

A review on diagnosis and treatment of type 2 diabetes

Submitted To:

Department of Pharmacy

Faculty of Allied Health Science

Daffodil International University

Submitted By:

Hamidul Islam

Id:191-29-272

Batch:21 DSC -C

Department of Pharmacy

Faculty of Allied Health Science

Daffodil International University

APPROVAL

This project, A review on diagnosis and treatment of type 2 diabetes submitted to the

Department of Pharmacy, Faculty of Allied Health Science, Daffodil International University

has been accepted as satisfactory for the partial fulfillment of the requirements for the degree

of Bachelor of Pharmacy and approved as to its style and contents.

BOARD OF EXAMINER

Professor Dr. Muniruddin Ahmed	
Professor and Head	

-

Department of Pharmacy

Faculty of Allied Health Science

Daffodil International University

Internal Examiner 1
Internal Examiner 2

Internal Examiner 3

Declaration

I hereby declare that this project report, A review on diagnosis andtreatment of type-2

diabetes is done by me under the supervision of Dr.Md. Sarowar Hossain ,Assistant

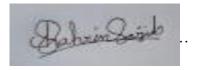
Professor Department of pharmacy, Faculty of Allied Health Science, Daffodil International

University. I am declaring that this project is my original work. I also declare that neither this

project nor any thereof has been submitted elsewhere for the award of Bachelor or any

degree.

Supervised By:



Dr.Md. Sarowar Hossain

Associate Professor ,Department of pharmacy

Faculty of Allied Health Science

Daffodil International University

Submitted By:

Hami dul

Hamidul Islam

Faculty of Allied Health Science

Daffodil International University

Acknowledgment

First I would like to convey my heartfelt gratitude to the Almighty Allah for giving me the chance to study this subject, the capability to complete my project work, and finally the ability to write up the project work & results in order to fulfill the requirements for the Bachelor of Pharmacy degree.

I want to express my gratitude to **Prof. Dr. Muniruddin Ahmed**, Professor and Head, Department of Pharmacy, Daffodil International University, for his support and for allowing me to finish this project.

I place on record, my sincere thank you to **Dr.Md. Bellal Hossain**, Dean and Faculty of Allied Health Sciences of Daffodil International University for the continuous encouragement.

I would like to express my respect and appreciation to my teacher and supervisor **Dr.Md. Sarowar Hossain**, Associate Professor, Department of Pharmacy, Faculty of Allied Health Science, Daffodil International University, for providing me proper guideline and inspiration for completion of my project work.

Finally, I would like to express my gratitude towards my parents and other family members for their kind cooperation and encouragement which helped me in completion of this project.

Dedication
To my beloved parents, my teachers, my supervisor and my friends.
© Daffodil International University

<u>v</u>

Abstract

A chronic metabolic illness called type 2 diabetes is characterized by elevated blood sugar levels brought on by insulin resistance and insufficient insulin production. Glycated hemoglobin levels, oral glucose tolerance tests, and fasting plasma glucose levels are all used in the diagnosis of type 2 diabetes. Early detection and intervention are essential for treating type 2 diabetes, and treatment includes pharmacological therapy, such as oral antidiabetic drugs and insulin therapy, as well as lifestyle changes like a nutritious diet and frequent exercise. Maintaining ideal glucose control, avoiding or delaying complications, and enhancing quality of life are the objectives of treatment. A multidisciplinary approach involving the patient, the healthcare provider, and other stakeholders, such as family members and carers, is necessary for the successful management of type 2 diabetes.

Keywords:Type 2 diabetes mellitus, Treatment, Oral antidiabetic agents, Injectable antidiabetic agents, Older people, Renal impairment, Future treatments.

List Of Contents

Serial No	Topic	Page No.
01	Title	i
02	Abstract	vi
03	List of Contents	vii
04	List of table	xi

Chapter 1

Serial no	<u>Topic</u>	Page no
01	General Introduction	1-2
02	Etiology	2-3
3	Lifestyle, geneticsand medical conditions	3
3.1	Lifestyle factors	3-4
3.2	Genetic factors	4-5
3.3	Medical condition	5

4	Pathophysiology	6-7
6	Screening and Diagnosis	7-8
7	Management	8
8	Epidemiology	8-9

Chapter 2

<u>Serial no</u>	<u>Topic</u>	Page no
<u>01</u>	Literature review	10-11

Chapter 3

Serial no	Topic	Page no
<u>01</u>	Purpose of the study	12-13

Chapter 4

<u>Serial no</u>	<u>Topic</u>	Page no
<u>01</u>	Methodology	14-15

Chapter 5

Serial no	<u>Topic</u>	Page no
O1	Result	16
02	Plasma glucose specific test	17
2.1.1	The EPG test	17
2.1.2	The RPG test	18
2.1.3	The OSTT	18
2.1.4	Capillary blood glucose	19
	meters	
2.1.5	A1C testing	19
2.1.6	Capillary blood A1c testing	20
2.2	Lifestyle modification for	22-28
	type 2 diabetes	
2.3	Medications	28
2.3.1	Metformin	28-31
2.3.2	Sulfonylureas	31-34
2.3.3	DPP-4 inhibitors	34-35
2.3.4	GLP-1 receptor agonist	35-36
2.3.5	SGLT2 inhibitors	36-37
2.4	Insulin Therapy	37-38

2.5	Emerging Therapies	41-43

Chapter 6

Serial no	Topic	Page no
01	Discussion	44-45

Chapter 7

Serial no	Topic	Page no
<u>01</u>	Conclusion	46

Chapter 8

Serial no	<u>Topic</u>	Page no
<u>01</u>	Reference	47-54

List Of table

Serial no	<u>Topic</u>	Page no
Table 1	Summary of testing for type-	21
	2 diabetes	

Table 2	Listing of the drug classes	39-41
	currently approved in the	
	United States, followed by	
	the drug names and relevant	
	references.	

Chapter One

Introduction

General Introduction

More than 400 million people worldwide have type 2 diabetes mellitus (T2DM). More than 640 million people will have diabetes worldwide in 2040.[1] In type 2 diabetes, the body either stops producing enough insulin or develops resistant to it, making it difficult to keep blood sugar levels within normal range. The amount of glucose (sugar) in the blood is controlled in part by the hormone insulin. Glucose builds up in the blood and can eventually cause a number of health issues when the body does not react to insulin effectively. Increased thirst, frequent urination, weariness, blurred vision, wounds that take a long time to heal, and

tingling or numbness in the hands or feet are all signs of type 2 diabetes. Some people, nevertheless, might not have any symptoms at all.

Obesity, leading a sedentary lifestyle, having a family member with the disease, and having certain medical disorders like high blood pressure or high cholesterol are all risk factors that can raise the likelihood of getting type 2 diabetes. The normal course of treatment for type 2 diabetes is taking drugs to help regulate blood sugar levels along with lifestyle adjustments like adopting a nutritious diet and increasing physical activity. In order to treat their illness, some persons may additionally need insulin therapy.

Effective management of type 2 diabetes is crucial to preventing or delaying consequences such heart disease, renal disease, nerve damage, and visual loss. The risk of these consequences can be decreased by routinely checking cholesterol, blood pressure, and blood sugar levels.

Etiology

The way your body processes blood sugar (glucose) is impacted by type 2 diabetes, a chronic illness. It accounts for around 90–95% of all diagnosed cases of diabetes worldwide, making it the most prevalent kind. Numerous risk factors play a part in the epidemiology of type 2 diabetes, which is complicated and multifactorial.

A literature review revealed that there are little statistics on the prevalence of type 2 DM in all of Africa. Studies looking at data patterns in Africa show that prevalence is dramatically rising in both rural and urban settings, affecting both genders equally.[11]

Less than 10% of DM occurrences in Africa appear to be type 1 DM, with type 2 DM causing the majority of the disease burden.[11] According to a 2011 report from the Centre for Disease Control and Prevention (CDC), around 25.8 million Americans (7.8% of the population) were estimated to have type 2 diabetes in 2010, accounting for 90% to 95% of cases.[12]

Lifestyle, geneticsand medical conditions

The main causes of type 2 diabetes are genetics and lifestyle choices.[15] Numerous lifestyle factors are known to play a significant role in the onset of type 2 DM. These include excessive alcohol consumption, smoking, sedentary behavior, and lack of physical activity.16 About 55% of type 2 DM cases have been found to be influenced by obesity.[17] It is thought that the rise in type 2 DM in children and adolescents between the 1960s and 2000s was caused by an increase in the prevalence of childhood obesity.[18]

Lifestyle factors:

Several lifestyle choices can raise the risk of type 2 diabetes, including:

Sedentary living: Living a sedentary lifestyle and getting little exercise can raise your chance of developing type 2 diabetes and cause you to gain weight.

- ✓ Diet that is unhealthy: Type 2 diabetes risk can be raised by a diet that is high in sugar, saturated fats, and processed foods.
- ✓ Obesity: Having an excessive body mass index or being obese raises the risk of type 2 diabetes. Extra body fat can result in insulin resistance, which raises blood sugar levels.
- ✓ Smoking: Smoking is linked to a number of chronic illnesses, including type 2 diabetes.

