EFFECT OF PROBIOTIC IN YOGHURT ON GLUCOSE AND LIPID PROFILE IN DM2 PATIENT

RESEARCH PROJECT SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

Bachelor

in

Department of Therapeutic Nutrition

Submitted by

Abdulrahman Mohammed Abdullah Drmosh
Abdulrahman Taha Mohammed Al-Shehari
Abrar Amin Abdo Alareda
Ahmed Mohammed Abdullah Almatwakla
Alia'a Mohammed Ameen Al-emad
Arwa Yasser Farook Mughalis
Dawod Ahmed Mohammed Abdo Saeed
Malak Mohammed Ahmed Nagy Al-Jomai
Seham Mohammed Ali Al-Edresi
Weam Abather Mohammed ALghashm

Supervisor

Dr. Mohammed Alsebaeai

Assistance Professor (Ph. D) in Food Science and Nutrition

DEPARTMENT OF THERAPEUTIC NUTRITION

INTERNATIONAL MALAYSIAN UNIVERSITY

YEMEN

2022

EFFECT OF PROBIOTIC IN YOGHURT ON GLUCOSE AND LIPID PROFILE IN DM2 PATIENT

RESEARCH PROJECT PRESENTED BY

Abdulrahman Mohammed Abdullah Saeed Drmosh

Abdulrahman Mohammed Abdullah drmosh

Abdulrahman Taha Mohammed Al-Shehari

Abrar Amin Abdo Alareda

Ahmed Mohammed Abdullah Almatwakla

Alia'a Mohammed Ameen Al-emad

Arwa Yasser Farook Mughalis

Dawod Ahmed Mohammed Abdo Saeed

Malak Mohammed Ahmed Nagy Al-Jomai

Seham Mohammed Ali Al-Edresi

Weam Abather Mohammed ALghashm

TO

International Malysian University

IN PARTIAL FULFILMENT OF THE
REQUIREMENTS FOR THE AWARD OF

Bachelor of Therapeutic Nutrition

YEAR

2022

DECLARATION BY STUDENT

CERTIFICATE

We are hereby certify that we had personally carried out the work depicted in the research project entitled, "**Effect of Probiotic in Yoghurt on Glucose and Lipid Profile in DM2 Patient**"

No part of the research project has been submitted for the award of any other degree prior to this date.

Name of the Candidate	Signature
Abdulrahman Mohammed Abdullah Drmosh	
Abdulrahman Taha Mohammed Al-Shehari	
Abrar Amin Abdo Alareda	
Ahmed Mohammed Abdullah Almatwakla	
Alia'a Mohammed Ameen Al-emad	
Arwa Yasser Farook Mughalis	
Dawod Ahmed Mohammed Abdo Saeed	
Malak Mohammed Ahmed Nagy Al-Jomai	
Seham Mohammed Ali Al-Edresi	
Weam Abather Mohammed ALghashm	

DECLARATION BY GUIDE

Name of the guide **Dr. Mohammed Alsebaeai**

Department **Therapeutic Nutrition**

This is to certify that in the department of Therapeutic Nutrition of this collage has fulfilled the requirements prescribed for the bachelor degree of the International Malaysian University

The research project entitled, "**Effect of Probiotic in Yoghurt on Glucose and Lipid Profile in DM2 Patient**" was carried out under my direct supervision. No part of the research project was submitted for the award of any degree or bachelor prior to this date.

Date Signature

THE EFFECT OF PROBIOTIC IN YOGHURT ON GLUCOSE AND LIPID PROFILE IN DM2 PATIENT

By

Abdulrahman Mohammed Abdullah Drmosh
Abdulrahman Taha Mohammed Al-Shehari
Abrar Amin Abdo Alareda
Ahmed Mohammed Abdullah Almatwakla
Alia'a Mohammed Ameen Al-emad
Arwa Yasser Farook Mughalis
Dawod Ahmed Mohammed Abdo Saeed
Malak Mohammed Ahmed Nagy Al-Jomai
Seham Mohammed Ali Al-Edresi
Weam Abather Mohammed ALghashm

Research project submitted in the partial fulfilment of the requirements for the degree of "**Bachelor in Therapeutic Nutrition "** Department of Therapeutic Nutrition International Malaysian University, Yemen.

APPROVED BY ADVISORY COMMITTEE AND EXAMMINERS

Chairman/Supervisor	**Dr. Mohammed Alsebaeai** Faculty of Agriculture and Food Science Ibb University
Internal Examiner	**Prof. Foud Alswadi** Faculty of Medical Science IMU
External Examiner:	**Dr. Eqbal Alhakim** Faculty of Agriculture and Food Science Ibb University

Acknowledgement

First and foremost, We bow our head with great reverence to the Almighty Allah for all these blessings towards us. In Addition, We are highly thankful to ***Dr. Mohammed Alsebaeai.***

We thank ***Dr. Qahera Alhelaly****,* ***Prof. Foud Alswadi and Dr. Eqbal Alhakim for*** *providing and support us during carry out our research work..*

At the very onset, We feel immense pleasure to express our deep sense of gratitude and indebtedness to our ***Mothers and Fathers*** *for their keep interest, constructive criticism, valuable guidance, persistent promptness and constant encouragement throughout the period of our study.*

We also give special thanks to those who are directly or indirectly involved to help us during our research work.

Date:

Place: …….. ***Researchers***

Abstract

Background: Type II is the most common form of diabetes. Millions of people around the world have been diagnosed with Type II diabetes, and many more remain undiagnosed. People with diabetes are at a greater risk of developing cardiovascular diseases such as heart attack and stroke. The fermented dairy products consumed today are generated through controlled microbial culturing and enzymatic conversions of major and minor milk components. Several study was reported that there are associated between Diabetes Millions and microorganism.

Objective: The objective of study was to estimate the effect of Yoghurt on the glucose measurement and lipid profile in DM 2 Patient

Materials and Methods: The study included 9 patients aged >30 years with T2DM. The patients were administered probiotic (Nana Ative) daily for 30 days, which consisted of probiotics microorganism strain**.** The patients were examined for clinical assessment such as (Skin, Hair, Nail and Eye), Anthropometric assessments such as (Weight, Height, BMI and Body Fat) and the laboratory assessment such as (TC, TG, HDL, VLDL, Estimated Average Glucose, HOMA-IR and FBG)

Results: The consumption of probiotic (Yoghurt) caused a powerful significant decrease in TG (210.56 in the begging to 141.89 mg/ dL in the end of experiment) and TC concentrations (177.89 in the begging to 168.13 mg/ dL After 4 week) in Yoghurt after the 4 weeks of intervention period. The BMI and body fat of participates were increased while the Fast Blood Glucose (FBG) in DM patient treated with Yoghurt were increased. HOMA-IR and HbA1C in DM patient treated with Yoghurt were increased after the 4 weeks of intervention period. The VLDL and LDL were Decrease during the experiment while HDL were Increased after the 4 weeks of intervention period

Conclusion: This study found that, the consumption of Yemeni yoghurt was increase HOMA-IR, HbA1C, EAG and FBG while decrease the lipid profile.

Key words

Yoghurt, Diet, BMI, DM2, Yemen

مشروع تخرج

(تأثير البروبيوتك في الزبادي علي سكر ومكونات الدهون في مرضي السكري من النوع الثاني)

الملخص

الخلفية: داء السكري من النوع الثاني هو النوع الاكثر شيوعًا بين انواع السكري. تم تشخيص إصابة الملايين من الأشخاص حول العالم بمرض السكري من النوع الثاني ، ولا يزال الكثيرون غير مشخصين. الأشخاص المصابون بداء السكري أكثر عرضة للإصابة بأمراض القلب والأوعية الدموية مثل النوبات القلبية والسكتة الدماغية. يتم إنتاج منتجات الألبان المخمرة المستهلكة اليوم من خلال الزراعة الميكروبية الخاضعة للرقابة والتحويلات الأنزيمية لمكونات الحليب الرئيسية والثانوية. تم اجراء العديد من الدراسات التي اكدت أن هناك علاقة بين مرض السكري والكائنات الحية الدقيقة النافعة.

الهدف: هدفت الدراسة الى تقدير تأثير الزبادي على قياس نسبة الجلوكوز ومكونات الدهون في مريض السكري من النوع الثاني.

المواد وطرق العمل: شملت الدراسة 9 مرضى تزيد أعمارهم عن 25 عامًا يعانون من السكري من النوع الثاني. تم إعطاء المرضى البروبيوتيك (Nana Ative) يوميًا لمدة 30 يومًا. فحص المرضى للتقييم السريري مثل (الجلد والشعر والأظافر والعين) والتقييمات الجسمانية مثل (الوزن والطول ومؤشر كتلة الجسم ودهون الجسم) والتقييمات المخبرية مثل (الكولسترول ، الدهون الثلاثية ، الليبوبروتني مرتفع الكثافة ومنخفض الكثافة والمنخفض جدا، تقدير المتوسط الجلوكوز، مقاومة الانسولين ، كمية السكر الصائم)

النتائج: تسبب استهلاك البروبيوتيك (الزبادي) في انخفاض معنوي قوي في الدهون الثلاثية من 210.56 إلى 141.89 مجم / ديسيلتر في نهاية التجربة و كميه الكوليسترول من 177.89 إلى 168.33 مجم / ديسيلتر. ازداد مؤشر كتلة الجسم ودهون الجسم ونسبة الجلوكوز الصائم و

تقدير المتوسط الجلوكوز و مقاومة الانسولين في مريض DM المعالج الزبادي بعد 4 أسابيع من التجربة. انخفض VLDL و LDL أثناء التجربة بينما زاد HDL بعد 4 أسابيع من التجربة.

الخلاصة: وجدت هذه الدراسة أن استهلاك الزبادي اليمني زاد من مؤشر كتلة الجسم ودهون الجسم ونسبة الجلوكوز الصائم و تقدير المتوسط الجلوكوز و مقاومة الانسولين مع انخفاض مستوى الدهون والكوليسترول بشكل عام.

الكلمات المفتاحية

الزبادي ، الحمية ، مؤشر كتلة الجسم ، السكري النوع الثاني ، اليمن

Abbreviations

BMI	Body Mass Index
WHO	The World Health Organization
Kg	Kilogram
Yr	Year
BF	Body Fat
LDL	Low Density Lipoprotein
HDL	High Density Lipoprotein
VLDL	Very Low Density Lipoprotein
%	Percentage
m2	Meter square
M	Meter
et al.	et alia (and associates)
Etc	(et cetera) and the others
Fig.	Figure
i.e.	(ed est) that is
Ml	Milliliter
Mm	Millimeter
SD	Standard deviation
Sec	Second
M	Mean
AOAC	Association of Official Agricultural Chemists
Cm	centimeter
Mins	minutes
DM	Diabetes Mellitus
TC,	Total cholesterol
TG,	Triglyceride
µl	Microliter

µg	Microgram
EAG	Estimated Average Glucose
HOMA-IR	Homeostatic Model Assessment for Insulin Resistance
FBG	Fast Blood Glucose

List of Tables

List of Figure

List of Photo

Contents

Chapter-I

Introduction

Chapter-I

Introduction

1.1 Overview

The global prevalence of type 2 diabetes mellitus (T2DM) is projected to grow beyond 700 million patients by 2045 (IDF, 2020), at a cost to society of greater than two trillion US dollars (Bommer et al., 2018). The World Health Organisation (WHO) and the United Nations (UN) have made T2DM prevention a top health priority (WHO, 2016). One in fifteen individuals in the United Kingdom (UK) has a diagnosis of diabetes, of which T2DM accounts for around 90%, a current cohort of greater than three million people. Population estimations suggest one million patients already suffer from undiagnosed T2DM. Of these cases, 60% are considered preventable through lifestyle and dietary intervention [5]. Obesity, central adiposity and body mass index (BMI) play a pivotal role in the pathophysiology of T2DM, a chronic metabolic disease characterized by hyperglycemia and associated with insulin resistance and/or insufficient pancreatic insulin production (ADA, 2010). Unrecognized or suboptimal T2DM may lead to both micro- and macro vascular complications associated with hypertension, renal failure, susceptibility to infection, limb amputations and blindness with their subsequent disability (Lederberg and McCray, 2001).

Dairy products are one of the main trends in the food industry, in addition to be widely consumed and recognized as health promoters (Yilmaz-Ersan et al., 2020), they also represent one of the largest segments of the functional food market (Akin and Ozcan, 2017).

Yogurt is one of the fermented milk products best known for being a functional food and probiotics, therefore, overtaking a great market success level overall compared to other probiotic products (Parvarei et al., 2021),

Its nutritional composition is rich in vitamins, minerals and proteins of high biological value, being available in various textures and flavors (Fabersani et al., 2018).

The yogurt production occurs from the coagulation and gelling of milk, which occurs through the action of the bacteria *Streptococcus thermophilus* and *Lactobacillus delbrueckii subsp*, which ferment lactose, producing organic acids such as lactic acid and bioactive peptides contributing to the unique flavor and texture and characteristic of yogurt (Yerlikaya et al., 2021).

The yogurt is considered an excellent vehicle for probiotic microorganisms and can be classified into two groups, which are standard culture yogurt and probiotic yogurt, therefore probiotic cultures in yogurt must remain alive in adequate numbers from the time of manufacture to consumption (Fazila, et al., 2018). According to Global Market Insights (2020), the size of the global market for probiotics exceeded $2 billion globally in 2018 and it is estimated to grow by more than 7.3% between 2019 and 2026.

The word "probiotic" comes from the Greek language "pro" and "bios", meaning "for all life", in other words, each substance or organism that prolongs life (Asgari et al., 2020). According to the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) (2002), probiotics are "live microorganisms that provide health benefits to the host when administered in adequate amounts". Therefore, in recent years new definitions have been added to probiotic terminologies, such as 'para-probiotics' (dead/inactivated cells of probiotics) and 'post-biotics' (healthy probiotic metabolites) (Zendeboodi et al., 2020).

