

Market Research on Popular Anti-Diabetic Drugs



B. Pharm (Honours Project Report)

**A dissertation submitted to the Department of
Pharmacy, Daffodil International University for the
partial fulfillment of Bachelor of Pharmacy Degree**

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APPROVAL

This Project, **Market Research on Popular Anti-diabetic drugs** submitted by **Arafat Rahman** to the Department of Pharmacy, 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.

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I hereby declare that, this project report is done by us under the supervision of **Nazmus Saqueeb Lecturer**, Department of Pharmacy, Daffodil International University, partial fulfillment of the requirements for the degree of Bachelor of Pharmacy. I am declaring that this Project is my original work. I also declare that neither this project nor any part thereof has been submitted elsewhere for the award of Bachelor or any degree.

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Acknowledgement

I praise the name of almighty Allah who has given me power, patience and ability to complete my B.Pharm (Hons.) project work and the opportunity to study in this subject.

I am proud fully indebted to **Nazmus Saqueeb** Lecturer, Department of Pharmacy, Daffodil International University, for his ingenious supervision, valuable criticism, active encouragement, cordial operating along with unique direction of every Day work. I wish to convey my thanks and heartiest regard to him for providing important data and extended cooperation.

I feel proud to express my heartiest gratitude to my reverend teacher Assistant Professor, **Md. Arifur Rahman Fahim**, Head, Department of Pharmacy, Daffodil International University, for his mastermind direction, dexterous management, adept analysis, keen interest, optimistic counseling and unremitting backup.

I wish to convey my thanks and heartiest regard to Professor, **Dr. Md. Selim Reza**, Advisor, Department of Pharmacy, Daffodil International University.

It is also great pleasure for me to offer my indebtedness to all my respected teacher of Department of Pharmacy, Daffodil International University for extending their helping hands and affectionate attitude whenever I needed.

I would like extend my thanks to the office staff of Department of Pharmacy, Daffodil International University. My special heartfelt thanks extend to all of my classmates and friends for their supportive help. Cordial thanks to my parents and to all well wisher for their wholehearted inspiration and open-ended support throughout the period of the project of the research work.

Finally, I am deeply indebted to my father Md. Motiur Rahman and my mother Arjumand Baju for their endless moral support and sacrifice to complete this project work and again also grateful to Allah for this entire research work.

28May, 2015

Arafat Rahman



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ABBREVIATIONS

DM=Diabetes Mellitus

IDF= International Diabetes Federation

WHO= The World Health Organization

NIDDM=Non insulin-dependent diabetes mellitus

IDDM= Insulin-dependent diabetes mellitus

GDM= Gestational diabetes mellitus

LADA=Latent autoimmune diabetes of adults

MODY=Maturity-onset diabetes of the young

FPG= Fasting plasma glucose test

OGTT= Oral glucose tolerance test

ACEIs= Angiotensin converting enzyme inhibitors

ARBs= Angiotensin receptor blockers

EMA= European Medicines Agency

FDA= U.S. Food and Drug Administration

GLP=Glucagon-like peptide

TZDs=Thiazolidinediones

PPRE=Peroxisome proliferator responsive elements

RPG= Random plasma glucose

Abstract

Diabetes Mellitus is now a major public health problem in the developed as well as developing countries. Now a day it ranked seventh among the leading causes of death. Market research is a systematic, objective collection and analysis of data about the target market and competition. The purpose of market research of antidiabetic drug is to identify the most popular antidiabetic drugs. For this purpose, Different hospitals were visited and over 100 prescriptions for diabetic patients were collected. After proper investigation, it was found that **Comet/Comet XR 1gm /500mg** (Generic name : Metformin ; Manufacturer : Square Pharmaceuticals Ltd) , **Met**(Generic name : Metformin ; Manufacturer : Opsonin Pharma Ltd.) , **Amaryl** (Generic Name : Glimepiride ; Manufacturer : Sanofi-aventis Bangladesh Ltd) , **Diaplus** (Generic name: Glipizide ; Manufacturer : Pacific Pharmaceuticals ltd) , **Metfo** (Generic name : Metformin ; Manufacturer: Pacific Pharmaceuticals Ltd .) **Metfar** (Generic :Metformin ; Manufacturer : The white horse Pharma) , Novomix (Generic name : Medium acting Insulin , Manufacturer : Novo Nordisk Pharma (Private) Ltd.) , **Maxulin30/70** (Generic name : Medium acting Insulin ; Manufacturer : Incepta Pharmaceuticals Ltd) **Mixtard 30/70** (Generic name : Medium acting Insulin ; Manufacturer : Novo Nordisk Pharma (private) Ltd.) , **Comprid / Comprid XR** (Generic name: Gliclazide ; Manufacturer : Square Pharmaceuticals Ltd), **Diemerol 80** (Generic name : Gliclazide ; Manufacturer : Drug International Ltd) , **Dieta / Dieta-2** (Generic name : Glimepiride ; Manufacturer : Pacific Pharmaceuticals Ltd) , **Lijenta** (Generic name :Linagliptin ; Manufacturer : NIPRO JMI Pharma.) are most commonly used & are at top level for selling anti diabetic drugs in Bangladesh.

CHAPTER 1

(Introduction of Diabetes Mellitus)

1. 1 Diabetes Mellitus

Diabetes Mellitus is now a major public health problem in the developed countries as well as developing countries. Diabetes is a disorder of metabolism -- the way our bodies use digested food for growth and energy. Most of the food we eat is broken down into glucose, the form of sugar in the blood. Glucose is the main source of fuel for the body.

After digestion, glucose passes into the bloodstream, where it is used by cells for growth and energy. For glucose to get into cells, insulin must be present. Insulin is a hormone produced by the pancreas, a large gland behind the stomach.

When we eat, the pancreas automatically produces the right amount of insulin to move glucose from blood into our cells. In people with diabetes, however, the pancreas either produces little or no insulin, or the cells do not respond appropriately to the insulin that is produced. Glucose builds up in the blood, overflows into the urine, and passes out of the body. Thus, the body loses its main source of fuel even though the blood contains large amounts of sugar.

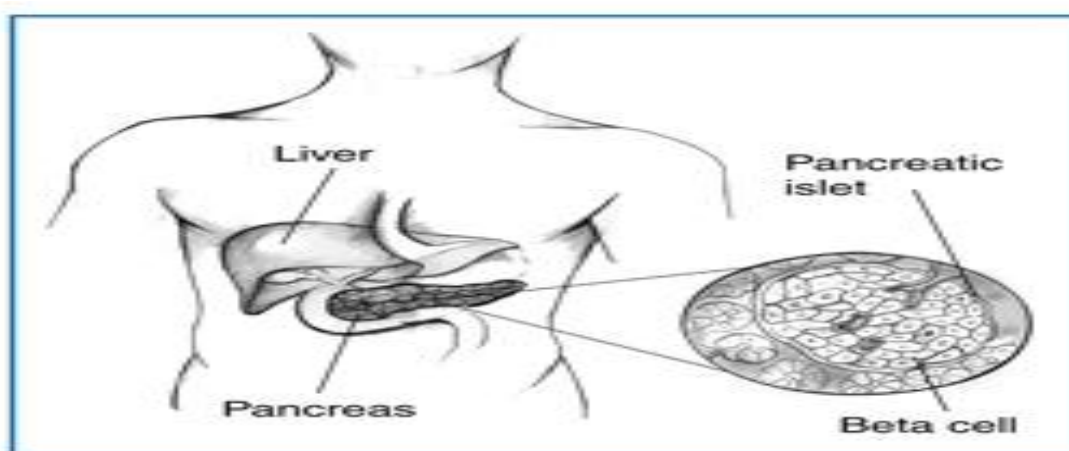


Fig1.1: How diabetes produced

1.2 History

Diabetes was one of the first diseases described, with an Egyptian manuscript from c. 1500 BCE mentioning "too great emptying of the urine. The first described cases are believed to be of type 1 diabetes. Indian physicians around the same time identified the disease and classified it *asmadhumeha* or "honey urine", noting the urine would attract ants. The term "diabetes" or "to pass through" was first used in 230 BCE by the Greek Appollonius of Memphis. The disease was

considered rare during the time of the Roman empire, with Galen commenting he had only seen two cases during his career. This is possibly due the diet and life-style of the ancient people, or because the clinical symptoms were observed during the advanced stage of the disease. Galen named the disease "diarrhea of the urine" (diarrhea urinosa). The earliest surviving work with a detailed reference to diabetes is that of Aretaeus of Cappadocia (2nd or early 3rd century CE). He described the symptoms and the course of the disease, which he attributed to the moisture and coldness, reflecting the beliefs of the "Pneumatic School". He hypothesized a correlation of diabetes with other diseases and he discussed differential diagnosis from the snakebite which also provokes excessive thirst. His work remained unknown in the West until the middle of the 16th century when, in 1552, the first Latin edition was published in Venice.

Type 1 and type 2 diabetes were identified as separate conditions for the first time by the Indian physicians Sushruta and Charaka in 400-500 CE with type 1 associated with youth and type 2 with being overweight. The term "mellitus" or "from honey" was added by the Briton John Rolle in the late 1700s to separate the condition from diabetes insipidus, which is also associated with frequent urination. Effective treatment was not developed until the early part of the 20th century, when Canadians Frederick Banting and Charles Herbert Best isolated and purified insulin in 1921 and 1922. This was followed by the development of the long-acting insulin NPH in the 1940s.

1.3 Prevalence of Diabetes Mellitus

The number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. Quantifying the prevalence of diabetes and the number of people affected by diabetes, now and in the future, is important to allow rational planning and allocation of resources.

As of 2013, 382 million people have diabetes worldwide. Type 2 makes up about 90% of the cases. This is equal to 8.3% of the adult population with equal rates in both women and men.

In 2014, the International Diabetes Federation (IDF) estimated that diabetes resulted in 4.9 million deaths. The World Health Organization (WHO) estimated that diabetes resulted in 1.5 million deaths in 2012, making it the 8th leading cause of death. The discrepancy between the two estimates is due to the fact that cardiovascular diseases are often the cause of death for individuals with diabetes; the IDF uses modeling to estimate the amount of deaths that could be

attributed to diabetes. More than 80% of diabetic deaths occur in low and middle-income countries

The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. The prevalence of diabetes is higher in men than women, but there are more women with diabetes than men. The urban population in developing countries is projected to double between 2000 and 2030. The most important demographic change to diabetes prevalence across the world appears to be the increase in the proportion of people >65 years of age .

The 10 countries estimated to have the highest numbers of people with diabetes in 2000 and 2030 are listed in table 1.1

Table 1.1: The list of countries with the highest numbers of estimated cases of diabetes for 2000 and 2030

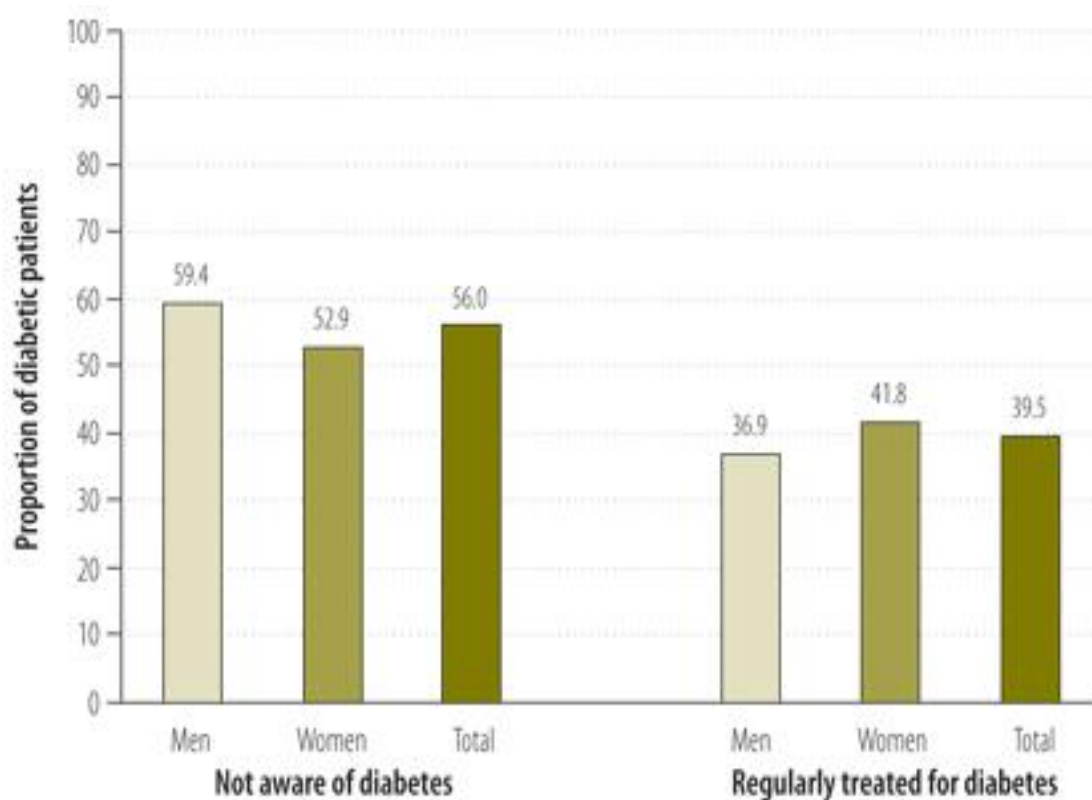
Ranking	2000		2030	
	Country	Diabetic people (millions)	Country	Diabetic people (millions)
1	India	31.7	India	79.4
2	China	20.8	China	42.3
3	U.S.	17.7	U.S.	30.3
4	Indonesia	8.4	Indonesia	21.3
5	Japan	6.8	Pakistan	13.9
6	Pakistan	5.2	Brazil	11.3
7	Russian Federation	4.6	Bangladesh	11.1
8	Brazil	4.6	Japan	8.9
9	Italy	4.3	Philippines	7.8
10	Bangladesh	3.2	Egypt	6.7

1.4 Prevalence of Diabetes Mellitus in Bangladesh

In Bangladesh, which had a population of 149.8 million in 2011, a recent meta-analysis showed that the prevalence of diabetes among adults had increased substantially, from 4% in 1995 to 2000 and 5% in 2001 to 2005 to 9% in 2006 to 2010.5 According to the International Diabetes Federation, the prevalence will be 13% by 2030.

