiproliferative effects of ellagic acid and its colonic metabolite, urolithins, on human bladder cancer T24 cells. *Food and chemical toxicology*, *59*, 428-437.

Qu, W., Breksa III, A. P., Pan, Z., Ma, H., and Mchugh, T. H. (2012). Storage stability of sterilized liquid extracts from pomegranate peel. *Journal of food science*, 77(7), C765-C772.

Qu, W., Pan, Z., Zhang, R., Ma, H., Zhu, B., Wang, Z., and Atungulu, G. G. (2009). Integrated extraction and anaerobic digestion process for recovery of nutraceuticals and biogas from pomegranate marc. *Transactions of the ASABE*, 52(6), 1997-2006.

Rafter, J. (2002). Lactic acid bacteria and cancer: mechanistic perspective. *British Journal of Nutrition*, *88*(S1), S89-S94.

Rahimi, H. R., Arastoo, M., and Ostad, S. N. (2012). A comprehensive review of *Punica granatum* (pomegranate) properties in toxicological, pharmacological, cellular and molecular biology researches. *Iranian journal of pharmaceutical research: IJPR*, *11*(2), 385.

Rana, S., Morya, R. K., Malik, A., Bhadada, S. K., Sachdeva, N., and Sharma, G. (2016). A relationship between vitamin D, parathyroid hormone, calcium levels and lactose intolerance in type 2 diabetic patients and healthy subjects. *Clinica Chimica Acta*, *462*, 174-177.

Rana, T. S., Narzary, D., and Ranade, S. A. (2010). Systematics and taxonomic disposition of the genus *Punica* L. *Pomegranate. Fruit Veg Cereal Sci Biotechnol*, *4*, 19-25.

Randazzo, C. L., Restuccia, C., Romano, A. D., and Caggia, C. (2004). *Lactobacillus casei*, dominant species in naturally fermented Sicilian green olives. *International Journal of Food Microbiology*, *90*(1), 9-14.

Randhir, R., Kwon, Y. I., and Shetty, K. (2008). Effect of thermal processing on phenolics, antioxidant activity and health-relevant functionality of select grain sprouts and seedlings. *Innovative Food Science & Emerging Technologies*, *9*(3), 355-364.

Rangaswamy, V., and Ramakrishna, S. V. (2008). Lactic acid production by *Lactobacillus delbrueckii* in a dual reactor system using packed bed biofilm reactor. *Letters in applied microbiology*, *46*(6), 661-666.

Rashid, R. (2008). Optimization and modeling of lactic acid production from pineapple waste. *Faculty of Chemical and Natural Resources Engineering. Universiti Teknologi Malaysia*.

Rault, A., Bouix, M., and Béal, C. (2009). Fermentation pH influences the physiological-state dynamics of *Lactobacillus bulgaricus* CFL1 during pH-controlled culture. *Appl. Environ. Microbiol.*, 75(13), 4374-4381.

Redon, E., Loubiere, P., and Cocaign-Bousquet, M. (2005). Transcriptome analysis of the progressive adaptation of *Lactococcus lactis* to carbon starvation. *Journal of bacteriology*, *187*(10), 3589-3592.

Rios, J. L., Francini, F., and Schinella, G. R. (2015). Natural products for the treatment of type 2 diabetes mellitus. *Planta medica*, *81*(12/13), 975-994.

Riyanti, S., Suganda, A.G. and Suganda, E.Y. (2016). Dipeptidyl Peptidase-IV Inhibitory Activity of Some Indonesian Medicinal Plants. *Asian J Pharm Clin Res*, 9 (2), 375-377.

Rodríguez, H., Curiel, J. A., Landete, J. M., de las Rivas, B., de Felipe, F. L., Gómez-Cordovés, C., and Muñoz, R. (2009). Food phenolics and lactic acid bacteria. *International journal of food microbiology*, *132*(2-3), 79-90.

Roels, J.A. (1983) Energetics and Kinetics in Biotechnology, Elsevier Biomedical Press, Amsterdam.