 Smoking can raise the chance of developing insulin resistance and diabetes.
- ✓ Sleep: Lack of sleep or poor sleep can increase the risk of type 2 diabetes by causing insulin resistance.
- ✓ Stress: Long-term stress can alter hormone levels, causing insulin resistance and raising the risk of type 2 diabetes.
- ✓ Alcohol consumption: Drinking too much alcohol can cause weight gain, high blood pressure, and high triglyceride levels, all of which raise the risk of type 2 diabetes.

Genetic factors:

The following list of recognized genetic factors:

- ✓ Family history: Type 2 diabetes often runs in families, and having a first-degree family who has the condition raises your risk of getting it yourself.
- ✓ Mutations in the genetic code: Some genetic changes can raise the risk of type 2 diabetes.

 An increased chance of acquiring the condition has been linked, for instance, to mutations in the TCF7L2 gene.

- ✓ Ethnicity: When compared to other ethnic groups, some have a higher chance of getting type 2 diabetes, including African Americans, Hispanic Americans, and Native Americans.
- ✓ Epigenetic modifications: DNA methylation is one epigenetic change that can modify gene expression and lead to the emergence of type 2 diabetes.
- ✓ Genes linked to obesity: It has been discovered that several genes, including FTO and MC4R, are linked to a higher risk of type 2 diabetes.

Medical condition:

Blood sugar (glucose) metabolism is impacted by type 2 diabetes, a long-term medical disorder. In order to maintain normal blood sugar levels, the body either fails to create enough insulin in this state or fights its effects. The pancreas produces the hormone insulin, which aids in the body's utilization of glucose as fuel. Glucose builds up in the bloodstream and raises blood sugar levels when the body either stops producing enough insulin or becomes resistant to it.

The eyes, kidneys, nerves, and cardiovascular system are just a few of the body's systems and organs that can suffer long-term damage from high blood sugar levels. Increased thirst, frequent urination, fuzziness of vision, exhaustion, and poor wound healing are all typical signs of type 2 diabetes. Obesity, sedentary lifestyles, and unhealthful eating habits are all known risk factors for type 2 diabetes. But other elements, such as genetics, might also be important. As well as medicine and insulin therapy in some situations, treatment often entails lifestyle modifications like weight loss, exercise, and a nutritious diet.

Pathophysiology

Insulin insensitivity, which is caused by insulin resistance, decreasing insulin production, and eventually failing pancreatic beta-cells, are characteristics of type 2 diabetes mellitus (DM)[.28,29] The liver, muscle cells, and fat cells receive less glucose as a result of this. As blood sugar levels rise, fat is broken down more quickly. A recent discovery in the pathogenesis of type 2 diabetes is the presence of poor alpha-cell function.[30]

Numerous mechanisms, such as the following, play a role in the pathophysiology of T2DM:

- ✓ Insulin resistance: One of the main contributors to the emergence of T2DM is insulin resistance. It is caused by a confluence of genetic and environmental variables and is characterized by lowered insulin sensitivity in target organs like the liver, skeletal muscle, and adipose tissue. Hyperglycemia and dyslipidemia are brought on by insulin resistance, which also increases lipolysis in adipose tissue, impairs skeletal muscle glucose absorption, and increases the synthesis of hepatic glucose.
- ✓ Beta-cell dysfunction: The pancreatic beta-cells, which secrete insulin, are a key contributor to the emergence of T2DM. The beta-cells boost insulin secretion to counteract insulin resistance in the early stages of the disease. However, over time,

chronic hyperglycemia and insulin resistance cause beta-cell exhaustion and dysfunction, which reduces insulin secretion.

- Glucotoxicity and lipotoxicity: Prolonged exposure to elevated blood glucose levels (glucotoxicity) and free fatty acids (lipotoxicity) can result in cellular damage and dysfunction, which contributes to the pathogenesis of T2DM. Beta-cell activity may be hampered by glucose toxicity, which may also lead to a rise in insulin resistance and the emergence of diabetic complications. Lipotoxicity can lead to insulin resistance in target tissues and impair beta-cell function, which can lead to beta-cell apoptosis and the emergence of T2DM.
- ✓ Inflammation: A feature of T2DM, chronic low-grade inflammation is a key factor in the emergence of insulin resistance and beta-cell dysfunction. Beta-cell dysfunction can result from impaired insulin signaling caused by inflammatory cytokines such tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6).
- ✓ Genetics: T2DM can develop for a variety of reasons, including genetics. It has been discovered that a number of genes, including those involved in insulin production, insulin sensitivity, and beta-cell function, are linked to an elevated risk of T2DM.

Screening and Diagnosis

There are numerous tests that can be used to detect and diagnose DM. A positive screen is similar to a diagnosis of pre-diabetes or diabetes mellitus since the test that is advised for screening is also the one that is used to make a diagnosis.[32] Although about 25% of type 2 diabetes patients have microvascular complications at the time of diagnosis, indicating that

they have had the disease for at least 5 years.[33] It continues to be based on the American Diabetic Association (ADA) guidelines from 1997 or the World Health Organization (WHO) National Diabetic Group criteria from 2006, which call for a single elevated glucose reading with symptoms (polyuria, polydipsia, polyphagia, and weight loss), otherwise elevated values on two occasions, either of fasting plasma glucose (FPG) 37.0 mmol/L (126 mg/dL) or with an oral glucose tolerance test (OGTT), two hours.[32]

Fasting plasma glucose (FPG) testing monitors blood glucose levels following an overnight fast and is the most used type 2 diabetes screening test. A FPG level of less than 100 mg/dL (5.6 mmol/L) is considered normal, however a level of 100-125 mg/dL (5.6-6.9 mmol/L) or above on two separate occasions is diagnostic for diabetes. The oral glucose tolerance test (OGTT), another type of diabetes screening test, involves drinking a glucose solution and monitoring blood glucose levels before and two hours after the drink. A result of 200 mg/dL (11.1 mmol/L) or higher on two different occasions is diagnostic for diabetes, while a value of 140-199 mg/dL (7.8-11.0 mmol/L) shows prediabetes. A normal OGTT result is less than 140 mg/dL (7.8 mmol/L).

Management

By altering one's dietary and lifestyle habits, studies have shown that maintaining a body mass index of 25 kg/m2, eating a diet high in fiber and unsaturated fat and low in saturated and trans fats and glycemic index, regular exercise, quitting smoking, and moderate alcohol consumption resulted in a significant decrease in the incidence of type 2 DM[.5,16,35-37] asserting that changing one's lifestyle can prevent the bulk of type 2 DM. A medical nutrition assessment should be given to type 2 diabetic patients, and lifestyle suggestions should be made in accordance with each patient's unique physical and functional capabilities[.38]

Epidemiology

Numerous risk factors for type 2 diabetes have been identified by epidemiological studies, including age, obesity, physical inactivity, poor diet, a family history of the disease, and ethnicity. Type 2 diabetes is more common in some communities than others; greater rates have been seen among some ethnic groups, including African Americans, Hispanics, and Native Americans. The International Diabetes Federation estimates that the prevalence of diabetes among adults worldwide will be 9.3% in 2019, with type 2 diabetes making up 90–95% of all cases. Type 2 diabetes is more common in low- and middle-income nations, and it is expected to rise in the coming years as a result of population expansion, aging, urbanization, and lifestyle modifications.

Heart disease, renal disease, nerve damage, retinopathy, and foot ulcers are all type 2 diabetic complications. With estimated annual direct and indirect expenditures in the billions of dollars, diabetes has a significant financial impact as well. Type 2 diabetes requires a multifaceted strategy for care and prevention that includes pharmacological interventions like oral hypoglycemic drugs and insulin therapy along with lifestyle changes like healthy eating and frequent exercise. Reducing the burden of type 2 diabetes also requires public health initiatives that support healthy lifestyles and expand access to healthcare.

Chapter Two

Literature review

The literature review of the diagnosis and treatment of type 2 diabetes covers a range of studies and meta-analyses evaluating various treatment strategies for this condition.

- ✓ Fasting blood sugar and/or hemoglobin A1C (HbA1c) levels are used to diagnose T2DM.

 A fasting plasma glucose level below 126 mg/dL or a HbA1c level above 6.5%, respectively, is considered to be a sign of diabetes by the American Diabetes Association (ADA). By repeat testing on a different day, the diagnosis should be verified.
- ✓ Glycemic control and the prevention or delay of problems are the two main objectives of treatment for T2DM. A change in lifestyle, medication, and insulin therapy are all necessary for the treatment of T2DM.

- ✓ The cornerstone of T2DM management is lifestyle change. It include quitting smoking, losing weight, adopting a healthy diet, and exercising frequently. The ADA suggests setting a weekly target of at least 150 minutes of moderate-intensity aerobic activity and at least twice weekly of weight training.
- ✓ When lifestyle changes alone are not enough to achieve glycemic control, pharmaceutical medication is advised. The selection of a drug is influenced by a number of elements, including patient preferences, cost, cost-effectiveness, and side effect profile. Medications including metformin, sulfonylureas, DPP-4 inhibitors, GLP-1 receptor agonists, SGLT2 inhibitors, and insulin are among the most often used ones.