All these figures indicate that the magnitude of health problems related to diabetes in Bangladesh has been increasing rapidly. It has been observed that the prevalence of diabetes was significantly higher in the urban than rural community of Bangladesh. So it is likely that the prevalence has been increasing with increasing urbanization. It has also been observed that the complications of diabetes were more frequent among the rural than urban and in poor than rich diabetic population.

Table 1.2: Diabetics aged 35 years or older who are not aware of their condition and receiving regular treatment, Bangladesh, 2011



1.5 Types of Diabetes Mellitus

Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced. There are three main types of diabetes mellitus :

- **Type 1 DM** results from the body's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is unknown.
- **Type 2 DM** begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The primary cause is excessive body weight and not enough exercise.
- **Gestational diabetes**, is the third main form and occurs when pregnant women without a previous history of diabetes develop a high blood glucose level.

1.5.1 Type 1 Diabetes Mellitus

Type 1 diabetes mellitus is characterized by loss of the insulin-producing beta cells of the islets of Langerhans in the pancreas, leading to insulin deficiency. This type can be further classified as immune-mediated or idiopathic. The majority of type 1 diabetes is of the immune-mediated nature, in which a T-cell-mediated autoimmune attack leads to the loss of beta cells and thus insulin. It causes approximately 10% of diabetes mellitus cases in North America and Europe. Most affected people are otherwise healthy and of a healthy weight when onset occurs. Sensitivity and responsiveness to insulin are usually normal, especially in the early stages. Type 1 diabetes can affect children or adults, but was traditionally termed "juvenile diabetes" because a majority of these diabetes cases were in children.

"Brittle" diabetes, also known as unstable diabetes or labile diabetes, is a term that was traditionally used to describe the dramatic and recurrent swings in glucose levels, often occurring for no apparent reason in insulin-dependent diabetes. This term, however, has no biologic basis and should not be used. Still, type 1 diabetes can be accompanied by irregular and unpredictable hyperglycemia, frequently with ketosis, and sometimes with serious hypoglycemia. Other complications include an impaired counter regulatory response to hypoglycemia, infection, gastroparesis (which leads to erratic absorption of dietary carbohydrates), and endocrinopathies (e.g., Addison's disease). These phenomena are believed to occur no more frequently than in 1% to 2% of persons with type 1 diabetes.

Type 1 diabetes is partly inherited, with multiple genes, including certain HLA genotypes, known to influence the risk of diabetes. In genetically susceptible people, the onset of diabetes can be triggered by one or more environmental factors, such as a viral infection or diet. There is some evidence that suggests an association between type 1 diabetes and Coxsackie B4 virus. Unlike type 2 diabetes, the onset of type 1 diabetes is unrelated to lifestyle.

1.5.2 Type 2 Diabetes Mellitus

Type 2 diabetes mellitus is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. The defective responsiveness of body tissues to insulin is believed to involve the insulin receptor. However, the specific defects are not known. Diabetes mellitus cases due to a known defect are classified separately. Type 2 diabetes is the most common type.

In the early stage of type 2, the predominant abnormality is reduced insulin sensitivity. At this stage, hyperglycemia can be reversed by a variety of measures and medications that improve insulin sensitivity or reduce glucose production by the liver.

Type 2 diabetes is due primarily to lifestyle factors and genetics. A number of lifestyle factors are known to be important to the development of type 2 diabetes, including obesity (defined by a body mass index of greater than thirty), lack of physical activity, poor diet, stress, and urbanization. Excess body fat is associated with 30% of cases in those of Chinese and Japanese descent, 60–80% of cases in those of European and African descent, and 100% of Pima Indians and Pacific Islanders. Those who are not obese often have a high waist–hip ratio.

Dietary factors also influence the risk of developing type 2 diabetes. Consumption of sugar-sweetened drinks in excess is associated with an increased risk. The type of fats in the diet is also important, with saturated fats and trans fatty acids increasing the risk and polyunsaturated and monounsaturated fat decreasing the risk. Eating lots of white rice appears to also play a role in increasing risk. A lack of exercise is believed to cause 7% of cases.

1.3 Table : A comparison between *Type 1 DM and Type 2 DM* are given bellow:

Comparison of type 1 and 2 diabetes		
Feature	Type 1 diabetes	Type 2 diabetes
Onset	Sudden	Gradual
Age at onset	Mostly children	Mostly in adults
Body size	Thin or normal	Often obese
Ketoacidosis	Common	Rare
Autoantibodies	Usually present	Absent
Endogenous insulin	Low or absent	Normal, or increased decreased
Concordance in identical twins	50%	90%
Prevalence	~10%	~90%

1.5.2.1 Effects of Hypoglycemia and Hyperglycemia

The symptoms of diabetes in the elderly can be masked, making the disease more difficult to diagnose. Warning signs like increased thirst, frequent urination and vision problems may be

overlooked because of the common affects of aging on the body. For example, a normal decrease in thirst due to age can offset the typical increased thirst experienced by people with diabetes. Changes such as mental confusion, incontinence and other health complications related to diabetes are more often the presenting symptoms.

Hypoglycemia (low blood sugar) and hyperglycemia (high blood sugar) are the two most common, yet threatening, diabetes-related emergencies experienced by the elderly. Unfortunately, they are commonly overlooked because cognitive impairment, such as dementia or other mental illness can make it difficult for the elderly to recognize the symptoms of diabetes-related emergencies.

Symptoms of Hypoglycemia: Hypoglycemia typically occurs when a senior parent or other elderly person with diabetes misses a meal or snack. Symptoms of hypoglycemia include:

- ❖ Cold, clammy skin
- ❖ Trembling or feelings of nervousness
- ❖ Lack of motor coordination and fatigue
- ❖ Irritability or confusion
- ❖ Blurred vision, headache or dizziness
- ❖ Nausea or stomach pain
- ❖ Fainting or unconsciousness

These are just some of the most common effects of hypoglycemia in the elderly. If your parent or another elderly person exhibits symptoms of hypoglycemia, immediately administer a form of sugar that can be easily absorbed, such as glucose tablets, juice or soda pop.

Symptoms of Hyperglycemia: Hyperglycemia (high blood sugar) is caused by too much food, reduced activity, missed insulin or even another illness and may develop over hours or days. The most common hyperglycemia symptoms are:

- ❖ Increased thirst and urination

- ❖ Sweet odor to the breath
- ❖ Fatigue
- ❖ Agitation and confusion
- ❖ High levels of ketones in the urine
- ❖ Weight loss

If anyone you know, especially an elderly person, is suffering from the effects of hypoglycemia or hyperglycemia, be sure to check with their physician or call for emergency care.

1.5.3 Gestational Diabetes Mellitus

Gestational diabetes mellitus (GDM) resembles type 2 diabetes in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness. It occurs in about 2–10% of all pregnancies and may improve or disappear after delivery. However, after pregnancy approximately 5–10% of women with gestational diabetes are found to have diabetes mellitus, most commonly type 2. Gestational diabetes is fully treatable, but requires careful medical supervision throughout the pregnancy. Management may include dietary changes, blood glucose monitoring, and in some cases insulin may be required.

Though it may be transient, untreated gestational diabetes can damage the health of the fetus or mother. Risks to the baby include macrosomia (high birth weight), congenital cardiac and central nervous system anomalies, and skeletal muscle malformations. Increased fetal insulin may inhibit fetal surfactant production and cause respiratory distress syndrome. Hyperbilirubinemia may result from red blood cell destruction. In severe cases, perinatal death may occur, most commonly as a result of poor placental perfusion due to vascular impairment. Labor induction may be indicated with decreased placental function. A Caesarean section may be performed if there is marked fetal distress or an increased risk of injury associated with macrosomia, such as shoulder dystocia.

1.5.4 Other Types

Prediabetes: It indicates a condition that occurs when a person's blood glucose levels are higher than normal but not high enough for a diagnosis of type 2 DM. Many people destined to develop type 2 DM spend many years in a state of prediabetes.

Latent autoimmune diabetes of adults: LADA is a condition in which type 1 DM develops in adults. Adults with LADA are frequently initially misdiagnosed as having type 2 DM, based on age rather than etiology.

Idiopathic diabetes: Some forms of type 1 diabetes have no known etiologies. Some of these patients have permanent insulinopenia and are prone to ketoacidosis, but have no evidence of autoimmunity. Although only a minority of patients with type 1 diabetes fall into this category, of those who do, most are of African or Asian ancestry. Individuals with this form of diabetes suffer from episodic ketoacidosis and exhibit varying degrees of insulin deficiency between episodes. This form of diabetes is strongly inherited, lacks immunological evidence for β -cell autoimmunity, and is not HLA associated. An absolute requirement for insulin replacement therapy in affected patients may come and go.

Other specific types of diabetes Genetic defects of the β -cell: Several forms of diabetes are associated with monogenetic defects in β -cell function. These forms of diabetes are frequently characterized by onset of hyperglycemia at an early age (generally before age 25 years). They are referred to as maturity-onset diabetes of the young (MODY) and are characterized by impaired insulin secretion with minimal or no defects in insulin action. They are inherited in an autosomal dominant pattern. Abnormalities at six genetic loci on different chromosomes have been identified to date. The most common form is associated with mutations on chromosome 12 in a hepatic transcription factor referred to as hepatocyte nuclear factor (HNF)-1 α . A second form is associated with mutations in the glucokinase gene on chromosome 7p and results in a defective glucokinase molecule. Glucokinase converts glucose to glucose-6-phosphate, the metabolism of which, in turn, stimulates insulin secretion by the β -cell. Thus, glucokinase serves as the “glucose sensor” for the β -cell. Because of defects in the glucokinase gene, increased plasma levels of glucose are necessary to elicit normal levels of insulin secretion. The less common forms result from mutations in other transcription factors, including HNF-4 α , HNF-1 β , insulin promoter factor (IPF)-1, and NeuroD1.

Point mutations in mitochondrial DNA have been found to be associated with diabetes mellitus and deafness. The most common mutation occurs at position 3243 in the tRNA leucine gene,

leading to an A-to-G transition. An identical lesion occurs in the MELAS syndrome (mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like syndrome); however, diabetes is not part of this syndrome, suggesting different phenotypic expressions of this genetic lesion.

Genetic defects in insulin action: There are unusual causes of diabetes that result from genetically determined abnormalities of insulin action. The metabolic abnormalities associated with mutations of the insulin receptor may range from hyperinsulinemia and modest hyperglycemia to severe diabetes. Some individuals with these mutations may have acanthosis nigricans. Women may be virilized and have enlarged, cystic ovaries. In the past, this syndrome was termed type A insulin resistance. Leprechaunism and the Rabson-Mendenhall syndrome are two pediatric syndromes that have mutations in the insulin receptor gene with subsequent alterations in insulin receptor function and extreme insulin resistance. The former has characteristic facial features and is usually fatal in infancy, while the latter is associated with abnormalities of teeth and nails and pineal gland hyperplasia.

