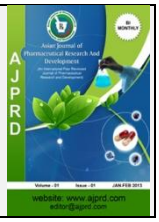
Available online on 15.04.2019 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

Open Access to Pharmaceutical and Medical Research



Open Access

Review Article

Review on Management Prevention and Treatment of Diabetes Mellitus

Sugave Ramling V, Nagoba Shivappa N*, Ningule Ganesh M, Patil Pooja Y

Channabasweshwar Pharmacy College, Latur, Maharashtra, India.

A B S T R A C T

Diabetes mellitus is the third leading cause of death (after heart disease and cancer) in many developed countries it affect about 6-8% of general population. The complication occurs in diabetes mellitus affect the eye, kidney and nervous system. Diabetes is major cause of blindness, renal failure and heart attack. And another is diabetes insipidus. India is the diabetes capital of the world. In India 50 million peoples suffering from type-2 diabetes. This country has major challenge & burden of economic condition to face. Because diabetes mellitus insulin therapy have higher cost & demand is more. But medical experts that timely detection and right management can go a long way in helping patients lead a normal life. That required to more demanding new drug that have need to develop more bioavailability and less toxicity of drugs. Oral hypoglycemic drugs these drugs lower blood glucose levels and are effective orally. Some natural antidiabetic drugs used in treatment of diabetes mellitus, gymnema, pterocarpus, Jamun, bitter guard etc.

Keywords:-Diabetes mellitus, oral hypoglycemic agent, Insulin, blood glucose levels bitter guard.

A R T I C L E I N F O: Received 24 Jan 2019; Review Completed 28 March 2019; Accepted 1April 2019; Available online 15 April 2019

Cite this article as:

Sugave Ramling V., Nagoba Shivappa N.*, Ningule Ganesh M., Patil Pooja Y. , Review On Management Prevention and Treatment of Diabetes Mellitus, Asian Journal of Pharmaceutical Research and Development. **2019; 7(2):56-62,**

DOI: http://dx.doi.org/10.22270/ajprd.v7i2.478

***Address for Correspondence:**

Dr. Nagoba Shivappa N, Associate Professor and Head,Department of Pharmaceutics, Channabasweshwar Pharmacy College,Kava Road, Latur-413512, Dist. Latur. (MS), India

INTRODUCTION

Diabetes mellitus is a common metabolic disorder characterized by increased abnormal blood glucose level (hyperglycemia) due to insufficient production of insulin by pancreatic cell.

In healthy person, the blood glucose level is (fasting 70-100 mg/dl)

In hypoglycemia (blood glucose < 45mg/dl) these time following symptoms occurs headache, confusion, anxiety and seizures.

In Diabetes mellitus Normal blood glucose levels are 82-110 mg/dl (fasting) and about 140-180 mg/dl (after meal).

The increase in blood glucose levels, in accordance with the values given below is indicating of diabetes:

Non fasting plasma glucose level ≥ 200 mg/dl, Fasting plasma glucose level ≥126 mg/dl, 2 hour post load glucose ≥ 200 mg/dl after consumption of a 75g oral glucose load.

Severity of the disease complications closely correlates to glycosylated hemoglobin (HbA1c) levels, a parameter frequently employed as an index for monitoring the disease and for therapy prognosis.

The symptoms of diabetes are the manifestation of metabolic disturbances. These include: polyphagia, polyurea, polydipsia, appearance of ketone bodies in breath and urine (ketonuria), glycosuria, ketoacidosis, weakness/ fatigue, xerosis, visual changes, skin and mucous membrane infections.

These metabolic disturbances are predisposing factors for cardiovascular, hepatic and renal complications. These complications are due to formation of Advanced Glycosylation End products conversion of glucose to fructose and sorbitol, microvascular and macro vascular damage, impaired immune response and impaired

detection due to neuropathy, increased plasma viscosity due to RBC modifications, failing lipid metabolism, etc.[1,2]

CLASSIFICATION OF DIABETES MELLITUS

There are two types of diabetes mellitus

Primary Or Idiopathic Diabetes Mellitus

It is most common with unknown cause of diabetes. It is further divided into three types
Type 1 diabetes (5-10%)
Type 2 diabetes (90-95%)
Gestational diabetes. (2% to 10%)

Secondary diabetes mellitus

In this type of diabetes mellitus have definite cause of hyperglycemia.
Chronic diseases
Hormonal disturbances
Steroid medications etc.

