IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

REVIEW ON: ALLOPATHIC ANTI-DIABETIC DRUGS

[1]Ashish M.Gore, [2]Mayur M. Mote, [3]Prathmesh A. Baravkar

[1]Bachelor of Pharmacy,

[1] Sarsam College of Pharmacy, Taluka-Baramati, District-pune

Abstract :

Diabetes is a metabolic disease that occurs due to decreased insulin and/or insulin secretion in the body. As the disease progresses, pathological changes such as kidney disease, retinopathy, cardiovascular problems will inevitably occur in the body. There are two types of diabetes, type 1 and type 2; type 2 diabetes (T2D) is by far the more common type. Since diabetes affects many biological functions, many classes of drugs with different types of activity must be used to treat diabetic patients. Traditionally, there are five main classes of oral anticoagulants (OHA) used to treat TD2 patients. Most antidiabetic drugs are taken orally, except for insulin, exenatide, and pramlintide. There are many types of type 2 antidiabetic drugs, and their selection depends on the nature of the diabetes, the patient's age and condition, and many other factors. Treatments include drugs that increase the amount of insulin produced by the pancreas. This review briefly describes the drugs used in the treatment of diabetes.

Keywords: Diabetes, Pathophysiology, Antidiabetics drug.

I. INTRODUCTION

Diabetes is a global problem of carbohydrate, fat and lipid metabolism that causes excessive blood sugar, causes serious endocrine disruption and causes millions of deaths worldwide. Affecting more than 230 million people worldwide.

Diabetes Mellitus is an endocrine disease caused by insulin, and decreased insulin action can also be caused by insulin, a pancreatic hormone synthesized by pancreatic beta cells, which is not directly involved in food metabolism in the body by promoting insulin. . Diabetes is generally divided into two types, type 1 diabetes and type 2 diabetes. Type 1 diabetes is usually caused by the immune system in the beta cells of the pancreas, and obesity plays an important role in the development of T2D. Genetic Disorders Exocrine Pancreatic Disease Type 1 Diabetes Insulin Dependent Type 2 Non-Insulin Dependent Type 1: Diabetes Mellitus IDDM, the patient must take insulin regularly It can occur at any age and is often detected by testing in children. Type 2: Type 2 diabetes is a type of diabetes that is not dependent on insulin. Insulin receptors on insulin-producing cells do not normally respond to insulin.

2.Pathophysiology

Glucose homeostasis in the body is regulated by various hormones. However, two hormones, insulin and glycogen, play a major role in regulating glucose levels. When blood sugar rises, B cells secrete insulin. Insulin also lowers blood sugar. Produces glucose by inhibiting glycolysis and gluconeogenesis in the liver.Increase the amount of glucose in the liver, muscle and fat tissue

3.Treatment :
3.1.1. Drug class: Biguanides –

Metformin-

– **Structure of Metformin**

Trade Names : Fortamet, Glucophage, Glucophage XR, Glumetza, Rimet **Generic Names:** Metformin, Metformin extended release –

Mechanism of action:

Biguanides do not cause insulin release, but they do. This is important. Metformin is not effective in pancreatectomized animals and in people with type 1 diabetes.

1.Although the details are not clear, recent studies have confirmed that role in the treatment of metformin's effects. main features This plays an important role in lowering blood sugar.
2. Improve insulin-mediated glucose uptake and action in skeletal muscle and fat, thus overcoming insulin resistance in type 2 diabetes.

3. Interferes with the mitochondrial respiratory chain and promotes peripheral glucose utilization via anaerobic glycolysis.

Activation of AMPK by metformin appears to be an indirect result of interference with cellular respiration and a decrease in the body's ATP and other energy sources.

Metformin also delays the digestion of glucose, other hexose sugars, amino acids, and B vitamins. And delayed absorption (Cmax decreased by 40%, AUC decreased by 25%, and Tmax prolonged by 35 minutes compared to ingestion) Fasting)

volume of distribution: 850 mg per dose of 654 Â± 358 L.

Binding to plasma proteins: Not recommended

Steady-state plasma concentration: within 24 to 48 hours

Elimination: Elimination unchanged in the urine (no hepatic metabolism or biliary excretion.)