The concept of probiotics is to restore and maintain a microflora advantageous to the human body. Probiotics are found in a number of fermented dairy products, infant formula, and dietary supplements. Basic research on probiotics has suggested several modes of action beneficial for the human body and clinical research has proven its preventive and curative features in different intestinal and extraintestinal diseases (Broekaert and Walker, 2006).

Chronic diseases cause considerable disablement in patients and represent a substantial economic burden on healthcare resources. Research has demonstrated a crucial role of nutrition in the prevention of chronic disease. Thus, positive, strain-specific effects of probiotics have been shown in diarrheal diseases, inflammatory bowel diseases, irritable bowel syndrome, and Helicobacter pylori-induced gastritis, and in atopic diseases and in the prevention of cancer.

As the majority of probiotics naturally inhabit the human intestinal microflora, their use has been regarded as very safe. However, in view of the range of potential benefits on health that might be achieved by the use of some probiotic bacteria, major and thorough evaluation is still necessary (Broekaert and Walker, 2006).

1.2 Aim of the Study

1.2.1 General Objectives

The objective of study was to estimate the effect of Yoghurt on the glucose measurement and lipid profile in DM 2 Patient

1.2.2 Specific Objectives

Specific objectives of study were as following:

1. To determine the impact of probiotic in the nutritional assessment of DM 2 Patient
2. To determine the impact of probiotic in the anthropometric measurement of DM 2 Patient
3. To determine the impact of probiotic in the laboratory assessment of DM 2 Patient

Chapter-II

Review of Literature

Chapter-II

Review of Literature

2.1. Diabetes Mellitus

2.1.1. Definition of Diabetes Mellitus

The terms “Diabetes” and “Mellitus” are derived from Greek language. “Diabetes” denotes “a passer through, a siphon” whereas the “Mellitus” means “sweet”. It is believed that Greeks entitled it such way, due to the exaggerated urine proportions produced by diabetic patients which attracted flies and bees (Piero et al 2015; Patlak, 2002). From the very first described case of DM 3000 years ago by the ancient Egyptians and Araetus of Cappadocia (81-133AD) to 1675 when British Thomas Willis rediscover the sweetness of urine and blood of patients (Ahmed, 2002: White, 2014). since now huge improvement in the knowledge for DM has been achieved. Some theories support that economic6 and insurance7 status would play a major role on the express of DM (type II). Moreover a recent study showed that race would also have an important factor on DM prevalence (type I and II) (Heidemann, et al., 2016)..

2.1.2. Classification and diagnosis of diabetes

Three main types of DM are known type I associated with full insulin deficiency, type II-progressive insulin deficiency (Gale, 2001). and gestational DM which is diagnosed in 2nd or 3rd semester of pregnancy. Currently, although type I cannot be prevented, type II is preventable with good health, exercising and healthy diet. Early diagnosis is the key in diabetes management. Nevertheless, type II have affected high population and lead to complications in several body parts, heart, nerves, eyes, kidney and so on Wu et al., 2016). Diabetes falls into three below general categories:

2.1.2.1. Type I diabetes

Type I accounts for only about 5—10% of all cases of diabetes; however, its incidence continues to increase worldwide and it has serious short-term and long-term implications. Type I indicates the process of beta-cell destruction in the

pancreas that may ultimately lead to diabetes mellitus in which "insulin is required for survival" to prevent the development of ketoacidosis, coma and death. Management of Type I diabetes is best undertaken in the context of a multidisciplinary health team and requires continuing attention to many aspects, including insulin administration, blood glucose monitoring, meal planning, and screening for diabetes-related complications. These complications consist of microvascular and macrovascular disease, which account for the major morbidity and mortality associated with Type I diabetes (Daneman, 2006).

2.1.2.2. Type II diabetes

Type II is the most common form of diabetes. Millions of people around the world have been diagnosed with Type II diabetes, and many more remain undiagnosed. People with diabetes are at a greater risk of developing cardiovascular diseases such as heart attack and stroke if the disease is left undiagnosed or poorly controlled. They also have elevated risks for sight loss, foot and leg amputation due to damage to the nerves and blood vessels, and renal failure requiring dialysis or transplantation (Pasinetti, 2011). Before people develop Type II diabetes, they almost always have "pre-diabetes" −blood glucose levels that are higher than normal but not yet high enough to be diagnosed as diabetes. Recent research has shown that some long-term damage to the body, especially the heart and circulatory system, may already be occurring during pre-diabetes (DePaula, 2008).

In Type II diabetes, either the body does not produce enough insulin or the cells ignore it. Insulin is necessary in order for the body to be able to use glucose for energy. After food consumption, the body breaks down all sugars and starches into glucose, which is the basic fuel for the cells. Insulin takes the sugar from the blood into the cells. When glucose builds up in the blood instead of going into the cells, it can lead to diabetes complications.

2.1.2.3. Gestational diabetes mellitus (GDM)

Gestational diabetes is diabetes found for the first time when a woman is pregnant. Women who are overweight, have had gestational diabetes before or

have a strong family history of diabetes are at a higher risk of developing gestational diabetes. Untreated gestational diabetes may cause problems to the baby. Both the mother and the baby are at increased risk for Type II diabetes for the rest of their lives (Harris, 1991).

2.1.3. Diagnostic Tests for Diabetes Mellitus

The diagnosis of diabetes mellitus is easily established when a patient presents the classic symptoms of hyper-glycaemia and has a random blood glucose value of 200 mg/dL (11.1 mmol/L) or higher, and confirmed on another occasion. The following tests are used for the basic diagnosis:

A fasting plasma glucose (FPG) test measures blood glucose in a person who has not eaten anything for at least 8 hours. This test is used to detect diabetes and pre-diabetes

An oral glucose tolerance test (OGTT) measures blood glucose after a person fasts at least 8 hours and 2 hours after the person drinks a glucose-containing beverage. This test can be used to diagnose diabetes and pre-diabetes. The FPG test is the preferred test for diagnosing diabetes because of its convenience and low cost. However, it may miss some diabetes or pre-diabetes that can be found with the OGTT. The FPG test is most reliable when done in the morning. Research has shown that the OGTT is more sensitive than the FPG test for diagnosing pre-diabetes, but it is less convenient to administer

A random plasma glucose test, also called a casual plasma glucose test, measures blood glucose without regard to when the person being tested last ate. This test, along with an assessment of symptoms, is used to diagnose diabetes but not pre-diabetes. Test results indicating that a person has diabetes should be confirmed with a second test on a different day (Twillman, 2002). The current WHO diagnostic criteria for diabetes should be maintained − fasting plasma glucose ≥ 7.0mmol/l (126mg/dl) or 2−h plasma glucose ≥ 11.1mmol/l (200mg/dl) (Report of a WHO Consultation, 1999).

2.1.4. Prevention / Delay of Type II Diabetes

Before people develop Type II diabetes, they almost always have "pre-diabetes" −blood glucose levels that are higher than normal but not yet high enough to be diagnosed as diabetes. Pre-diabetes is a serious medical condition that can be treated. A recently completed study carried out by scientists in the United States conclusively showed that people with pre-diabetes can prevent the development of Type II diabetes by making changes in their diet and by increasing their level of physical activity. They may even be able to bring their blood glucose levels back to the normal range.

Lifestyle changes are of outmost importance. A balanced diet and an increase of the level of physical activity can help maintain a healthy weight, stay healthier for longer and reduce the risk of diabetes. The results of the Diabetes Prevention Program (DPP) proved that weight loss through moderate diet changes and physical activity can delay or prevent Type II diabetes (Haus, 2010). The Diabetes Prevention Program (DPP) was a major multicenter clinical research study aimed at discovering whether modest weight loss through dietary changes and increased physical activity or treatment with the oral diabetes drug metformin (Glucophage) could prevent or delay the onset of type II diabetes in study participants.

2.1.5. Old and new approaches to treatment

Diabetes is now ranked as the sixth leading cause of death by disease in the U.S (National diabetes fact sheet, Atlanta 2004). Its treatment as well as the management of diabetes-related complications remains a top priority for governments worldwide, since the economic burden in 2007 alone exceeded $174 billion (Dall et al, 2007).

2.1.5.1. Pharmacological treatment

Old approaches to the treatment of this chronic progressive disease include diet modification and oral hypoglycemic medications, which have proven inadequate, while insulin therapy only solves the problem temporarily. Even with the newest pharmaco-therapies, patients continue to develop macro- and microvascular complications. Diabetes is associated with increased cardiac- and

stroke-related deaths, kidney failure, blindness, and 60% of non-trauma lower-limb amputations (National Diabetes Fact Sheet, Atlanta 2004).

Alternative treatments targeting different models of this disease require careful and responsible examination. As shown below, apart from insulin treatment, it is possible to gain diabetes control after gastrointestinal bypass surgeries.

2.1.5.1.1. Insulin therapy

Diabetes, being one of the primary causes of increased cardiovascular morbidity and mortality in Western countries, constitutes a large burden to health care systems in terms of both direct and indirect costs. Therefore, efficient glucose control (attainment of normal HbA1C, prandial and postprandial glucose levels) is essential to the prevention of the life-threatening complications of this disease.

Insulin is a hormone that treats diabetes by controlling the amount of sugar (glucose) in the blood. When used as a medication, it is derived from either pork (porcine), beef (no longer available in the U.S.), or is genetically made to be identical to human insulin (Buysschaert, 2000).

Patients with type I diabetes mellitus depend on external insulin (most commonly injected subcutaneously) for their survival because the hormone is no longer produced internally. Patients with type II diabetes mellitus are insulin resistant, have relatively low insulin production, or both; certain patients with Type II diabetes may eventually require insulin if other medications fail to control blood glucose levels adequately.

There are many types of insulin used to treat diabetes. They are classified by how fast they start to work, when they reach their "peak" level of action (i.e. when the concentration of insulin in the blood is highest), and how long their effects last.

The types of insulin include:

- Rapid-acting insulin, which starts working within a few minutes and lasts for a couple of hours.

- Regular- or short-acting insulin, which takes about 30 minutes to work and lasts for 3 to 6 hours.
- Intermediate-acting insulin, which takes 2 to 4 hours to work and its effects can last for up to 18 hours.
- Long-acting insulin, which takes 6 to 10 hours to reach the bloodstream, but it can keep working for an entire day (Tuomilehto, 2001).

2.1.5.1.2. Non-Insulin Diabetes Treatment

There is a relatively new class of drugs called incretinmimetics, which mimic certain substances that can be found in the stomach and intestinal tract. These substances are normally released in response to food intake and signal the release of insulin from the pancreas. Since this reaction is reduced in people with type II diabetes, incretinmimetics work to stimulate insulin release and help lower blood sugar. The doctor may recommend incretinmimetics if a patient has not been able to adequately control their blood sugar with other types of treatment. These medications are taken by injection, either once or twice a day.

For people with type II diabetes, medications called DPP-4 inhibitors can be taken alone or in combination with other diabetes medications. DPP-4 inhibitors prevent the breakdown of incretin hormones. In turn, the incretins can help their body produce insulin to lower elevated blood sugar levels (Gkaliagkousi, 2007).

2.1.5.2. Non-pharmacological treatment

When it comes to non-pharmacological treatment of diabetes mellitus − especially type II diabetes− lifestyle modification alone can prevent development of diabetes in impaired glucose tolerance patients. It can also be the sole therapeutic tool in early diabetes.

After being diagnosed with diabetes, a behavior and lifestyle modification is required. Health care providers should advice all diabetics not to initiate tobacco and emphasize stopping smoking in smokers as utmost priority for diabetic smokers (Diabetes care 1993), since it increases the risk of renal failure, visual

impairment, foot ulcers, leg amputations and heart attacks in people with diabetes. The effects of stopping smoking in diabetes are substantial. The incidence of micro and macro vascular complications was significantly increased in smokers compared to non-smokers (Buysschaert, 2000).

As concerns alcohol, consumption of large amounts can cause hypoglycaemia and this can occur many hours after alcohol intake, particularly if no food has been consumed beforehand.

2.1.6. Diet and Diabetes Mellitus

The major environmental factors that lead to type II diabetes are sedentary lifestyle and over nutrition leading to obesity (Harris, 1991). Sedentary lifestyle is more common in urbanized societies.

Dietary advice is essential upon diagnosis of diabetes. Normal advice includes:

- Reducing intake of fatty foods
- Eating mainly vegetables, fruit, cereal, rice and pasta (using wholemeal products where possible)
- Eating only small amounts of refined sugar (jam, sweets etc.)
- Eating at regular intervals
- Carrying glucose tablets, sweets or products in case of hypoglycaemia
- Exercising regularly; not only does it help reduce hyperglycaemia, but it also reduces insulin resistance by reducing obesity.

Most cases are preventable with healthy lifestyle changes and some can even be reversed. Taking steps to prevent and control diabetes doesn’t mean living in deprivation. While eating right is important, patients don’t have to give up sweets entirely or resign themselves to a lifetime of “health food”

Carbohydrates have a big impact on your blood sugar levels −more so than fats and proteins. In general, patients should limit highly refined carbohydrates like white bread, pasta, and rice, as well as soda, candy, and snack foods. Focus instead

on high-fiber complex carbohydrates−also known as slow-release carbs. Slow-release carbs help keep blood sugar levels even because they are digested more slowly, thus preventing the body from producing too much insulin. They also provide lasting energy and help people stay full longer (Gross, 2005).

2.1.7. Exercise and Diabetes Mellitus

Physical activity reduces the risk of developing type II diabetes by 30-50% and risk reductions are observed with as little as 30 minutes of moderate exercise per day (Gkaliagkousi 2007). Regular exercise improves glycaemic control in all forms of diabetes. Insulin resistance is the major cause of hypoglycemia in type II diabetes and physical exercise is the best way to reduce insulin resistance (Goodpaster et al 2010). Physical activity improves insulin sensitivity in many ways. Fat accumulation in the liver is the main cause of insulin resistance in obesity. Exercise can reduce the free fatty acid load to liver and thereby reduce hepatic insulin resistance (Haus et al 2010). Exercise recommended is moderate exercise for 30 minutes a day (Tuomilehto et al 2001) or moderate physical activity like brisk walking at least 150 minutes per week (Diabetes Prevention Programme research group in *NEJM* 2002). Putative protective mechanisms include reduction of body weight; reduction of insulin resistance, and thereby the associated consequences of the metabolic syndrome, including hypertension, dyslipidaemia and inflammation; and enhancement of endothelial function (Gkliagkousi 2007).