Type I diabetes mellitus (Insulin dependent diabetes mellitus IDDM)

In this type of diabetes mellitus body's failure of insulin production by β-cells of islets of Langerhans in pancreas cells, leading to insulin deficiency. This type can be further classified in as immune mediated or idiopathic. Most of type 1 diabetes is of immune mediated nature, in which a T-cell mediated autoimmune attack leads to loss of β-cells and thus insulin. Only about 10% of all people are suffer from this type of diabetes have called type 1 diabetes mellitus.

Type II diabetes mellitus (non insulin dependent diabetes mellitus)

In this type of diabetes mellitus 90% peoples are suffering from this type 2 disease. Individuals who have insulin resistance, diminished tissue sensitivity to insulin, impaired β-cell function (delayed or inadequate insulin release) and excessive or inappropriate glucagon secretion. Type II diabetes may occur at any age but more common in people older than the age of 40.

There are probably many different causes of this form of diabetes. Although the specific etiology is not known, autoimmune destruction of β-cells does not occur but it is attributed to typical genetic makeup, familial history, obesity and defect in insulin receptor.

Gestational diabetes

Diabetes can occur temporarily during pregnancy, and it occurs in 2% to 10% of all pregnancies. Significant hormonal changes during pregnancy can lead to blood sugar elevation in genetically predisposed individuals.

SECONDARY DIABETES

It is the type of diabetes mellitus and has a definite cause of hyperglycemia. Secondary diabetes refers to elevated blood sugar levels from another medical condition. Secondary diabetes may develop when the pancreatic tissue is responsible for the production of insulin is destroyed by disease, such as chronic pancreatitis (inflammation of the pancreas by toxins like excessive alcohol), trauma, or surgical removal of the pancreas etc.[3]

Epidemiology of Diabetes Mellitus

India is the diabetes capital of the world. In India 50 million peoples suffering from type-2 diabetes. This has major challenge to face. However, medical experts feel that timely detection and right management can go a long way in helping patients lead a normal life. Diabetes might be one of the most talked about diseases across the world and especially in India, but awareness about the same can well be estimated by the fact that India today has more people with type-2 diabetes (more than 50 million) than any other nation. With the country having the highest number of diabetic patients in the world, the sugar disease is posing an enormous health problem to our country today. Often known as the diabetes capital of the world, India has been witnessing an alarming rise in incidence of diabetes according to the International Journal of Diabetes in Developing Countries. According to a World Health Organization (WHO) fact sheet on diabetes, an estimated 3.4 million deaths are caused due to high blood sugar.

The WHO also estimates that 80 per cent of diabetes deaths occur in low and middle-income countries and projects that such deaths will double between 2016 and 2030. It has been further estimated that the global burden of type-2 diabetes is expected to increase to 438 million by 2030 from 285 million people (recorded in 2010). Similarly, for India this increase is estimated to be 58%, from 51 million people in 2010 to 87 million in 2030. But debates, discussions and deliberations aside, the fundamental thing is to know what exactly diabetes is diabetes. 4

As of 2016, 422 million people have diabetes worldwide, up from an estimated 382 million people in 2013 and from 108 million in 1980. Accounting for the shifting age structure of the global population, the prevalence of diabetes is 8.5% among adults, nearly double the rate of 4.7% in 1980. Type 2 makes up about 90% of the cases. Some data indicate rates are roughly equal in women and men, but male excess in diabetes has been found in many populations with higher type 2 incidence, possibly due to sex-related differences in insulin sensitivity, consequences of obesity and regional body fat deposition, and other contributing factors such as high blood pressure, tobacco smoking, and alcohol intake.