Rosenblat, M., Hayek, T., and Aviram, M. (2006). Anti-oxidative effects of pomegranate juice (PJ) consumption by diabetic patients on serum and on macrophages. *Atherosclerosis*, *187*(2), 363-371.

Rosenblat, M., Volkova, N., Attias, J., Mahamid, R., and Aviram, M. (2010). Consumption of polyphenolic-rich beverages (mostly pomegranate and black currant juices) by healthy subjects for a short term increased serum antioxidant status, and the serum's ability to attenuate macrophage cholesterol accumulation. *Food & function*, *1*(1), 99-109.

Rozenberg, O., Howell, A., and Aviram, M. (2006). Pomegranate juice sugar fraction reduces macrophage oxidative state, whereas white grape juice sugar fraction increases it. *Atherosclerosis*, *188*(1), 68-76.

Saarela, M., Virkajärvi, I., Nohynek, L., Vaari, A., and Mättö, J. (2006). Fibres as carriers for *Lactobacillus rhamnosus* during freeze-drying and storage in apple juice and chocolate-coated breakfast cereals. *International journal of food microbiology*, *112*(2), 171-178.

Sabokbar, N., and Khodaiyan, F. (2015). Characterization of pomegranate juice and whey based novel beverage fermented by kefir grains. *Journal of food science and technology*, *52*(6), 3711-3718.

Sarian, M. N., Ahmed, Q. U., So'ad, M., Zaiton, S., Alhassan, A. M., Murugesu, S., and Latip, J. (2017). Antioxidant and antidiabetic effects of flavonoids: A structure-activity relationship-based study. *BioMed research international*, *2017*.

Sattanathan, K., Dhanapal, C. K., Umarani, R., and Manavalan, R. (2011). Beneficial health effects of rutin supplementation in patients with diabetes mellitus. *Journal of Applied Pharmaceutical Science*, *1*(8), 227.

Saxena, M., Saxena, J., and Pradhan, A. (2012). Flavonoids and phenolic acids as antioxidants in plants and human health. *International Journal of Pharmaceutical Sciences Review and Research*, *16*(2), 130-134.

Scheen, A. J. (2012). DPP-4 inhibitors in the management of type 2 diabetes: a critical review of head-to-head trials. *Diabetes & metabolism*, *38*(2), 89-101.

Scheinbach, S. (1998). Probiotics: functionality and commercial status. *Biotechnology Advances*, 16(3), 581-608.

Schrezenmeir, J., and de Vrese, M. (2001). Probiotics, prebiotics, and synbiotics—approaching a definition–. *The American journal of clinical nutrition*, *73*(2), 361s-364s.

Seeram, N. P., Adams, L. S., Henning, S. M., Niu, Y., Zhang, Y., Nair, M. G., and Heber, D. (2005). *In vitro* antiproliferative, apoptotic and antioxidant activities of punicalagin, ellagic acid and a total pomegranate tannin extract are enhanced in combination with other polyphenols as found in pomegranate juice. *The Journal of nutritional biochemistry*, *16*(6), 360-367.

Seeram, N. P., Zhang, Y., McKeever, R., Henning, S. M., Lee, R. P., Suchard, M. A., and Nguyen, M. (2008). Pomegranate juice and extracts provide similar levels of plasma and urinary ellagitannin metabolites in human subjects. *Journal of medicinal food*, *11*(2), 390-394.

Servin, A. L. (2004). Antagonistic activities of lactobacilli and bifidobacteria against microbial pathogens. *FEMS microbiology reviews*, *28*(4), 405-440.

Sestili, P., Martinelli, C., Ricci, D., Fraternale, D., Bucchini, A., Giamperi, L., and Stocchi, V. (2007). Cytoprotective effect of preparations from various parts of *Punica granatum* L. fruits in oxidatively injured mammalian cells in comparison with their antioxidant capacity in cell free systems. *Pharmacological Research*, *56*(1), 18-26.

Seth, M., and Chand, S. (2000). Biosynthesis of tannase and hydrolysis of tannins to gallic acid by *Aspergillus awamori*—optimisation of process parameters. *Process Biochemistry*, *36*(1-2), 39-44.