2.2. Dairy products

2.2.1. Introduction

The fermented dairy products consumed today are generated through controlled microbial culturing and enzymatic conversions of major and minor milk components. Fermentation improves shelf life, increases microbiological safety, adds flavor, and enhances palatability and organoleptic qualities. The fermentation process involves a series of complex reactions carried out by microorganisms, which transform milk constituents rendering new molecules of enhanced nutritive value and digestibility. Moreover, fermentation generates metabolites that can be major contributors of a daily healthful diet (Marco, Heeney et al. 2017). The

contributions of milk components and dairy products to human health have been comprehensively reviewed (Tunick and Van Hekken 2015). These can be summarized as enhancing muscle building, lowering blood pressure, reducing low density lipoprotein cholesterol, and preventing diabetes, obesity and cancer, among others. Additionally, due to the reduced consumption of dietary fiber in Western societies and the overall decrease of microbial diversity in processed foods, fermented dairy products could be the perfect carriers for reseeding the gut microbiota. The above listed health benefits and the fact that they are viewed as natural products have placed yoghurt, kefir, and cheese in the forefront of consumers' preferences. In the present chapter we describe existing data regarding the microbiota found in fermented dairy products and the advances in knowledge of microbial properties that may benefit human health.

2.2.2. Fermented dairy products

Fermentation is one of the oldest forms of milk preservation and has been used by humans since ancient times (Markowiak and Slizewska 2017). The beneficial effects of fermented dairy products was empirically known by Romans, Greeks and Egyptians. They produced different types of sour milk from buffalo, cow, or goat´s milk. However, it was not until the 20th century that the beneficial properties of lactic acid bacteria (LAB) started to be scientifically substantiated by the immunologist Élie Metchnikoff, who was awarded the Nobel Prize in 1908. He concluded that the unusual high numbers of Balkan centenarians was due to the consumption of sour milk containing large numbers of the lactic acidproducing bacterium *Lactobacillus bulgaricus bacillus*, currently classified as *Lactobacillus delbrueckii subsp. bulgaricus*. In the book 'The Prolongation of Life' (Metchnikoff 1908), Metchnikoff recommended the daily consumption of milk fermented with pure cultures of this Lactobacillus to discourage microbial putrefactive growth in the colon, setting the stage for further studies on beneficial effects of LAB in fermented products.

2.2.3. Yoghurt

Among fermented dairy products, yoghurt is consumed the most in Western societies, being a common component in the daily diet of populations from the Netherlands and Scandinavian countries. Although yoghurt has been manufactured commercially for over a century, its concept has changed over time into a very segmented market. Today fermented dairy products include a broad catalog of flavored, low-fat, drinkable, probiotic, and other products marketed as health-promoting. The European Codex Alimentarius Commission explicitly defines yoghurt as the product of milk fermentation by *Streptococcus thermophilus and L. delbrueckii subsp. bulgaricus (L. bulgaricus)* (Codex-Alimentarius 2003). According to the Codex STAN 243-2003 these microorganisms must reach a minimum of 107 cfu/g, be viable, active, and abundant in the product until the set expiration date. However, differences in labeling laws allow, for example in the United Kingdom, to include any Lactobacillus species in fermented milks labeled as 'yoghurt'. In this case, the term 'yoghurt-like product' is used and defined as an alternative dairy product in which *L. bulgaricus* can be substituted by other Lactobacillus species for the fermentation, or yoghurt containing probiotic bacteria, when probiotic or alternative organisms are added to yoghurt (Guarner, Perdigon et al. 2005).

Yoghurt is an excellent source of macro- and micronutrients like high-quality, digestible proteins and carbohydrates, minerals, and vitamins. It contributes to the growth and fitness of muscle mass and helps maintaining bone health due to their calcium and phosphorus content. The nutritional value of yoghurt has been recognized by the Canadian Food Guide (Health-Canada 2011), USA Department of Agriculture (USDA 2010), and the British Nutrition Foundation (BNF 2015). These international agencies recommend the inclusion of fermented dairy products in the daily diet. Furthermore, they emphasize that food guides must state whether dairy products are fermented or non-fermented since fermented dairy products have additional health claims compared to non-fermented products (Chilton, Burton et al. 2015

2.2.4. The definition of Probiotics

The definition of probiotics has been modified with increasing knowledge in the field of how they function. The term is derived from the Greek language meaning 'for life. In the past there have been many attempts to define the term 'probiotic', one of the first being described by Lilly & Stillwell in 1965. They defined probiotics as "substances secreted by one microorganism, which stimulates the growth of another". The focus of this definition was to distinguish them from and make it clear that they are the opposite of antibiotics. Subsequently, in 1974, Parker defined them as "organisms and substances which contribute to intestinal microbial balance" (Schrezenmier & de Vrese, 2001). In 1989, Fuller tried to improve on Parker's definition by proposing the following definition: "live microbial feed supplement, which beneficially affect the host (animal or human) by improving its intestinal microbial balance" (Salminen et al., 1999; Vilsojevic & Shah, 2008). Then, Havenaar & Huis In't Veld (1992) defined probiotics acceptably as 'a viable mono- or mixed culture of microorganisms which applied to animal or man, beneficially affects the host by improving the properties of the indigenous microflora'. Schrezenmeir & de Vrese (2001) defined the term probiotic as "a preparation of or a product containing viable, defined microorganisms in sufficient numbers, which alter the microflora by implantation or colonization, in a compartment of the host and by that, exert beneficial effects on host health". Among these descriptions and definitions, there were many others, until the Food and Agriculture Organization of the United Nations-World Health Organization (FAO-WHO) officially defined probiotics as: "live microorganisms that when administered in adequate amounts confer a significant health benefit on the host" (FAO, 2001). This definition was later endorsed by the International Scientific Association for Probiotics and Prebiotics (ISAPP) and is currently the most accepted definition of probiotics by scientists worldwide (Reid, 2006)

2.2.5. Desirable properties for a probiotic strain

A microbial strain has to fulfil a number of specific properties or criteria for it to be regarded as a probiotic. These criteria are classified into safety, performance and technological aspects (Gibson & Fuller, 2000). The criteria are further

dependent on specific purpose of the strain and on the location for the expression of the specific property. With regards to safety, the probiotic strain must be of human origin, isolated from the gastrointestinal tract (GIT) of healthy individuals. They should possess GRAS (generally regarded as safe) status, be nonpathogenic, and without previous association with diseases such as infective endocarditis or gastrointestinal disorders. Probiotic strains must not deconjugate bile salts and they should carry no antibiotic resistance genes that can be transferred to pathogens (Collins et al., 1998; Saarela et al., 2000). The strain must not induce an immune reaction in the host, i.e. the host must be immuno-tolerant to the probiotic (Havenaar & Huis int' Veld, 1992). The strain itself, its fermentation products or its cell components after its death, should be non-pathogenic, non-toxic, non-allergic, non-mutagenic or non-carcinogenic even in immunocompromised individuals (Collins et al., 1998; Havenaar & Huis int' Veld, 1992). It must have antimutagenic and anticarcinogenic properties and not promote inflammation in individuals (Collins et al., 1998). A probiotic strain should possess a desirable antibiogram profile. It must also be genetically stable with no plasmid transfer mechanism (Havenaar & Huis int' Veld, 1992; Ziemer & Gibson, 1998)

In addition, technological aspects must be taken into account before selecting a probiotic strain. Strains should be capable of being prepared on a large scale and should be able to multiply rapidly, with good viability and stability in the product during storage. The strains must not produce off flavours or textures once incorporated into foods. They should be metabolically active within the GIT and biologically active against their identified target. Probiotic strains must be resistant to phages and have good sensory properties (Collins et al., 1998; Kolida et al., 2006; Lacroix & Yildirim, 2007; Mattila-Sandholm et al., 2002; Saarela et al., 2000;). Therefore probiotic containing foods and products need to be of good quality and must have high enough numbers of viable probiotic cells to ensure that consumers get the optimal benefits from the product (Alakomi et al., 2005). Probiotic strains have to be good vehicles for specific target delivery of peptides and recombinant proteins within the human GIT (Dunne et al., 2001; Parracho et al., 2007).

2.2.6. Probiotic products

Probiotics can be consumed either as food components or as non-food preparations (Stanton et al., 1998). Foods containing probiotics are referred to by others as functional foods. This refers to foods with nutrient or non-nutrient components that affect targeted function(s) in the body resulting in a positive health effect (Bellisle et al., 1998). Thus, functional foods have a physiological or psychological effect beyond basic nutritional value (Clydesdale, 1997). Several probiotic LAB strains are available to consumers in both traditional fermented foods and in supplemented form (Kourkoutas et al., 2005). The majority of probiotics are incorporated into dairy products such as milk powders, yoghurt, soft-, semi-hard and hard cheeses and ice cream (Desmond et al., 2005; Dinakar & Mistry, 1994; Stanton et al., 2001; Stanton et al., 2005). These products offer a suitable environment for probiotic viability and growth (Özer et al., 2009; Ross et al., 2002). There is an increase in use of other foods as vehicles for probiotics. This is partly due to allergenicity of some consumers to milk products. Non-dairy products such as malt-based beverages and fruit juices (Champagne & Raymond, 2008; Rozada Sanchez et al., 2007; Sheehan et al., 2007), meat sausages (Ruiz-Moyano et al., 2008), capsules, and freeze-dried preparations (Berni-Carnani et al., 2007) are among these alternatives. Growing vegetarian alternatives have also led to soy-based probiotic foods (Farmworth et al., 2007). Recently, Aragon-Alegro et al. (2007) added probiotic chocolate mousse to the list of alternatives.

2.2.7. Beneficial effects of probiotics

The benefits attributed to probiotics can either be nutritional or therapeutic (Prasad et al., 1998). Benefits associated are, however, strain specific (Saarela et al., 2000).

2.2.8. Nutritional benefits

Microbial action in the gut, specifically by beneficial cultures, has been shown to enhance the bioavailability, quantity and digestibility of certain nutrients (Parvez et al., 2006). Ingestion of probiotics is associated with improved production of riboflavin, niacin, thiamine, vitamin B6, vitamin B12 and folic acid (Gorbach,

1997; Hargrove & Alford, 1978). Probiotics play a role in increasing bioavailability of calcium, iron, manganese, copper, phosphorous (Alm, 1982; McDonough et al., 1983) and increase the digestibility of protein and fat in yoghurt (Fernandes et al., 1987). Enzymatic hydrolysis of protein and fat leads to an increase in free amino acids and short chain fatty acids (SCFAs). Organic acids such as acetate and lactate produced during fermentation by LAB lower the pH of intestinal contents thereby creating undesirable conditions for harmful bacteria (Mack et al., 1999; Parvez et al., 2006).

2.2.9. Therapeutic benefits

Patients prefer medicine with little or no side effects for treatment of their ailments. Probiotics provide such an alternative, being living, non-pathogenic organisms, which are extremely safe as indicated by their GRAS status. Probiotic bacteria are claimed to alleviate and prevent conditions such as lactose intolerance, allergies, diarrheal diseases, lowering of serum cholesterol, reduction of the risk associated with mutagenicity and carcinogenicity and inhibition of pathogens, as well as stimulation of the immune system (Collins & Gibson, 1999; Shah, 2007). Positive effects of probiotics are not confined to the gut only, but can extend to other parts of the body. For instance, probiotics are known to have anti-inflammatory benefit when administered parenterally (Shiel et al., 2004).

Lactose malabsorption (also referred to as lactose intolerance or lactose indigestion) is the inability to hydrolyze lactose (Adams & Moss, 2000; Salminen et al., 1998a). It is caused by a deficiency of the enzyme β-D-galactosidase (lactase) (Buller & Grand, 1990). The undigested lactose passes to the colon where it is attacked by resident lactose fermenters (Adams & Moss, 2000). Colonic lactose fermentation results in high levels of glucose in blood and hydrogen gas in breath (Buller & Grand, 1990; Mombelli & Gismondo, 2000; Scrimshaw & Murray, 1988; Shah, 1993; Vesa et al., 2000). Probiotics strains and the traditional yoghurt cultures, Lactobacillus d+elbrueckii spp. *bulgaricus* and *Streptococcus thermophilus* produce β-Dgalactosidase thereby improving tolerance to lactose (Adams & Moss, 2000; Fooks et al., 1999, Shah, 2000c)

Constipation, a disorder of motor activity of the large bowel characterized by bowel movements that are less frequent than normal (Salminen et al., 1998b), pain during defecation, abnormal swelling and incomplete emptying of colon contents (Salminen et al., 1998a), can also be relieved by probiotic use. *Lactobacillus reuteri, Lactobacillus rhamnosus and Propionibacterium freudenreichii* are probiotic strains shown to improve the condition (Ouwenhand et al., 2002). Incidences of antibiotic associated diarrhoea caused by Clostridium difficile (Fuller, 2003; Tuohy et al., 2003; Vasiljevic & Shah, 2008) and rotavirus diarrhoea (Salminen et al., 1998a) can also reduced by administration of probiotics. Strains associated with reduction of diarrhoea include Bifidobacterium spp, B. animalis Bb12 (Fuller, 2003, Guandalini et al., 2000), L. rhamnosus GG, L. acidophilus, L. bulgaricus (Fuller, 2003; Goldin, 1998; Gorbach, 2000; Sazawal et al., 2006) and Saccharomyces boulardii (Kotowska et al., 2005, Sazawal et al., 2006). The effect of probiotics against diarrhoea is the most researched and substantiated claim, with documented clinical applications (BergogneBérézin, 2000; Cremonini et al., 2002; Marteau et al., 2001, McNaught & MacFie, 2001; Reid et al., 2003; Sullivan & Nord 2005).