The WHO estimates that diabetes mellitus resulted in 1.5 million deaths in 2012, making it the 8th leading cause of death. However another 2.2 million deaths worldwide were attributable to high blood glucose and the increased risks of cardiovascular disease and other associated complications (e.g. kidney failure), which often lead to premature death and are often listed as the underlying cause of death certificates rather than diabetes. For example, in 2014, the International Diabetes Federation (IDF) estimated that diabetes resulted in 4.9 million deaths worldwide, using modeling to estimate the total number of deaths that could be directly or indirectly attributed to diabetes.

Diabetes mellitus occurs throughout the world but is more common (especially type 2) in more developed countries. The greatest increase in rates has however been seen in

low- and middle-income countries, where more than 80% of diabetic deaths occur. The fastest prevalence increase is expected to occur in Asia and Africa, where most people with diabetes will probably live in 2030. The increase in rates in developing countries follows the trend of urbanization and lifestyle changes, including increasingly sedentary lifestyles, less physically demanding work and the global nutrition transition, marked by increased intake of foods that are high energy-dense but nutrient-poor (often high in sugar and saturated fats, sometimes referred to as the "Western-style" diet). The global prevalence of diabetes might increase by 55% between 2013 and 2035.[5]

History of Diabetes Mellitus

Diabetes was one of the first diseases described, with an Egyptian manuscript from c. 1500 BCE mentioning "too great emptying of the urine". The Ebers papyrus includes a recommendation for a drink to be taken in such cases. The first described cases are believed to be of type 1 diabetes. Indian physicians around the same time identified the disease and classified it as *madhumeha* 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 Apollonius 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 to the diet and lifestyle of the ancients, 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 1552, when 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.

Diabetes mellitus has been known since ancient times its treatments were known since the middle Ages, and the elucidation of its pathogenesis occurred mainly in the 20th century. Non-progressing Type II diabetics almost went undiagnosed. The discovery of the role of the pancreas in diabetes was made by Joseph Von Mering and Oskar Minkowski in 1889. They found that upon complete removal of the pancreas from dogs, the dogs exhibited all the signs and symptoms of diabetes and died shortly afterwards. In 1910, Sir Edward Albert Sharpey-Schafer of Edinburgh in Scotland suggested that diabetics lacked a single chemical which was normally produced by the pancreas. Name of this chemical was later proposed to be insulin (Himsworth, 1936). In 1921, Frederick Grant Banting and Charles Herbert Best repeated the work of Von Mering and Minkowski but went a step further and managed to show that they could reverse the induced diabetes in dogs by giving them an extract from the pancreatic islets of Langerhans of healthy dogs. Plant derived medications have also found immense use in the management of diabetes mellitus. Notes that there is a new trend in the world to turn to phytodrugs to avoid the adverse effects associated with conventional hypoglycemic agents. Many plant species have been used to treat life- threatening diseases including diabetes mellitus. A World Health Organization (WHO) study shows that 80% of the world population solely relies on medicinal plants for their primary health care needs. To date, the catalogue of antidiabetic medicinal plants is growing at a pleasantly high rate particularly in the African continent. Perhaps this is advised by the economic situation in African, which has driven African diabetics to seek cheaper treatment and management options. This overreliance on antidiabetic medicinal plants has probably invoked scientists to bioassay these plants in an effort to elucidate more hypoglycemic medicinal plants. The antidiabetic potential of some medicinal plants extracts has been demonstrated in human and animal models of type II diabetes. However, more detailed research on the antidiabetic plants is inevitable to ameliorate the concerns of in vivo safety and efficacy[5,6]

Etymology of Diabetes Mellitus

The terms "Diabetes" and “Mellitus” are derived from Greek. “Diabetes” denotes "a passer through; a siphon" whereas the "Mellitus" denotes "sweet". It is thought that the Greeks named it so due to the excessive amounts of urine produced by diabetics attracted flies and bees. The traditional way of diagnosing diabetes mellitus in ancient Chinese was by observing whether ants are attracted to a person's urine or not. In medieval ages, the European doctors tested for diabetes by tasting the urine themselves, a scene occasionally depicted in Gothic beliefs.[6]

MANAGEMENT AND PREVENTION OF DIABETES MELLITUS

- Diabetes mellitus prevented by advising peoples include nutrition, physical activity, therapy and meditation.
- The diagnosis of diabetes is frequently carried out by oral glucose tolerance test as per WHO criteria a person suffering from diabetes if his/her blood glucose level more than or above 126mg/dl.
- Physical Activity
- Weight Loss
- Reduce Smoking
- Drug Therapy is Prescribed When Necessary.