Alterations in the structure and function of the insulin receptor cannot be demonstrated in patients with insulin-resistant lipotrophic diabetes. Therefore, it is assumed that the lesion(s) must reside in the postreceptor signal transduction pathways.

Infections: Certain viruses have been associated with β -cell destruction. Diabetes occurs in patients with congenital rubella, although most of these patients have HLA and immune markers characteristic of type 1 diabetes. In addition, coxsackievirus B, cytomegalovirus, adenovirus, and mumps have been implicated in inducing certain cases of the disease.

Uncommon forms of immune-mediated diabetes: In this category, there are two known conditions, and others are likely to occur. The stiff-man syndrome is an autoimmune disorder of the central nervous system characterized by stiffness of the axial muscles with painful spasms. Patients usually have high titers of the GAD autoantibodies, and approximately one-third will develop diabetes.

Anti-insulin receptor antibodies can cause diabetes by binding to the insulin receptor, thereby blocking the binding of insulin to its receptor in target tissues. However, in some cases, these antibodies can act as an insulin agonist after binding to the receptor and can thereby cause hypoglycemia. Anti-insulin receptor antibodies are occasionally found in patients with systemic lupus erythematosus and other autoimmune diseases. As in other states of extreme insulin resistance, patients with anti-insulin receptor antibodies often have acanthosis nigricans. In the past, this syndrome was termed type B insulin resistance.

1.6 Signs and symptoms

The classic symptoms of untreated diabetes are weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes. Several other signs and symptoms can mark the onset of diabetes, although they are not specific to the disease. In addition to the known ones above, they include blurry vision, headache, fatigue, slow healing of cuts, and itchy skin. Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. A number of skin rashes that can occur in diabetes are collectively known as diabetic dermadromes.

If you think that you have diabetes, visit your doctor immediately for a definite diagnosis. Common symptoms include the following:

- Frequent urination
- Excessive thirst
- Unexplained weight loss
- Extreme hunger
- Sudden vision changes
- Tingling or numbness in the hands or feet
- Feeling very tired much of the time
- Very dry skin
- Sores that are slow to heal
- More infections than usual

Some people may experience only a few symptoms that are listed above. About 50 percent of people with type 2 diabetes don't experience any symptoms and don't know they have the disease.

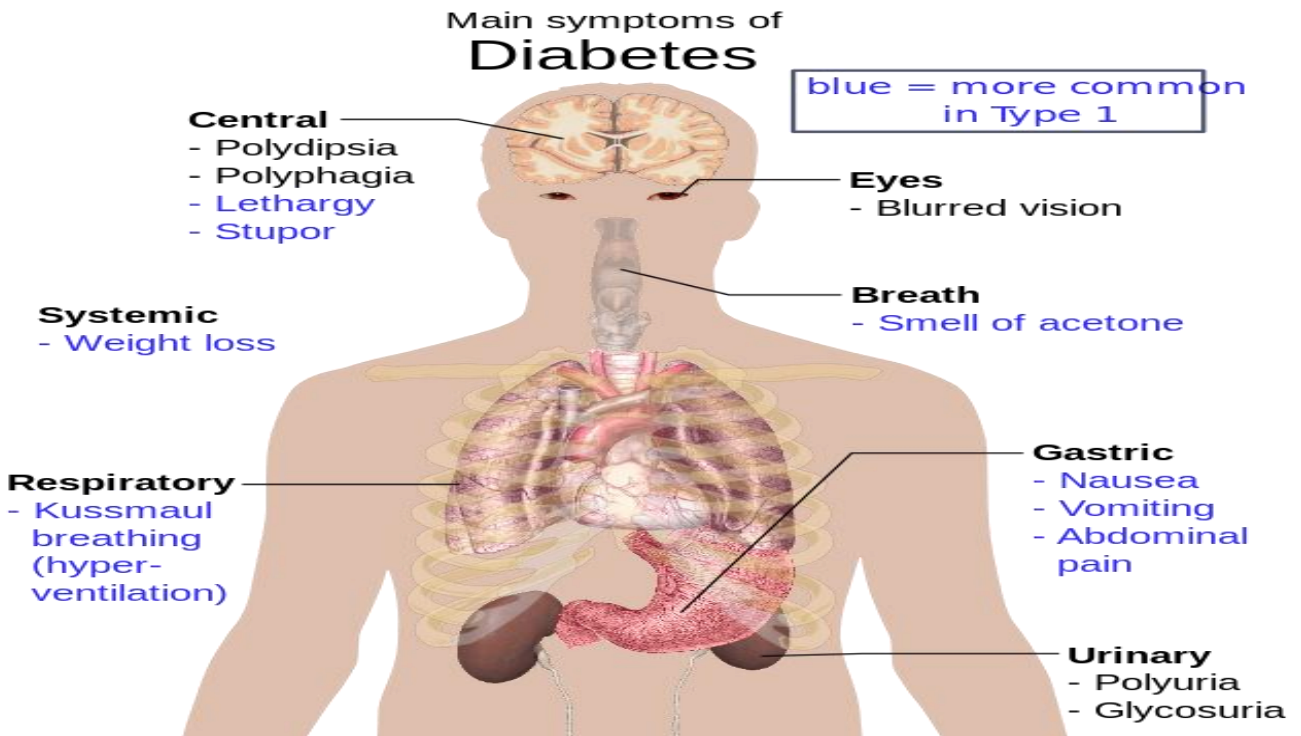


Fig1.2: Main symptoms of diabetes

1.7 Effects of Diabetes in our body

It can take work to get your diabetes under control, but the results are worth it. If you don't make the effort to get a handle on it, you could set yourself up for a host of complications. Diabetes can take a toll on nearly every organ in your body, including the:

- ❖ Heart and blood vessels
- ❖ Eyes
- ❖ Kidneys
- ❖ Nerves
- ❖ Gums and teeth

1.7.1 Heart and Blood Vessels

Heart disease and blood vessel disease are common problems for many people who don't have their diabetes under control. You're twice as likely to have heart problems and strokes as people

who don't have the condition. Blood vessel damage or nerve damage may also cause foot problems that, in rare cases, can lead to amputations. More than half the legs and feet removed are not lost because of an injury, but as a result of this disease.

Symptoms: You might not notice warning signs until you have a heart attack or stroke. Problems with large blood vessels in your legs can cause leg cramps, changes in skin color, and less sensation.

The good news: Many studies show that controlling your diabetes can help you avoid these problems, or stop them from getting worse if you have them.

1.7.2 Eyes

Diabetes is the leading cause of new vision loss in the U.S. in adults 20 to 74 years old. It can lead to eye problems, some of which can cause blindness if not treated:

- ❖ Glaucoma
- ❖ Cataracts
- ❖ Diabetic retinopathy

Symptoms: Vision problems, sight loss, or pain in your eye if you have diabetes-related eye disease.

The good news: Studies show that regular eye exams and timely treatment of these kinds of problems could prevent up to 90% of diabetes-related blindness.

1.7.3 Kidney Disease

Diabetes is the leading cause of kidney failure in adults in the U.S., accounting for almost half of new cases. Symptoms: You might not notice any problems with early diabetes-related kidney disease. In later stages it can make your legs and feet swell.

The good news: Drugs that lower blood pressure (even if you don't have high blood pressure) can cut your risk of kidney failure by 33%.

1.7.4 Effect on Nerves

The effect of diabetes on nerves can be very serious as the nerves are involved in so many of our body functions, from movement and digestion through to sex and reproduction.

The presence of nerve damage is commonly noticed by:

- ❖ Numbness or tingling in the hands or feet
- ❖ Lack of arousal in the penis or clitoris
- ❖ Excessive sweating or
- ❖ Diagnosis of delayed stomach emptying.

Treatments for neuropathy concentrate on reducing pain but medication such as blood pressure lowering drugs may also be prescribed to help prevent development of the condition.

1.7.5 Effect on Digestion

Diabetes can affect digestion in a number of ways. If diabetes has caused nerve damage, this can lead to nausea, constipation or diarrhea.

1.8 Pathophysiology

Insulin is the principal hormone that regulates the uptake of glucose from the blood into most cells of the body, especially liver, muscle, and adipose tissue. Therefore, deficiency of insulin or the insensitivity of its receptors plays a central role in all forms of diabetes mellitus.

The body obtains glucose from three main places: the intestinal absorption of food, the breakdown of glycogen, the storage form of glucose found in the liver, and gluconeogenesis, the generation of glucose from non-carbohydrate substrates in the body.^[1] Insulin plays a critical role in balancing glucose levels in the body. Insulin can inhibit the breakdown of glycogen or the process of gluconeogenesis, it can stimulate the transport of glucose into fat and muscle cells, and it can stimulate the storage of glucose in the form of glycogen. Insulin is released into the

blood by beta cells (β -cells), found in the islets of Langerhans in the pancreas, in response to rising levels of blood glucose, typically after eating. Insulin is used by about two-thirds of the body's cells to absorb glucose from the blood for use as fuel, for conversion to other needed molecules, or for storage. Lower glucose levels result in decreased insulin release from the beta cells and in the breakdown of glycogen to glucose. This process is mainly controlled by the hormone glucagon, which acts in the opposite manner to insulin.

If the amount of insulin available is insufficient, if cells respond poorly to the effects of insulin (insulin insensitivity or insulin resistance), or if the insulin itself is defective, then glucose will not be absorbed properly by the body cells that require it, and it will not be stored appropriately in the liver and muscles. The net effect is persistently high levels of blood glucose, poor protein synthesis, and other metabolic derangements, such as acidosis.

When the glucose concentration in the blood remains high over time, the kidneys will reach a threshold of reabsorption, and glucose will be excreted in the urine (glycosuria). This increases the osmotic pressure of the urine and inhibits reabsorption of water by the kidney, resulting in increased urine production (polyuria) and increased fluid loss. Lost blood volume will be replaced osmotically from water held in body cells and other body compartments, causing dehydration and increased thirst (polydipsia).

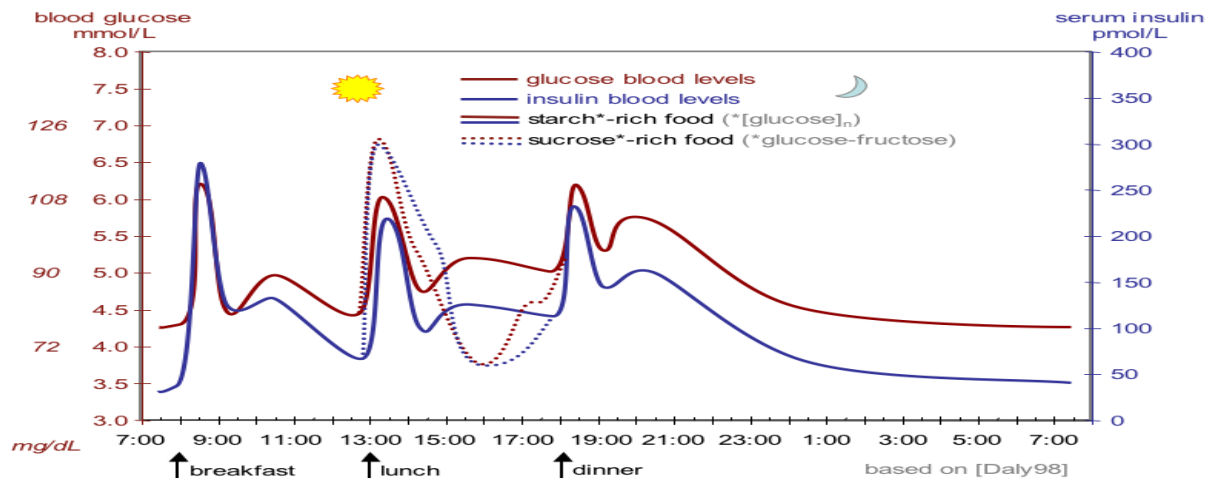


Fig 1.3: The fluctuation of blood sugar (red) and the sugar-lowering hormone insulin (blue) in humans during the course of a day with three meals — one of the effects of a sugar-rich vs a starch-rich meal is highlighted