Elimination half-life: approximately 6.2 hours

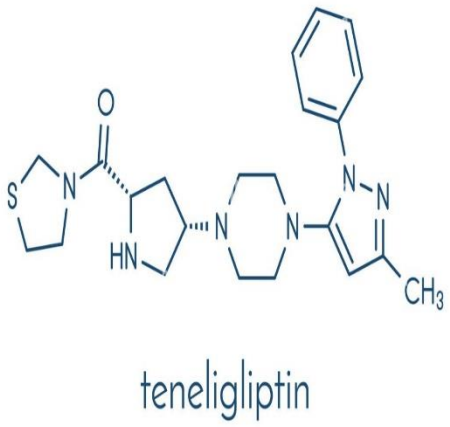
Side effects: common diarrhea, vomiting, constipation, bloating, metallic taste, weight loss medium can lead to renal failure and metformin toxicity Contraindications renal disease (men: SrCr > 1.5 mg / dl; women: SrCr > 1.4 mg / dl), cardiovascular drugs. treatment, acute or chronic metabolic acidosis and liver function. Forms Lozenges, delayed-release tablets, oral medications Areas of Use Type 2 diabetes, polycystic ovary syndrome, weight gain due to anti-inflammatory drugs.

Initial dose: 500 mg twice daily with food in the morning and evening, 850 mg once daily with food, or 500 mg extended-release

once daily with food Dosage: 2000-2550 mg daily in divided doses or 2000 mg° extended-release once daily.

3.1.2 Drug category: Dipeptidyl peptidase 4 inhibitor

Teneligliptin :



Struture of Teneligliptin

Teneligliptin (INN; brand name Tenelia) is a medication for the treatment of type2 diabetes, belonging to the class of anti-inflammatory drugs called dipeptidyl peptidase 4 inhibitors or "liptins".

Mechanism of action:

Although DPP-4 inhibitors share a common mechanism of action, they have considerable heterogeneity. DPP-4 inhibitors can be divided into peptide mimetics (such as sitagliptin, vildagliptin, saxagliptin, and alogliptin) and non-peptide mimetics (such as alogliptin and linagliptin Ting).

Teneligliptin,{(2S,4S)-4-[4-(3-methyl-1-phenyl-1H-pyrazol-5-yl)piperazin-1-yl]pyrrolidin-2-yl}(1,3-thiazolidin-3-yl)methanone hemipentahydrobromide hydrate, has a unique structure of five consecutive rings and is a peptide mimetic. The X-ray cocrystal structure of teneligliptin and DPP-4 shows that a significant interaction occurs between the benzene ring of pyrazole and the common S2 subsite of DPP-4, which not only increases the potency of the drug, but also improves its medicinal effect. .

Pharmacology:

Teneligliptin is a potent, selective and long-acting DPP-4 inhibitor with a potency of about 24 hours, and has a special pharmacological property: It passes through Cytochrome P450 (CYP) 3A4 and contains Flavin, which is metabolized by monooxygenase 3 (FMO3). ex. is not changed by the kidneys.

Adverse drug reaction:

1.Headache.

2.Hypoglycemia.

3..Nasopharyngitis

.4.Constipation.

5.Gastrointestinal symptoms.

3.1.3 Medications: **Insulin**

Insulin is secreted endogenously from the pancreatic beta cells. People with type 1 diabetes are completely insulin deficient, and people with type 2 diabetes may also have reduced endogenous insulin production. All people with type 1 diabetes require insulin as a lifelong treatment. Insulin is usually used in combination with oral antibiotics in people with type 2 diabetes or as monotherapy as the disease progresses. Various mutations and other changes in the insulin molecule have given rise to different types of insulin. These drugs are characterized and regulated by their pharmacodynamic and pharmacokinetic properties, such as onset, peak, and duration of action. Most importantly, insulin is classified as rapid-acting, short-acting, intermediate-acting, or long-acting.

Mechanism of action by drug class: Insulin reduces blood glucose by stimulating peripheral glucose uptake (especially by skeletal muscle and fat) and inhibiting hepatic glucose production.

Drug Class Recommended Use Type 1 Diabetes*, Type 2 Diabetes*, Hyperkalemia, DKA*/Diabetic Coma ï Drug Class Dosage Starting dose: 0.5 to 1 unit/kg daily Sub-Q (high interpatient dose variability)

❀ Dose adjustment: adjust dose to complete before meals and at bedtime ❝glycemic values 80-140 mg/dl

❀ Renal therapy dose: CrCl 10–50 ml/min: give 75% of normal dose °CrCl <10 ml/min: give 25-50% of normal dose; monitor clo.