Structured education programmes. It is now considered standard care to offer people with diabetes education to help them manage their diabetes themselves on a day-to-day basis. This should be offered in a structured way and based upon theories of adult learning. Group education is

now invariably offered as it offers economic advantages over one-to-one education as well as peer support. Examples of such programmes include DAFNE (Dose Adjustment for Normal Eating) in type 1 diabetes and DESMOND (Diabetes Education for Self Management in the Ongoing and Newly Diagnosed) in type 2 diabetes.

DIET

- Diet is very important for diabetes mellitus patient, suggest healthy diet given. Eat regular meals based on starchy foods such as bread, pasta, potatoes, rice and cereals.
- Choose high-fiber varieties of these foods, for example, whole meal bread and whole meal cereals which have a lower glycaemic index.
- Try to cut down on fat, particularly saturated (animal) fats. Monounsaturated fats such as olive oil are preferred.
- Use less butter, margarine, cheese and eat fewer fatty meals.
- Choose low-fat dairy foods, for example, skimmed milk and low-fat yoghurt. Grill, steam or oven bake instead of frying or cooking with oil or other fats.
- Try to eat at least five portions of fruit and vegetables every day. This provides vitamins and fiber as well as helping to balance the overall diet.
- Cut down on sugar and sugary foods. Sugar can still be used as an ingredient in foods and baking as part of a healthy diet. Use sugar-free, low-sugar or diet squashes and fizzy drinks, as sugary drinks cause blood glucose levels to rise quickly.
- Use less salt as high intake can raise blood pressure. Food can be flavored with herbs and spices instead of salt.
- Drink alcohol in moderation. Two units/day for a woman and three for a man. A small glass of wine or half a pint of normal strength beer is one unit. Never drink on an empty stomach as alcohol can exacerbate hypoglycemia.

Carbohydrates and Sweeteners

The blood glucose level is closely affected by carbohydrate intake. Previous guidance for people with diabetes recommended eating about the same amount of carbohydrate at approximately the same time each day and generally advised & restriction of carbohydrates**.** A number of people for this advice, Examples of carbohydrates with a low glycaemic index include beans, pulses and starchy foods like whole meal pasta and wholegrain bread. Total carbohydrate consumption should not exceed 45–60% of energy intake, with monounsaturated fat and carbohydrate combined making up 60–70% of energy intake. Sucrose or 'sugar' may be included in the diet, according to the new guidance, but sucrose should account for no more than 10% of total energy and should be spaced throughout the day, rather than being consumed all in one go. Sugar alcohols, for example, sorbitol, maltitol and xylitol, often used as sugar substitutes in diabetic foods, are expensive and may cause diarrhea. They are therefore considered to confer little advantage over sucrose. Non-nutritive or intense sweeteners such as aspartame, saccharin, acesulphame K, cyclamate and sucralose may be useful, especially for those who are overweight.

Alcohol:

Must be restricted to the same maximum weekly quantities as for the general population, that is, 14 units (women) and 21 units (men), with 1–2 alcohol-free days per week. In these quantities, alcohol has cardio protective effects.