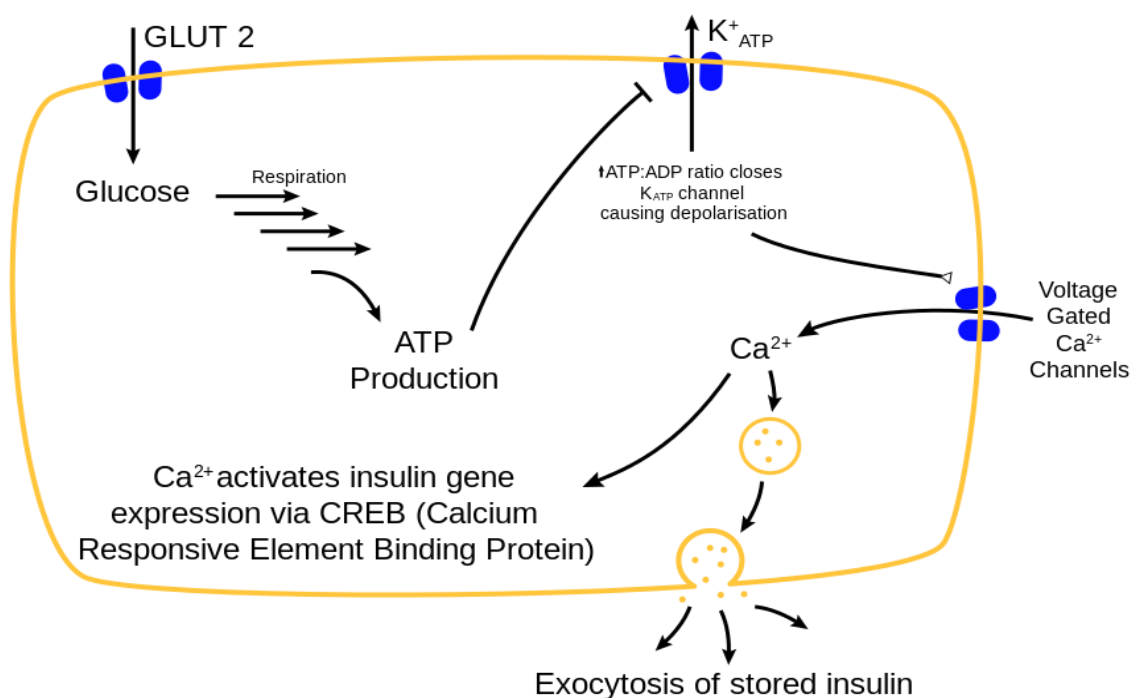


Fig1.4: Mechanism of insulin release in normal pancreatic beta cells — insulin production is more or less constant within the beta cells. Its release is triggered by food, chiefly food containing absorbable glucose.

1.9Diagnosis

Blood tests are used to diagnosis diabetes and prediabetes because early in the disease type 2 diabetes may have no symptoms. All diabetes blood tests involve drawing blood at a health care provider's office or commercial facility and sending the sample to a lab for analysis. Lab analysis of blood is needed to ensure test results are accurate. Glucose measuring devices used in a health care provider's office, such as finger-stick devices, are not accurate enough for diagnosis but may be used as a quick indicator of high blood glucose.

Testing enables health care providers to find and treat diabetes before complications occur and to find and treat prediabetes, which can delay or prevent type 2 diabetes from developing.

Any one of the following tests can be used for diagnosis:

- An **A1C** test, also called the hemoglobin A1c, HbA1c, or glycohemoglobin test
- A **fasting plasma glucose (FPG)** test

- **An oral glucose tolerance test (OGTT)**

Not all tests are recommended for diagnosing all types of diabetes. See the individual test descriptions for details.

Another blood test, the random plasma glucose (RPG) test, is sometimes used to diagnose diabetes during a regular health checkup. If the RPG measures 200 micrograms per deciliter or above, and the individual also shows symptoms of diabetes, then a health care provider may diagnose diabetes.

Symptoms of diabetes include

- increased urination
- increased thirst
- unexplained weight loss

Other symptoms can include fatigue, blurred vision, increased hunger, and sores that do not heal.

Any test used to diagnose diabetes requires confirmation with a second measurement unless clear symptoms of diabetes exist.

The following table provides the blood test levels for diagnosis of diabetes for nonpregnant adults and diagnosis of prediabetes.

Blood Test Levels for Diagnosis of Diabetes and Prediabetes			
	A1C (percent)	Fasting Plasma Glucose (mg/dL)	Oral Glucose Tolerance Test (mg/dL)
Diabetes	6.5 or above	126 or above	200 or above
Prediabetes	5.7 to 6.4	100 to 125	140 to 199
Normal	About 5	99 or below	139 or below

Definitions: mg = milligram, dL = deciliter
For all three tests, within the prediabetes range, the higher the test result, the greater the risk of diabetes.

Fig 1.5: Blood test level for Diagnosis of Diabetes and Prediabetes.

1.9.1 A1C Test

The A1C test is used to detect type 2 diabetes and prediabetes but is not recommended for diagnosis of type 1 diabetes or gestational diabetes. The A1C test is a blood test that reflects the average of a person's blood glucose levels over the past 3 months and does not show daily fluctuations. The A1C test is more convenient for patients than the traditional glucose tests because it does not require fasting and can be performed at any time of the day.

The A1C test result is reported as a percentage. The higher the percentage, the higher a person's blood glucose levels have been. A normal A1C level is below 5.7 percent.

An A1C of 5.7 to 6.4 percent indicates prediabetes. People diagnosed with prediabetes may be retested in 1 year. People with an A1C below 5.7 percent may still be at risk for diabetes, depending on the presence of other characteristics that put them at risk, also known as risk factors. People with an A1C above 6.0 percent should be considered at very high risk of developing diabetes. A level of 6.5 percent or above means a person has diabetes.

Laboratory analysis: When the A1C test is used for diagnosis, the blood sample must be sent to a laboratory using a method that is certified by the NGSP to ensure the results are standardized. Blood samples analyzed in a health care provider's office, known as point-of-care tests, are not standardized for diagnosing diabetes.

Abnormal results: The A1C test can be unreliable for diagnosing or monitoring diabetes in people with certain conditions known to interfere with the results. Interference should be suspected when A1C results seem very different from the results of a blood glucose test. People of African, Mediterranean, or Southeast Asian descent or people with family members with sickle cell anemia or a thalassemia are particularly at risk of interference.

False A1C test results may also occur in people with other problems that affect their blood or hemoglobin such as chronic kidney disease, liver disease, or anemia.

Changes in Diagnostic Testing: In the past, the A1C test was used to monitor blood glucose levels but not for diagnosis. The A1C test has now been standardized, and in 2009, an international expert committee recommended it be used for diagnosis of type 2 diabetes and prediabetes.

1.9.2 Fasting Plasma Glucose Test

The FPG test is used to detect diabetes and prediabetes. The FPG test has been the most common test used for diagnosing diabetes because it is more convenient than the OGTT and less expensive. The FPG test measures blood glucose in a person who has fasted for at least 8 hours and is most reliable when given in the morning.

People with a fasting glucose level of 100 to 125 mg/dL have impaired fasting glucose (IFG), or prediabetes. A level of 126 mg/dL or above, confirmed by repeating the test on another day, means a person has diabetes.

1.9.3 Oral Glucose Tolerance Test

The OGTT can be used to diagnose diabetes, prediabetes, and gestational diabetes. Research has shown that the OGTT is more sensitive than the FPG test, but it is less convenient to administer. When used to test for diabetes or prediabetes, the OGTT measures blood glucose after a person fasts for at least 8 hours and 2 hours after the person drinks a liquid containing 75 grams of glucose dissolved in water.

If the 2-hour blood glucose level is between 140 and 199 mg/dL, the person has a type of prediabetes called impaired glucose tolerance (IGT). If confirmed by a second test, a 2-hour glucose level of 200 mg/dL or above means a person has diabetes.

WHO diabetes diagnostic criteria				
Condition	2 hour glucose	Fasting glucose	HbA _{1c}	
Unit	mmol/l(mg/dl)	mmol/l(mg/dl)	mmol/mol	DCCT %

Normal	<7.8 (<140)	<6.1 (<110)	<42	<6.0
Impaired fasting glycaemia	<7.8 (<140)	$\geq 6.1 (\geq 110)$ & <7.0 (<126)	42-46	6.0–6.4
Impaired glucose tolerance	$\geq 7.8 (\geq 140)$	<7.0 (<126)	42-46	6.0–6.4
Diabetes mellitus	$\geq 11.1 (\geq 200)$	$\geq 7.0 (\geq 126)$	≥ 48	≥ 6.5

1.10 Prevention

There is no known preventive measure for type 1 diabetes. Type 2 diabetes can often be prevented by a person being a normal body weight, physical exercise, and following a healthful diet. Dietary changes known to be effective in helping to prevent diabetes include a diet rich in whole grains and fiber, and choosing good fats, such as polyunsaturated fats found in nuts, vegetable oils, and fish. Limiting sugary beverages and eating less red meat and other sources of saturated fat can also help in the prevention of diabetes. Active smoking is also associated with an increased risk of diabetes, so smoking cessation can be an important preventive measure as well.

1.11 Management

Diabetes mellitus is a chronic disease, for which there is no known cure except in very specific situations. Management concentrates on keeping blood sugar levels as close to normal ("euglycemia") as possible, without causing low blood sugar. This can usually be accomplished with a healthful diet, exercise, and use of appropriate medications (insulin in the case of type 1 diabetes; oral medications, as well as possibly insulin, in type 2 diabetes). Learning about the

disease and actively participating in the treatment is vital for people with diabetes, since the complications of diabetes are far less common and less severe in people who have well-managed blood sugar levels. The goal of treatment is an HbA_{1c} level of 6.5%, but should not be lower than that, and may be set higher. Attention is also paid to other health problems that may accelerate the deleterious effects of diabetes. These include smoking, elevated cholesterol levels, obesity, high blood pressure, and lack of regular exercise. Specialized footwear is widely used to reduce the risk of ulceration, or re-ulceration, in at-risk diabetic feet. Evidence for the efficacy of this remains equivocal, however.

1.11.1 Life style

People with diabetes can benefit from education about the disease and treatment, good nutrition to achieve a normal body weight, and sensible exercise, with the goal of keeping both short-term and long-term blood glucose levels within acceptable bounds. In addition, given the associated higher risks of cardiovascular disease, lifestyle modifications are recommended to control blood pressure.

1.11.2 Medications

Medications used to treat diabetes do so by lowering blood sugar levels. There are a number of different classes of anti-diabetic medications. Some are available by mouth, such as metformin, while others are only available by injection like insulin. Type 1 diabetes can only be treated with insulin, typically with a combinations of regular and NPH insulin, or synthetic insulin analogs.

Metformin is generally recommended as a first line treatment for type 2 diabetes, as there is good evidence that it decreases mortality. It works by decreasing production of glucose by the liver. Several other groups of drugs, mostly given by mouth, may also decrease blood sugar in type II DM. These include agents that increase insulin release, agents that decrease absorption of sugar from the intestines, and agents that make the body more sensitive to insulin. When insulin is used in type 2 diabetes, a long-acting formulation is usually added initially, while continuing oral medications. Doses of insulin are then increased to effect.

Since cardiovascular disease is a serious complication associated with diabetes, some recommend blood pressure levels below 120/80 mmHg; however, evidence only supports less than or equal to somewhere between 140/90 mmHg to 160/100 mmHg. Amongst medications that lower blood pressure, angiotensin converting enzyme inhibitors (ACEIs) improve outcomes in those with DM while the similar medications angiotensin receptor blockers (ARBs) do not. Aspirin is also recommended for patient with cardiovascular problems, however routine use of aspirin has not been found to improve outcomes in uncomplicated diabetes.

1.11.3 Pancreatic transplantation

A pancreas transplant is occasionally considered for people with type 1 diabetes who have severe complications of their disease, including end stage kidney disease requiring kidney transplantation.

1.11.4 Support

In countries using a general practitioner system, such as the United Kingdom, care may take place mainly outside hospitals, with hospital-based specialist care used only in case of complications, difficult blood sugar control, or research projects. In other circumstances, general practitioners and specialists share care in a team approach. Home tele health support can be an effective management technique.

1.12 Other animals

In animals, diabetes is most commonly encountered in dogs and cats. Middle-aged animals are most commonly affected. Female dogs are twice as likely to be affected as males, while according to some sources; male cats are also more prone than females. In both species, all breeds may be affected, but some small dog breeds are particularly likely to develop diabetes, such as Miniature Poodles. The symptoms may relate to fluid loss and polyuria, but the course may also be insidious. Diabetic animals are more prone to infections. The long-term complications recognized in humans are much rarer in animals. The principles of treatment (weight loss, oral antidiabetics, subcutaneous insulin) and management of emergencies (e.g. ketoacidosis) are similar to those in humans.

