International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 07-05-2023, Accepted: 21-05-2023, Published: 07-06-2023
Volume 8, Issue 2, 2023, Page No. 155-159

Anti-diabetic drugs and therapy used in the treatment of diabetes mellitus: A review

Mayuri Jagtap[1*], Pratiksha Vadde[1], Vikesh Kukade[2], Dr. Rajendra Patil[3]
[1] Final year B pharmacy, Delonix society's Baramati College of Pharmacy, Barhanpur Tal-Baramati, Dr. Babasaheb Ambedkar Technological University, Maharashtra, India
[2] Assistant Professor of Delonix society's Baramati College of Pharmacy, Barhanpur Tal-Baramati, Dr. Babasaheb Ambedkar Technological University, Maharashtra, India
[3] Principal of Delonix society's Baramati College of Pharmacy, Barhanpur Tal-Baramati, Dr. Babasaheb Ambedkar Technological University, Maharashtra, India

Abstract
Diabetes Mellitus is a chronic, developing condition. Impact of diabetes mellitus across the globe is a global pandemic. Diabetes mellitus (DM) is a long-term condition characterised by chronic metabolic imbalance, increased or decreased secretions, and high blood glucose levels (hyperglycemia). Additionally, the pancreatic beta cells' ability to secrete are completely lost. Currently, the drugs are used for pharmacologic therapy, which lowers the high blood glucose in DM. To date, there are no drugs that can completely or permanently cure DM; they can only prevent and treat the Illness. We have outlined the anti-diabetic allopathic and ayurvedic medications used to treat diabetes mellitus in this paper.This paper includes evidence to support the.in this report we have also prove the great contribution of yoga in the treatment of Diabetes mellitus.

Keywords: diabetes mellitus, ayurvedic, allopathic, yoga

Introduction
In 1899, diabetes was first identified. It is first tested by removing a dog's pancreas, after which diabetes is allowed to set up.two types of diabetes exist. Diabetes insipidus is a condition in which the pituitary hormone vasopressin's secretion or reaction is compromised, leading to excessive production of diluted urine and frequently accompanying dehydration and unquenchable thirst. A series of metabolic diseases known as diabetes mellitus are characterised by persistent hyperglycemia brought on by deficiencies in insulin secretion, insulin action, or both. The beta cells in the pancreas completely stop secreting, which is another characteristic of the condition.

- **Insulin-dependent diabetes mellitus, often known as type 1 diabetes**
  In that person insulin is not produced so it is given externally, there is no other option.

- **Insulin non- Dependent mellitus often known as type 2 diabetes**
  In that person low insulin can release so drugs are given to that person to increase the release of insulin by beta-cells of pancreas. Hence it is not complete depend upon insulin.

Gestational diabetes
Pregnancy diabetes the term "gestational diabetes" describes the beginning of women's glucose intolerance during pregnancy. Due to being overweight or obese during pregnancy, pregnant women's bodies are unable to produce enough insulin, which is the primary cause of gestational diabetes. At 24 to 28 weeks of pregnancy, the majority of pregnant women get a gestational diabetes screening. Untreated gestational diabetes can lead to issues for the unborn child, such as stillbirth and early birth.

HbA1C method [20]
HbA1C test
The most accurate & reliable approach for detecting diabetes mellitus is the Glycosylated Haemoglobin (HbA1C) method. >126 mg/dl is the fasting blood glucose level. Blood sugar levels postmeal are above 200 mg/. The average HbA1C value is 6.5 g%. Diabetes mellitus is identified when the HbA1C value is greater than 6.5g%.
If it is less than 4 g%, the person does not have any type of diabetes. If it is between 5.5 and 5.5 g%, the person is prediabetic, which means that although they do not now have diabetes, they may do so in the future. Therefore, that person needs to take measures because it could exceed 6.5 g% without them.

Mechanism of action of insulin
Insulin ties to a particular insulin receptor that is present on the cell surface. reduces cAMP levels in some tissues by preventing the activity of the enzyme adenylate cyclase. By phosphodiesterase enzyme stimulation, it enhances cAMP metabolism. Insulin impacts the metabolism of glucose, fatty acids, and amino acids because cells produce less cAMP. Insulin makes it easier for potassium to enter cells.

Allopathic anti-diabetic medications used to treat diabetes mellitus [1-4]
Sulfonylureas
Mechanism of action
Inhibit the ATP-sensitive potassium channels, which causes the beta cells to depolarize and release insulin. Only when 30% or more of the beta cells are functioning are drugs effective. No discernible impact on blood sugar in the absence of pancrease (beta cells). effective only in people with Type 2 diabetes.