Fats:

Since obesity is a major problem in type 2 diabetes and fats contain more than twice the energy content per unit mass than either carbohydrate or protein, consumption of fats should be limited. Monounsaturated fats have a lower atherogenic potential and are therefore recommended as the main source of dietary fat. Intake of fat should be less than 35% of total energy consumption, with saturated and trans- unsaturated fats accounting for less than 10% of energy intake and monounsaturated fats providing 10–20%. Examples of monounsaturated fats are olive oil and rapeseed (also known as canola) oil. Saturated fats are chiefly of animal origin, for example, beef, pork, lamb, whole milk products with some found in plants, for example, cocoa butter, coconut oil and palm oil. Trans-unsaturated fats are found in hydrogenated vegetable oils and hard margarines. N-6 polyunsaturated fats such as cornflower, sunflower, safflower,

Soyabean oil and seed oils should account for less than 10% of energy intake, and n-3 polyunsaturated fats (fish oils) should be eaten as fish, rather than fish oil supplements, once or twice a week.

Protein:

The protein for adults without nephropathy, protein intake is recommended as less than 1 g/kg of body weight, equivalent to about 10–20% of total energy intake. For those with nephropathy, protein intake may need to be further restricted, but this requires expert dietetic advice and supervision.

Fibre:

There is no quantitative dietary recommendation for fibre intake. Dietary fibre has useful properties in that it is physically bulky, and it delays the digestion and absorption of complex carbohydrates, thereby minimising hyperglycemia. For the average person with type 2 diabetes, 15 g of soluble fiber from fruit, vegetables or pulses is likely to produce a 10% improvement in fasting blood glucose, gyrated hemoglobin and low-density lipoprotein cholesterol (LDL-C). Insoluble fibre from cereals, whole meal bread, rice and pasta has no direct effect on glycemia; **Salt** Sodium chloride should be limited to a maximum of 6 g/day. A reduction in salt intake from 12 to 6 g/day has been shown to produce a reduction in systolic blood pressure of 5 mmHg and a reduction of 2–3 mmHg in diastolic pressure.

Obesity Management in Type 2:

Diabetes Obesity management is a very important issue in type 2 diabetes owing to the insulin resistance which occurs as a consequence of excess adipose tissue. any loss of weight in those who are overweight or obese is of benefit in diabetes in that it is associated with an improvement in dyslipidaemia, hypertension and glycaemic control, bariatric surgery can lead to profound improvements. Recent studies have shown that

laparoscopic banding can induce remission of type 2 diabetes in 48% of individuals.