1.13 Research

Inhalable insulin has been developed. The original products were withdrawn due to side effects. Afrezza, under development by pharmaceuticals company MannKind Corporation, was approved by the FDA for general sale in June 2014.

An advantage to inhaled insulin is that it may be more convenient and easy to use.

CHAPTER 2

(Anti -Diabetic Drugs)

2.1 Anti diabetic drugs

Drugs used in diabetes treat diabetes mellitus by lowering glucose levels in the blood. With the exceptions of insulin, exenatide, liraglutide and pramlintide, all are administered orally and are thus also called oral hypoglycemic agents or oral antihyperglycemic agents. There are different classes of anti-diabetic drugs, and their selection depends on the nature of the diabetes, age and situation of the person, as well as other factors.

Diabetes mellitus type 1 is a disease caused by the lack of insulin. Insulin must be used in Type I, which must be injected.

Diabetes mellitus type 2 is a disease of insulin resistance by cells. Type 2 diabetes mellitus is the most common type of diabetes. Treatments include (1) agents that increase the amount of insulin secreted by the pancreas, (2) agents that increase the sensitivity of target organs to insulin, and (3) agents that decrease the rate at which glucose is absorbed from the gastrointestinal tract.

Several groups of drugs, mostly given by mouth, are effective in Type II, often in combination. The therapeutic combination in Type II may include insulin, not necessarily because oral agents have failed completely, but in search of a desired combination of effects. The great advantage of injected insulin in Type II is that a well-educated patient can adjust the dose, or even take additional doses, when blood glucose levels measured by the patient, usually with a simple meter, as needed by the measured amount of sugar in the blood.

Many anti-diabetes drugs are available as generics. These include:

- ❖ Sulfonylureas - glimepiride, glipizide, glyburide
- ❖ Biguanides - metformin
- ❖ Thiazolidinediones (Tzd) - pioglitazone, Actos generic
- ❖ Alpha-glucosidase inhibitors - Acarbose
- ❖ Meglitinides - nateglinide
- ❖ Combination of sulfonylureas plus metformin - known by generic names of the two drugs

No generics are available for dipeptidyl peptidase-4 inhibitors (Januvia, Onglyza) and other combinations.

2.2 Comparison

The following table compares some common anti-diabetic agents, generalizing classes, although there may be substantial variation in individual drugs of each class. When the table makes a comparison such as "lower risk" or "more convenient" the comparison is with the other drugs on the table.

Compound (medication)	Mechanism of action	Preferred patient type
<u>Sulfonylureas</u> (Daonil®, Glimel, Euglocon®=glibenclamide or Glyburide®; Diabinese=Chlorpropamide; Rastinon®=Tolbutamide; Melizide, Glucotrol®, Minidiab®=glipizide; Diamicron®=gliclazide)	increase Insulin secretion chronically	insulinopenic, lean
<u>Meglitinides</u> (Repaglinide =Prandin®, Nateglinide=Starlix™)	increase Insulin secretion acutely	hyperglycemic postprandially
<u>α - glucosidase inhibitors</u> (Voglibose; Acarbose = Glucobay®; miglitol)	decrease postprandial carbohydrate absorption	hyperglycemic postprandially
<u>Biguanidines</u> (Metformin=Glucophage®; Diabex®; Diaformin)	decrease hepatic glucose production decrease insulin resistance	overweight, with fasting hyperglycemia
<u>Thiazolidinediones, glitazones</u> (Actos®=pioglitazone; Avandia®=rosiglitazone, Rezulin® =troglitazone)	decrease insulin resistance decrease hepatic glucose production	insulin-resistant, overweight, dyslipidemic and renally impaired
<u>Insulin</u>	decrease hepatic glucose production increase cellular uptake of glucose	patients with a diabetic emergency newly diagnosed with significant hyperglycemia, or those with hyperglycemia despite maximal doses of oral agents

Most anti-diabetic agents are contraindicated in pregnancy, in which insulin is preferred.

2.3 Sensitizers: Insulin sensitizers address the core problem in Type II diabetes—insulin resistance.

2.3.1 Biguanides

Biguanides reduce hepatic glucose output and increase uptake of glucose by the periphery, including skeletal muscle. Although it must be used with caution in patients with impaired liver or kidney function, metformin, a biguanide, has become the most commonly used agent for type 2 diabetes in children and teenagers. Among common diabetic drugs, metformin is the only widely used oral drug that does not cause weight gain.

Typical reduction in glycated hemoglobin (A1C) values for metformin is 1.5–2.0%

- ❖ Metformin (Glucophage) may be the best choice for patients who also have heart failure, but it should be temporarily discontinued before any radiographic procedure involving intravenous iodinated contrast, as patients are at an increased risk of lactic acidosis.
- ❖ Phenformin (DBI) was used from 1960s through 1980s, but was withdrawn due to lactic acidosis risk.
- ❖ Buformin also was withdrawn due to lactic acidosis risk.

Metformin is usually the first-line medication used for treatment of type 2 diabetes. In general, it is prescribed at initial diagnosis in conjunction with exercise and weight loss, as opposed to in the past, where it was prescribed after diet and exercise had failed. There is an immediate release as well as an extended-release formulation, typically reserved for patients experiencing GI side-effects. It is also available in combination with other oral diabetic medications.

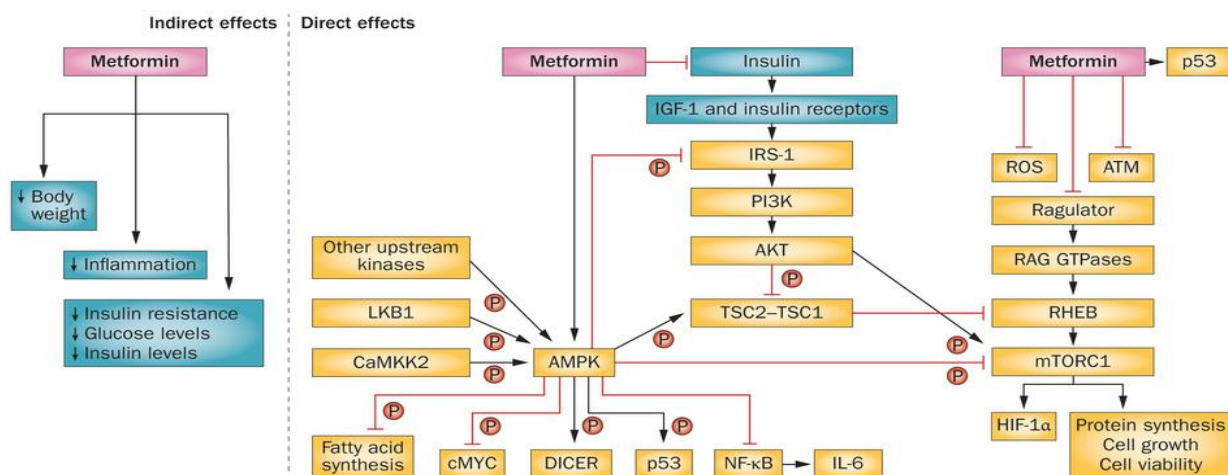


Fig2.1: How Metformin works.

Table 2.1: A list of commonly used Metformin drugs In Bangladesh

Brand Name	Dosages	Manufacturer	Price
BIGMET	Tablet	Renata Ltd	500mg=200tk / 850mg=250tk
COMET/COMET XR 1gm /500mg	Tablet	Square Pharmaceuticals Ltd	500mg × 100s pack=200tk / 1 gm × 30s pack= 210tk
DAOMIN	Tablet	ACME Laboratories Ltd	500mg × 100s pack=200 MRP
DIABEX	Tablet	Gaco Pharmaceuticals Ltd	500mg × 50s pack=50tk
FORMET	Tablet	Bio-pharma Laboratories Ltd	500mg × 100s pack=110 .00MRP
GLUCOMET/ GLUCOMET 500XR /750XR	Tablet	Aristopharma Ltd	500mg × 100s pack=200 MRP / 850 × 50s pack=150.0MRP
GLUNOR	Tablet	Eskayef Bangladesh Ltd	500mg × 50s pack=100MRP

Phenformin is an antidiabetic drug from the biguanide class. It was marketed as DBI by Ciba-Geigy, but was withdrawn from most markets in the late 1970s due to a high risk of lactic acidosis, which was fatal in 50% of cases.

Phenformin was discovered in 1957 by Ungar, Freedman and Seymour Shapiro, working for the US Vitamin Corporation. Clinical trials begun in 1958 showed it to be effective, but with gastrointestinal side effects. Phenformin, along with buformin and metformin, inhibits the growth and development of cancer.

When given orally for type 2 diabetes mellitus, the dosage is 200–400 mg, twice daily, for adults.

Buformin (1-butylbiguanide) is an oral antidiabetic drug of the biguanide class, chemically related to metformin and phenformin. Buformin was marketed by German pharmaceutical company Grünenthal as Silubin.

The daily dose of buformin is 150–300 mg by mouth.

2.3.2 Thiazolidinediones

Thiazolidinediones (TZDs), also known as "glitazones," bind to PPAR γ , a type of nuclear regulatory protein involved in transcription of genes regulating glucose and fat metabolism. These PPARs act on peroxysome proliferator responsive elements (PPRE). The PPREs influence insulin-sensitive genes, which enhance production of mRNAs of insulin-dependent enzymes. The final result is better use of glucose by the cells.

Typical reductions in glycated hemoglobin (A1C) values are 1.5–2.0%. Some examples are:

- ❖ rosiglitazone (Avandia): the European Medicines Agency recommended in September 2010 that it be suspended from the EU market due to elevated cardiovascular risks.
- ❖ pioglitazone (Actos)
- ❖ troglitazone (Rezulin): used in 1990s, withdrawn due to hepatitis and liver damage risk.

Multiple retrospective studies have resulted in a concern about rosiglitazone's safety, although it is established that the group, as a whole, has beneficial effects on diabetes. The greatest concern is an increase in the number of severe cardiac events in patients taking it. The ADOPT study showed that initial therapy with drugs of this type may prevent the progression of disease, as did the DREAM trial.

Concerns about the safety of rosiglitazone arose when a retrospective meta-analysis was published in the New England Journal of Medicine. There have been a significant number of publications since then, and a Food and Drug Administration panel voted, with some controversy, 20:3 that available studies "supported a signal of harm," but voted 22:1 to keep the drug on the market. The meta-analysis was not supported by an interim analysis of the trial designed to evaluate the issue, and several other reports have failed to conclude the controversy. This weak evidence for adverse effects has reduced the use of rosiglitazone, despite its important and sustained effects on glycemic control. Safety studies are continuing. In contrast, at least one

large prospective study, PROactive 05, has shown that pioglitazone may decrease the overall incidence of cardiac events in people with type 2 diabetes who have already had a heart attack.

Table 2.2 : A list of commonly used Pioglitazone group of drugs in Bangladesh

Brand Name	Dosages Form	Company Name	Price
ADPAS	Tablet	General Pharmaceuticals Ltd.	15mg × 30s pack= 240.00 MRP
DIAGLIT	Tablet	Beximco Pharmaceuticals Ltd.	30mg × 30s pack= 450.00 MRP
DIATAG	Tablet	ACI Ltd.	45mg × 30s pack= 450.00 MRP
PIOGLIN	Tablet	Renata Ltd	30mg × 10s pack=150.00MRP
GLUCOZON	Tablet	Aristopharma Ltd.	15mg × 30s pack= 210.00 MRP

Table 2.3: A list of commonly used Rosiglitazone group of drugs in Bangladesh:

Brand Name	Dosages Form	Company Name	Price
ROGLIT 4	Tablet	Pacific Pharmaceutical Ltd	4mg x 30s pack: 240.00 MRP
ROMEROL	Tablet	Drug International Ltd.	2mg x 50s pack: 250.00 MRP; 4mg x 30s pack: 240.00 MRP
ROSIT-2	Tablet	Delta Pharma Ltd.	2mg x 30s pack: 150.02 MRP
SENSULIN	Tablet	Square Pharmaceutical Ltd.	2mg x 30s pack: 150.00 MRP; 4mg x 30s pack:

			240.00 MRP
TAZONE-4	Tablet	Kemiko Pharmaceuticals Ltd.	4mg x 30s pack: 240.00 MRP

2.4 Secretagogues : Secretagogues are drugs that increase insulin output from the pancreas.

2.4.1 Sulfonylureas

Sulfonylureas were the first widely used oral anti-hyperglycaemic medications. They are insulin secretagogues, triggering insulin release by inhibiting the KATP channel of the pancreatic beta cells. Eight types of these pills have been marketed in North America, but not all remain available. The "second-generation" drugs are now more commonly used. They are more effective than first-generation drugs and have fewer side-effects. All may cause weight gain.