Settachaimongkon, S., Nout, M. R., Fernandes, E. C. A., Hettinga, K. A., Vervoort, J. M., van Hooijdonk, T. C., ... and van Valenberg, H. J. (2014). Influence of different proteolytic strains of *Streptococcus thermophilus* in co-culture with *Lactobacillus delbrueckii* subsp. bulgaricus on the metabolite profile of set-yoghurt. *International journal of food microbiology*, *177*, 29-36.

Shah, N. P. (2001). Functional foods from probiotics and prebiotics. *Food technology*.

Shah, N. P. (2007). Functional cultures and health benefits. *International dairy journal*, *17*(11), 1262-1277.

Shah, N., and Jelen, P. (1990). Survival of lactic acid bacteria and their lactases under acidic conditions. *Journal of Food Science*, *55*(2), 506-509.

Shahidi, F., and Yeo, J. (2016). Insoluble-bound phenolics in food. *Molecules*, *21*(9), 1216.

Shahidi, F., Wanasundara, U. N., and Amarowicz, R. (1994). Natural antioxidants from low-pungency mustard flour. *Food Research International*, *27*(5), 489-493.

Shaygannia, E., Bahmani, M., Zamanzad, B., and Rafieian-Kopaei, M. (2016). A review study on *Punica granatum* L. *Journal of evidence-based complementary & alternative medicine*, *21*(3), 221-227.

Sheehan, V. M., Ross, P., and Fitzgerald, G. F. (2007). Assessing the acid tolerance and the technological robustness of probiotic cultures for fortification in fruit juices. *Innovative Food Science & Emerging Technologies*, *8*(2), 279-284.

Shiphrah, V.H., Sahu, H., Thakur, A.R. and Chaudhuri, S.R. (2013). Screening of bacteria for lactic acid production from whey water. *American Journal of Biochemistry and Biotechnology*, 2, 118-123.

Shohaib, T., Shafique, M., Dhanya, N., and Divakar, M. C. (2011). Importance of flavonoids in therapeutics. *Hygeia JD Med*, *3*(1), 1-18.

Shostak, K., and Chariot, A. (2011). NF-κB, stem cells and breast cancer: the links get stronger. *Breast Cancer Research*, *13*(4), 214.

Shrime, M. G., Bauer, S. R., McDonald, A. C., Chowdhury, N. H., Coltart, C. E., and Ding, E. L. (2011). Flavonoid-Rich Cocoa Consumption Affects Multiple

Cardiovascular Risk Factors in a Meta-Analysis of Short-Term Studies. *The Journal of nutrition*, *141*(11), 1982-1988.

Shubhada, N., D.L. Rudresh, S.L. Jagadeesh, D.P. Prakash and Raghavendra, S. (2018). Fermentation of Pomegranate Juice by Lactic Acid Bacteria. *International Journal of Current Microbiology and Applied Sciences*, 7(8), 4160-4173.

Shuler, M. L., and Kargi, F. (2002). Bioprocess Engineering: Basic Concepts. 2nd. *Upper Saddle*.

Sikder, J., Chakraborty, S., Sharma, V., and Drioli, E. (2014). Kinetic of lactic acid production from sugarcane juice using *Lactobacillus plantarum* NCIM 2912. *Asia-Pacific Journal of Chemical Engineering*, *9*(3), 374-381.

Silveira, M. S., Fontes, C. P., Guilherme, A. A., Fernandes, F. A., and Rodrigues, S. (2012). Cashew apple juice as substrate for lactic acid production. *Food and Bioprocess Technology*, *5*(3), 947-953.

Sindhu, S. C., and Khetarpaul, N. (2001). Probiotic fermentation of indigenous food mixture: effect on antinutrients and digestibility of starch and protein. *Journal of Food Composition and Analysis*, *14*(6), 601-609.

Singh, R. P., Chidambara Murthy, K. N., and Jayaprakasha, G. K. (2002). Studies on the antioxidant activity of pomegranate (*Punica granatum*) peel and seed extracts using *in vitro* models. *Journal of agricultural and food chemistry*, *50*(1), 81-86.