- Patients who struggle to control their blood sugar levels despite making lifestyle changes and using oral drugs are advised to start insulin therapy. The degree of hyperglycemia, the existence of concomitant conditions, patient preferences, and cost all play a role in the selection of an insulin regimen. Basal-bolus, premixed insulin, and basal insulin are the insulin regimens that are most frequently utilized.
- Insulin insensitivity, which is caused by insulin resistance, decreasing insulin production, and eventually failing pancreatic beta-cells, are characteristics of type 2 diabetes mellitus (DM)[.28,29] The liver, muscle cells, and fat cells receive less glucose as a result of this. As blood sugar levels rise, fat is broken down more quickly. A recent discovery in the pathogenesis of type 2 diabetes is the presence of poor alpha-cell function.[30]
- A literature review revealed that there are little statistics on the prevalence of type 2 DM in all of Africa. Studies looking at data patterns in Africa show that prevalence is dramatically rising in both rural and urban settings, affecting both genders equally.[11]

Chapter Three
Purpose of the study

Purposes of a study on the diagnosis and treatment of type 2 diabetes:

- Understanding the causes and risk factors: Investigation into the root causes of type 2 diabetes aids in the discovery of the risk factors that fuel its growth. These risk factors include obesity, inactivity, heredity, and way of life elements like smoking and food. Identifying people who are at high risk of getting the illness and informing preventative steps can be aided by understanding these characteristics.
- Treatments being developed: Type 2 diabetes has been studied, and as a result, a number of treatments, including prescription drugs, dietary adjustments, and surgical procedures, have been created. Researchers can improve patient outcomes by creating more effective medicines by better understanding the underlying mechanics of the disease and how it affects the body.
- Preventing complications: Heart disease, stroke, renal failure, and blindness are a some of the consequences that can result from type 2 diabetes. The condition can be studied to find strategies to treat or prevent these side effects, enhancing the quality of life for those who have it.
- Informing public health policy: Strategies and policies for lowering the prevalence of type 2 diabetes can be informed by research on the condition. This includes programs to encourage a healthy diet and regular exercise, to increase access to healthcare, and to lessen the social and economic factors that contribute to the condition.

In conclusion, research on type 2 diabetes is crucial for understanding its causes and risk factors, devising efficient therapies, avoiding complications, and informing public health policies aimed at lowering its incidence.

Chapter Four

Methodology

Search strategy:

The search strategy used to find pertinent papers for the review should be discussed in the methods section. This might entail manually scanning reference lists of pertinent papers, getting in touch with subject-matter experts, or searching electronic databases like PubMed, google scholar, rechearchgate, MEDLINE, or Cochrane Library.

Study selection criteria:

The methodology section should include the inclusion and exclusion standards for research that were taken into account for the review.

Data extraction:

The methods section has to explain how the data from the listed research were obtained. In order to do this, it may be necessary to use a standardized data extraction form to gather details on the study's design, sample size, treatments, results, and other pertinent factors.

Data synthesis:

The methods section should outline the steps taken to compile and evaluate the data from the included research. This could entail combining the data of several research using statistical techniques like deta-analysis.

Overall, the methodology section of a review article should provide a clear and transparent description of the methods used to conduct the review and evaluate the quality of the included studies, in order to ensure that the findings are robust and trustworthy.

Chapter Five Result

Result

Blood tests to detect blood glucose levels are frequently used to diagnose type 2 diabetes. The condition can be identified with a hemoglobin A1c test, an oral glucose tolerance test, or a fasting plasma glucose test. Medication and lifestyle modifications are frequently used as type 2 diabetes treatments. The main objective is to control blood sugar levels to avoid problems including renal disease, nerve damage, and blindness

Diagnosis and Treatment

Diagnosis

Plasma-glucose specific tests

Because they measure the pathophysiological result of diabetes (i.e., the level of extra glucose in the blood), glucose-specific tests are frequently preferred. They are also accessible during a clinical office visit, affordable, and straightforward to purchase. Here, we go through the characteristics of the FPG, RPG, and OGTT tests as well as the support for their application.

The FPG test

Type 2 diabetes is frequently diagnosed with the FPG (Fasting Plasma Glucose) test. After you've fasted (not eaten anything) for at least eight hours, this test measures the amount of glucose (sugar) in your blood. Your doctor will take a blood sample from you for the FPG test, which determines your fasting blood glucose level. You have impaired fasting glucose (IFG), which increases your risk of type 2 diabetes, if your fasting blood glucose level is between 100 and 125 mg/dL. Type 2 diabetes may be identified if your fasting blood glucose level is 126 mg/dL or above.

The FPG concentration diagnostic for diabetes was reduced from 140 to 126 mg/dl in 2003 as a result of concerns that the previous level was too low to accurately diagnose diabetes that presents as postprandial hyperglycemia. When IFG was diagnosed, the FPG concentration was lowered to its current range of 100-125 mg/dl.[22]

Studies looking at FPG have confirmed a lot of what is already known about the pathophysiology of diabetes, and there is strong evidence that it is a reliable predictor of diabetes complications at the present diagnostic threshold. However, data supporting the prediabetes cutoff and its association with complications are not as clear, clinicians should be aware. Furthermore, studies examining glucose-lowering therapy and the ADA diabetes

management guidelines have emphasized A1C rather than FPG as a measure of glucose control. In order to guide future medical decision-making, it is likely helpful to also look at a baseline A1C when making a diagnosis of diabetes or pre-diabetes with FPG.

The RPG test

The RPG (or "casual" plasma glucose) measurement has the advantages of being simple to get the day of an office visit, requiring no fasting, and frequently being included in a basic metabolic panel ordered for other causes. It requires rapid processing and can necessitate a second office visit for confirmatory testing, which are some of the FPG's practical drawbacks. The standard RPG cutoff is 200 mg/dl, and it should be present along with signs of polyuria, polydipsia, and unexplained weight loss to suggest a second test for diagnostic confirmation. Pre-diabetes is indicated by an RPG of 140 to 199 mg/dl.18 An RPG below 200 mg/dl is insensitive but close to 100% specific for OGTT-based diagnosis27, which makes it unlikely that a false-positive diagnosis will result in the presence of symptoms.

The OGTT

Type 2 diabetes can be diagnosed by a test called the OGTT (Oral Glucose Tolerance Test).

After consuming a sugary liquid, the subject undergoes a test to see how well their body can digest glucose.

The 2-hour post-load plasma glucose threshold was established based on the possibility of diabetic microvascular consequences. In a study of Pima Indians, Rushforth et al.29 looked at the relationship between FPG and 2-hour plasma glucose and the presence of diabetic retinopathy and nephropathy. Based on sensitivity and specificity, they found that a 2-hour

plasma glucose level of 250 mg/dl and an FPG of 136 mg/dl were the best levels for diagnosis. According to a second study9, the current 2-hour plasma glucose cut-off of 200 mg/dl had an 87.5% sensitivity and a 75.8% specificity for the presence of diabetic retinopathy. Finally, a European diabetes epidemiology group evaluated 13 prospective European cohort studies for risk of death according to the various glucose categories in the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe study31. IGT without IFG—defined as 2-hour plasma glucose measurements between 140 and 199 mg/dl with FPG less than 110 mg/dl—was demonstrated by this group to be linked to a higher risk of passing away. The risk ratio for men was 1.8, whereas it was 2.6 for women.

Capillary blood glucose meters

The most common technique for determining point glucose levels during clinic visits is capillary glucose measurement, which is also advised for patients to use for self-monitoring. Their utility in screening and diagnosis, however, is constrained by meter imprecision and the significant variations among meters.[14] A laboratory test should be used to confirm any aberrant glucose readings recorded with a capillary glucose meter.

A1C testing

An overall assessment of a person's diabetes management is provided by an A1C test, which evaluates the average blood sugar level over the previous two to three months. The hemoglobin A1C test and glycated hemoglobin test are other names for the A1C test. The amount of hemoglobin with sugar molecules attached, a protein found in red blood cells that transports oxygen, is quantified. Blood is drawn for the test from an arm vein, typically in a

medical facility or testing facility. A laboratory is subsequently contacted to do the analysis on the blood sample.

The American Diabetes Association (ADA) suggests that persons with type 2 diabetes aim for an A1C of fewer than 7%. However, depending on factors like age, general health, and other medical conditions, individual targets may change. People with diabetes who have their blood sugar under control should have their A1C tested at least twice a year, and more frequently if they are having trouble doing so. Doctors might modify drugs or other treatment options based on test results to better control blood sugar and reduce the risk of diabetic complications.

Capillary blood A1C testing

Capillary blood A1C measurement, commonly known as "point-of-care" (POC) A1C testing, is quickly gaining popularity as a technique for office-based diabetes control monitoring. Rapid POC A1C measurement led to more frequent intensification of the diabetic regimen when A1C reached 7% in a study42 of 597 patients (79% of whom were female and 96% of whom were African Americans). A1C significantly decreased in the rapid-test group in the same study's 275 patients with two follow-up visits (from 8.4 to 8.1%) but not in the usual group (from 8.1 to 8.0%).