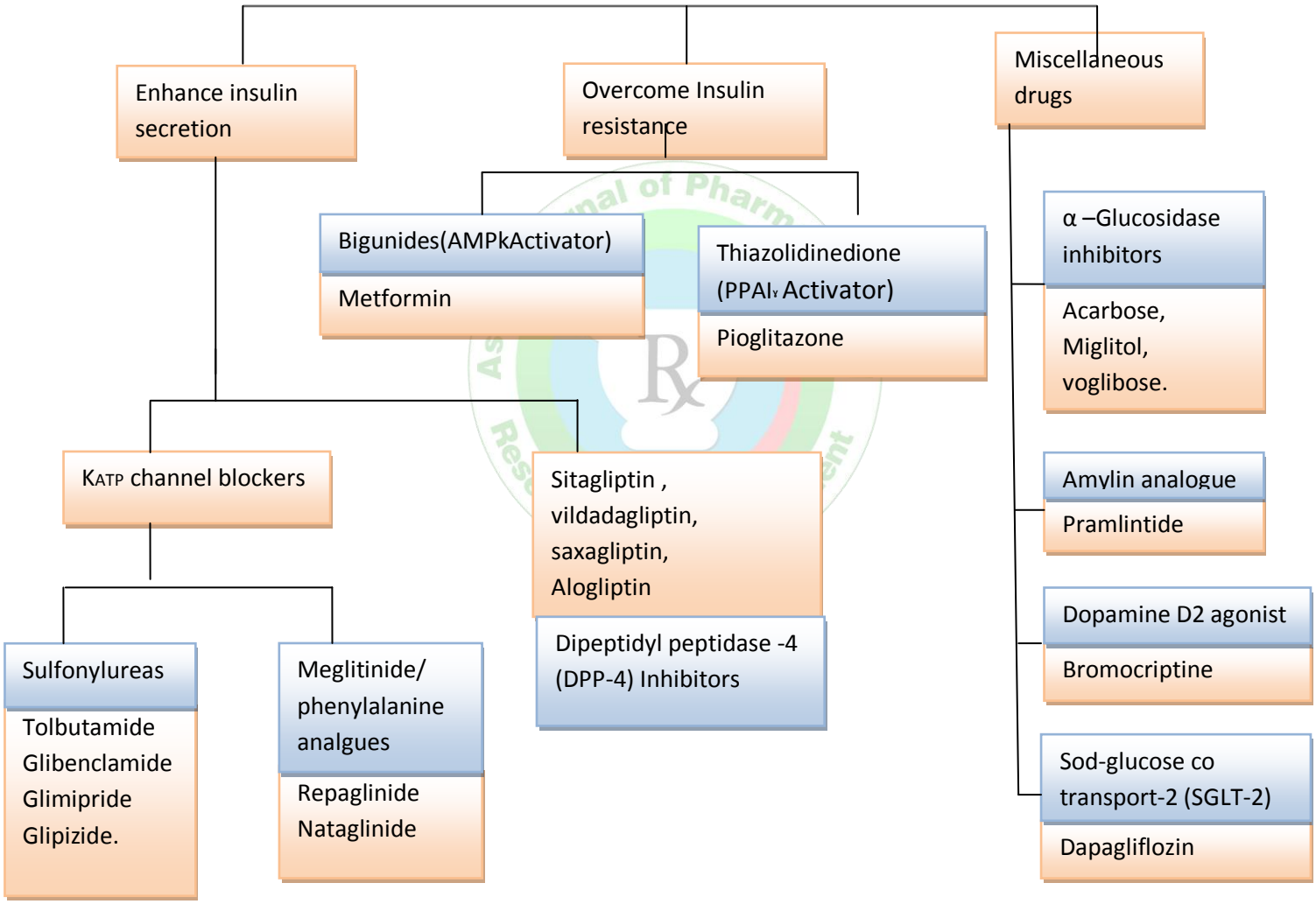
Insulin therapy in type 1 diabetes:

All patients with type 1 diabetes require treatment with insulin in order to survive. Exogenous insulin is used to mimic the normal physiological pattern of insulin secretion as closely as possible for each individual patient. However, a balance is required between tight glycaemic control and hypoglycaemia risk. If the risk of hypoglycaemia is high, then it may be necessary to aim for less tight glycaemic control. There is a wide variety of insulin preparations available which differ in species of origin, onset of action, time to peak effect and duration of action .[7]

Regulation of Insulin Secretio:

β–cell has glucoreceptor which is activated by the glucose → glucose enters in the cells through glucose transporter and indirectly inhibits to the ATP sensitive K+ channel and intracellular Ca2+ → secretion of insulin. y Somatostatin (GHIH) inhibits insulin as well as glucagon. y Insulin inhibits the glucagon secretion. y Glucagon increases/stimulates the release of insulin as well as somatostatin. Adrenergic α2 receptor activation → decreases cAMP and K+ channel ↑ → decreases insulin secretion. ‡ Adrenergic β2 receptor activation → increase cAMP and K+ channel ↓ → increase insulin secretion. ‡ Cholinergic–Muscarinic activation → ↑ IP3/DAG and K+ channel ↓ → increase insulin secretion.[8]

ORAL ANTIDIABETIC DRUGS [9,10]



ORAL HYPOGLYCAEMIC DRUGS:

These drugs lower blood glucose levels and are effective orally. The chief draw back of insulin is—it must be given by injection. Orally active drugs have always been more demand. The early sulfonamides tested in 1940s produced hypoglycaemia as side effect. the first clinically acceptable sulfonylurea tolbutamide was introduced in 1957.