Adverse Drug Class: Common - Hypoglycemia (anxiety, blurred vision, palpitations, tremor, slurred speech, sweating), weight gain –

Drug Class Adverse Reactions: Rare/severe/important. ➞ Diabetes Mellitus (seizures/coma), edema, lipoatrophy or lipohypertrophy at the injection site ➞

- Acetazolamide
- Diuretic
- Oral contraceptive
- Albuterol
- phenothiazine
- Asparaginase
- Estrogen
- Terbutaline
- Corticosteroid →
- HIV
- Thyroid hormone

Insulin Types;

1.Insulin glulisine

2 .Insulin Lispro

3. NPH

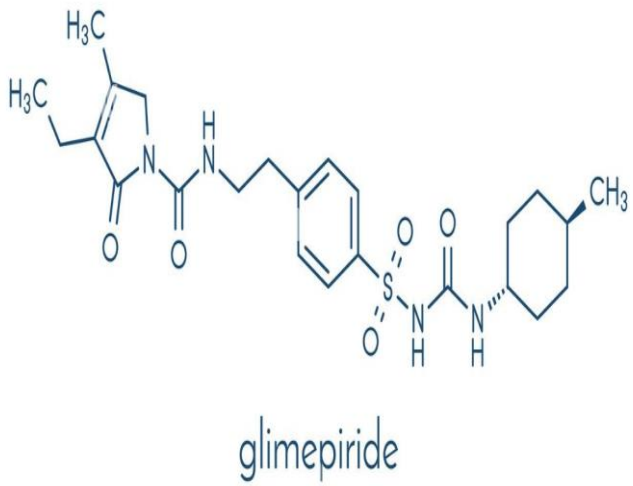
4. Regular insulin

5. Insulin glargine

3.1.4 Drug Class: Sulfonylureas

Sulfonylureas are used as an adjunct to diet and exercise in patients with type 2 diabetes. Although sulfonylureas are routinely used as monotherapy, sulfonylureas are often used in combination with other drugs when glycemic targets are not being achieved in people. Sometimes oral antibiotics in the same formulation. The general recommendation for taking the drug is to start with a low dose and then increase the dose according to the patient's response while monitoring for signs and symptoms of hypoglycemia, which is not good. Use caution in people with kidney or liver disease. HbA1c decreased from 1% to 2%.

▪ **Glimepiride**



Structure of Glimepiride

▪ **Brand Name**: - Amali

▪ **Brand Name**: - Glimepiride

▪ **Mode of Action:** -

Glimepiride, like other sulfonylureas, is an insulin secretagogue and is only effective in patients with beta-compartment diabetes. It acts by activating ATP-dependent potassium channels in the cell membrane of pancreatic beta cells, preventing the release of potassium from the cell, causing iatrogenic depolarization. Depolarization activates voltage-dependent calcium channels in the cell membrane, causing increased intracellular calcium and subsequent exocytosis of insulin into the bloodstream. Insulin then activates cell membrane receptors, leading to the expression of GLUT-4 and the entry of glucose into the cell, reducing blood glucose. In addition, glimepiride has been shown to interact with Epac3, a nucleotide modifier that mediates insulin granule exocytosis. A study conducted on healthy volunteers highlighted the effectiveness of glimepiride. The results show a relationship between glimepiride blood and insulin release in normoglycemic and hyperglycemic conditions.

Pharmacology:

Like all sulfonylureas, glimepiride acts as an insulin secretagogue. It lowers blood sugar by stimulating the release of insulin from pancreatic beta cells and by causing an increase in the insulin receptor. Not all minor sulfonylureas have the same risk of hypoglycemia. –

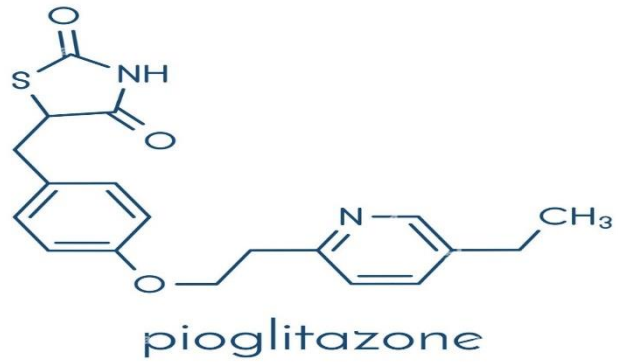
Agreement: - Tablets.

Dose:Starting dose: 1-2 mg once daily with breakfast.

3.1.5.Drug Class: **Thiazolidinediones**

Thiazolidinediones, pioglitazone and rosiglitazone, may decrease insulin sensitivity by increasing insulin secretion. They are used as an adjunct to diet and exercise in people with type 2 diabetes. Although not usually used as monotherapy, they are often used in combination with other oral medications and/or insulin in patients who are not achieving glycemic goals. Recent clinical data suggest that patients taking thiazolidinediones may have an increased risk of myocardial infarction and death and should be used with caution in patients with a history of heart disease. Not recommended for use in patients with NYHA Class III and IV heart failure. The similar thiazolidinedione troglitazone has been withdrawn from the market due to hepatic failure and death. It is recommended that patients with impaired liver function not use. HbA1c decreased from 1% to 1.5%.