Sulfonylureas bind strongly to plasma proteins. Sulfonylureas are useful only in Type II diabetes, as they work by stimulating endogenous release of insulin. They work best with patients over 40 years old who have had diabetes mellitus for under ten years. They cannot be used with type I diabetes, or diabetes of pregnancy. They can be safely used with metformin or -glitazones. The primary side-effect is hypoglycemia.

Typical reductions in glycated hemoglobin (A1C) values for second-generation sulfonylureas are 1.0–2.0%.

First-generation agents

- ❖ tolbutamide (Orinase, Rastinon brand name)
- ❖ acetohexamide (Dymelor)
- ❖ tolazamide (Tolinase)
- ❖ chlorpropamide (Diabinese)

Second-generation agents

- ❖ glipizide (Glucotrol, Minidiab, Glibenese)
- ❖ glyburide or glibenclamide (Diabeta, Micronase, Glynase, Daonil, Euglycon)
- ❖ glimepiride (Amaryl)
- ❖ gliclazide (Uni Diamicron)
- ❖ glycopyramide
- ❖ gliquidone (Glurenorm)

Table 2.4: A list of commonly used Glibenclamide group of drugs In Bangladesh :

Brand name	Dosages Form	Company Name	Price
DAOSIN	Tablet	Gaco Pharmaceuticals Ltd	100s pack: 27.83 MRP
DIBENOL	Tablet	Square Pharmaceuticals Ltd	300s pack: 84.00 MRP
DICON	Tablet	Jayson Pharmaceuticals Ltd	100s pack: 28.00 MRP
GLUBAN	Tablet	Kemiko Pharmaceuticals Ltd	100s pack: 28.00 MRP
GLUCON	Tablet	Opsonin Pharma Limited	100s pack: 28.00 MRP

Table 2.5: A list of commonly used Gliclazide group of drugs In Bangladesh:

Brand Name	Dosages Form	Company Name	Price
ADMIRA MR	Tablet	Unimed & Unihealth Manufacturers Ltd	30spack: 180.00 MRP
COMPRID	Tablet	Square Pharmaceuticals Ltd	40s pack: 240.00 MRP
CONSUCON	Tablet	Incepta Pharmaceuticals Ltd.	50s pack: 300,00 MRP
DIAB	Tablet	Rephco Laboratories Ltd	50s pack: 300.00 MRP
DIAPRO	Tablet	Beximco Pharmaceuticals Ltd.	50s pack: 350.00 IP
DIMEROL-MR	Tablet	Drug International Ltd.	50s pack: 300.00 MRP

Table 2.6: A list of commonly used **Glimepiride** group of drugs In Bangladesh:

Brand Name	Dosages Name	Company Name	price
ADGLIM	Tablet	Unimed & Unihealth Manufacturers Ltd.	1mg x 30s pack: 90.00 MRP; 2mg x 30s pack: 150.00 MRP
AMARYL	Tablet	Sanofi-aventis Bangladesh Ltd	1mg x 30s pack: 184.20 MRP; 2mg x 30s pack: 360.00 MRP; 3mg x 30s pack: 465.00 MRP
CONDIA	Tablet	RAK Pharmaceuticals Pvt. Ltd	1mg x 30s pack: 90.00 MRP
DACTUS	Tablet	ACME Laboratories Ltd.	1mg x 50s pack: 150.00 MRP; 2mg x 40s pack: 200.00 MRP
DIALON	Tablet	Eskayef Bangladesh Ltd.	1mg x 50s pack: 125.00 MRP; 2mg x 30s pack: 120.00 MRP; 4mg x 20s pack: 120.00 MRP
DIARYL	Tablet	Beximco Pharmaceuticals Ltd.	1mg x 30s pack: 90.00 IP; 2mg x 30s pack: 150.00 IP; 2mg x 30s pack: 210.00 IP
DIETA	Tablet	Pacific Pharmaceuticals	1mg x 50s pack: 90.00 MRP; 2mg x 30s pack: 150.00 MRP; 4mg x 30s pack: 240.00 MRP

Table 2.7: A list of commonly used **Glipizide** group of drugs In Bangladesh

Brand Name	Dosages Form	Company Name	Price
ACTINE	Tablet	Aristopharma Ltd.	5mg x 50s pack: 200.00 MRP
DIACTIN	Tablet	Beximco Pharmaceuticals Ltd.	5mg x 100s pack: 150.00 IP
DIAPIZI	Tablet	Medimet Pharmaceuticals Ltd	2.5mg x 100s pack: 100.00 MRP
DIAPLUS	Tablet	Pacific Pharmaceuticals Ltd.	5mg x 50s pack: 100.00 MRP
GLIMEROL	Tablet	Drug International Ltd.	5mg x 100s pack: 150.00 MRP

2.5 Nonsulfonylurea secretagogues

2.5.1 Meglitinides

Meglitinides help the pancreas produce insulin and are often called "short-acting secretagogues." They act on the same potassium channels as sulfonylureas, but at a different binding site. By closing the potassium channels of the pancreatic beta cells, they open the calcium channels, thereby enhancing insulin secretion.

They are taken with or shortly before meals to boost the insulin response to each meal. If a meal is skipped, the medication is also skipped.

Typical reductions in glycated hemoglobin (A1C) values are 0.5–1.0%.

- repaglinide (Prandin, NovoNorm)
- nateglinide (Starlix)

Adverse reactions include weight gain and hypoglycemia.

Table 2.8: A list of commonly used **Nateglinide** group of drugs In Bangladesh:

Brand Name	Dosages Form	Company Name	Price
STARLIX	Tablet	Novartis (Bangladesh) Ltd	84s pack: 2155.44 MRP

Table 2.9: A list of commonly used **Repaglinide** group of drugs In Bangladesh:

Brand Name	Dosages Form	Company Name	Price
DIANORM	Tablet	Rephco Laboratories Ltd	1mg x 30s pack: 112.50 MRP
DIAREPA	Tablet	Techno Drugs	1mg x 30s pack: 274.80 MRP
GLIMET	Tablet	Drug International Ltd	1mg x 50s pack: 150.00 MRP
GLURETOR	Tablet	Pacific Pharmaceuticals Ltd	0.5mg x 30s pack: 84.00 MRP
SINGLIN	Tablet	Renata Ltd.	0.5mg x 100s pack: 200.00 MRP

2.6 Alpha-glucosidase inhibitors

Alpha-glucosidase inhibitors are oral anti-diabetic drugs used for diabetes mellitus type 2 that work by preventing the digestion of carbohydrates (such as starch and table sugar). Carbohydrates are normally converted into simple sugars (monosaccharides), which can be absorbed through the intestine. Hence, alpha-glucosidase inhibitors reduce the impact of carbohydrates on blood sugar.

Alpha-glucosidase inhibitors are "diabetes pills" but not technically hypoglycemic agents because they do not have a direct effect on insulin secretion or sensitivity. These agents slow the digestion of starch in the small intestine, so that glucose from the starch of a meal enters the

bloodstream more slowly, and can be matched more effectively by an impaired insulin response or sensitivity. These agents are effective by themselves only in the earliest stages of impaired glucose tolerance, but can be helpful in combination with other agents in type 2 diabetes.

Examples of alpha-glucosidase inhibitors include:

- ❖ Acarbose- Precose
- ❖ Miglitol - Glyset
- ❖ Voglibose

Even though the drugs have a similar mechanism of action, there are subtle differences between acarbose and miglitol. Acarbose is an oligosaccharide, whereas miglitol resembles a monosaccharide. Miglitol is fairly well absorbed by the body, as opposed to acarbose. Moreover, acarbose inhibits pancreatic alpha-amylase in addition to alpha-glucosidase.

2.6.1 Natural alpha glucosidase inhibitors

There are a large number of plants with Alpha-glucosidase inhibitor action.

For example, research has shown the culinary mushroom Maitake (*Grifola frondosa*) has a hypoglycemic effect. The reason Maitake lowers blood sugar is because the mushroom naturally contains an alpha glucosidase inhibitor. Another plant attracting a lot of attention is *Salacia oblonga*.

2.6.2 Role in clinical use

Alpha-glucosidase inhibitors are used to establish greater glycemic control over hyperglycemia in diabetes mellitus type 2, particularly with regard to postprandial hyperglycemia. They may be used as monotherapy in conjunction with an appropriate diabetic diet and exercise, or they may be used in conjunction with other anti-diabetic drugs.

Alpha-glucosidase inhibitors may also be useful in patients with diabetes mellitus type 1; however, this use has not been officially approved by the Food and Drug Administration.

2.6.3 Mechanism of action

Alpha-glucosidase inhibitors are saccharides that act as competitive inhibitors of enzymes needed to digest carbohydrates: specifically alpha-glucosidase enzymes in the brush border of

the small intestines. The membrane-bound intestinal alpha-glucosidases hydrolyze oligosaccharides, trisaccharides, and disaccharides to glucose and other monosaccharides in the small intestine.

Acarbose also blocks pancreatic alpha-amylase in addition to inhibiting membrane-bound alpha-glucosidases. Pancreatic alpha-amylase hydrolyzes complex starches to oligosaccharides in the lumen of the small intestine.

Inhibition of these enzyme systems reduces the rate of digestion of carbohydrates. Less glucose is absorbed because the carbohydrates are not broken down into glucose molecules. In diabetic patients, the short-term effect of these drugs therapies is to decrease current blood glucose levels: the long-term effect is a small reduction in hemoglobin A1c level

2.6.4 Dosing

Since alpha-glucosidase inhibitors are competitive inhibitors of the digestive enzymes, they must be taken at the start of main meals to have maximal effect. Their effects on blood sugar levels following meals will depend on the amount of complex carbohydrates in the meal.

These medications are rarely used in the United States because of the severity of their side-effects (flatulence and bloating). They are more commonly prescribed in Europe. They do have the potential to cause weight loss by lowering the amount of sugar metabolized.

Table 2.10: A list of commonly used **Acarbose** group of drugs in Bangladesh :

Brand Name	Dosages Form	Company Name	Price
ACARID	Tablet	White Horse Pharma	50mg x 30s pack: 300.00 MRP
SUGATROL	Tablet	Pacific Pharmaceuticals Ltd.	50mg x 30s pack: 300.00 MRP; 100mg x 30s pack: 450.00 MRP

2.7 Insulin

Insulin (from the Latin, insula meaning island) is a peptide hormone produced by beta cells in the pancreas. It regulates the metabolism of carbohydrates and fats by promoting the absorption of glucose from the blood to skeletal muscles and fat tissue and by causing fat to be stored rather than used for energy. Insulin also inhibits the production of glucose by the liver.

Insulin is usually given subcutaneously, either by injections or by an insulin pump. Research of other routes of administration is underway. In acute-care settings, insulin may also be given intravenously. In general, there are three types of insulin, characterized by the rate which they are metabolized by the body. They are rapid acting insulins, intermediate acting insulins and long acting insulins.