The capillary blood A1C test findings are often accessible in a few minutes. The A1C test offers an average of blood sugar levels over the past two to three months, which can be used to diagnose type 2 diabetes and track how well the condition is controlled in those who already have it. The American Diabetes Association advises type 2 diabetics to have an A1C test at least twice annually to track their blood sugar control. However, those who have

recently received a diagnosis or are not maintaining their blood sugar goals may require more frequent testing.

Test Name	Mode of Action
Plasma glucose specific test	Measure how much sugar circulating in
	blood.
Thee EPG test	determines your fasting blood glucose level.
The RPG test	Predict the diagnosis of diabetes.
The OSTT	Measure bodys response to sugar.
Capillary blood glucose meters	Determining point glucose levels during
	clinic visits.
A1C testing	Evaluates the average blood sugar level over
	the previous two to three months.
Capillary blood A1c testing	Average of blood sugar levels over the past
	two to three months.

Table 1: Summary of testing for type-2 diabetes

Lifestyle modifications for type 2 diabetes

The two primary drivers of energy balance are dietary intake and physical activity[4], and they are regarded as the cornerstones of treatment for diabetic patients. All patients should be recommended to get about seven hours of sleep each night because adequate rest is also essential for preserving energy levels and overall health[3]. Sleep deprivation worsens insulin resistance, hypertension, hyperglycemia, and dyslipidaemia[6], while evidence suggests a link between 6 to 9 hours of sleep per night and a decrease in cardiometabolic risk factors. On the other hand, people suspected of having obstructive sleep apnoea should be screened, and they should be sent to a sleep expert for assessment and treatment[3].

The management of type 2 diabetes must include lifestyle changes. Dietary adjustments are intended to decrease consumption of simple carbs and increase consumption of high-fiber foods, like vegetables and whole grains. People with type 2 diabetes are advised by the American Diabetes Association to consume a diet that contains 45–60% of calories from carbohydrates, 15–20% from protein, and 20–35% fromfat. Additionally advised for enhancing insulin sensitivity and controlling blood sugar levels is physical activity. Simple forms of exercise include brisk walking and moderate-intensity activities for at least 150 minutes per week.

Here are some lifestyle modifications that can be helpful for people with type 2 diabetes:

- ✓ Healthy diet: Co-morbidities in a diabetic patient must also be taken into account when dietary intervention is being explored. The dietary advice can help people reach their ideal weight, blood sugar, blood pressure, lipid profile, and sleep apnea levels[4,7], as well as reduce their risk of depression and sleep apnea and improve their overall health-related quality of life[8–9].
- ✓ Numerous randomized controlled trials have shown the metabolic advantages of nutritional advice in lowering HbA1c; these studies generally depend on the severity of the disease[10,11].
- ✓ A balanced diet can lower the risk of problems and help control blood sugar levels. The nutrients required for optimum health can be obtained through a diet high in whole grains, fruits, vegetables, lean meats, and healthy fats. Alcohol consumption, as well as sugary and processed foods, must be restricted.
- Macronutrient distribution: To recommend a healthy ratio of proteins, fats, and carbs, there is insufficient evidence. A number of dietary patterns, such as the Mediterranean diet, vegetarian or vegan diet, Dietary Approaches to Stop Hypertension (DASH), low-fat diet, and low-carb diet, have been examined. These dietary patterns have shown some modest effectiveness in the management of diabetes, but many studies that have sought to distribute the best ratio of macronutrients have failed to find valid results. More research is required because the advantages only materialize when weight loss is also achieved.[12]
- ✓ Index and glycaemic load: Regarding the effects of a low glycaemic index diet, there is a lot of uncertainty. The conclusions of the numerous investigations are not universally agreed upon. There are articles that dispute this claim, despite the fact that several associations promote these diets because they show superior glycaemic control when

compared to foods with a high glycaemic index in particular[12]. They base this disparity on the varying definitions of glycaemic index, the fact that fiber does not factor in, and the fact that different people have different glycaemic reactions to the same food. They believe that it cannot be proven that the effect is caused solely by the glycaemic load of the food[15].

- ✓ Fiber: Consuming fiber, particularly the fiber that contains natural resources, has been found to lower cardiovascular risk factors and to worsen diabetics' glycemic control[27,31]. Studies have indicated that increased daily fiber intake results in a modestly significant effect on diabetes, though. This, however, is far from the actual daily consumption (more than 50 g/d)[17].
- ✓ It is generally advised that diabetic patients consume fiber and whole grains in amounts that are at least comparable to those advised for the general population; roughly 25 g/d for women and 38 g/d for men, or 14 g per 1000 kcal[13]. This is to account for the modest beneficial effects on cardiovascular risk factors.
- Sucrose and fructose:Contrary to popular belief, sucrose replacement for isocaloric levels of starch does not adversely affect glycaemic or lipid responses at intakes of 10% to 35% of total energy[18]. Free fructose, which is naturally present in foods like fruit, did not worsen glycaemic control more than other types of sugar, however it should be avoided in excess of 12% of daily calories[28]. To avoid consuming too many calories, which can lead to weight gain if ingested in big amounts, it is advised to limit these sugars in the diet. Additionally, sugary beverages have been shown to raise the risk of diabetes and cardiovascular disease in the healthy population that consume them since they contain significant amounts of quickly absorbed carbs. When they are sweetened with fructose-

free sugar, it is very dangerous. Despite the paucity of studies on diabetic people, there is no reason to believe they won't experience the same outcomes. These beverages are therefore not recommended[19].

- Non caloric sweeteners: There are sweeteners that have fewer calories than natural simple sugars. Most are made of plastic. With the exception of aspartame, which has 4 kcal/g, they do not add calories and do not raise blood sugar levels. Diabetic individuals can utilize these sweeteners. They have the advantage of lowering the number of calories in the diet when used to replace glucose[20].
- Proteins: It's interesting to distinguish between diabetic patients with kidney problems and those who don't. The typical recommendation for protein intake in healthy individuals is between 15% and 20%; however, after examining the available research, no conclusive findings could be made. Various randomized clinical trials that have looked at these results can be found in the literature. The HbA1c, triglycerides, total cholesterol, and/or LDL cholesterol all improve when 28% to 40% of the diet's energy is consumed as proteins, according to some studies[21], while other studies[22] have not found any change in any of these factors. Reducing protein intake below the norm in people with kidney disease—whether we're talking about micro or macroalbuminuria—has undergone several tests and meta-analyses. Following a low-protein diet has not been found to enhance glycemic management, cardiovascular risk factors, or the progression of renal disease[12]. There is no distinction between proteins of animal or vegetable origin in terms of proteinuria[13].
- ✓ Finally, even while proteins do not directly alter blood glucose management in persons with T2DM, they do raise the insulin response, making it unwise to utilize proteins when hypoglycemia is present.

- ✓ Fat:Epidemiological research has connected lipids to cardiovascular risk factors like obesity[38]. There is no ideal fat proportion, just as there isn't one for the other immediate principles. As a general rule, diabetic patients should adhere to the recommendations for the general population (between 20% and 35%), paying particular attention if the patient is overweight, in which case the percentage should be at the lower limits. Diabetes patients frequently consume more fat than is advised[24] despite these recommendations.
- Monounsaturated and polyunsaturated fats can be distinguished from saturated fats. It should also be highlighted that trans fatty acids, despite being a form of unsaturated fat, have negative effects on the body due to their unique structure. In fact, studies have shown that the kind of fat consumed matters more than the quantity.
- ✓ In this regard, the guidelines for diabetes patients are the same as for the general population because there are few research on the consumption of saturated fatty acids or cholesterol in diabetic patients: With a contribution of cholesterol under 300 mg/dL, a contribution of saturated fat under 10%, and a minimum intake of trans fatty acids, it is preferable to choose monounsaturated and polyunsaturated fatty acids (including omega-3 fatty acids). Monounsaturated fatty acids can reduce cardiovascular risk factors and enhance glycemic management, according to certain studies that looked at the Mediterranean diet pattern[25], particularly if saturated fatty acids are substituted for them.
- ✓ Omega-3 fatty acids: Omega-3 supplements have demonstrated a clear cardiovascular benefit, despite mixed results[26]. Consuming goods strong in omega-3s can help avoid cardiovascular disease, though[27].

- ✓ Alcohol: One serving of alcohol per day for women and two servings per day for males should be consumed in moderation. This contribution must be swapped for other goods in order to prevent unnecessary energy usage. Although studies have shown that moderation can enhance glycaemic control and lower cardiovascular events, moderate consumption does not affect glycaemic control.
- ✓ Despite the information above, it is important to remember that alcohol use can also cause late hypoglycemia to manifest. We should caution the patient to pay attention to any indications of hypoglycemia since this is especially true for individuals receiving therapy with hypoglycaemic medications [13].
- ✓ Sodium: Patients with diabetes mellitus must adhere to the recommendation for the general population to cut their sodium intake to fewer than 2300 mg/d. Reduced salt consumption should be tailored to each person's needs when they also have hypertension, which is fairly common[28].
- Specific supplements: Researchers have examined the possible advantages of dietary supplements for diabetic patients that contain certain particular nutrients. Due to the addition of antioxidants such vitamins and carotenes, micronutrients like chromium, or other herbs to the diet, credible data has not been seen to substantiate benefits in glycaemic control supplementation. The general population's guidelines for vitamins and minerals still apply; a diverse diet provides them[23].
- ✓ Regular exercise: Blood sugar levels can be lowered by exercise and insulin sensitivity can be increased. Aim for 150 minutes or more per week of moderately intense aerobic activity, such as brisk walking, cycling, or swimming. Exercises for strength training can also aid in muscle growth and health improvement.