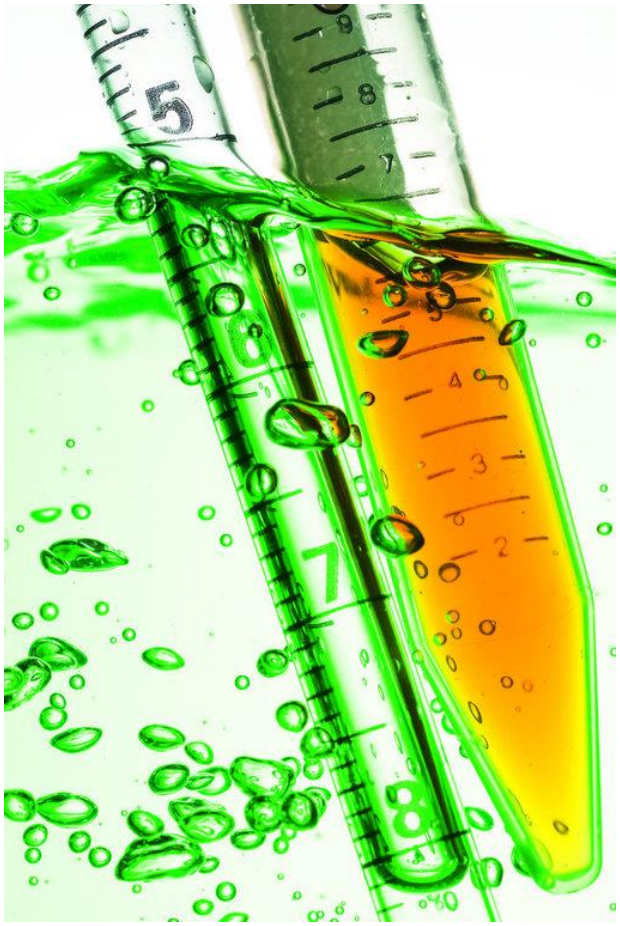
Inflammatory bowel disease (IBD) and irritable bowel syndrome (IBS) are other intestinal disorders that can be treated with varying degrees of success using probiotics. IBD is a collection of disorders including ulcerative colitis, Crohn's disease and pouchitis, characterized by chronic or recurrent inflammation, ulceration and abnormal narrowing of the GIT resulting in abdominal pain, diarrhoea and gastrointestinal bleeding (Hanauer, 2006; Marteau et al., 2001). IBS is typically characterized by abdominal pain, excessive flatus, variable bowel habit and bloating (Madden & Hunter, 2002). Several studies have been conducted to investigate the efficacy of probiotics in treatment of IBD (Guandalini, 2002; Ma et al., 2004; Zhang et al., 2005). The tested strains against IBD include among others VSL#3 probiotic (Gionchetti et al., 2000), *Bifidobacterium longum* (Furrie et al., 2005) and *Lactobacillus rhamnosus GG* (Gupta et al., 2000). Combination of *Lactobacillus acidophilus* and *Bifidobacterium infantis* (Hoyos, 1999) and of *Bifidobacterium bifidus, Bifidobacterium infantis* and *Streptococcus thermophilus*

were shown to reduce incidences of ulcerative colitis (Bin- Nun et al., 2005). Several studies reported the success of *bifidobacteria* for the alleviation of IBS (Mahony et al., 2005; Brenner et al., 2009; Jankovic et al., 2010). Alfredo (2004) demonstrated the efficacy of Lactobacillus plantarum LP01 and *Bifidobaccterium* breve BR0 as short-term therapy for IBS. Although some of the results obtained were very encouraging, there is need for larger, randomized, double-blinded, placebo-controlled clinical trials to substantiate these claims.

Hereditary allergic conditions of increasing importance in developing countries such as eczema, asthma, atopic dermatitis and rhinitis can be treated with probiotics (Holgate, 1999; Kalliomaki et al., 2003; Salminen et al., 1998a). Tested probiotics with antiallergenic properties include *Bifidobacterium lactis Bb-12* (Isolauri et al., 2000) and Lactobacillus GG (Isolauri et al., 2000; Kalliomaki et al., 2001; Kalliomaki et al., 2003; Lee et al., 2008; Mirkin, 2002; Vanderhoof & Young, 2003). However, contradictory studies report on the poor efficiency of probiotics in allergy alleviation (Helin et al., 2002; Vliagoftis et al., 2008) and highlight the need for more convincing and conclusive research in allergy treatment.

Probiotics have the ability to lower levels of cholesterol in serum, contributing to the prevention of cardiovascular disease (Fooks et al., 1999; Proviva, 2002). This ability has been shown for *Lactobacillus johnsonii* and *L. reuterii* using animal models (Mombelli & Gismondo, 2000). They also reduce the risk of cancer (Sanders, 1999) due to their activity against certain tumors (Chen & Yao, 2002). Several studies indicated that probiotics in a diet reduces the risk of cancer (Sanders, 1999). Anticarcinogenic effects of *Bifidobacterium bifidum* and *Lactobacillus acidophilus* were shown using clinical trials in humans (Fooks, 1999).

Chapter-III



Materials and Methods

Chapter-III

Materials and Methods

3.1. Material

Table 3:1 The materials used in experiment

	Chemical	Company
1.	Yoghurt	Nana company

3.2. Instruments

Table 3:2 The Instruments used in experiment

	Instruments	Company
1.	Bio-system BTS 350	Rosha Company
2.	Mindray BS-240	Rosha Company
3.	A1cCheck Pro Glycohemoglubin Analyzer	Rosha Company
4.	Cobas e 411 analyzer	Rosha Company

3.3. Sample size

The study included 9 patients aged >25 years with T2DM who were overweight or obese. The patients were administered probiotic (Nana Ative) daily for 30 days, which consisted of probiotics microorganism strain.

Photo 3:1 Photo of Yoghurt

3.4. Nutritional assessment

3.5. Clinical assessments

Clinical assessment was evaluated according to physical examination such as Skin, Hair, Nail and Eye.

3.6. Anthropometric assessments

Participants were weighted without shoes and heavy clothing using digital scale, with a precision of 0.1 kg and height was measured without shoes to the nearest tenth of a centimeter using a portable stadiometer (Seca model 207 Germany); body mass index (BMI) was calculated by dividing weight (kg) by height square (m2)

3.6.1. Height:

In order to measure height subject was first asked to stand straight without shoes on horizontal platform with heels together and hanging the arms loose. Head was made at Frankfurt plane, buttocks and shoulder blades in contact with vertical surface of stadiometer. He was asked to take deep breath and stand tall to aid the straightening of the spine and shoulders relaxed. Movable headboard was lowered until it touches crown of head. Height measurement was taken at maximum inspiration, with examiner’ s eyes in level with headboard to avoid parallax error. Reading was taken to nearest millimetre. For reading falling between two values, lower reading was recorded (Gibson, 1993).

3.6.2. Weight:

Measurement was taken after bladder was emptied and minimal clothing. The balance was placed on hard, flat surface and the scale was made zero. Subject was asked to stand unassisted, in the centre of the platform and look straight ahead standing relaxed but still. Body weight was recorded to nearest 0.1 kg (Gibson, 1993).

3.6.3. **BMI:**

Body mass index is a simple calculation using a person height and person height and weight. The formula is a person weight in kilograms kg /m2 is a person weight in kilograms and m2 is their height in meters squared. The BMI is classified to:

- BMI, ≤18. 5 was considered as underweight
- BMI, 18.5 - 24.9 was considered as normal
- BMI, 25.0 - 29.9 was considered as overweight or pre obese
- BMI, ≥30 was considered as obese

3.6.4. Fat %:

The body fat can be estimated from body mass index (BMI), a person mass in kilograms divided by the square of the height in meters ; if weight is measure in pounds and height in inches, the result can be converted to by multiplying by 703

Child body fat percentage = 1.51×BMI - 0.70 × age – 3.6 × sex +1.4

Adult body fat percentage = 1.20×BMI - 0.23 × age – 10.8 × sex +5.4

Where sex is 0 for females and 1 for males

- Man 13 to 21 %body fat
- Woman 23 to 31 % body fat

3.7. Laboratory assessments

3.7.1. Sample collection

Fasting Blood samples (10 ml) were taken before and after the 6 weeks of intervention after an overnight 10e12 h fasting between 8 and 9 a.m. The serum samples were separated from whole blood by centrifugation at 3500 rpm for 10 min (Hettich D-78532; Tuttlingen, Germany) and were frozen at 70 \C, immediately until assay.

3.7.2. The producer

Fasting plasma glucose (FPG) levels were quantified via the glucose oxidase/peroxidase method with commercially available kits. Serum insulin levels were assessed using. HbA1C was measured by A1cCheck Pro Glycohemoglubin Analyzer.

Serum concentrations of TC, TG, LDL, VLDL and HDL were measured using the standard enzymatic methods with available Mindray BS-240 instrument. insulin resistance (HOMA-IR) was calculated using Cobas e 411 analyzer.

Photo 3:2 Photo of Mindray BS-240

Photo 3:3 Bio-system BTS 350

Photo 3:4 Photo of A1cCheck Pro Glycohemoglubin Analyzer

Photo 3:5 Cobas e 411 analyzer

3.8. Data Analysis and Statistical Methods

The data were enter in Windows Excel and then scrutinize in the same software. Then, the data were import to SPSS for analysis.

3.9. Ethical consideration

An ethical clearance was granted by patient and IMU, IBB, Yemen.

Chapter-IV

Result and Discussion

Chapter-IV

Results and Discussion

A total of 9 patients with type 2 diabetes were recruited in the study. We sought to assess the effects of Yoghurt on biochemical factors including insulin parameters and lipid profile among patients with type 2 diabetes.

4.1. Baseline characteristics of study participants.

Baseline characteristics of study participants were presented in Table (4.1). Nine persons were screened. The age of participate ranged from 25-77 Years while the gender of participants were 44.44% male and 55.55% female. The Diabetes duration (Year) were ranged from 1-5 Years while the Physical Activity (%) of participants were 88.88% Moderate Physical Activity and 11.11 % Low Physical Activity.

Table: 4.1 Baseline characteristics of study participants.

	Participates
Age	25-77
Sex	4 Male 5 Female
Diabetes duration (Year)	1-5 Years
Physical Activity (%)	
High	
Moderate	88.88%
Low	11.11 %

4.2. Clinical assessment of DM patient

Table (4:2) showed the clinical assessment of DM 2 patient before and after treatment of yoghurt. The result showed that the clinical assessment such as Skin, Hair, Nail, Eye were normal before and after treatment.

4.3. The anthropometric measurements of patients

The anthropometric measurements of patients after and before treatment with yoghurt were shoed in table (4:3) As shown in Table , no significant alterations were reported for BMI and weight parameters after the intervention period in probiotic.

4.3.1. Effects of yoghurt on the Weight of the DM2 patients

Effects of yoghurt on the weight of the DM2 patients were showed in table (4:3) Fig (4:1). The results showed that the weight was increasing during the study due to the adulteration of yoghurt by starch.

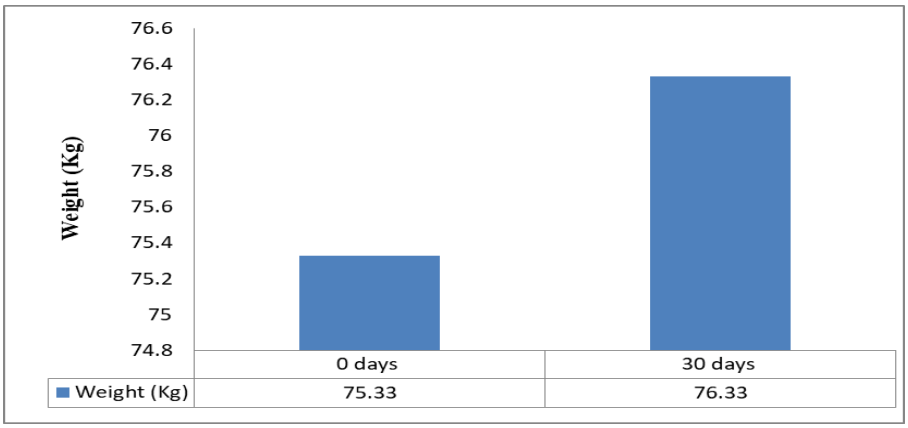


Fig. 4.1 Evaluation of weight (Kg) in DM patient treated with Yoghurt

4.3.2. Effects of yoghurt on the BMI of DM2 patients

Body mass index (BMI) – the weight in kilograms divided by the square of the height in meters (kg/m2) – is a commonly used parameter to classify obesity in adults. The World Health Organization (WHO) defines obesity when BMI is equal to or more than 30, and overweight when BMI is equal to or more than 25. The table (4:3) and Fig (4:2) showed the Effects of yoghurt on the BMI of DM2 patients. The

result showed that, there were significant increase in BMI during experiment due to the adulteration of yoghurt by starch.