Slana, M., Žigon, D., Makovec, T., and Lenasi, H. (2011). The response of filamentous fungus *Rhizopus nigricans* to flavonoids. *Journal of basic microbiology*, *51*(4), 433-441.

Sluiter, A., Sluiter, J., Wolfrum, E., Reed, M., Ness, R., Scarlata, C., and Henry, J. (2016). Improved methods for the determination of drying conditions and fraction insoluble solids (FIS) in biomass pretreatment slurry. *Biomass and Bioenergy*, *91*, 234-242.

Soobrattee, M. A., Neergheen, V. S., Luximon-Ramma, A., Aruoma, O. I., and Bahorun, T. (2005). Phenolics as potential antioxidant therapeutic agents: mechanism and actions. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, *579*(1), 200-213.

Sreekumar, S., Sithul, H., Muraleedharan, P., Azeez, J. M., and Sreeharshan, S. (2014). Pomegranate fruit as a rich source of biologically active compounds. *BioMed research international*, *2014*.

Srivastava, J. K., Dubey, P., Singh, S., Bhat, H. R., Kumawat, M. K., and Singh, U. P. (2015). Discovery of novel 1, 3, 5-triazine-thiazolidine-2, 4-diones as dipeptidyl peptidase-4 inhibitors with antibacterial activity targeting the S1 pocket for the treatment of type 2 diabetes. *RSC Advances*, *5*(19), 14095-14102.

Stalikas, C. D. (2007). Extraction, separation, and detection methods for phenolic acids and flavonoids. *Journal of separation science*, *30*(18), 3268-3295.

Stankovic, M. S. (2011). Total phenolic content, flavonoid concentration and antioxidant activity of *Marrubium peregrinum* L. extracts. *Kragujevac J Sci*, *33*(2011), 63-72.

Stiles, M. E., and Holzapfel, W. H. (1997). Lactic acid bacteria of foods and their current taxonomy. *International journal of food microbiology*, *36*(1), 1-29.

Sumner, M. D., Elliott-Eller, M., Weidner, G., Daubenmier, J. J., Chew, M. H., Marlin, R., and Ornish, D. (2005). Effects of pomegranate juice consumption on myocardial perfusion in patients with coronary heart disease. *The American journal of cardiology*, *96*(6), 810-814.

Syed, D. N., Afaq, F., and Mukhtar, H. (2007). Pomegranate derived products for cancer chemoprevention. In *Seminars in cancer biology* (Vol. 17, No. 5, pp. 377-385). Academic Press.

Taneja, N. (2012). *Maximizing viability of Lactobacillus paracasei subsp. paracasei L. casei 431 during processing and ambient storage: a thesis presented in partial fulfillment of the requirements for the degree of Master of Technology in Food Technology, Massey University, Palmerston North, New Zealand* (Doctoral dissertation, Massey University).

Tango, M. S. A., and Ghaly, A. E. (1999). Amelioration of lactic acid production from cheese whey using micro-aeration. *Biomass and Bioenergy*, *17*(3), 221-238.

Tezcan, F., Gültekin-Özgüven, M., Diken, T., Özçelik, B., and Erim, F. B. (2009). Antioxidant activity and total phenolic, organic acid and sugar content in commercial pomegranate juices. *Food Chemistry*, *115*(3), 873-877.

Thakur, A., and Joshi, V. K. (2017). Preparation of Probiotic Apple Juice by Lactic Acid Fermentation. *International Journal of Food and Fermentation Technology*, *7*(1), 67-85.

Thavasi, V., Bettens, R. P. A., and Leong, L. P. (2009). Temperature and solvent effects on radical scavenging ability of phenols. *The Journal of Physical Chemistry A*, *113*(13), 3068-3077.

Tian, Q., Giusti, M. M., Stoner, G. D., and Schwartz, S. J. (2005). Screening for anthocyanins using high-performance liquid chromatography coupled to electrospray ionization tandem mass spectrometry with precursor-ion analysis, product-ion analysis, common-neutral-loss analysis, and selected reaction monitoring. *Journal of chromatography A, 1091*(1-2), 72-82.