- ✓ Weight loss: In addition to enhancing insulin sensitivity, weight loss might also lessen type 2 diabetes consequences. Even a small weight decrease of 5-10% can greatly enhance blood sugar regulation.
- ✓ Stress management: Finding appropriate strategies to manage stress is essential since stress can affect blood sugar levels. This may involve routines like yoga, deep breathing, or meditation.
- ✓ Quit smoking: Quitting smoking is an important lifestyle change to take into consideration because it can reduce the risk of complications from type 2 diabetes.
- Regular check-ups:Checkups with a healthcare professional on a regular basis can help monitor cholesterol, blood pressure, and blood sugar levels as well as spot and treat any potential issues.It's important to remember that lifestyle changes should be customized to each person's unique demands and preferences. A customised plan for controlling type 2 diabetes through lifestyle changes can be created with the assistance of a healthcare professional and/or a certified dietitian.

Medications

To control problems and lower blood sugar levels in type 2 diabetic patients, medications are frequently employed. Metformin, which acts by lowering glucose synthesis in the liver and enhancing insulin sensitivity, is the drug of choice for the majority of people with type 2 diabetes. The management of type 2 diabetes frequently involves the use of medications, particularly for those who are unable to regulate their blood sugar levels solely through lifestyle changes. Here are a few typical treatments for type 2 diabetes:

Metformin

The first-line treatment for type 2 diabetes is frequently metformin. By decreasing the liver's ability to produce glucose and raising the body's sensitivity to insulin, it decreases blood sugar levels. Typically, it is consumed orally once or twice per day. An oral medicine called metformin is used to treat type 2 diabetes mellitus. Additionally, it is used to treat PCOS, a hormonal condition that affects women of reproductive age. The biguanide medication class includes metformin, which reduces the amount of glucose the liver produces. Additionally, it increases the body's sensitivity to insulin.

The dosage of metformin is often taken orally, with meals, and is based on the patient's condition and treatment response. Usually, low initial doses are followed by gradually rising doses. Both immediate-release and extended-release versions of the medicine are offered; the latter is typically taken once daily. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and stomach pain are among the side effects of metformin. Typically, these negative effects are minor and eventually disappear. Lactic acidosis is a dangerous disease that metformin can occasionally cause. When lactic acid levels in the blood get too high, this happens. Patients with kidney or liver issues or those who take high doses of the medicine are more likely to experience this. It is essential to inform your doctor about all other medications you are taking, including over-the-counter medicines and herbal supplements, because metformin can interact with them. While most people find metformin to be safe, it should not be used while pregnant or breast-feeding. Metformin is used to treat diabetes and PCOS, but some evidence indicates it may also be beneficial for other illnesses. Cancer, heart disease, and neurological diseases are a few of these. To completely comprehend the advantages and disadvantages of metformin for these illnesses, more study in these areas is necessary.

Mechanism of action

[30]The intestinal barrier's integrity is maintained by mucosal AMP-activated protein kinase (AMPK), which is triggered by metformin and can alter the composition of the gut microbiota[59]. These outcomes, along with the activation of AMPK[60] in hepatocytes, seem to constitute the mechanism by which metformin lowers blood and liver levels of lipopolysaccharide (LPS).

Metformin can inhibit gluconeogenesis by four different mechanisms after entering the liver from the intestines[33]: (1) through activating hepatic AMPK through liver-kinase B1 and decreased energy charge (9, 10); (2) through the inhibition of glucagon-induced cAMP production by blocking adenylcyclase (11); (3) at high concentrations (5 mmol/L) inhibiting NADH coenzyme Q oxidoreducta 4. Inhibition of mitochondrial glycerol phosphate dehydrogenase (mG3PDH)[58], which prevents lactate gluconeogenesis. It should activate AMPK.

Additionally, the Peutz-Jeghers protein LKB1 is how metformin functions. Because LKB1 is a tumour suppressor, activating AMPK via LKB1[62] might prevent cell proliferation.

Indications

Metformin is primarily prescribed to treat type 2 diabetes mellitus, especially when lifestyle modifications alone are ineffective at regulating blood sugar levels. Additionally, it may be used off-label to treat gestational diabetes and polycystic ovarian syndrome (PCOS).

Contraindications

- ✓ Hypersensitivity:Patients who have a history of medication hypersensitivity should not use metformin.Metformin shouldn't be taken in patients with severe renal impairment (eGFR less than 30 mL/min/1.73 m2) since it raises the possibility of lactic acidosis.
- ✓ Metformin is not recommended for use in individuals with acute or chronic metabolic acidosis, including diabetic ketoacidosis, as it may make their situation worse.
- ✓ Hepatic impairment:Patients with hepatic impairment shouldn't use metformin since it raises the risk of lactic acidosis.
- ✓ Heart failure: Patients with congestive heart failure shouldn't use metformin because it can make their situation worse, especially if they are in unstable state.
- ✓ Recent myocardial infarction or unstable angina: Patients with recent myocardial infarction or unstable angina should temporarily stop taking metformin since these conditions may raise the risk of lactic acidosis.
- ✓ Alcohol abuse: Alcohol usage should be avoided since it raises the risk of lactic acidosis in metformin users.

It is crucial to remember that these are not the only instances where metformin should not be taken. Any medicine should be started or stopped after consulting a healthcare professional.

Side effects

The most frequent ones, which are typically minor and temporary, are gastrointestinal, including anorexia, nausea, abdominal pain, and diarrhea. Metformin also reduces vitamin B12 absorption through the digestive tract. Lactic acidosis is far less typical. There were no cases of lactic acidosis in a review[35] of 347 randomized trials and prospective cohort

studies. However, because to the high case-fatality rate, it is extremely important. All conditions that increase the risk of hypoperfusion and hypoxemia, such as sepsis, heart failure, dehydration, and acute or gradual renal impairment, are referred to as predisposing factors.

Sulfonylureas

Sulfonylureas are a group of drugs that stimulate the pancreas to produce more insulin. They are taken orally once or twice a day, and one of their side effects is hypoglycemia, or low blood sugar. A class of oral hypoglycemic medications called sulfonamides is used to treat type 2 diabetes. They function by encouraging the pancreas to produce more insulin, which reduces blood glucose levels. Sulfonylureas come in a variety of forms, including first-generation medications like tolbutamide and hydrochloride, as well as second-generation medications like glipizide, glyburide, and glimepiride. Due to their higher potency, shorter half-life, and lower risk of hypoglycemia, second-generation sulfonylureas are more often used nowadays.

The dosage of sulfonylureas is frequently modified based on the patient's blood glucose levels, and they are normally given once or twice daily with meals. They can be used alone or in combination with other oral hypoglycemic agents, insulin, or other diabetic treatments, and they often reduce HbA1c levels by 1-2%. Although hypoglycemia is the most frequent adverse effect of sulfonylureas, it can occasionally be very severe and is normally well tolerated. Patients should be instructed to regularly check their blood sugar levels and be aware of the symptoms and signs of hypoglycemia. Shaking, perspiration, bewilderment, and loss of consciousness are some of these symptoms. Sulfonylureas may also cause weight gain, gastrointestinal issues such nausea and diarrhea, skin rashes, and liver malfunction as side effects. When treating patients with liver or kidney illness, as well as the elderly,

sulfonylureas should be used cautiously. Hypoglycemia may be more likely to affect these patients. Sulfonylureas are an oral hypoglycemic drug class that are frequently used in type 2 diabetes, to sum up. Although they can result in hypoglycemia and other potential side effects, they lower blood glucose levels. These adverse effects should be regularly watched for in patients, and they should be reminded to take their medications as prescribed.

Pharmacokinetics

Specific reactions are caused by variations in the pharmacokinetic and binding characteristics of insulin secretagogues. One can distinguish between first- and second-generation sulfonylureas. Second-generation sulfonylureas include glimepiride, glipizide, gliclazide, and gliburide (sometimes referred to as glibenclamide in Europe)[29]. These agents of the next generation are more effective and cause fewer side effects[22]. Despite the fact that second-generation sulfonylureas are similarly effective, there are differences in the how they are absorbed, metabolized, and how long they last. For instance, glyburide possesses active metabolites that extend the duration of its action.

Repaglinide and Nateglinide are the two glinides. Regalinide is a member of the meglitinide family, not the sulfonylurea family. Nateglinide, a phenylalanine derivative, differs structurally from sulfonylureas and meglitinide. Due to their shorter half-lives and alternative sulfonylurea receptor binding sites, which result in faster absorption and a quicker stimulus to insulin production, they both result in less hypoglycemia and less weight gain[22].

Sulfonylureas decrease fasting plasma glucose concentrations while meglitinides decrease postprandial glucose as a result of their different pharmacokinetics[36].