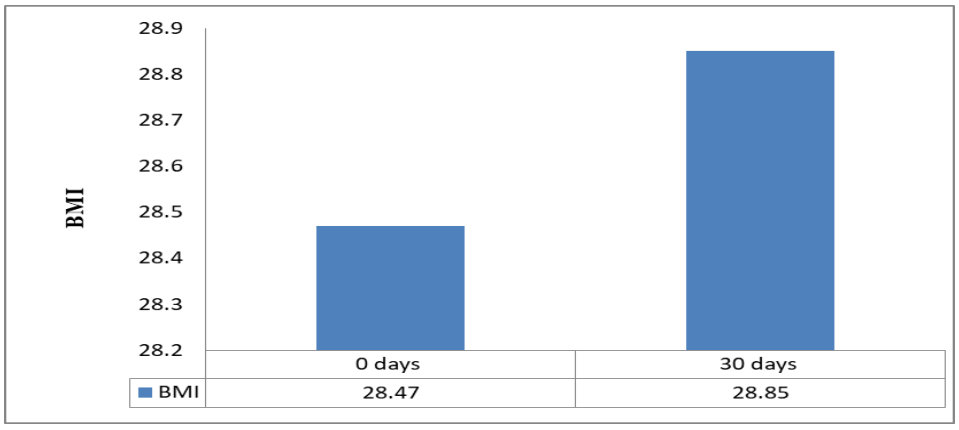


Fig. 4.2 Evaluation of BMI in DM patient treated with Yoghurt

4.3.3. Effects of yoghurt on the Body fat of the DM2 patients

Body mass index is a simple calculation using a person height and person height and weight. The formula is a person weight in kilograms kg /m2 is a person weight in kilograms and m2 is their height in meters squared, the body fat was calculated by using BMI. The table (4:3) and fig (4:3) showed Effects of yoghurt on the Body fat of the DM2 patients. The Body fat was increase during the study due to the adulteration of yoghurt by starch.

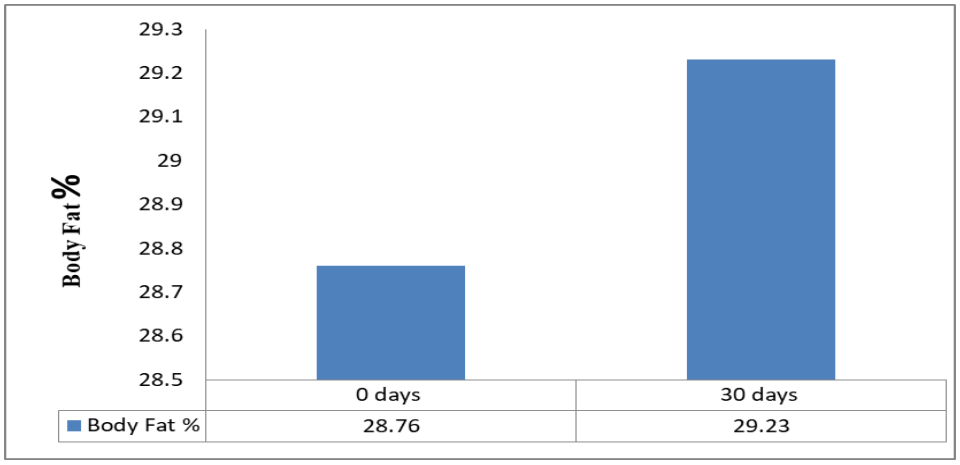


Fig. 4.3 Evaluation of Body Fat % in DM patient treated with Yoghurt

Table: 4.2 The anthropometric measurements of volunteers

	Test	V1		V2		V3		V4		V5		V6		V7		V8		V9	
		A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
1.	Skin	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
2.	Hair	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
3.	Nail	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
4.	Eye	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+

Table 4.3 The Anthropometric Measurements of Volunteers

	Test	V1		V2		V3		V4		V5		V6		V7		V8		V9	
		A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
1.	**Wt:(Kg)**	70	70	83	84	72	72	65	70	73	73	81	83	90	90	80	80	64	65
2.	Ht: (M)	1.78	1.78	1.60	1.60	1.70	1.70	1.50	1.50	1.53	1.53	1.70	1.70	1.55	1.55	168	168	1.60	1.60
3.	BMI	22.09	22.09	32.42	32.81	24.91	24.91	28.89	31.11	31.19	31.19	28.03	28.72	37.46	37.46	28.35	28.34	25	25.39
4.	B F %	20.43	20.43	35.59	36.29	31.39	31.39	36.17	38.83	44.21	44.21	30.083	30.91	52.20	52.20	26.32	26.32	35.18	35.65

Table 4.5 Laboratory assessment of DM patient

	Test	V1		V2		V3		V4		V5		V6		V7		V8		V9		References
		A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	
1.	**F.B.S**	118	180	117	157	190	270	97	121	95	167	220	197	170	150	105	134	98	145	**<100 mg/dl**
2.	**HOMA-IR**	1	3	0.5	1.9	2.8	4.1	1.2	2	2.3	4.3	5.1	4.9	3.1	4.6	2.2	3.1	1.4	3.2	**Less than 1.0**
3.	**HbA1C**	9.8	9.5	5.4	6.3	10.9	11.7	5.5	5.8	7.3	9	8.6	9	7.4	9.2	6	5.6	6.7	6.4	**4.0 -5.6%**
4.	**EAG**	215	209	118	136	239	257	121	128	160	198	189	198	162	202	132	123	147	138	**60 – 110 mg/dl**
5.	**TG**	230	145	220	120	165	145	290	120	205	120	245	120	165	135	220	242	155	130	**60 – 165**
6.	**TC**	175	170	180	170	180	205	170	140	171	150	170	140	195	140	190	210	170	190	**Up to 200**
7.	**HDL**	35	39	36	38	36	41	34	33	34	39	34	36	39	37	38	42	34	38	**55**
8.	**LDL**	115	107	120	112	111	105	98	88	96	96	87	88	123	85	118	120	115	126	**<100**
9.	**VLDL**	46	29	44	24	33	29	58	24	41	24	49	24	33	27	44	48	31	26	**Less Than 32**

4.4. The laboratory measurements of patients

The laboratory measurements of patients were presented in table (4:3)

4.4.1. Effects of yoghurt on the HOMA-IR of the DM2 patients

The effects of yoghurt on the HOMA-IR of the DM2 patients was presented in Fig (4.4). HOMA-IR was increase from (2.18 in the begging to 3,46 in the end of experiment) in Yoghurt after the 4 weeks of intervention period this is due to the adulteration of yoghurt by starch.

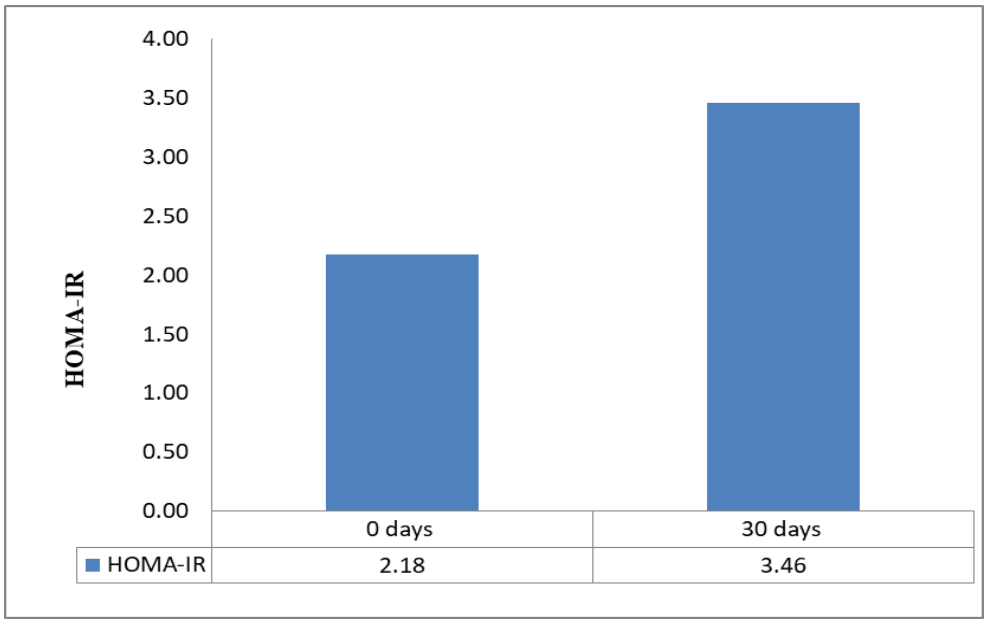


Fig. 4.4 Evaluation of HOMA-IR in DM patient treated with Yoghurt

4.4.2. Effects of yoghurt on the Estimated Average Glucose of the DM2 patients

The effects of yoghurt on the Estimated Average Glucose of the DM2 patients was presented in Fig (4:5). Estimated Average Glucose concentrations were increased from (164.78 in the begging to 176.56 mg/ dL in the end of experiment) in Yoghurt after the 4 weeks of intervention period.

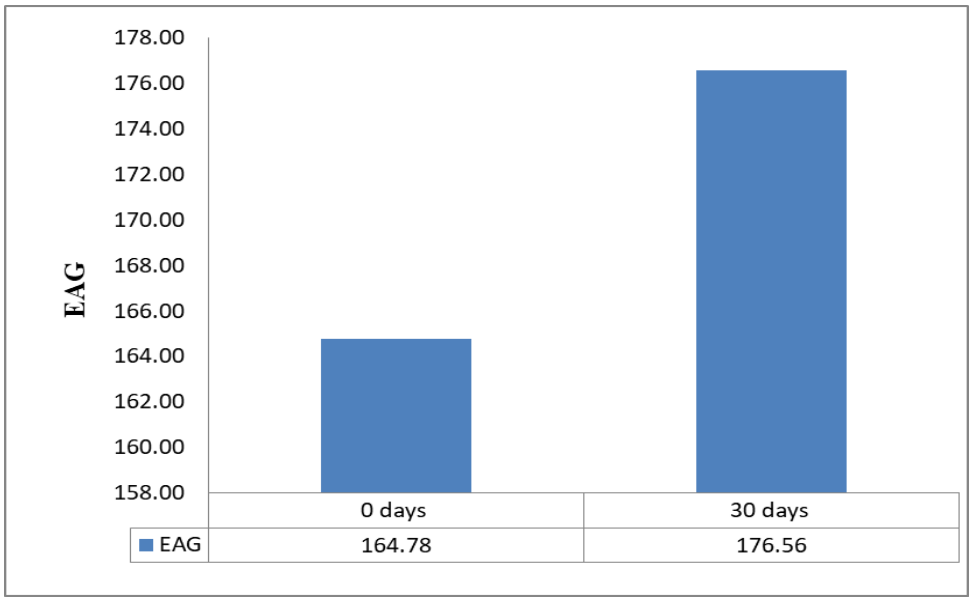


Fig. 4.5 Evaluation of Estimated Average Glucose in DM patient treated with Yoghurt

4.4.3. Effects of yoghurt on the Fast Blood Glucose (FBG) of the DM2 patients

Fast Blood Glucose (FBG) concentrations were increased from (134.44 in the begging to 169 mg/ dL in the end of experiment) in Yoghurt after the 4 weeks of intervention period. as presented in Fig (4:6).

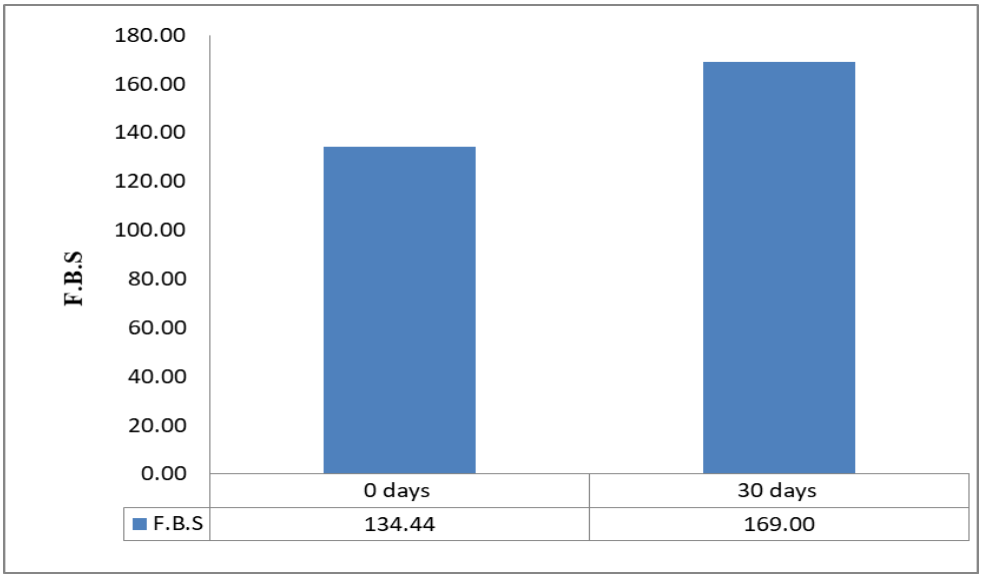


Fig. 4.6 Evaluation of Fast Blood Glucose (FBG) in DM patient treated with Yoghurt

4.4.4. Effects of yoghurt on the TG of the DM2 patients

According to Table 4:3 Fig (4:7), it reported that consumption of probiotic (Yoghurt) caused a powerful significant decrease in TG (210.56 in the begging to 141.86 mg/ dL in the end of experiment)

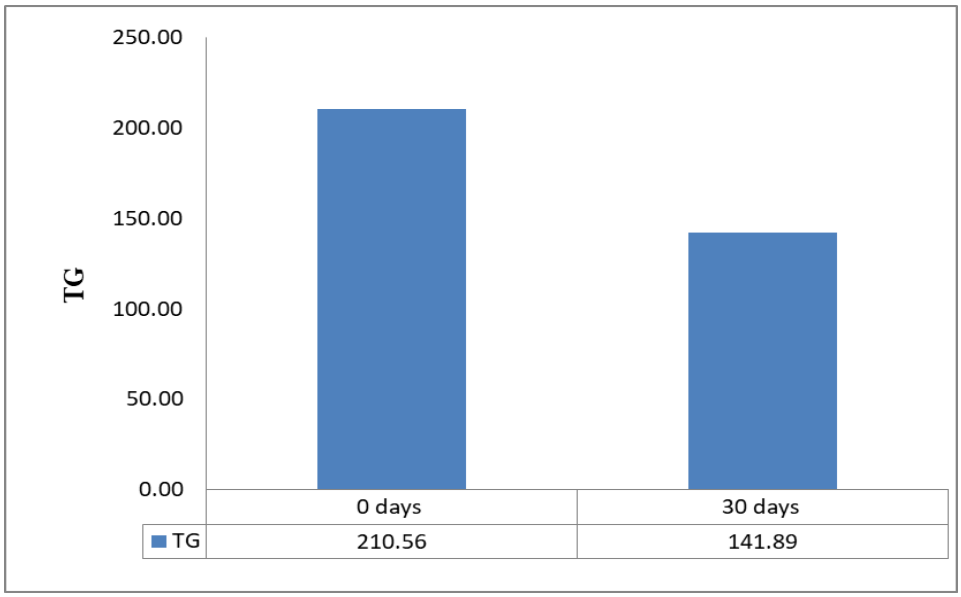


Fig. 4.7 Evaluation of Total Triglyceride (TG) in DM patient treated with Yoghurt

4.4.5. Effects of yoghurt on the TC of the DM2 patients

The effects of yoghurt on the TC of the DM2 patients was presented in Fig (4.8). TC concentrations (177.89 in the begging to 168.33 mg/ dL in the end of experiment) in Yoghurt after the 4 weeks of intervention period.