Tomita, S., Saito, K., Nakamura, T., Sekiyama, Y., and Kikuchi, J. (2017). Rapid discrimination of strain-dependent fermentation characteristics among *Lactobacillus* strains by NMR-based metabolomics of fermented vegetable juice. *PloS one*, *12*(7), e0182229.

Tongnual, P., and Fields, M. L. (1979). Fermentation and relative nutritive value of rice meal and chips. *Journal of Food Science*, *44*(6), 1784-1785.

Tranchimand, S., Brouant, P., and Iacazio, G. (2010). The rutin catabolic pathway with special emphasis on quercetinase. *Biodegradation*, *21*(6), 833-859.

Tripathy, B. B., Chandalia, H. B., and Das, A. K. (2012). *RSSDI textbook of diabetes mellitus*. JP Medical Ltd.

Tuorila, H., and Cardello, A. V. (2002). Consumer responses to an off-flavor in juice in the presence of specific health claims. *Food Quality and Preference*, *13*(7-8), 561-569.

Tzulker, R., Glazer, I., Bar-Ilan, I., Holland, D., Aviram, M., and Amir, R. (2007). Antioxidant activity, polyphenol content, and related compounds in different fruit juices and homogenates prepared from 29 different pomegranate accessions. *Journal of Agricultural and Food Chemistry*, *55*(23), 9559-9570.

Vamanu, E., Vamanu, A., Popa, O., and Câmpeanu, G. (2005). Isolation of a *Lactobacillus plantarum* strain used for obtaining a product for the preservation of fodders. *African Journal of Biotechnology*, *4*(5), 403-408.

Van den Berghe, G., Wouters, P. J., Bouillon, R., Weekers, F., Verwaest, C., Schetz, M., ... and Lauwers, P. (2003). Outcome benefit of intensive insulin therapy in the critically ill: Insulin dose versus glycemic control. *Critical care medicine*, *31*(2), 359-366.

Van Hylckama Vlieg, J. E., Veiga, P., Zhang, C., Derrien, M., and Zhao, L. (2011). Impact of microbial transformation of food on health—from fermented foods to fermentation in the gastro-intestinal tract. *Current opinion in biotechnology*, *22*(2), 211-219.

Vandepitte, J., Verhaegen, J., Engbaek, K., Rohner, P., Piot, P., Heuck, C. C., and Heuck, C. C. (2003). *Basic laboratory procedures in clinical bacteriology*. World Health Organization.

Vasudha, S., and Mishra, H. N. (2013). Non dairy probiotic beverages. *International Food Research Journal*, *20*(1).

Vergara, C. M. D. A. C., Honorato, T. L., Maia, G. A., and Rodrigues, S. (2010). Prebiotic effect of fermented cashew apple (*Anacardium occidentale* L) juice. *LWT-Food Science and Technology*, *43*(1), 141-145.

Vessal, M., Hemmati, M., and Vasei, M. (2003). Antidiabetic effects of quercetin in streptozocin-induced diabetic rats. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology*, *135*(3), 357-364.

Viladomiu, M., Hontecillas, R., Lu, P., and Bassaganya-Riera, J. (2013). Preventive and prophylactic mechanisms of action of pomegranate bioactive constituents. *Evidence-Based Complementary and Alternative Medicine*, *2013*.

Villarreal-Soto, S. A., Beaufort, S., Bouajila, J., Souchard, J. P., and Taillandier, P. (2018). Understanding Kombucha Tea Fermentation: A Review. *Journal of food science*, *83*(3), 580-588.

Vitas, J. S., Malbaša, R. V., Grahovac, J. A., and Lončar, E. S. (2013). The antioxidant activity of kombucha fermented milk products with stinging nettle and winter savory. *Chemical Industry and chemical Engineering Quarterly*, *19*(1), 129-139.

Viuda-Martos, M., Ruiz Navajas, Y., Sánchez Zapata, E., Fernández-López, J., and Pérez-Álvarez, J. A. (2010). Antioxidant activity of essential oils of five spice plants widely used in a Mediterranean diet. *Flavour and Fragrance Journal*, 25(1), 13-19.