Mechanism of action

Both sulfonylureas and glinides base their mechanism of action on increasing insulin secretion, which is regulated by ATP-sensitive potassium channels (KATP potassium channel) located in the membrane of pancreatic beta cells. Although the receptor's binding site is different for sulfonylureas and glinides, they both induce channel closure and cell depolarization. This leads to an increase in cytoplasmic calcium levels and insulin secretion[22].

Side effects

The main issues with these medications include loss of efficacy, hypoglycemia, and weight gain. Due to an aggravation of islet dysfunction brought on by beta cell failure, insulin secretagogues lose their potency over time (secondary failure)[38,37]. As a result, a smaller and smaller proportion of patients are able to maintain good glycaemic control. Although the course of the disease may also be related to this effect, other medications have showed a higher rate of secondary failures[80]. Numerous similar pathways induced by insulin therapy can lead to weight increase, and this has been seen in various studies[41,42]. When administered in tandem, metformin may, however, counteract the effect on weight gain[41,43]. Sulfonylureas of various generations have been demonstrated to increase body weight, and the degree of this increase seems to be correlated with a susceptibility for hypoglycemia. It might also happen with meglitinides because their profiles are similar[37], however it seems to happen less frequently because of their brief action[38].

The most frequent side effect[43,44] is hypoglycemia, which is more likely to occur while using long-acting sulfonylureas such glimepiride[45]. A much lower risk of hypoglycemia

exists with the newest generation of sulfonylureas. Meglitinides often have a lower risk of hypoglycaemia[22], making them helpful for people who want to prevent hypoglycaemic occurrences. Older people with variable eating habits (meglitinides may be helpful in these patients), malnutrition, alcohol consumption, renal insufficiency, hepatic failure, hypothyroidism, or drug interactions are risk factors for hypoglycemia[46,47]. In older people, whose results from trials have revealed that aggressive control may not have significant advantages and may present some risk[2,] the risk of hypoglycemia as well as considerations of the risk-to-benefit relationship are particularly pertinent.

DPP-4 inhibitors

DPP-4 inhibitors are a group of drugs that lower blood sugar levels by boosting insulin secretion and decreasing the liver's ability to produce glucose. One or two oral doses are given each day. Type 2 diabetes is treated using a class of oral drugs known as dyspeptic peptidase-4 (DPP-4) inhibitors. They function by inhibiting the DPP-4 enzyme, which is responsible for breaking down the incretin hormones that control blood sugar. Incretin hormones can be kept active longer by blocking DPP-4, which raises insulin production, lowers glucagon secretion, and lowers blood sugar levels. DPP-4 inhibitors include medications like sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), and alogliptin (Nesina), among others. There is little chance of hypoglycemia (low blood sugar) with these drugs and they are typically well tolerated.

DPP-4 inhibitors have been linked to headaches, nausea, diarrhea, and abdominal pain as well as upper respiratory tract infections. In rare instances, they could also result in joint discomfort or pancreatitis (pancreatic inflammation). Following metformin and lifestyle changes, DPP-4 inhibitors are frequently used as a second-line treatment for type 2 diabetes.

To further enhance blood sugar control, they can also be taken along with other drugs like sulfonylureas or insulin. The advantages and hazards should be discussed with your healthcare physician because they might not be appropriate for everyone.

GLP-1 receptor agonists

37 | Page @Daffodil International University

GLP-1 receptor agonists are a class of drugs that boost insulin secretion and lessen hepatic glucose synthesis. Once a week or every day, they are frequently injected. Type 2 diabetes is managed with drugs called GLP-1 receptor agonists (GLP-1RAs). The hormone GLP-1, which is made in the intestine, increases the production of insulin from the pancreas, which controls blood glucose levels. The actions of GLP-1RAs are similar to those of GLP-1 in the body, raising insulin secretion while lowering glucagon secretion. Lower blood sugar levels are the result of this. Exenatide, liraglutide, dulaglutide, semaglutide, and lixisenatide are a few of the several GLP-1RAs that are offered for sale. Depending on the particular prescription, they are commonly given by subcutaneous injection and taken once a day or once a week. GLP-1RAs have also been demonstrated to have positive effects on the body outside of how they affect blood glucose levels. By reducing hunger and boosting sensations of fullness, for instance, they can promote weight loss. They may also improve the cardiovascular system by lowering the risk of heart attacks and strokes, for example.

Particularly when the medicine is first begun or the dose is increased, GLP-1RAs can produce nausea, vomiting, diarrhea, and stomach pain. However, these adverse effects frequently get better with time. Although the danger seems modest, some people on GLP-1RAs have also been reported to have thyroid malignancies and pancreatitis.GLP-1RAs are a possible alternative to other drugs for people with type 2 diabetes who have not been able to control their blood sugar levels adequately. Patients with cardiovascular disease or obesity

may also benefit from them. The possible advantages and hazards must be carefully weighed before beginning treatment, as with any medicine.

SGLT2 inhibitors

A class of drugs known as SGLT2 inhibitors works to lower blood sugar levels by decreasing the kidneys' ability to reabsorb glucose and increasing the excretion of glucose through the urine. Once daily, they are consumed orally.

By decreasing the amount of glucose reabsorbed by the kidneys and increasing glucose excretion in the urine, sodium-glucose cotransporter 2 (SGLT2) inhibitors are a class of drug used to treat type 2 diabetes. Since these drugs don't depend on insulin to function, they're a great choice for patients with type 2 diabetes who don't produce enough insulin or are insulinresistant. Here are some key points to know about SGLT2 inhibitors:

- Mechanism of Action: The proximal tubules of nephrons, where glucose reabsorption typically takes place in the kidneys, are blocked by SGLT2 inhibitors. Lower blood glucose levels result from blocking SGLT2, which causes glucose to be eliminated in the urine instead. By 30 to 50%, SGLT2 inhibitors lessen the absorption of glucose.
- Effectiveness: SGLT2 inhibitors have been demonstrated to decrease HbA1c (a marker of long-term blood glucose control), lower blood sugar levels, and encourage weight loss.
 Additionally, they are linked to lower blood pressure and a lower risk of cardiovascular disease.
- Side Effects: Both vaginal yeast infections and urinary tract infections are brought on by
 SGLT2 inhibitors. In particular for those with kidney illness or those taking specific

other drugs, dehydration, hypotension, and ketoacidosis are also risks. SGLT2 inhibitors, however, only occasionally cause negative side effects.

Canagliflozin, dapagliflozin, empagliflozin, ertugliflozin, and ipragliflozin are a few examples of SGLT2 inhibitors that are offered for sale.SGLT2 inhibitors are a generally safe and efficient class of medications treating type 2 diabetes. They function without the need for insulin and lower the risk of cardiovascular disease. Like all medications, they should only be taken as directed by a healthcare professional.

Insulin therapy

Insulin therapy may be required in those with type 2 diabetes that is more severe or poorly controlled. In order to administer insulin, a syringe or an insulin pump is typically used. Diabetes treatment known as insulin therapy uses insulin to help manage blood sugar levels. Diabetes is a condition when the body can't utilise insulin effectively or doesn't create enough of it. Blood sugar levels are controlled by the hormone insulin. Interruption of this mechanism might result in elevated blood sugar levels, which are harmful to the body. The insulin used in insulin therapy comes in a variety of forms. These consist of long-acting insulin, intermediate-acting insulin, short-acting insulin, and rapid-acting insulin. Depending on the person's unique requirements and type of diabetes, different types of insulin are utilized.

Blood sugar levels after meals are managed with rapid-acting insulin. It starts working after 15 minutes and can continue for up to four hours. Before meals, short-acting insulin, commonly referred to as normal insulin, is frequently administered to regulate blood sugar levels. Within 30 minutes, it begins to operate, and it can persist for up to six hours. Blood

sugar levels between meals are normally managed using intermediate-acting insulin. Beginning to work after a few hours, it can last up to 18 hours. Overnight blood sugar management often involves the administration of long-acting insulin. Starting to work can take several hours, and it can last up to 24 hours. Injections, insulin pens, and insulin pumps are just a few of the ways that insulin therapy can be administered. The most popular approach is injection, which entails injecting insulin subcutaneously (under the skin) with an insulin syringe or insulin pen. Insulin pumps are discreet devices worn on the body that continuously inject insulin through a catheter inserted under the skin. Blood sugar levels are kept within a target range via insulin therapy. Age, general health, and other variables may affect this range. For insulin therapy to be effective and to allow for any necessary treatment plan modifications, regular blood sugar monitoring is essential. Although it needs careful monitoring and supervision, insulin therapy can be a successful diabetes treatment. Diabetic patients should talk to their doctor about their alternatives before deciding whether to start insulin therapy. They will be able to decide which strategy suits their needs the best thanks to this.

It is crucial to remember that type 2 diabetes medication management should be customized to meet the unique requirements and preferences of each patient. Based on variables such blood sugar levels, age, and general health, working with a healthcare expert can assist choose the most suitable drug regimen. In order to get the best blood sugar control, it's also essential to adhere to the medication schedule exactly as instructed and monitor blood sugar levels often.