Examples of rapid acting insulins include

- ❖ Regular insulin (Humulin R, Novolin R)
- ❖ Insulin lispro (Humalog)
- ❖ Insulin aspart (Novolog)
- ❖ Insulin glulisine (Apidra)
- ❖ Prompt insulin zinc (Semilente, Slightly slower acting)

Examples of intermediate acting insulins include

- ❖ Isophane insulin, neutral protamine Hagedorn (NPH) (Humulin N, Novolin N)
- ❖ Insulin zinc (Lente)

Examples of long acting insulins include

- ❖ Extended insulin zinc insulin (Ultralente)
- ❖ Insulin glargine (Lantus)
- ❖ Insulin detemir (Levemir)

Table 2.11 : A list of commonly used Insulins in Bangladesh:

Brand Name	Drug Class	Dosages Form	Company Name	Price
ACTRAPID	Short Acting Insulin	Injection	Novo Nordisk/ Transcom	3ml (prefilled syringe) x 5s pack: 2720.00 MRP
HUMULIN R	Short Acting Insulin	Injection	Eli Lilly/Int. Agencies	100 i.u x 4ml

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			(Bd.)	vial: 266.88 MRP
INSUL R	Short Acting Insulin	Injection	Popular Pharmaceuticals Ltd.	40 i.u x 10ml vial: 195.00 MRP
INSULIN ACTRAPID HM	Short Acting Insulin	Injection	Novo Nordisk/ Transcom	40 i.u x 10ml vial: 232.00 MRP
LANTUS	Long Acting Insulin	Injection	Sanofi-aventis Bangladesh Ltd.	3ml (prefilled pen with injection device) x 5s pack: 5395.75 MRP
MAXSULIN 30/70	Medium Acting Insulin	Injection	Incepta Pharmaceuticals Ltd.	40 i.u x 10ml vial: 195.00 MRP
NOVOMIX 30	Medium Acting Insulin	Injection	Novo Nordisk/ Transcom	3ml (prefilled injection) x 5s pack: 3810.00 MRP
MIXTARD 50 Novolet	Medium Acting Insulin	Injection	Novo Nordisk/ Transcom	3ml (prefilled syringe) x 5s pack: 2720.00 MRP
INSULIN MIXTARD 50 HM	Medium Acting Insulin	Injection	Novo Nordisk/ Transcom	3ml cartidge x 5s pack: 1662.00 MRP
MAXSULIN R	Short Acting Insulin	Injection	Incepta Pharmaceuticals Ltd.	40 i.u x 10ml vial: 195.00 MRP; 100 i.u x 10ml vial: 415.00 MRP

2.8 Peptide analogs

2.8.1 Injectable Incretin mimetics

Incretins are insulin secretagogues. The two main candidate molecules that fulfill criteria for being an incretin are glucagon-like peptide-1 (GLP-1) and gastric inhibitory peptide (glucose-dependent insulintropic peptide, GIP). Both GLP-1 and GIP are rapidly inactivated by the enzyme dipeptidyl peptidase-4

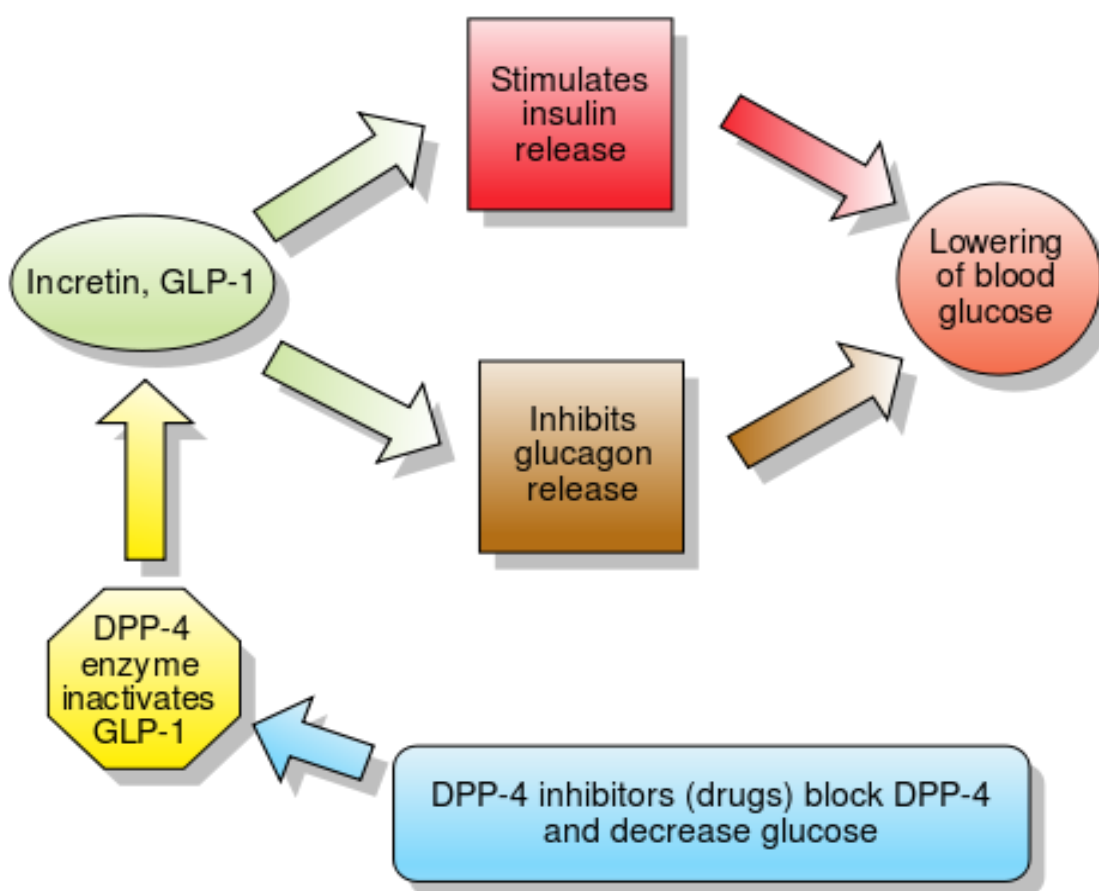


Fig 2.2: Mechanism of action of peptide analogs (Injectable Incretin mimetics)

2.8.2 Injectable Glucagon-like peptide analogs and agonists

Glucagon-like peptide (GLP) agonists bind to a membrane GLP receptor. As a consequence, insulin release from the pancreatic beta cells is increased. Endogenous GLP has a half-life of only a few minutes, thus an analogue of GLP would not be practical.

- Exenatide (also Exendin-4, marketed as Byetta) is the first GLP-1 agonist approved for the treatment of type 2 diabetes. Exenatide is not an analogue of GLP but rather a GLP agonist. Exenatide has only 53% homology with GLP, which increases its resistance to degradation by DPP-4 and extends its half-life. Typical reductions in A1C values are 0.5–1.0%.
- Liraglutide, a once-daily human analogue (97% homology), has been developed by Novo Nordisk under the brand name Victoza. The product was approved by the European Medicines Agency (EMA) on July 3, 2009, and by the U.S. Food and Drug Administration (FDA) on January 25, 2010.
- Taspoglutide is presently in Phase III clinical trials with Hoffman-La Roche.
- Lixisenatide (Lyxumia) Sanofi Aventis.

These agents may also cause a decrease in gastric motility, responsible for the common side-effect of nausea, and is probably the mechanism by which weight loss occurs.

2.8.3 Dipeptidyl Peptidase-4 Inhibitors

GLP-1 analogs resulted in weight loss and had more gastrointestinal side-effects, while in general DPP-4 inhibitors were weight-neutral and increased risk for infection and headache, but both classes appear to present an alternative to other antidiabetic drugs. However, weight gain and/or hypoglycaemia have been observed when DPP-4 inhibitors were used with sulfonylureas; effect on long-term health and morbidity rates are still unknown.

Dipeptidyl peptidase-4 (DPP-4) inhibitors increase blood concentration of the incretin GLP-1 by inhibiting its degradation by dipeptidyl peptidase-4.

Examples are:

- ❖ vildagliptin (Galvus) EU Approved 2008

- ❖ sitagliptin (Januvia) FDA approved Oct 2006
- ❖ saxagliptin (Onglyza) FDA Approved July 2009
- ❖ linagliptin (Tradjenta) FDA Approved May 2, 2011

2.8.4 Injectable Amylin analogues

Amylin agonist analogues slow gastric emptying and suppress glucagon. They have all the incretins actions except stimulation of insulin secretion. As of 2007, pramlintide is the only clinically available amylin analogue. Like insulin, it is administered by subcutaneous injection. The most frequent and severe adverse effect of pramlintide is nausea, which occurs mostly at the beginning of treatment and gradually reduces. Typical reductions in A1C values are 0.5–1.0%

2.9 Natural substances

2.9.1 Plants

A number of medicinal plants have been studied for the treatment of diabetes, however there is insufficient evidence to determine their effectiveness. Cinnamon has blood sugar-lowering properties; however whether or not it is useful for treating diabetes is unknown. Researchers from Australia's Swinburne University have found extracts from Australian Sandalwood and Indian Kino tree slows down two key enzymes in carbohydrate metabolism. Bioassay-directed fractionation techniques led to isolation of isoorientin as the main hypoglycemic component in *Gentiana olivieri*.

2.9.2 Element

While chromium supplements have no beneficial effect on healthy people, there might be an improvement in glucose metabolism in individuals with diabetes, although the evidence for this effect remains weak. Vanadyl sulfate, a salt of vanadium, is still in preliminary studies. There is tentative research that thiamine may prevent some diabetic complications however more research is needed.

CHAPTER 3

(Experimental)

3.1 Experimental

For this experiment, 100 prescriptions were collected. They are observed by the following ways:

Table no 3.1: Observation of prescriptions from different patients.

No. of Prescriptions	Patients	Brand name	Drug class/ Generic name
1	Male	Met	Biguanide (metformin)
2	Male	Diasulin	Medium acting insulin
3	Male	Comet XR 500	Biguanide (metformin)
4	Male	Galvurmet	Biguanide (metformin)
5	Female	Dieta 2	Glimepiride
6	Female	Lijenta	Linagliptin
7	Male	Janmet 500 , Lozide	Bigunide(metformin), Gliclazide
8	Female	Amaryl-2,	Glimepiride,
9	Male	Sacrin	Glimepiride
10	Male	Metfo	Biguanide(metformin)
11	Female	Compid-XR	Gliclazide
12	Male	Dieta	Glimepiride
13	Male	Sugamet	Metformin
14	Male	Dieta 2	Glimepiride
15	Female	Met	Metformin
16	Male	Metfo 500	Metformin
17	Male	Novomix	Insulin
18	Male	Met 500	Metformin
19	Female	Diasulin , Met	Insulin, Metformin
20	Male	Diasulin , Metfo	Insulin , Metformin
21	Male	Maxulin	Short acting Insulin
22	Female	Mixtard	Medium acting insulin
23	Male	Mixtard 30	Medium acting Insulin

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24	Male	Mixtard 30 , Met 850	Medium acting Insulin, Metformin
25	Male	Met500	Metformin
26	Female	Janmet	Metformin
27	Female	Mixtard , Met 850	Medium acting Insulin, Metformin
28	Male	Metfo 500	Metformin
29	Male	comprid	Gliclazide
30	Male	Glipita M 50/500	Metformin
31	Female	Comprid XR	Gliclazide
32	Male	Metfo , Amaryl	Metformin, Glimepiride
33	Male	Metfo	Metformin
34	Male	Diasulin , Metfo XR	Insulin , Metformin
35	Female	Consucon , Informet	Gliclazide, Metformin
36	Female	Consucon 80	Gliclazide
37	Male	Consucon MR , Informet	Gliclazide, Metformin
38	Female	Consucon MR , Informet	Gliclazide, Metformin
39	Male	Novomix , Lijenta	Medium acting insulin, Linagliptin
40	Male	Novomix, Comet , Lijenta	Medium acting insulin, Metformin, Linagliptin
41	Female	Diasulin MR 60	Medium acting Insulin
42	Male	Novomix	Medium acting insulin
43	Male	Novomix, Lijenta , comet 850 mg	Medium acting insulin, Linagliptin , metformin
44	Female	Novomix , dieta , Lijenta	Medium acting insulin, Glimeride, Linagliptin
45	Female	Met 850	Metformin
46	Female	Maxulin N	Medium acting Insulin

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47	Female	Maxulin N, Metfo	Medium acting Insulin , Metromin
48	Female	Novomix, Lijenta	Medium acting insulin, Linagliptin
49	Male	Met 850	Metformin
50	Male	Novomix, Comet 850 , Glipita 50	Medium acting insulin , Metformin
51	Female	Comet 850 , Amaryl	Metformin , Glimepiride
52	Female	Maxsulin 30/70	Medium acting Insulin
53	Male	Maxulin , Metfo	Medium acting Insulin , Metformin
54	Female	Diaplus	Glipizide
55	Female	Diaplus , Met	Glipizide , Metformin
56	Male	Novomix , Lijenta , Comet 850	Medium acting insulin, Linagliptin , Metformin
57	Male	Compid –XR , GlipitaM 50/500	Gliclazide,, Metformin
58	Female	Mixtard, comet 850	Medium acting Insulin, Metformin
59	Female	Maxulin 30/70	Medium acting insulin,
60	Male	Daomin , Maxulin 30/70	Metformin, Medium acting Insulin
61	Male	Dimerol 80 , Metfo 500	Gliclazide, Metfromin
62	Female	Dimerol 80 , Metfo 850	Gliclazide, Metfromin
63	Female	Dimerol 80 , Metfo 850	Gliclazide, Metfromin
64	Male	Diapro , Met 850	Gliclazide, Metfromin
65	Male	Diapro , Metfo	Gliclazide, Metfromin
66	Male	Diapro , Met 850	Gliclazide, Metfromin
67	Female	Mixtard , Met 850	Medium acting insulin, Metformin
68	Female	Mixtard , Metfo	Medium acting insulin, Metformin