Viuda-Martos, M., Ruiz-Navajas, Y., Fernández-López, J., Sendra, E., Sayas-Barberá, E., and Pérez-Álvarez, J. A. (2011). Antioxidant properties of pomegranate

(*Punica granatum* L.) bagasses obtained as co-product in the juice extraction. *Food Research International*, *44*(5), 1217-1223.

Vodnar, D. C., Paucean, A., Dulf, F. V., and Socaciu, C. (2010). HPLC characterization of lactic acid formation and FTIR fingerprint of probiotic bacteria during fermentation processes. *Notulae Botanicae Horti Agrobotanici Cluj-Napoca*, *38*(2), 109-113.

Vuong, T., Martineau, L. C., Ramassamy, C., Matar, C., and Haddad, P. S. (2007). Fermented Canadian lowbush blueberry juice stimulates glucose uptake and AMP-activated protein kinase in insulin-sensitive cultured muscle cells and adipocytes. *Canadian Journal of Physiology and Pharmacology*, *85*(9), 956-965.

Walker, W. A. (2008). Mechanisms of action of probiotics. *Clinical Infectious Diseases*, *46*(Supplement_2), S87-S91.

Wang, C. Y., Ng, C. C., Su, H., Tzeng, W. S., and Shyu, Y. T. (2009). Probiotic potential of noni juice fermented with lactic acid bacteria and bifidobacteria. *International journal of food sciences and nutrition*, *60*(sup6), 98-106.

Wang, D., Lu, J., Miao, A., Xie, Z., and Yang, D. (2008). HPLC-DAD-ESI-MS/MS analysis of polyphenols and purine alkaloids in leaves of 22 tea cultivars in China. *Journal of Food Composition and Analysis*, *21*(5), 361-369.

Wang, N. F., Yan, Z., LI, C. Y., Jiang, N., and Liu, H. J. (2011). Antioxidant activity of peanut flour fermented with lactic acid bacteria. *Journal of Food Biochemistry*, *35*(5), 1514-1521.

Wang, R., Ding, Y., Liu, R., Xiang, L., and Du, L. (2010). Pomegranate: constituents, bioactivities and pharmacokinetics. *Fruit, vegetable and cereal science and biotechnology*, *4*(2), 77-87.

Wang, Y. C., Yu, R. C., and Chou, C. C. (2006). Antioxidative activities of soymilk fermented with lactic acid bacteria and bifidobacteria. *Food microbiology*, *23*(2), 128-135.

Wang, Y. C., Yu, R. C., Yang, H. Y., and Chou, C. C. (2003). Sugar and acid contents in soymilk fermented with lactic acid bacteria alone or simultaneously with bifidobacteria. *Food Microbiology*, *20*(3), 333-338.

Wardani, S. K., Cahyanto, M. N., Rahayu, E. S., and Utami, T. (2017). The effect of inoculum size and incubation temperature on cell growth, acid production and curd formation during milk fermentation by *Lactobacillus plantarum* Dad 13. *International Food Research Journal*, *24*(3).

Wayne, P. A. (2012). Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; approved standard, 11th ed. CLSI document M02-A11. CLSI.

Wei, Q. K., Chen, T. R., and Chen, J. T. (2007). Using of Lactobacillus and Bifidobacterium to product the isoflavone aglycones in fermented soymilk. *International journal of food microbiology*, *117*(1), 120-124.

Wijayanti, E. D., Setiawan, N. C. E., and Malang, A. F. P. I. (2017). The effect of lactic acid fermentation on fig (*Ficus carica*) fruit flavonoid. *Journal of Biological Researches*, *23*(1), 40.

Wink, M. (2010). Annual plant reviews, functions and biotechnology of plant secondary metabolites, 39, 1-20. John Wiley & Sons.

Wong, Y. M., and Siow, L. F. (2015). Effects of heat, pH, antioxidant, agitation and light on betacyanin stability using red-fleshed dragon fruit (*Hylocereus polyrhizus*) juice and concentrate as models. *Journal of food science and technology*, *52*(5), 3086-3092.