CLASSIFICATION

A. Enhance Insulin secretion

1. Sulfonylureas (K-ATPas Channel blockers)
   - First generation: Tolbutamide
   - Second generation: Glibenclamide (Glyburide), Glipizide, Gliclazide, Glimepiride
2. Meglitinide/phenylalanine analogues Repaglinide, Nateglinide

3. Glucagon-like peptide-1 (GLP-1) receptor agonists (Injectable drugs) Exenatide, Liraglutide
4. Dipeptidyl peptidase-4 (DPP-4) inhibitors Sitagliptin, Vildagliptin, Saxagliptin, Alogliptin, Linagliptin

B. Overcome Insulin resistance

1. Biguanide (AMPK activator) Metformin
2. Thiazolidinediones (PPAR γ activator) Pioglitazone

C. Miscellaneous antidiabetic drugs

1. α-Glucosidase inhibitors Acarbose, Miglitol, Voglibose
2. Amylin analogue Pramlintide
3. Dopamine-D2 receptor agonist Bromocriptin
4. Sodium-glucose cotransport-2 (SGLT-2) inhibitor Dapagliflozin

Sulfonylureas (K-ATPas Channel blockers) The generic formula of sulfonylureas (SUs) is—

All SUs have similar pharmacological profile, their sole significant action being lowering of blood glucose level in normal subjects and in type 2 diabetics, but not in type 1 diabetics. Being more potent and clinically superior, only the second generation SUs are employed now. All first generation compounds have been discontinued except tolbutamide which is infrequently used.

Mechanism of action:

Sulfonylureas provoke a quick release of insulin from pancreas, the mechanism of which the rate of insulin secretion at any glucose concentration is increased, i.e. insulin release is provoked even at low-glucose concentration risking production of severe and unpredictable hypoglycaemia. In type 2 DM the kinetics of insulin release in response to glucose or meals is delayed.[11]

GLIMEPIRIDE:-

Sold under the trade name **Amaryl** among others is medium-to-long-acting sulfonylurea antidiabetic medication. It is taken by mouth. It is sometimes classified as either the first third-generation sulfonylurea, or as second-generation.

In 2016 it was the 61st most prescribed medication in the United States with more than 12 million prescriptions.

Medical uses

Glimepiride is indicated to treat type 2 diabetes mellitus; its mode of action is to increase insulin secretion by the pancreas. However it requires adequate insulin synthesis as prerequisite to treat appropriately. It is not used for type 1 diabetes because in type 1 diabetes the pancreas is not able to produce insulin

Contraindication

Its use is contraindicated in patients with hypersensitivity to glimepiride or other sulfonylureas.

Adverse effect

Side effects from taking glimepiride include gastrointestinal tract (GI) disturbances, occasional allergic reactions, and rarely blood production disorders including thrombocytopenia, leukopenia, and hemolytic anemia. In the initial weeks of treatment, the risk of hypoglycemia may be increased. Alcohol consumption and exposure to sunlight should be restricted because they can worsen side effects.

Interaction

Nonsteroidal anti-inflammatory drugs (such as salicylates), sulfonamides, chloramphenicol, coumadin and probenecid may potentiate the hypoglycemic action of glimepiride. Thiazides, other diuretics, phothiazides, thyroid products, oral contraceptives, and phenytoin tend to produce hyperglycemia.

Pharmacokinetic

Two generic oral tablets of glimepride, 2mg each.

Gastrointestinal absorption is complete, with no interference from meals. Significant absorption can occur within one hour, and distribution is throughout the body, 99.5% bound to plasma protein. Metabolism is by oxidative biotransformation, it is hepatic and complete. First, the medication is metabolized to M_1 metabolite by CYP2C9. M_1 possesses about $\frac{1}{3}$ of pharmacological activity of glimepiride, yet it is unknown if this results in clinically meaningful effect on blood glucose. M_1 is further metabolized to M_2 metabolite by cytosolic enzymes. M_2 is pharmacologically inactive. Excretion in the urine is about 65%, and the remainder is excreted in the feces.