Market Research on Popular Anti- Diabetic Drugs

69	Male	Maxulin 30/70	Medium acting insulin
70	Male	Mixtard	Medium acting insulin
71	Female	Dimerol 80 , Comet 850	Gliclazide, Metformin
72	Female	Mixtard , Metfo 850	Medium acting insulin, Metformin
73	Female	Mixtard 30 (u-100)	Medium acting insulin
74	Male	Comet XR, Lozide	Metformin, Gliclazide
75	Male	Mixterd 30/70 , Comet 850	Medium acting insulin, Metformin
76	Male	Janmet 500 , Maxulin 30/70	Metformin, Medium acting Insulin
77	Male	Metfo 500	Metformin
78	Male	Mixtard 30/70, Met	Medium acting insulin, Metformin
79	Female	Mixtard 30 PF.	Medium acting insulin
80	Female	Pride	Glimepiride
81	Male	Pride , Comet	Glimepiride, Metformin
82	Male	Amaryl , Met	Glimepiride , Metformin
83	Male	Comet , Lijenta	Metformin, Linagliptin
84	Male	Mixtard , Metfar	Medium acting insulin, Metformin
85	Male	Metfo	Metformin
86	Male	Mixtard30/70	Medium acting Insulin
87	Female	Dieta ,Comet500	Glimepiride, Metformin
88	Female	Comet 500	Metformin
89	Male	Diasulin , Metfar 500	Medium acting insulin, Metformin
90	Male	Mixtard 30/70 , Metfar	Medium acting insulin, Metformin
91	Male	Maxulin30/70 , Daomin	Medium acting insulin,

			Metformin
92	Male	Mixtard 30/70	Medium acting insulin
93	Male	Met	Metformin
94	Male	Comet XR	Metformin
95	Female	Compid –XR , GlipitaM 50/500	Gliclazide,, Metformin
96	Female	Novomix , Met	Medium acting insulin, Metformin
97	Female	Amaryl -2 , Glipita M 50/500	Glimepiride , Metformin
98	Male	Amaryl , Comet XR	Glimepiride , Metformin
99	Male	Novomix , Comet	Medium acting insulin, Metformin
100	Male	Maxulin 30/70 , Comet XR	Medium acting insulin, Metformin

From the above chart, we noticed that Metformin group(**Met, Metfo, Comet XR, Comet 500, Janmet, Compid / Compid XR etc**) of drugs are most commonly used in our country for the treatment of Diabetes mellitus. In case of Insulin preparations, Medium acting Insulin(**Novomix, Maxulin 30/70, Mixtard 30/70**) is mostly prescribed by the doctors.

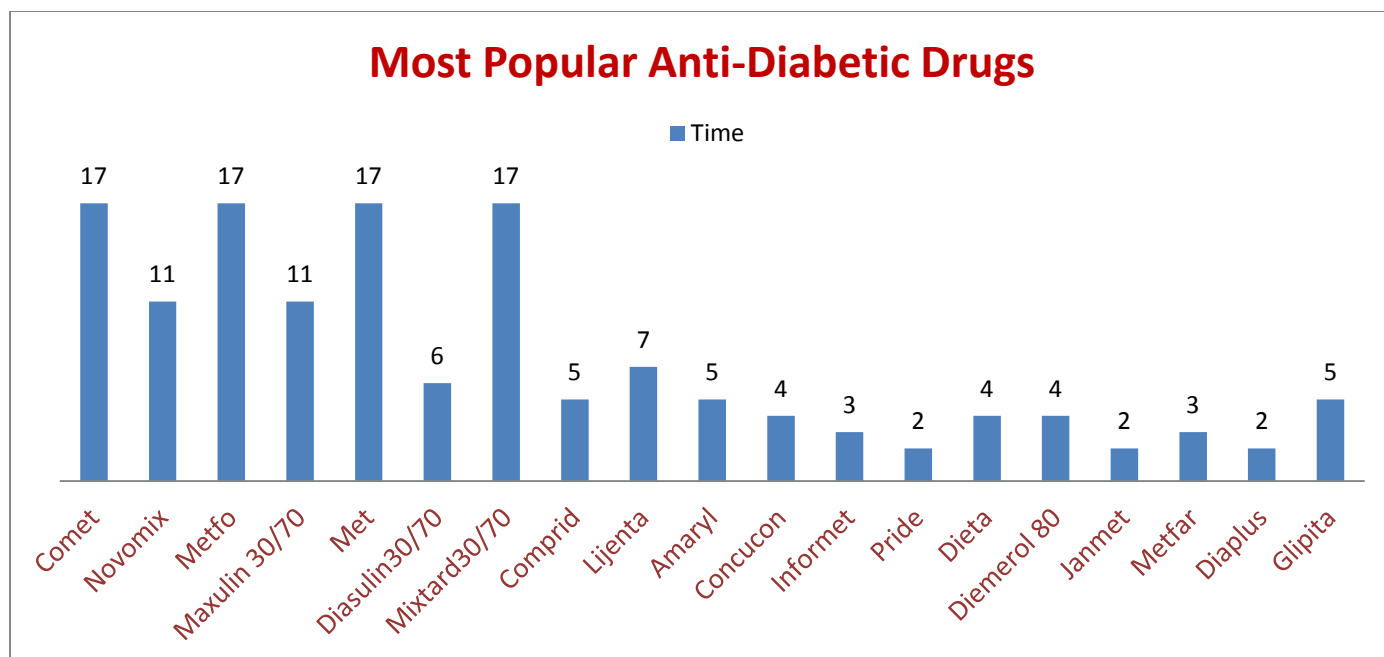
CHAPTER 4

(Results and Discussion)

Results and discussion

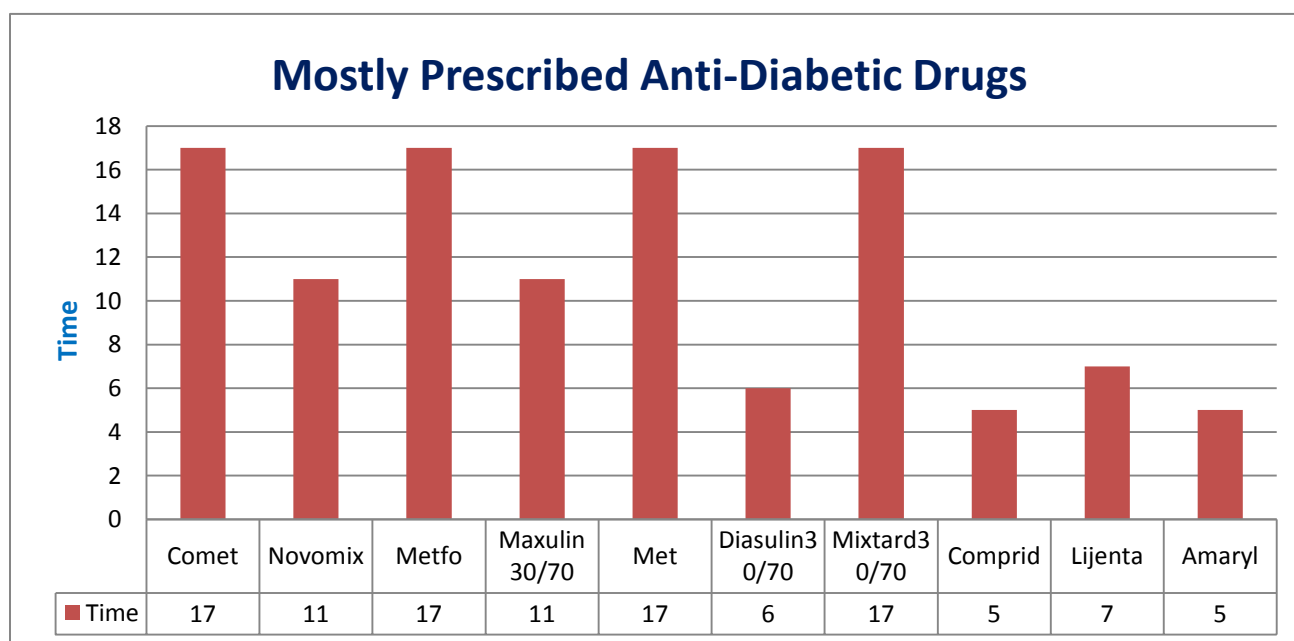
Different hospitals were visited and prescriptions were collected from these hospitals. Different prescriptions had different types of anti diabetes drugs. Some types of drugs were present in most of the prescriptions. 100 prescriptions were observed. Males are more sensitive to diabetes than female. Some drugs are the most popular (Such as Metformin group of drugs; Met, Metfo, Comet, Compride). The drugs were divided into different classes. The generic names of these drugs were also found out. Some companies are at high stage for selling the anti diabetes drugs. **Comet/Comet XR 1gm /500mg** (Generic name : Metformin ; Manufacturer : *Square Pharmaceuticals Ltd*) was prescribed 17 times , **Met** (Generic name : Metformin ; Manufacturer : *Opsonin Pharma Ltd.*) was prescribed 17 times , **Amaryl** (Generic Name : Glimepiride ; Manufacturer : *Sanofi-aventis Bangladesh Ltd*) was prescribed 5 times , **Diaplus** (Generic name: Glipizide ; Manufacturer : *Pacific Pharmaceuticals Ltd*)was prescribed 2 times, **Metfo** (Generic name : Metformin ; Manufacturer: *Pacific Pharmaceuticals Ltd* .) was prescribed 17 times. **Metfar** (Generic :Metformin ; Manufacturer : *The white horse Pharma*)was prescribed 3 times , **Novomix** (Generic name : Medium acting Insulin , Manufacturer : *Novo Nordisk Pharma (Private) Ltd.*) was prescribed 11 times , **Maxulin30/70** (Generic name : Medium acting Insulin ; Manufacturer : *Incepta Pharmaceuticals Ltd*) was prescribed 11 times, **Mixtard 30/70** (Generic name : Medium acting Insulin ; Manufacturer : *Novo Nordisk Pharma (private) Ltd.*)was prescribed 17 times , **Comprid / Comprid XR** (Generic name: Gliclazide ; Manufacturer : *Square Pharmaceuticals Ltd*) was prescribed 5 times , **Diemerol 80** (Generic name : Gliclazide ; Manufacturer : *Drug International Ltd*) was prescribed 4times , **Dieta / Dieta-2** (Generic name : Glimepiride ; Manufacturer : *Pacific Pharmaceuticals Ltd*) was prescribed 4 times , **Lijenta** (Generic name :Linagliptin ; Manufacturer : *NIPRO JMI Pharma.*) was prescribed 7 times , **Janmet** (*Generic name: Metformin; Manufacturer : ACME pharmaceuticals Ltd*) was prescribed 2 times , **Glipita M 50/500** (Generic : Metformin ; Manufacturer: *Beximco Pharmaceuticals Ltd*) was prescribed 5 times, **Pride** (Generic name: Glimepiride ; Manufacturer : *The white horse Pharma*)was prescribed 2 times , **Consucon** (Generic name: Gliclazide ; Manuafacturer : *Incepta Pharmaceuticals Ltd*) was prescribed 4 times, **Informet** (Generic name: Metformin ; Manufacturer :*Beximco pharmaceuticals Ltd*) was prescribed 3 times, **Diasulin 30/70** (Generic name: Medium acting Insulin ; Manufacturer : *ACI Ltd.*) was prescribed 6 times, are the highest selling anti diabetic drugs in Bangladesh .

A graphical overview of the most popular anti-diabetic drugs are given bellow :



So the most frequently prescribed drugs are **Comet / Comet XR 1gm / 500mg , Met 500/850 mg, Novomix (insulin), Mixtard 30/70 (insulin) , Maxulin 30.70 (insulin) ,Diasulin 30/70 (insulin) , Metfo , Lijenta, Combrid/ Combrid XR.**

A graphical overview of mostly prescribed drugs are given bellow:



CHAPTER 5

(Conclusion)

Conclusion

Diabetes Mellitus is now a major public health problem in the developed as well as developing countries. Now a day it ranked seventh among the leading causes of death. Although the actual cure of Diabetes mellitus is not possible at all, but we can maintain our blood sugar level by using different types of anti- diabetic drugs.

From the above experiment we found that, the most frequently prescribed drugs are **Comet / Comet XR 1gm / 500mg** , **Met 500/850 mg**, **Novomix (insulin)**, **Mixtard 30/70 (insulin)** , **Maxulin 30.70 (insulin)** ,**Diasulin 30/70 (insulin)** , **Metfo** , **Lijenta**, **Compid/ Compid XR**, are the highest selling anti-diabetic drugs in Bangladesh.

CHAPTER 6

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