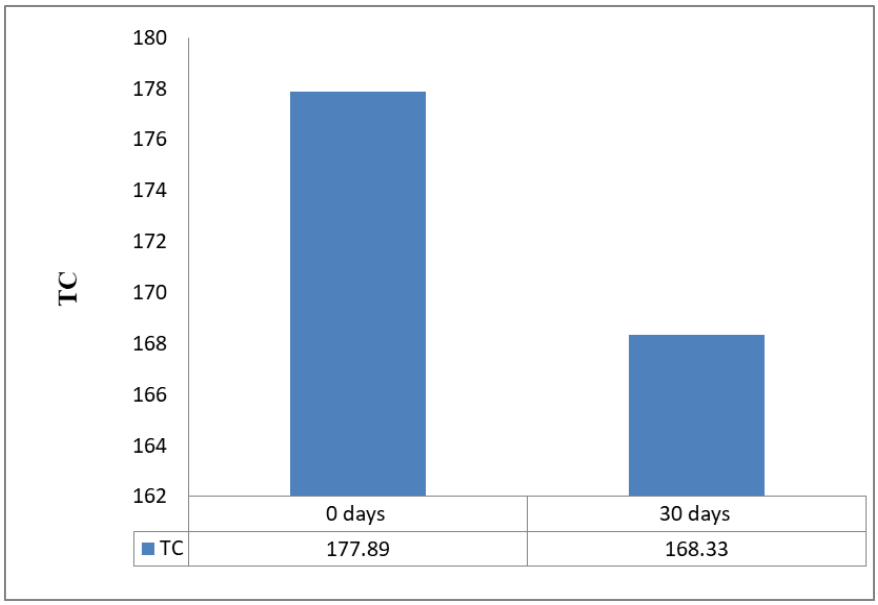


Fig. 4.8 Evaluation of Total Cholesterol (TC) in DM patient treated with Yoghurt

4.4.6. Effects of yoghurt on the HbA1C of the DM2 patients

There were increase in HbA1C concentrations (7.51 in the begging to 8.06 mg/ dL in the end of experiment) after the 4 weeks of intervention period, as showed in Fig (4.9).

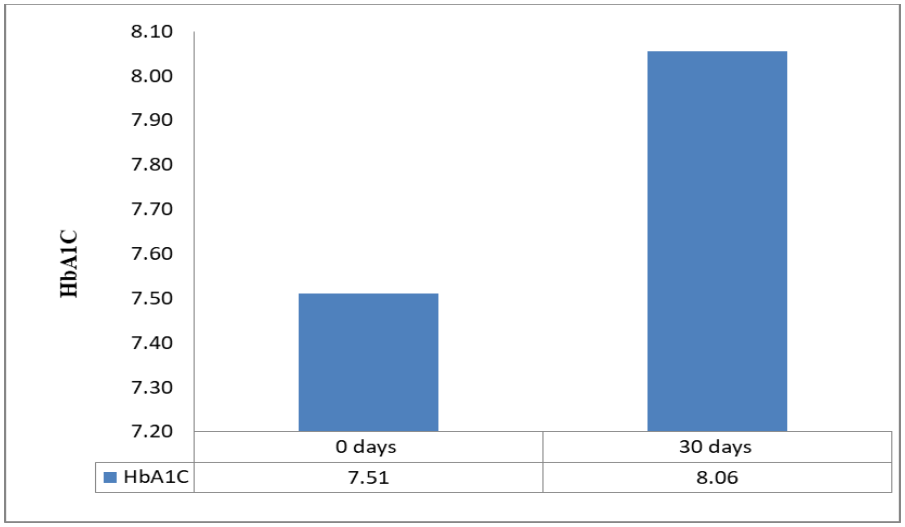


Fig. 4.9 Evaluation of HbA1C in DM patient treated with Yoghurt

4.4.7. Effects of yoghurt on the LDL and VLDL of the DM2 patients

The effects of yoghurt on the LDL and VLDL of the DM2 patients were presented in Fig (4.10,11)The VLDL and LDL were increase during the experiment.

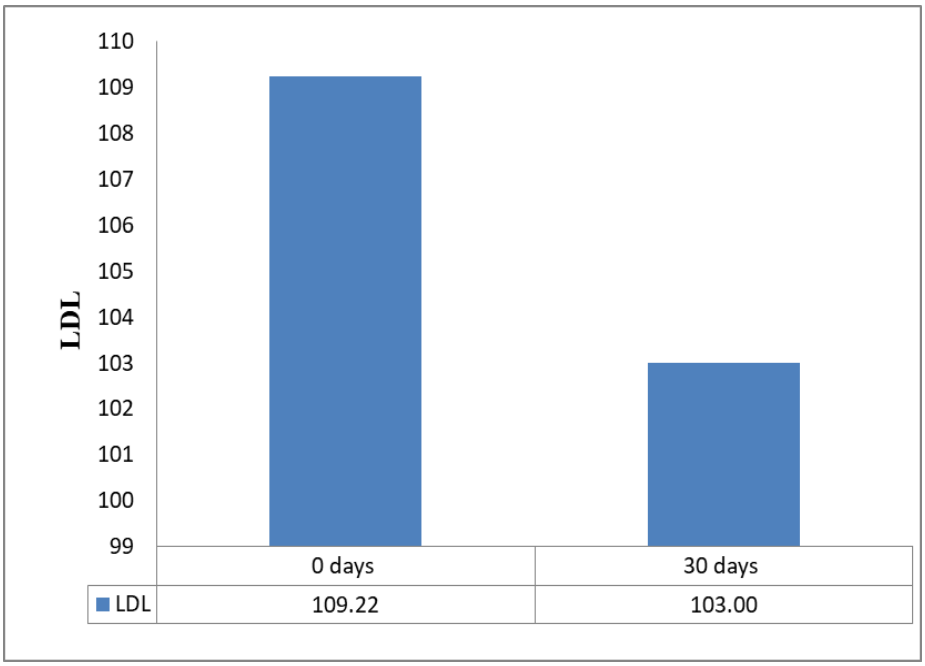


Fig. 4.10 Evaluation of LDL in DM patient treated with Yoghurt

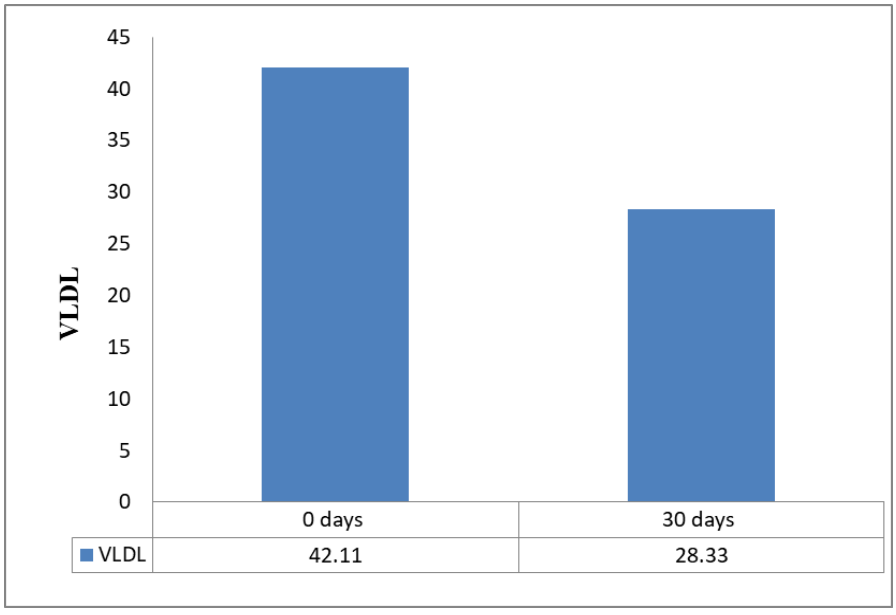


Fig. 4.11 Evaluation of VLDL in DM patient treated with Yoghurt

4.4.8. Effects of yoghurt on the HDL of the DM2 patients

The HDL was decrease after the 4 weeks of intervention period. as showed in Fig (4.12).

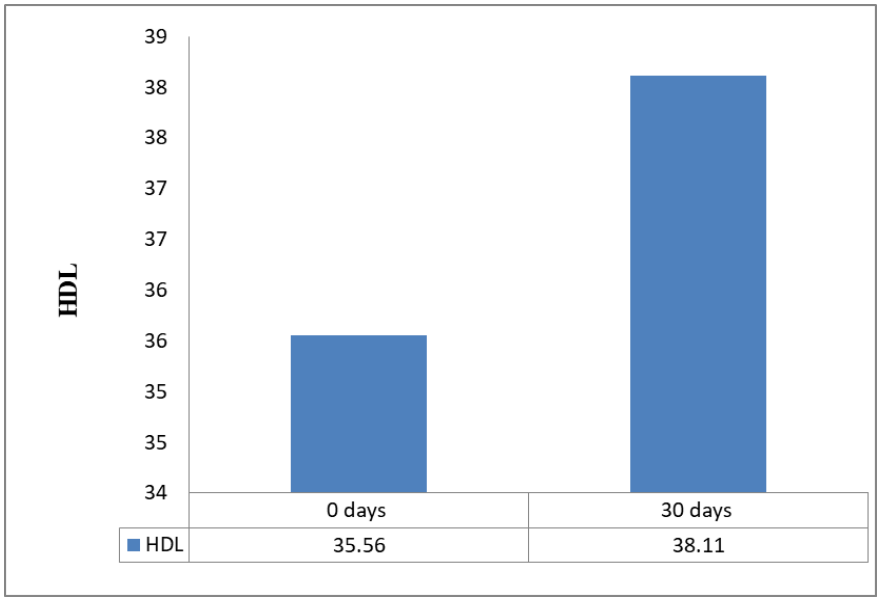


Fig. 4.12 Evaluation of HDL in DM patient treated with Yoghurt

Several studies showed benefits of probiotic use for improving blood glucose control in patients with GDM and T2DM (type 2 diabetes mellitus) Different result were found in study by Asemi et al.(2013) the effects of daily consumption of probiotic yoghurt were assessed on insulin resistance and serum insulin levels among Iranian healthy pregnant women; they reported that consumption of 200 g/day of probiotic yogurt enriched with Lactobacillus acidophilus LA5 and Bifidobacterium animalis BB, did not alter the FPG levels, however, it caused significant increase and decrease in fasting insulin levels and insulin resistance, respectively, which may prevent the development of insulin resistance and GDM (Asemi et al., 2013). One might say that as GDM has been proved to be caused by the hormonal changes and metabolic demands of pregnancy, along with genetic and environmental factors (Gilmartin et al., 2008), it would be different from other types of diabetes and the

related results of investigations. Our finding was differ from all study in term of Glucose and insulin resistance and this is due the adulteration of yoghurt by starch.

Asemi et al. (2013) evaluated the effects of daily consumption of probiotic yoghurt on insulin resistance and levels of insulin in the serum of pregnant women in the third trimester of gestation. The probiotic yoghurt used in this study was enriched with a probiotic culture of L. acidophilus LA5 and Bifidobacterium animalis BB12 with at least 107 Colony Forming Unities. Daily consumption of probiotic yoghurt for 9 weeks was effective in maintaining normal serum insulin levels in pregnant women and thus contributing to prevent the development of insulin resistance, which usually develops during the last trimester in pregnant women. The study demonstrated an improvement in glycemic control during the last trimester of pregnancy, extending in the postpartum period for 12 months.

In the study conducted by Badehnoosh et al. (2018) on 60 subjects with GDM they found that consumption of probiotic capsule containing Lactobacillus acidophilus, Lactobacillus casei and Bifidobacterium bifidum (2 × 109 CFU/g each) for 6 weeks had beneficial effects on glycemic response, and serum inflammatory and oxidative stress biomarkers.

Dolatkhah et al. (2015) conducted a study with women between 18 and 45 years of age with GDM between 24 and 28 weeks of pregnancy. The study was based on the daily consumption of probiotic capsules containing four bacterial strains (4 × 109 CFU) in lyophilized culture, or placebo. The probiotic supplement appeared to improve glucose metabolism and weight gain among pregnant women with GDM.

Karamali et al. (2016) analyzed the effects of probiotic supplementation on glycemic control and the lipid profiles over a period of 6 weeks. This study included 60 pregnant women with GDM, from 24 to 28 weeks of pregnancy. The probiotic group took a daily capsule containing 109 CFU/g L. acidophilus, L. casei, and Bifidobacterium bifidum. After 6 weeks of treatment with probiotics, glycaemia, triglycerides, and VLDL cholesterol concentration decreased compared with the

placebo group. In another 12-week study in pregnant women, probiotic supplementation containing the same strains, concluded that the probiotics had a positive effect on the metabolism of insulin, triglycerides, biomarkers of inflammation, and oxidative stress.