Pioglitazone -



Structure of Pioglitazone

- **Brand Name**: - Actos
- **Scientific Name**: - Pioglitazone
- **Mode of Action**:

  Pioglitazone selectively inhibits the nuclear receptor peroxisome proliferator-activated receptor gamma (PPAR-ÃŽ Â³) and to a lesser extent the nuclear receptor peroxisome proliferator-activated receptor gamma (PPAR-gamma), PPAR-alpha. It regulates the transcription of genes involved in the regulation of glucose and lipid metabolism in muscle, adipose tissue and liver. Thus, pioglitazone reduces insulin resistance in the liver and peripheral tissues, reduces hepatic gluconeogenesis and reduces blood glucose and glycated haemoglobin..

Pharmacology:

Pioglitazone is a thiazolidinedione that increases insulin sensitivity in tissues. It is well absorbed with an average bioavailability of 83% and reaches a maximum in approximately 1.5 hours.

Dosage form: - Tablets

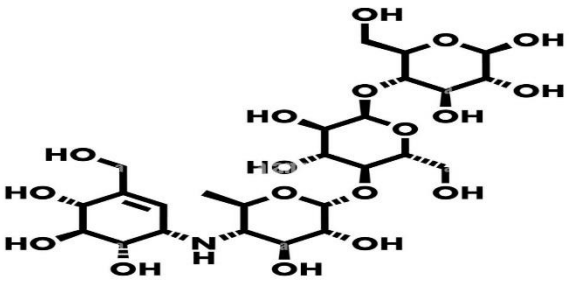
Dosage: - Initial dose: - 15-30 mg once daily without food

Corrective dose: -15-45 mg once daily

3.1.6. Drug Class: - Alpha-Glucosidase Inhibitors

Alpha-glucosidase inhibitors (AGI) are a group of anti-inflammatory drugs used in the treatment of type 2 diabetes, the methods of action, contraindications, side effects, care, and other important factors that doctors should pay attention to are included in the treatment of type 2 diabetes and its complications.

Acarbose :



: Structure of Acarbose

Acarbose (INN) is an antibiotic used to treat type 2 diabetes and prediabetes in some countries. It is a generic drug sold as Glucobay (Bayer AG) in Europe and China, Precose (Bayer Pharmaceuticals) in North America, and Prandase (Bayer AG) in Canada.

Common Name: - Precose

Mode of Action: -

Acarbose is a complex oligosaccharide that acts as a competitive, reversible inhibitor of pancreatic alpha-amylase and membrane-bound intestinal alpha-glucoside hydrolase. Pancreatic alpha-amylase hydrolyzes complex carbohydrates to oligosaccharides in the intestine. Intestinal alpha-glucosidase hydrolase breaks down oligosaccharides, trisaccharides, and disaccharides (sucrose, maltose) in the brush border of the small intestine into monosaccharides (glucose, fructose). Acarbose delays the digestion of carbohydrates, slowing the absorption of glucose, thereby reducing blood glucose levels.

Pharmacology:

Acarbose inhibits the enzymes required for carbohydrate digestion (glycoside hydrolases), particularly alpha-glucosidase of the brush border of the small intestine and pancreatic alpha-amylase. However, alpha-amylase bacteria from the intestinal microbiome can degrade acarbose.

Pancreatic alpha-amylase hydrolyzes complex starches and breaks down oligosaccharides that coat the cell membrane.

Dosage: - Initial dose: 25 mg orally 3 times daily with the first meal. Dose Increase: This dose can be increased up to 100 mg orally 3 times daily with the first meal of each meal.

4. **Conclusion:**

The advancement of sedentary lifestyle and the high prevalence of obesity have created a huge demand for sugar by increasing the number of patients and have led companies to increase their research and development investments to create targets. Many medical advances are considered to have brought nanotechnology into our daily lives. Nanoformulation research in the past few years has greatly contributed to the development of nanoparticle delivery systems for antiviral drugs. Long-term safety concerns and ethical concerns regarding nanoformulations require the FDA's strict guidelines for product regulation to support such protection and make the product useful, as discussed above. The main goal is to use appropriate ligands or drug combinations to achieve appropriate glycemic control through the long-term addition of two or more antidiabetic drugs. This ongoing technological development in nanotechnology holds promise for the development of effective hypoglycemic treatments in the future.