Wood, B. J. B. and Holzapfel, W. H. (1995). The lactic acid bacteria. In B. J. B. Wood and W. H. Holzapfel (eds.). The Genera of Lactic Acid Bacteria. Blackie Academic & Professional, London.

Wu, S., and Tian, L. (2017). Diverse phytochemicals and bioactivities in the ancient fruit and modern functional food pomegranate (*Punica granatum*). *Molecules*, *22*(10), 1606.

Yabe-Nishimura, C. (1998). Aldose reductase in glucose toxicity: a potential target for the prevention of diabetic complications. *Pharmacological reviews*, *50*(1), 21-34.

Yamasaki, M., Kitagawa, T., Koyanagi, N., Chujo, H., Maeda, H., Kohno-Murase, J. and Yamada, K. (2006). Dietary effect of pomegranate seed oil on immune function and lipid metabolism in mice. *Nutrition*, *22*(1), 54-59.

Yanez, R., Marques, S., Gírio, F. M., and Roseiro, J. C. (2008). The effect of acid stress on lactate production and growth kinetics in *Lactobacillus rhamnosus* cultures. *Process Biochemistry*, *43*(4), 356-361.

Yigzaw, Y., Gorton, L., Solomon, T., and Akalu, G. (2004). Fermentation of seeds of Teff (*Eragrostis teff*), grass-pea (*Lathyrus sativus*), and their mixtures: aspects of nutrition and food safety. *Journal of agricultural and food chemistry*, *52*(5), 1163-1169.

Yogisha, S., and Raveesha, K. A. (2010). Dipeptidyl Peptidase IV inhibitory activity of *Mangifera indica*. *J Nat Prod*, *3*, 76-79.

Yoon, K. Y., Woodams, E. E., and Hang, Y. D. (2004). Probiotication of tomato juice by lactic acid bacteria. *The Journal of microbiology*, *42*(4), 315-318.

Yoon, K. Y., Woodams, E. E., and Hang, Y. D. (2005). Fermentation of beet juice by beneficial lactic acid bacteria. LWT-Food Science and Technology, 38(1), 73-75.

Yoon, K. Y., Woodams, E. E., and Hang, Y. D. (2006). Production of probiotic cabbage juice by lactic acid bacteria. *Bioresource Technology*, *97*(12), 1427-1430.

Yuan, T., Wan, C., Ma, H., and Seeram, N. P. (2013). New phenolics from the flowers of *Punica granatum* and their in vitro α-glucosidase inhibitory activities. *Planta medica*, *79*(17), 1674-1679.

Zhang, Y. and Zhang, H. (2013). Microbiota associated with type 2 diabetes and its related complications. *Food Science and Human Wellness*, *2*(3-4), 167-172.

Zhang, Y., Krueger, D., Durst, R., Lee, R., Wang, D., Seeram, N., and Heber, D. (2009). International multidimensional authenticity specification (IMAS) algorithm for detection of commercial pomegranate juice adulteration. *Journal of agricultural and food chemistry*, *57*(6), 2550-2557.

Zheng, Z., Guo, X., Zhu, K., Peng, W., and Zhou, H. (2016). The optimization of the fermentation process of wheat germ for flavonoids and two benzoquinones using EKF-ANN and NSGA-II. *RSC Advances*, *6*(59), 53821-53829.

Zhou, Y., Han, L. R., He, H. W., Sang, B., Yu, D. L., Feng, J. T., and Zhang, X. (2018). Effects of Agitation, Aeration and Temperature on Production of a Novel Glycoprotein GP-1 by *Streptomyces kanasenisi* ZX01 and Scale-Up Based on Volumetric Oxygen Transfer Coefficient. *Molecules*, *23*(1), 125.

Zia, T., Hasnain, S. N., and Hasan, S. K. (2001). Evaluation of the oral hypoglycaemic effect *of Trigonella foenum-graecum* L.(methi) in normal mice. *Journal of Ethnopharmacology*, *75*(2-3), 191-195.