Recently, Jafarnejad et al. (2016) analyzed the effects of a mixture of probiotics (VSL#3) on the glycemic state and inflammatory markers in 72 GDM patients through a double blind and randomized controlled clinical trial. The study groups consumed either a probiotic or placebo capsules twice a day for 8 weeks. The study concluded that for women with GDM, a probiotic supplementation can modulate some of the inflammatory markers and improve glycemic control.

In the study of Lindsay et al. (2014), 149 pregnant women older than 18 years, before 34 weeks of pregnancy, were divided between probiotic and placebo groups and the aim of their study was to investigate the effects of probiotic capsule contained 100 mg Lactobacillus salivarius on metabolic parameters and pregnancy outcomes in pregnant women with GDM. No significant differences were observed between the groups concerning the postintervention fasting blood glucose and birth weight.

In addition, Lindsay et al. (2015) investigated the effects of probiotic supplementation on fasting maternal glycaemia in obese pregnant women with a Body Mass Index (BMI) of > 30 kg/m2 between 24 and 28 weeks of pregnancy. A probiotic or placebo capsule was ingested daily, each probiotic capsule containing 100 mg of lyophilised *Lactobacillus salivarius*. The study showed no effect of probiotic intervention during 4 weeks on glycaemia. Their findings were different maybe because of the use of other probiotic strain and/or different intervention duration.

Chapter-VI

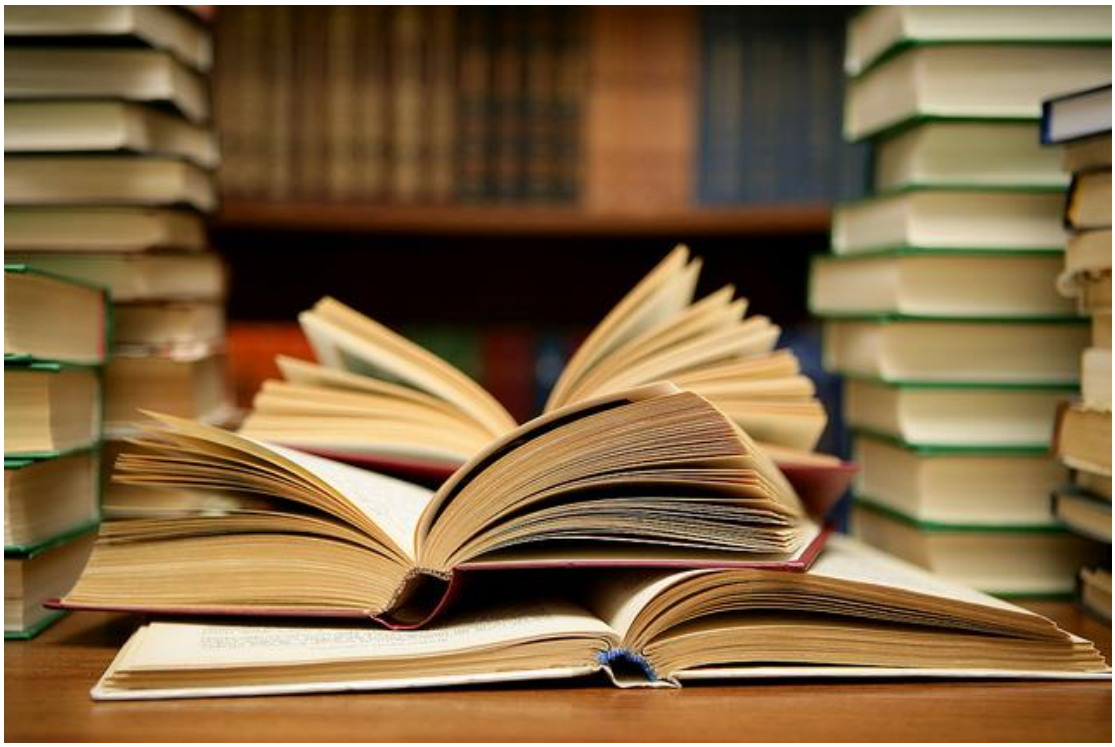
Summary & Conclusion

Chapter-V

Summary and Conclusion

Our study revealed that consumption of (Yoghurt) for 4 weeks, which consisted of probiotic bacteria strains. The effect of probiotic bacteria on patient of DM2 as the following

- There were nine participates with DM2 in this study
- The age of participates were ranged from 25-77 and the gender were 4 Male 5 Female, also the Diabetes duration (Year) were ranged from 1-5 Years.
- The BMI of participates was increased
- The body fat of participates was increased
- The consumption of probiotic (Yoghurt) caused a powerful significant decrease in TG (210.56 in the begging to 141.86 mg/ dL in the end of experiment) and TC concentrations (177.89 in the begging to 168.33 mg/ dL After 4 week) in Yoghurt after the 4 weeks of intervention period.
- Fast Blood Glucose (FBG) in DM patient treated with Yoghurt were increased
- HOMA-IR in DM patient treated with Yoghurt were increased
- Increase in HbA1C concentrations (7.51 in the begging to 8.06 mg/ dL in the end of experiment) after the 4 weeks of intervention period.
- The VLDL and LDL were Decrease during the experiment while HDL were increased after the 4 weeks of intervention period



References

References

Adams, M.R. & Moss, M.O., (2000). Food Microbiology. Second Edition, The Royal Society of Biochemistry, Cambridge, UK, pp. 318-323.

Ahmed, A. M. (2002). History of diabetes mellitus. Saudi medical journal, 23(4), 373-378. International Diabetes Federation. IDF Diabetes Atlas, Ninth Edition. 2019. https://www.diabetesatlas.org/en/. Accessed 01 Mar 2021.

Akin, Z., & Ozcan, T. (2017). Functional properties of fermented milk produced with plant proteins. LWT, 86, 25-30.

Alfredo S. 2004. Probiotics in the treatment of irritable bowel syndrome. Journal of Clinical Gastroenterology 38, S104-S106.

American Diabetes Association ADA, 2010. Diagnosis and classifcation of diabetes mellitus. Diabetes Care.;33(Suppl 1):S62–9. https://doi.org/10. 2337/dc10-S062.

Asgari, S., Pourjavadi, A., Licht, T. R., Boisen, A., & Ajalloueian, F. (2020). Polymeric carriers for enhanced delivery of probiotics. Advanced Drug Delivery Reviews.

BergogneBérézin, E., 2000. Treatment and prevention of antibiotic associated diarrhea. International Journal of Antimicrobial Agents 16, 521-526.

Bin-Nun A., Bromiker R., Wilschanski M., Kaplan M., Rudensky B., Caplan M., 2005. Oral probiotics prevent necrotising enterocolitis in very low birth weight neonates. Journal of Paediatrics 147, 192-196.

BNF. (2015). "Healthy Eating." Retrieved March 20, 2015, from http://www.nutrition.org.uk/healthyliving/healthyeating.html.

Bommer C, Sagalova V, Heesemann E, Manne-Goehler J, Atun R, Bärnighausen T, et al. Global economic burden of diabetes in adults: projections from 2015 to 2030. Diabetes Care. 2018;41(5):963–70.

Brenner D.M., Moeller M.J., Chey W.D., Schoenfeld S. 2009. The utility of probiotics in the treatment of irritable bowel syndrome: A systemic review. American journal of Gastroenterology 104, 1033-1049.

Broekaert, I. J., & Walker, W. A. (2006). Probiotics and chronic disease. Journal of clinical gastroenterology, 40(3), 270-274.

Buller H.A. & Grand R.J. 1990. Lactose intolerance. Annual Reviews in Medicine 41, 141-148. Champagne C.P and Raymond Y. 2008. Viability of Lactobacillus Rhamnosus R0011 in an apple-based fruit juice under simulated storage at the consumer level. Journal of Food Science 73, M221-M226.

Buysschaert, M., Dramais, A. S., Wallemacq, P. E., & Hermans, M. P. (2000). Hyperhomocysteinemia in type 2 diabetes: relationship to macroangiopathy, nephropathy, and insulin resistance. Diabetes care, 23(12), 1816-1822.

Buysschaert, M., Dramais, A. S., Wallemacq, P. E., & Hermans, M. P. (2000). Hyperhomocysteinemia in type 2 diabetes: relationship to macroangiopathy, nephropathy, and insulin resistance. Diabetes care, 23(12), 1816-1822.

Champagne C.P and Raymond Y. 2008. Viability of Lactobacillus Rhamnosus R0011 in an apple-based fruit juice under simulated storage at the consumer level. Journal of Food Science 73, M221-M226.

Chen, B.H. & Yao, Y.Q., 2002. Beneficial microbe composition, new protective material for the microbes, method to prepare the same and uses thereof. US Patent 6368591.

Chilton, S. N., J. P. Burton, et al. (2015). "Inclusion of fermented foods in food guides around the world." Nutrients 7(1): 390-404.

Codex-Alimentarius (2003). CODEX standard for fermented milks. Codex Stan 243-2003

Collins J.K, Thornton G and Sullivan G.O. 1998. Selection of probiotic strains for human applications. International Dairy Journal 8, 487-490.

Collins M.D. & Gibson G.R. 1999. Probiotics, prebiotics, and synbiotics: approaches for modulating the microbial ecology of the gut. American Journal of Clinical Nutrition 69, 1052S-1057S.

Cremonini, F., Di Caro, S., Santarelli, L., Gabrielli, M., Candelli, M., Nista, E.C., Lupascu, A., Gasbarrini, G. & Gasbarrini, A., 2002. Probiotics in antibiotic-associated diarrhea. Digestive and Liver Disease 21, S78-S80.

Dall, T., Mann, S. E., Zhang, Y., Martin, J., & Chen, Y. (2008). Economic costs of diabetes in the US in 2007. Diabetes Care, 31(3), 596.

Daneman, D. (2006). Type 1 diabetes. The Lancet, 367(9513), 847-858.

Depaula A.L., macedo A.L., rassi N., vencio S., machado C.A., Mota B.R., Silva L.Q., Halpern A., Schraibman V (2008).: Laparoscopic treatment of metabolic syndrome in patients with type 2 diabetes mellitus. SurgEndosc 22(12):2670-2678.

Diabetes Prevention Programme Research Group.: Reduction in the incidence of type2 diabetes with life style intervensions or metformin NEJM 2002;346:393-403.

Dinakar P. and Mistry V.V. 1994. Growth and viability of Bifidobacterium bifidum in cheddar cheese. Journal of Dairy Science 77, 2854-2864.

Fabersani, E., Grande, M. V., Aráoz, M. V. C., Zannier, M. L., Sánchez, S. S., Grau, A., & Honoré, S. M. (2018). Metabolic effects of goat milk yogurt supplemented with yacon flour in rats on a high-fat diet. Journal of Functional Foods, 49, 447-457.

Fazilah, N. F., Ariff, A. B., Khayat, M. E., Rios-Solis, L., & Halim, M. (2018). Influence of probiotics, prebiotics, synbiotics, and bioactive phytochemicals on the formulation of functional yogurt. Journal of Functional Foods, 48, 387-399

Fernandes C.F., Shahani K.M., Amer M.A. 1987. Therapeutic role of dietary lactobacilli and lactobacillic fermented dairy products. FEMS Microbiology Reviews 46, 343-356

Fooks, L.J., Fuller, R. & Gibson G.R., 1999. Prebiotics, probiotics and human gut microbiology. International Dairy Journal 9, 53-61.

Fuller, R., 2003. Probiotics - what they are and what they do. http://www.positivehealth.com/permit/Articles/Nutrition/fuller32.htm.

Furrie E., Macfarlane S., Kennedy A., Cummings J.H., Walsh S.V., O' Niell D.A., 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, 242-249.

Gale, E. A. (2001). The discovery of type 1 diabetes. Diabetes, 50(2), 217-226.

Gibson, G.R & Fuller, R 2000, 'Aspects of in vitro and in vivo research approaches directed towards identifying probiotics and prebiotics for human use', Journal of Nutrition, 130, 391-395.

Gionchetti P., Rizzello F., Venturi A., Brigidi P., Matteuzzi D., Bazzocchi G., Poggioli G.,

Gkaliagkousi, E., Shah, A., & Ferro, A. (2007). Pharmacological and non-pharmacological treatment of endothelial dysfunction: relevance to diabetes. The British Journal of Diabetes & Vascular Disease, 7(1), 5-10.

Gkaliagkousi, E., Shah, A., & Ferro, A. (2007). Pharmacological and non-pharmacological treatment of endothelial dysfunction: relevance to diabetes. The British Journal of Diabetes & Vascular Disease, 7(1), 5-10.

Goldin, B.R., 1998. Health benefits of probiotics. British Journal of Nutrition 20, S202-S207.

Goodpaster, B. H., DeLany, J. P., Otto, A. D., Kuller, L., Vockley, J., South-Paul, J. E., ... & Jakicic, J. M. (2010). Effects of diet and physical activity interventions on weight loss and cardiometabolic risk factors in severely obese adults: a randomized trial. Jama, 304(16), 1795-1802.

Gorbach S.L. 1997. Health benefits of probiotics. IFT Annual Meeting, Orlando, FL, Abstract 73-1.

Gorbach S.L. 1997. Health benefits of probiotics. IFT Annual Meeting, Orlando, FL, Abstract 73-1.

Gross, J. L., De Azevedo, M. J., Silveiro, S. P., Canani, L. H., Caramori, M. L., & Zelmanovitz, T. (2005). Diabetic nephropathy: diagnosis, prevention, and treatment. Diabetes care, 28(1), 164-176.

Gu, K., Cowie, C. C., & Harris, M. I. (1998). Mortality in adults with and without diabetes in a national cohort of the US population, 1971−1993. Diabetes care, 21(7), 1138-1145.

Guandalini S., Pensabene L., Zikri M.A., Dias J.A., Casali L.G., Hoekstra H 2000. Lactobacillus GG administered in oral rehydration solution to children with acute diarrhea: A multicenter European trial. Journal of Paediatric Gastroenterology and Nutrition 30, 214-216.

Guarner, F., G. Perdigon, et al. (2005). "Should yoghurt cultures be considered probiotic?" Br. J. Nutr. 93(6): 783-786.