Sl	Drug class	Drug name	Mechanism of action	Reference
no				
1	α-	Acarbose, miglitol, voglibose	Inhibits intestinal	[48-53]
	Glucosidase		carbohydrate	
	inhibitors		absorption	
2	Bile acid	Colesevelam	Unknown,possibly	[48-53]
	sequestrant		stimulates of incretin	
			secretion	
	a 10 1			540. 703
3	Sulfonylureas	Glyburide/glibenclamide;	Glucose-independent	[48-53]
		glipizide;glimeperide	insulin secretion	
4	Meglitinides	Repaglinide;nateglinide	Glucose-independent	[48-53]
'	Wegninges	Tepugiinide,nategiinide	insulin secretion	[10 33]
			msum secretion	
5	Glucagon-	Exenatide; liraglutide	Enhances glucose-	[48-53]
	like peptide-1		dependent insulin	
	agonists		secretion, inhibits	
			glucagon secretion,	
			delays gastric	
			emptying, stimulates	
			satiety	

6	Dipeptidyl	Sitagliptin;saxagliptin;	Enhances glucose-	[48-53]
	peptidase-4	linagliptin	dependent insulin	
	inhibitors		secretion, inhibits of	
			glucagon secretion	
7	Amylin	Pramlintide	Stimulates satiety,	[48-53]
	analog		reduces glucagon	
			secretion	
8	Biguanide	Metformin	Inhibits hepatic	[48-53]
			glucose production	
9	Peroxisome	Pioglitazone;rosiglitazone	Reducesectopic lipid	[48-53]
	proliferator-		accumulation, increases	
	activated		adiponectin, reduces	
	receptor-γ		deleterious cytokine	
	agonists		secretion	

Table 2.

Listing of the drug classes currently approved in the United States, followed by the drug names and relevant references.

Emerging therapies

Even if there are numerous ways to manage type 2 diabetes symptoms, new medications give patients fresh reasons to be hopeful.Novel drugs that target the many pathways involved in glucose metabolism are among the new treatments for type 2 diabetes. These include dual SGLT1 and SGLT2 inhibitors, which prevent both glucose absorption in the gut and kidneys. They also contain PPAR agonists, which enhance insulin sensitivity and lessen inflammation.Gene therapy, which includes inserting genes into the body to alter insulin signaling pathways, is one of the other cutting-edge treatments for type 2 diabetes. In addition, stem cell therapy, which includes regenerating pancreatic cells that produce insulin using stem cells.Here are some emerging therapies for type 2 diabetes:

GLP-1 inflammation-promoting insulin Agonists: The effects of the hormone glucagon-like peptide-1 (GLP-1) in the body are imitated by a class of drugs known as GLP-1 agonists. By promoting insulin release, slowing digestion, and suppressing appetite, GLP-1 controls blood sugar levels. GLP-1 agonists can be used alone or in conjunction with other diabetic treatments, and they are given via injection.

The sodium-glucose cotransporter 2 (SGLT2) inhibitors are a class of drugs that function by preventing the kidneys from reabsorbing glucose, causing more glucose to be discharged in the urine. Weight loss may result from this reduction in blood sugar levels. SGLT2 inhibitors are oral drugs that can be used either on their own or in conjunction with other diabetes treatments. Agonists of incretin axiolytics The hormones glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) are both activated by both incretin agonists. This dual activation can enhance weight loss, blood sugar regulation, and other advantages. Injection-based dual insulin agonists are still in the clinical testing stages.

Cell-Based Therapies: In order to reestablish regular insulin production, cell-based therapies include transplanting insulin-producing cells into the pancreas. Research on this strategy is currently underway as it is still in its early phases of development.

Gene Therapy: In order to replace or fix faulty genes, genes are delivered to bodily cells during gene therapy. Researchers are looking on gene therapy for type 2 diabetes to enhance insulin production and control blood sugar levels. There are a number of other type 2 diabetes treatment options being researched in addition to these new medicines. These include of synthetic pancreas systems, immunological therapy, and microbiome-based treatments. Although additional investigation is required to establish the efficacy and safety of these novel medicines, they represent fresh hope for type 2 diabetes patients. They might eventually play a crucial role in this condition management.

Treatment strategies for managing complications of type 2 diabetes

To avoid and manage type 2 diabetes-related problems, regular monitoring of blood sugar levels and other health indicators is essential. These side effects include nephropathy, neuropathy, and cardiovascular disease. Medication, lifestyle changes, and surgical procedures may all be used as treatment solutions for type 2 diabetic complications.

For instance, aspirin and statins may be beneficial for persons with type 2 diabetes and cardiovascular disease. Additionally, people might gain from modifying their way of life through regular exercise and a heart-healthy diet. Drugs like gabapentin or pregabalin, as well as dietary changes, may help people with neuropathy. To control pain and guard against

nerve damage, do this. Medication like ACE inhibitors or ARBs, as well as lifestyle changes to control blood pressure and lessen proteinuria, may be helpful for those with nephropathy.

Chapter Six

Discussion

The discussion of diagnosis and treatment of type 2 diabetes involves high blood sugar levels caused by the body's ineffective use of insulin characterize type 2 diabetes, a chronic metabolic condition. A number of blood glucose level tests, including the fasting blood glucose test, oral glucose tolerance test, and glycated hemoglobin (HbA1c) test, are used to diagnose type 2 diabetes.

The goal of type 2 diabetes treatment is to manage blood glucose levels by dietary changes, medication, and insulin therapy. Maintaining a nutritious diet, getting regular exercise, and managing your weight are all examples of lifestyle modifications. Blood glucose levels can be lowered with the help of drugs like metformin, sulfonylureas, and DPP-4 inhibitors. In some circumstances, insulin therapy may be required to control blood sugar levels. In addition to these therapies, people with type 2 diabetes should have routine medical examinations and tests to keep track of their kidney function, eye health, blood pressure, cholesterol, and blood glucose levels. To create a personalized treatment plan that takes into account the particular requirements and difficulties of controlling type 2 diabetes, constant collaboration with healthcare specialists is essential.

Chapter Seven Conclusion

Type 2 diabetes requires prompt and effective treatment to improve outcomes and reduce the risk of complications.Long-term problems like heart disease, neurological damage, and kidney failure can be avoided with early diagnosis and treatment.Despite the fact that there is currently no cure for type 2 diabetes, early detection and effective treatment can help people control their symptoms, avoid complications, and generally lead better lives. Type 2 diabetics can live full and healthy lives with the correct care.

Chapter Eight
Reference

48 | Page @Daffodil

- 1. International Diabetes Foundation. Diabetes: facts and figures [accessed 2016 Mar 22]
- 2. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, Peters AL, Tsapas A, Wender R, Matthews DR. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach: update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care. 2015;38:140–149
- 3. Garber AJ, Abrahamson MJ, Barzilay JI, Blonde L, Bloomgarden ZT, Bush MA, Dagogo-Jack S, DeFronzo RA, Einhorn D, Fonseca VA, et al. Consensus statement by the american association of clinical endocrinologists and american college of endocrinology on the comprehensive type 2 diabetes management algorithm--2016 executive summary. Endocr Pract. 2016;22:84–113
- 4. National Diabetes Education Program (NDEP) Guiding principles for the care of people with or at risk for diabetes [accessed 2016 Jan]
- 5. Cappuccio FP, Cooper D, D'Elia L, Strazzullo P, Miller MA. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Eur Heart J. 2011;32:1484–1492.
- 6. McNeil J, Doucet É, Chaput JP. Inadequate sleep as a contributor to obesity and type 2 diabetes. Can J Diabetes. 2013;37:103–108.

- 7. Esposito K, Maiorino MI, Ciotola M, Di Palo C, Scognamiglio P, Gicchino M, Petrizzo M, Saccomanno F, Beneduce F, Ceriello A, et al. Effects of a Mediterranean-style diet on the need for antihyperglycemic drug therapy in patients with newly diagnosed type 2 diabetes: a randomized trial. Ann Intern Med. 2009;151:306–314
- 8. Faulconbridge LF, Wadden TA, Rubin RR, Wing RR, Walkup MP, Fabricatore AN, Coday M, Van Dorsten B, Mount DL, Ewing LJ. One-year changes in symptoms of depression and weight in overweight/obese individuals with type 2 diabetes in the Look AHEAD study. Obesity (Silver Spring) 2012;20:783–793
- 9. Williamson DA, Rejeski J, Lang W, Van Dorsten B, Fabricatore AN, Toledo K. Impact of a weight management program on health-related quality of life in overweight adults with type 2 diabetes. Arch Intern Med. 2009;169:163–171.
- 10. Franz MJ, Boucher JL, Green-Pastors J, Powers MA. Evidence-based nutrition practice guidelines for diabetes and scope and standards of practice. J Am Diet Assoc. 2008;108:S52–S58
- 11.. Andrews RC, Cooper AR, Montgomery AA, Norcross AJ, Peters TJ, Sharp DJ, Jackson N, Fitzsimons K, Bright J, Coulman K, et al. Diet or diet plus physical activity versus usual care in patients with newly diagnosed type 2 diabetes: the Early ACTID randomised controlled trial. Lancet. 2011;378:129–139.