References:

1. Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TP, Clin Biochem Nutr, 2007;40:163-7.

2. Ribeiro C, Moat Calendar CS, Voltarelli FA, Arañojo MB, Botezelli JD, Effects on motor activity in neonatal rats using alloxan. J Diabetes Metab 2010; 1:107

3. Bastaki, S. Diabetes and Treatment, Int. Journal of Diabetes Metabolism, 2005;

4.M. Okur, I. Karantas, P. Siafaka, Diabetes Mellitus: a review of pathophysiology, current oral pathophysiology, current and future prospects of oral medicine, ACTA Pharm Sci, 2017 55 : 61;

5. Mayorov, Insulin also in type 2 diabetes, in the pathogenesis of diabetes. Melitus, 2011; 14:35

6. Ojha, U. Ojha, R. Muhammed, A. Chandrasekhar, H. Ojha, Current perspectives on the role of insulin and glucagon in the pathogenesis and treatment of type 2 diabetes, Clin Pharmacol, 2019 11: 57-65.

7.K. Kaku, Policy on pathophysiology and treatment of type 2 diabetes, JMAJ, 2010; 53: 41-46.

8. D. Stringer, P. Zahradka, C. Taylor, Glucose transporters: cellular links to insulin resistance and hyperglycemia in diabetes, Nutr. Rev Rev 2015;73:140-154.

9.Ratner RE, Research DPP. Update on Diabetes Prevention. Endocrinology Practice, 2006; 12 [1:20-4.]

10. C. Grimshaw, A. Jennings, R. Kamran, H. Ueno, N. Nishigaki, T. Kosaka, et al. Trelagliptin (SYR-472, Zafatek), a novel once-weekly treatment for type 2 diabetes, inhibits dipeptidyl peptidase 4 (DPP-4) via a non-covalent mechanism. PLOS. One, 2016; 11; 157-509.

11.T. Y. Nagai, Y. Yamamoto, A. Miyachi, H. Hamajim, E. Mieno et al., Effects of alogliptin on plasma glucagon and gastric emptying in patients with type 2 diabetes: a randomized controlled trial compared with metformin, Diabetes. resources. treatment. Yap, 2019;158:107892

12. S. Tsuru Fukuda, J. Anabuki, Y. Abe, K. Yoshida, S. Ishii, teneligliptin, a novel, potent and stable dipeptidyl peptidase 4 inhibitor, improves postprandial hyperglycemia and dyslipidemia after single and repeated doses, Eur. J. Pharmacol, 2012; 696:194–202

13. Yes. FDA approves new treatment for type 2 diabetes. FDA report, 2011; Access date: 13 December 2013.

14. Nakakawa, J. Sawa, Y. Kumeda, T. Shoji, et al., Improvement of glycemic control in hemodialysis patients with type 2 diabetes using teneligliptin: evaluation with continuous glucose monitoring, J. Diabetes. Sib, 2015; 29:1310-1313.

15. O. Swamy, S. Sharma, A. Panneerselvam, K. Singh, G. Parmar, P. Gadge, Teneligliptin in type 2 diabetes, diabetes. metadata. Completed. Obes, 2016; 9:251-260.

16. K. Kau, K. Kisanuki, M. Shibata, T. Oohira, Risk-benefit analysis of alogliptin in type 2 diabetes, Drug Saf, 2019;42:1311 - 1327.

17.Deacon CF, Holst JJ. Linagliptin is a xanthine-based dipeptidyl peptidase 4 inhibitor with poor efficacy in the treatment of type 2 diabetes. Expert Opinion in Drug Research, 2010;19:133-40.

18. McGill JB, Sloan L, Newman J, Patel S, Sos C, von Eynatten M, et al. Long-term efficacy and safety of linagliptin in patients with type 2 diabetes and severe renal impairment: a 1-year randomized, double-blind, placebo study. Diabetes Care, 2013; 3{2:237-44}

19. Whiting DR, Guariguanta L, Weil C. Shaw JEIDF Diabetes Atlas: Global estimates of diabetes prevalence 2011 and 2030. 94:311-21.

20. "Essentials of Clinical Pharmacology" 8th Edition, Maulana Azad, principal professor and Director of Pharmacology. Likewise, 286-301

21. https://www.news-medical.net/health/Metformin-Chemistry.aspx

22. https://images.app.goo.gl/X1vMLAsmzYLoVpzL9

23. https://images.app.goo.gl/RnXiJX5mck5zt36v6

24. https://images.app.goo.gl/sC3npPePJ9XodfWb7

25. https://images.app.goo.gl/Kxmm95TaYUVsBwZH6