Gupta P., Andrew H., Kirschner B.S., Guandalini S. 2000. Is Lactobacillus GG helpful in children with Crohn's disease? Results of a preliminary, open-label study. Journal of Paediatric Gastroenterology and Nutrition 31, 453-457.

Hanauer S.B. 2006. Inflammatory bowel disease: Epidemiology, pathogenesis, and therapeutic opportunities. Inflammatory Bowel Diseases 12, S3-S9.

HARRIS (1991) Epidemiologic correlated of NIDDM in Hispanics, whites and blacks in the US population. Diabetes Care ;14(suppl3):639-648.

Harris, M. I. (1991). Epidemiological correlates of NIDDM in Hispanics, whites, and blacks in the US population. Diabetes care, 14(7), 639-648.

Haus, J. M., Solomon, T. P., Marchetti, C. M., Edmison, J. M., Gonzalez, F., & Kirwan, J. P. (2010). Free fatty acid-induced hepatic insulin resistance is attenuated following lifestyle intervention in obese individuals with impaired glucose tolerance. The Journal of Clinical Endocrinology & Metabolism, 95(1), 323-327.

Havenaar R., & Huis int' Veld J.H.J. 1992. Probiotics: a general view. The Lactic Acid Bacteria in Health and Disease (Wood BJB, ed), pp. 209−224. Chapman & Hall, New York

Havenaar R., & Huis int' Veld J.H.J. 1992. Probiotics: a general view. The Lactic Acid Bacteria in Health and Disease (Wood BJB, ed), pp. 209−224. Chapman & Hall, New York

Health-Canada. (2011). "Eating Well with Canada's Food Guide." Retrieved February 26, 2018, from http://www.hc-sc.gc.ca/fn-an/food-guide-aliment/index-eng.php

Heidemann, D. L., Joseph, N. A., Kuchipudi, A., Perkins, D. W., & Drake, S. (2016). Racial and economic disparities in diabetes in a large primary care patient population. Ethnicity & disease, 26(1), 85.

Helin T., Haahtela S. & Haahtela T. 2002. No effect of oral treatment with an intestinal bacterial strain, Lactobacillus rhamnosus (ATCC 53103), on birch-pollen allergy: a placebo-controlled double-blind study. Allergy 57, 243-246

Holgate S.T., 1999. The epidermic of allergy and asthma. Nature 402, B2-B4.

Hoyos A.B. 1999. Reduced incidence of necrotising enterocolitis associated with enteral administration of Lactobacillus acidophilus and Bifidobacterium infantis to neonates in an intensive care unit. International Journal of Infectious Diseases 3, 197-202.

Isolauri, E., Arvola, T., Sutas, Y., Moilanen, E. & Salminen, S., 2000. Probiotics in the management of atopic eczema. Clinical and Experimental Allergy 30, 1604-1610.

Jankovic I., Sybesma W., Phothirath P., Ananta E., Mercenier A. 2010. Application of probiotics in food products-challenges and new approaches. Current Opinion in Biotechnology 21, 175-181Johansen H.N., Glitso V., & Knudsen K.E.B. 1996. Influence of extraction solvent and temperature on the quantitative determination of oligosaccharides from plant materials by high-performance liquid chromatography. Journal of Agricultural and Food Chemistry 44, 1470-1474

Kalliomaki, M., Salminen, S., Arvilomni, H., Kero, P., Koskinen, P. & Isolauri, E., 2001. Probiotics in primary prevention of atopic disease: a randomised placebocontrolled trial. Lancet 357, 1076-1079.

Kolida, S, Saulnier, D.M & Gibson, G.R 2006, 'Gastrointestinal Microflora: Probiotics', Advances in Applied Microbiology 59, 187-219.

Kotowska, M., Albrecht, P. & Szajewska, H., 2005. Saccharomyces boulardii in the prevention of antibiotic-associated diarrhea in children: a randomized double-blind placebocontrolled trial. Alimentary Pharmacology and Therapeutics 21, 583-590.

Lacroix C. & Yildirim S. 2007. Fermentation technologies for the production of probiotics with high viability and functionality. Current Opinion in Biotechnology 18, 176-183.

Lederberg J, McCray A. (2001) Ome sweet omics—a genealogical treasury of words. Scientist. 2001;15(7):8.

Lee Y.K and Salminen S. 1995. The coming of age of probiotics. Trends in Food science & Technology 6, 241-245.

Ma D., Forsythe P., Bienenstock J. 2004. Live Lactobacillus reuteri is essential for the inhibitory effect on tumour necrosis alpha-induced interleukin-8 expression. Infection and Immunity 72, 5308-5314.

Mackay, A.D., Taylor, M.D., Kibbler, C.C & Hamilton-Miller, J.M 1999, ' Lactobacillus endocarditis caused by a probiotic organism', Clinical Microbial Infections, vol. 5, pp. 290-292.

Madden J.A.J and Hunter O. 2002. A review of the role of gut microflora in irritable bowel syndrome and the effects of probiotics. British Journal of Nutrition 88, S67-S72.

Marco, M. L., D. Heeney, et al. (2017). "Health benefits of fermented foods: Microbiota and beyond." Curr. Opin. Biotechnol. 44: 94-102

Markowiak, P. and K. Slizewska (2017). "Effects of probiotics, prebiotics, and synbiotics on human health." Nutrients 9(9): 1021.

Marteau, P.R., de Vrese, M., Cellier, C.J. & Schreimeir, J., 2001. Protection from gastrointestinal diseases with the use of probiotics1-3, American Journal of Clinical Nutrition 73, 430S-436S.

McDonough F., Wells P., Wong N., Hitchins A., Bodewell C. 1983. Role of vitamins and minerals in growth stimulation of rats fed with yoghurt. Federation Proceedings 42, 556-558.

McNaught, C.E. & MacFie, J., 2001. Probiotics in clinical practice: a critical review of evidence. Nutrition Research 21, 343-353.

Merz, C. N. B., Buse, J. B., Tuncer, D., & Twillman, G. B. (2002). Physician attitudes and practices and patient awareness of the cardiovascular complications of diabetes. Journal of the American College of Cardiology, 40(10), 1877-1881.

Miglioli M., Campieri M. 2000. Oral bacteriotherapy as maintenance treatment in patients with chronic pouchitis: A double-blind, placebo-controlled trial. Gastroenterology 119, 305-309.

Mirkin, M.D., 2002. Atopic dermatitis eczema: http://www.drmirkin.com/morehealth/G108.htm.

Mombelli, B. & Gismondo, M.R., 2000. The use of probiotics in medical practice. International Journal of Antimicrobial Agents 16, 531-536.

Mombelli, B. & Gismondo, M.R., 2000. The use of probiotics in medical practice. International Journal of Antimicrobial Agents 16, 531-536.

NATIONAL DIABETES FACT SHEET (2004) general information and national estimates on diabetes in the United States, 2003, Centers for Disease Control and Prevention, Ed. Atlanta, GA, U.S. Department of Health and Human Services, Centers for Disease Control and Prevention

O'Mahony L., McCarthy J., Kelly P., Hurley G., Luo F., Chen K., O'Sullivan G.C., Kiely B., Collins J.K., Shanahan F., Quigley E.M. 2005. Lactobacillus and bifidobacterium in irritable bowel syndrome: symptom responses and relationship to cytokine profiles. Gastroenterology 128, 541-551.

Ouwenhand, A.C., Langstrom, H., Suomalainen, T. & Salminen, S. 2002. Effects of probiotics on constipation, fecal azoreductase activity and fecal mucin content in the elderly. Annals of Nutrition and Metabolism 46, 159-162.

Özer B., Kirmaci H.A., Şenel E., Atamer M., Hayaloğlu A. 2009. Improving the viability of Bifidobacterium bifidus BB-12 and Lactobacillus acidophilus LA-5 in white-brined cheese by microencapsulation. International Dairy Journal 19, 22-29.

Parvarei, M. M., Fazeli, M. R., Mortazavian, A. M., Nezhad, S. S., Mortazavi, S. A., Golabchifar, A. A., & Khorshidian, N. (2021). Comparative effects of probiotic and paraprobiotic addition on microbiological, biochemical, and physical properties of yogurt. Food Research International, 140, 110030.

Parvez S., Malik K.A., Kang S.A and Kim H.Y. 2006. Probiotics and their fermented food products are beneficial for health. Journal of Applied Microbiology 100, 1171-1185.

Pasinetti, G. M., Wang, J., Porter, S., & Ho, L. (2011). Caloric intake, dietary lifestyles, macronutrient composition, and Alzheimer's disease dementia. International journal of Alzheimer's disease, 2011.

Patlak, M. (2002). New weapons to combat an ancient disease: treating diabetes. The FASEB Journal, 16(14), 1853e-1853e.

Piero, M. N., Nzaro, G. M., & Njagi, J. M. (2015). Diabetes mellitus-a devastating metabolic disorder. Asian journal of biomedical and pharmaceutical sciences, 5(40),1.

Proviva, 2002. Health professionals. Documented beneficial effects. www.proviva.co.uk/hp_doc_ben.htm.

Reid G., Jass J., Sebulsky M.T., McCormick J.K. 2003. Potential uses of probiotics in clinical practice. Clinical Microbiology Reviews 16, 658-672.

Rozada-Sanchez R., Sattur A.P., Thomas K., Pandiella S.S. 2007. Evaluation of Bifidobacterium spp. for the production of a potentially probiotic malt-based beverage. Process Biochemistry 43, 848-854.

Saarela, M., Mogensen, G., Fondén, R., Mättö, J. & Mattila-Sandholm, T., 2000. Probiotic bacteria: safety, functional and technological properties. Journal of Biotechnology 84, 197-215.

Salminen, S, Ouwehand, A, Benno, Y & Lee, Y.K 1999, 'Probiotics: how should they be defined?', Trends in Food Science & Technology 10, 107-110

Sanders, M.E., 1999. Probiotics. Food Technology 53, 67-77.

Sazawal S., Hiremath G., Dhinga U., Malik P., Deb S., & Black R.E. 2006. Efficacy of probiotics in prevention of acute diarrhea: A meta-analysis of masked, randomised, placebo-controlled trials. The Lancet Infectious Diseases 6, 374-382.

Schrezenmeir, J. & de Vrese, M., 2001. Probiotics, prebiotics and synbiotics:Approaching a definition. American Journal of Clinical Nutrition 73, 361S-364S

Scrimshaw T.M., & Murray E.B. 1988. The acceptability of milk and milk products in populations with a high prevalence of lactose intolerance. American Journal of Clinical Nutrition 48, 1079S-1159S.

Shah N.P. 1993. Effectiveness of dairy products in alleviation of lactose intolerance. Food Australia 45, 268-271.

Shiel B., McCarthy J., O' Mahony L., Bennett M.W., Ryan P., Fitzgibbon J.J., Kiely B., Collins J.K., Shanahan F. 2004. Is the mucosal route of administration essential for probiotic function? Subcutaneous administration is associated with attenuation of murine colitis and arthritis. Gut 53, 694-700.

Sullivan A. & Nord C.E. 2005. Probiotics and gastrointestinal diseases. Journal of Internal Medicine 257, 78-92.

Tunick, M. H. and D. L. Van Hekken (2015). "Dairy products and health: Recent insights." J. Agric. Food Chem. 63(43): 9381-9388.

Tuomilehto, J., Lindström, J., Eriksson, J. G., Valle, T. T., Hämäläinen, H., Ilanne-Parikka, P., ... & Uusitupa, M. (2001). Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. New England Journal of Medicine, 344(18), 1343-1350.

USDA (2010). Dietary Guidelines for Americans Washington DC, USA, U.S. Government Printing Office.

Vanderhoof J.A. and Young R.J. 2003. Role of probiotics in the management of patients with food allergy. Annals of Allergy, Asthma and Immunology 90, 99-103

Vasiljevic T. and Shah N.P. 2008. Probiotics-from Metchnikoff to bioactives. International Dairy Journal 18, 714-728.

Vesa, T.H., Marteau, P. & Korpela, R., 2000. Lactose intolerance. Journal of the American College of Nutrition 19, 165S-175S.

Vliagoftis H., Kouranos V.D., Betsi G.I., Falagas M.E. 2008. Probiotics for the treatment of allergic rhinitis and asthma: systemic review of randomized controlled trials. Annals of Allergy and Asthma Immunology 101, 570-579.

White Jr, J. R. (2014). A brief history of the development of diabetes medications. Diabetes spectrum: a publication of the American Diabetes Association, 27(2), 82.

World Health Organisation. Global Report on Diabetes. 2016. https:// www.who.int/publications/i/item/9789241565257.

World Health Organization (1999). Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. Report of a WHO Consultation. Geneva: WHO.

Wu, H., Walker, J., Damhuis, R. A., Brewster, D. H., Wild, S. H., & Scottish Diabetes Research Network Epidemiology Group. (2016). Metformin and survival of people with type 2 diabetes and pleural mesothelioma: A population-based retrospective cohort study. Lung Cancer, 99, 194-199.

Yerlikaya, O., Saygili, D., & Akpinar, A. (2021). An application of selected enterococci using Bifidobacterium animalis subsp. lactis BB-12 in set-style probiotic yogurt-like products. Food Bioscience, 41, 101096.

Yilmaz-Ersan, L., Ozcan, T., & Akpinar-Bayizit, A. (2020). Assessment of socio-demographic factors, health status, and knowledge on probiotic dairy products. Food Science and Human Wellness, 9(3), 272-279.

Zendeboodi, F., Khorshidian, N., Mortazavian, A. M., & da Cruz, A. G. (2020). Probiotic: conceptualization from a new approach. Current Opinion in Food Science, 32, 103-123.

Zhang L., Li N., Caicedo R., Neu J. 2005. Alive and dead Lactobacillus rhamnosus GG decrease tumour necrosis factor-alpha-induced interleukin-8 production in Caco-2 cells. Journal of Nutrition 135, 1752-1756.