Mechanism of action :-

Like all sulfonylureas, glimepiride acts as an insulin secretagogue It lowers blood sugar by stimulating the release of insulin by pancreatic beta cells and by inducing increased activity of intracellular insulin receptors.[12]

NATURAL ANTIDIABETIC DRUGS:-

Gymnema (*Gymnema sylvstre*)
Pterocarpus (*Pterocarpus marsupium*)
Jamun (*Eugenia jambolana*)
Bitter guard (*Marmordica charantia*)
Neem (*Azadirachta indica*)

***Gymnema sylvestre* (Gurmar)**:

The drugs consist of dried leaves of Gymnema sylvestre belonging to family- Asclepidaceae. It rises up as a woody climber in tropical forests and found in central and southern India. So it was easy for them to use it as natural treatment for diabetes for more than two millennium Chemical constituents are gymnemic acid, innositol, hentriacontane, pentatriacontane.

***Momordica charentia* (Karela, bitter gourd):**

It consists of fresh green fruits.Momordica charentia belonging to family Cucurbitaceae. Chemical Constituents are- Chiratin (steroidal saponin) and mimordicin. Momordica charantia is not only a nutritious vegetable, but is also used in traditional medical practices to treat type 2 diabetes mellitus. In Southern India it is used in the dishes pachadi (which is considered a medicinal food for diabetics). Used in the treatment of diabeties.Other uses

are stomachic, carminative, tonics, treatment of rheumatism, gout, disorder of spleen and liver.

***Syzygium cumini* (jamun, jambul):**

It consists of mature fruits and dried seeds of Syzygium cumini belonging to family myretaceae. Chemical. Constituents are anthocyanin delphinidine-3-gentiobioside, malvidin 3-laminaribiosidea and ferulic acid. Many research studies have shown that jamun is one of the best medicines for treatment of diabetes. It is an Antidiabetic drug. Diabetics are advised to consume 1 tsp of this jamun seed powder in empty stomach early morning.

***Azadirachta indica* (Neem):**

Source of neem is Azadirachta indica of family maliaceae.Neem leaf extracts and seeds are used as an active.ingredient as an effective cure for.diabetes. It has been scientifical.proven after a number of tests and research by leading medical institutes, that neem parts have high efficacy in treating the disease (Shinde and Dhalwal, 2009). Natural neem tablets are being manufactured and exported the world over for treating large number of patients. Neem leaf extracts improve the blood circulation by dilating the blood vessels and also helpful in reducing the need for hypoglycaemic drugs.[13,14]

REFERENCES

1. Satyanarayana U., Chakrapani U. *etal* Biochemistry (with clinical concepts and case studies) Elsevier Publication 4th Edition, 2013:669.
2. Inamdar N.N., A companion to medicinal chemistry second edition, career publications, 2016:730.
3. Jangme C. M., Wadulkar R. D. *etal*, Pathophysiology, essential guide for pharmacy and other paramedical courses, 2018 :8.5-8.6.
4. Malik R., India is the diabetes capital of the world, times of India, Updated: Jan 28, 2016:01.
5. https://en.wikipedia.org/wiki/Diabetes_mellitus.
6. Piero M.N., Nzaro G.M., Diabetes mellitus – a devastating metabolic disorder, Asian Journal of Biomedical & Pharmaceutical Sciences, 2014; 4(4): 3.
7. Walker R., Whittlesea C. *etal*, Clinical Pharmacy and Therapeutics, 5th Edition, Elsevier Ltd., 2012:694-695.
8.
9. Shah U., Akabari A. *etal* The Pearson Guide to the GPAT and Other Competitive Examinations in Pharmacy,Pearson India education services PVT,LTD., 2017.
10. Tripathi K.D., Pharmacological Classification of Drugs With Doses And Preparations 5th Edition, 2014:42.
11. Seth V., Classification of Drugs with Drugs of Choice Aditya Medical Books Pvt. Ltd. 2009:65.
12. Tripathi K.D., Essentials of Medical Pharmacology 7th Edition, Jaypee Brothers Medical Publishers (P) Ltd., 2018; 270-271.
13. https://en.wikipedia.org/wiki/Glimepiride
14. Singh G.K., Bhandari A. *etal* A textbook of Pharmacognosy (as per education Regulation 1991), 1991:134.
15. Mishra R., Shuaib M. *etal* A reviews on herbal antidiabetic drugs, Journal of Applied Pharmaceutical Science 2011; 01(06):235-237.