- 12. Wheeler ML, Dunbar SA, Jaacks LM, Karmally W, Mayer-Davis EJ, Wylie-Rosett J, Yancy WS. Macronutrients, food groups, and eating patterns in the management of diabetes: a systematic review of the literature, 2010. Diabetes Care. 2012;35:434–445.
- 13. Evert AB, Boucher JL, Cypress M, Dunbar SA, Franz MJ, Mayer-Davis EJ, Neumiller JJ, Nwankwo R, Verdi CL, Urbanski P, et al. Nutrition therapy recommendations for the management of adults with diabetes. Diabetes Care. 2013;36:3821–3842.
- 14. Thomas D, Elliott EJ. Low glycaemic index, or low glycaemic load, diets for diabetes mellitus. Cochrane Database Syst Rev. 2009;(1):CD006296.
- 15. Franz MJ. Diabetes mellitus nutrition therapy: beyond the glycemic index. Arch Intern Med. 2012;172:1660–1661
- 16. Burger KN, Beulens JW, van der Schouw YT, Sluijs I, Spijkerman AM, Sluik D, Boeing H, Kaaks R, Teucher B, Dethlefsen C, et al. Dietary fiber, carbohydrate quality and quantity, and mortality risk of individuals with diabetes mellitus. PLoS One. 2012;7:e43127
- 17. Post RE, Mainous AG, King DE, Simpson KN. Dietary fiber for the treatment of type 2 diabetes mellitus: a meta-analysis. J Am Board Fam Med. 2012;25:16–23.
- 18. Sanz París A, Boj Carceller D, Melchor Lacleta I, Albero Gamboa R. Sugar and diabetes: international recommendations. Nutr Hosp. 2013;28 Suppl 4:72–80.
- 19. Stanhope KL, Schwarz JM, Keim NL, Griffen SC, Bremer AA, Graham JL, Hatcher B, Cox CL, Dyachenko A, Zhang W, et al. Consuming fructose-sweetened, not glucose-

sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans. J Clin Invest. 2009;119:1322–1334.

- 20. Serra-Majem L, Riobó Serván P, Belmonte Cortés S, Anadón Navarro A, Aranceta Bartrina J, Franco Vargas E, García-Closas R, Gómez-Candela C, Herrero Sancho E, La Vecchia C, et al. Chinchón declaration; decalogue on low- and no-calorie sweeteners (LNCS) Nutr Hosp. 2014;29:719–734.
- 21. Gannon MC, Nuttall FQ, Saeed A, Jordan K, Hoover H. An increase in dietary protein improves the blood glucose response in persons with type 2 diabetes. Am J Clin Nutr. 2003;78:734–741.
- 22. Wycherley TP, Noakes M, Clifton PM, Cleanthous X, Keogh JB, Brinkworth GD. A high-protein diet with resistance exercise training improves weight loss and body composition in overweight and obese patients with type 2 diabetes. Diabetes Care. 2010;33:969–976.
- 23.Melmed S, Polonsky KS, Larsen PR, Kronenberg HM. Disorders of Carbohydrate and Metabolism. Williams Textbook of Endocrinology 12th edition. New York: USA Press; 2011. pp. 1413–1414.
- 25. Vitolins MZ, Anderson AM, Delahanty L, Raynor H, Miller GD, Mobley C, Reeves R, Yamamoto M, Champagne C, Wing RR, et al. Action for Health in Diabetes (Look AHEAD) trial: baseline evaluation of selected nutrients and food group intake. J Am Diet Assoc. 2009;109:1367–1375.

- 26.Estruch R, Ros E, Salas-Salvadó J, Covas MI, Corella D, Arós F, Gómez-Gracia E, Ruiz-Gutiérrez V, Fiol M, Lapetra J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med. 2013;368:1279–1290.
- 27. Bosch J, Gerstein HC, Dagenais GR, Díaz R, Dyal L, Jung H, Maggiono AP, Probstfield J, Ramachandran A, Riddle MC, et al. n-3 fatty acids and cardiovascular outcomes in patients with dysglycemia. N Engl J Med. 2012;367:309–318.
- 28. Karlström BE, Järvi AE, Byberg L, Berglund LG, Vessby BO. Fatty fish in the diet of patients with type 2 diabetes: comparison of the metabolic effects of foods rich in n-3 and n-6 fatty acids. Am J Clin Nutr. 2011;94:26–33
- 29.Standards of Medical Care in Diabetes-2016: Summary of Revisions. Diabetes Care. 2016;39 Suppl 1:S4–S5.
- 30. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, Peters AL, Tsapas A, Wender R, Matthews DR. Management of hyperglycemia 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) Diabetes Care. 2012;35:1364–1379.
- 31. An H, He L. Current understanding of metformin effect on the control of hyperglycemia in diabetes. J Endocrinol. 2016;228:R97–106
- 32.Shin NR, Lee JC, Lee HY, Kim MS, Whon TW, Lee MS, Bae JW. An increase in the Akkermansia spp. population induced by metformin treatment improves glucose homeostasis in diet-induced obese mice. Gut. 2014;63:727–735.

33.Zhou G, Myers R, Li Y, Chen Y, Shen X, Fenyk-Melody J, Wu M, Ventre J, Doebber T, Fujii N, et al. Role of AMP-activated protein kinase in mechanism of metformin action. J Clin Invest. 2001;108:1167–1174.

34.Song R. Mechanism of Metformin: A Tale of Two Sites. Diabetes Care. 2016;39:187–189.

35. Alessi DR, Sakamoto K, Bayascas JR. LKB1-dependent signaling pathways. Annu Rev Biochem. 2006;75:137–163.

36. Salpeter SR, Greyber E, Pasternak GA, Salpeter EE. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. Cochrane Database Syst Rev. 2010;(4):CD002967.

37. Ferrannini E, DeFronzo RA. Impact of glucose-lowering drugs on cardiovascular disease in type 2 diabetes. Eur Heart J. 2015;36:2288–2296.

38.Lau DC, Teoh H. Impact of Current and Emerging Glucose-Lowering Drugs on Body Weight in Type 2 Diabetes. Can J Diabetes. 2015;39 Suppl 5:S148–S154.

39.Takahashi A, Nagashima K, Hamasaki A, Kuwamura N, Kawasaki Y, Ikeda H, Yamada Y, Inagaki N, Seino Y. Sulfonylurea and glinide reduce insulin content, functional expression of K(ATP) channels, and accelerate apoptotic beta-cell death in the chronic phase. Diabetes Res Clin Pract. 2007;77:343–350.

- 40. Maedler K, Carr RD, Bosco D, Zuellig RA, Berney T, Donath MY. Sulfonylurea induced beta-cell apoptosis in cultured human islets. J Clin Endocrinol Metab. 2005;90:501–506.
- 41.Kahn SE, Haffner SM, Heise MA, Herman WH, Holman RR, Jones NP, Kravitz BG, Lachin JM, O'Neill MC, Zinman B, et al. Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. N Engl J Med. 2006;355:2427–2443
- 42.Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33) UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998;352:837–853.
- 43. McIntosh B, Cameron C, Singh SR, Yu C, Ahuja T, Welton NJ, Dahl M. Second-line therapy in patients with type 2 diabetes inadequately controlled with metformin monotherapy: a systematic review and mixed-treatment comparison meta-analysis. Open Med. 2011;5:e35–e48.
- 44.Lim PC, Chong CP. What's next after metformin? focus on sulphonylurea: add-on or combination therapy. Pharm Pract (Granada) 2015;13:606.
- 45.Scott LJ. Repaglinide: a review of its use in type 2 diabetes mellitus. Drugs. 2012;72:249–272.
- 46.Gangji AS, Cukierman T, Gerstein HC, Goldsmith CH, Clase CM. A systematic review and meta-analysis of hypoglycemia and cardiovascular events: a comparison of glyburide with other secretagogues and with insulin. Diabetes Care. 2007;30:389–394.
- 47.Cryer PE, Davis SN, Shamoon H. Hypoglycemia in diabetes. Diabetes Care. 2003;26:1902–1912.

- 48.International Hypoglycaemia Study Group. Minimizing Hypoglycemia in Diabetes. Diabetes Care. 2015;38:1583–1591.
- 49. Ahren B, Schweizer A, Dejager S, Villhauer EB, Dunning BE, Foley JE. Mechanisms of action of the dipeptidyl peptidase-4 inhibitor vildagliptin in humans. *Diabetes Obes Metab* 13: 775–783, 2011
- 50.Baggio LL, Drucker DJ. Biology of Incretins: GLP-1 and GIP. *Gastroenterology* 132: 2131–2157, 2007
- 51. Fonseca V, Handelsman Y, Staels B. Colesevelam lowers glucose and lipid levels in type 2 diabetes: the clinical evidence. *Diabetes Obes Metab* 12: 384–392, 2010
- 52.Handelsman Y. Role of bile acid sequestrants in the treatment of type 2 diabetes. *Diabetes Care* 34, Suppl 2: S244–S250, 2011
- 53.Holst JJ, McGill MA. Potential new approaches to modifying intestinal GLP-1 secretion in patients with type 2 diabetes mellitus: focus on bile acid sequestrants. *Clin Drug Invest* 32: 1–14, 2012