Adverse effect
Anxiety, dizziness, drowsiness, headache, vomiting

Contraindications
Hypersensitivity to the drug, diabetic ketoacidosis.

Meglitinides
Mechanism of action
Being accustomed to Peroxisome proliferative activated receptor gamma (PPAR-Gamma) selective agonists are what it is. Muscles and adipose tissues with improved insulin sensitivity are due to PPAR Gamma. hepatic gluconeogenesis must be stopped. Effective only when insulin is present. These medications treat type 2 diabetes' insulin resistance. closes ATP-dependent potassium channels by binding to particular receptors on the membrane of beta cells. Blocking potassium channels depolarizes the membrane of the beta cell, which triggers calcium influx, a rise in intracellular calcium, and activation of insulin secretion. Meglitinides produce insulin substantially more quickly than sulfonylureas. Meglitinides ought to be taken with food because doing so will cause the pancreas to create insulin much more quickly. Meglitinides carry a lower risk of hypoglycemia than sulphonylurea.

Adverse effect
Diarrhea, nausea, vomiting, hypoglycemia, joint pain.

Contraindication
Severe liver dysfunction, hypersensitivity to any drug of this component.

Bigunides
Mechanism of action
In contrast to sulfonylurea, the action of biguanide is extra-pancreatic. Drugs decrease the blood glucose by activating AMPK (adenosine Mono Phosphate-activated protein Kinase) AMPK decreases the production of glucose and increases utilization of glucose in peripheral muscles. drug also inhibit the intestinal absorption of glucose. inhibit glucogenesis and glycolgenolysis whereas stimulate the glycolysis and tissue uptake of glucose.

Adverse effects
Lactic acidosis (more with Phenformin), Megaloblastic anaemia (more with metformin) due to vitamin B12 deficiency, Biguanides increase the intestinal production of lactate by anaerobic glycolysis.

Contraindications
Should not be used in the patients with hepatic disease, also in Type 1 diabetes patients

Thiazolidinediones
Mechanism of action
Selective agonist of the PPAR-Gamma peroxisome proliferative activated receptor (mechanism of action). The PPAR-gamma receptor is in charge of enhancing the sensitivity of muscles and adipose tissues to insulin. Hepatic gluconeogenesis must be stopped. Effective only when insulin is present. These in type 2 diabetes, medications are utilised to reverse insulin resistance. These medications also frequently raise HDL.

Adverse effects
Plasma enlargement is a negative consequence that should be avoided in CHF patients. Long-term use is linked to an increased risk of bladder cancer.

Contraindications
Patients who have osteoporosis and postmenopausal womens have should not take this medication, because it has high risk of bone fractures.

Anti-alpha glucosidase agent
Mechanism of action
The mucus membrane at the brush edge of the small intestine contains the enzyme alpha-glucosidase. Responsible for chopping up dietary carbs and making it easier for the body to absorb them. Because polysachharides are not directly absorbed by the body, they can change into monosachharides before being taken up by the body. The GIT absorbs fewer carbohydrates when this enzyme is inhibited. The main adverse impact brought on by the fermentation of unabsorbed carbohydrates is flatulence.

Acarbose
It is an oligosaccharide that comes from the microbial species Actinoplanes Utahensis. serves as an antagonist that competes with alpha-glucosidase. reduces the absorption of starch, dextrin, and diasaccharides via the digestive tract.

GLP-1 (glucagon-like peptide-1) agonists
Mechanism of action
Compared to intravenous glucose, oral glucose causes a four-fold increase in insulin release. GLP-1 is released by oral glucose, which enhances or facilitates the insulin release generated by glucose. Diabetes type 2 patients have lower GLP-1 secretion. Along with releasing insulin, GLP-1 also inhibits glucagon production and delays stomach emptying, both of which decrease hunger. Dipeptidyl peptidase-4 (DPP-4) breaks down GLP-1 quickly, giving it a half-life of just 1-2 minutes.

DPP-4 (dipeptidyl peptidase-4) Inhibitors
Mechanism of action
DPP-4 enzyme is responsible for breakdown of GLP-1. DPP-4 inhibitors prolong the action of endogeneous GLP-1by inhibiting its metabolism through DPP-4. DPP-4 inhibitors are effective orally & used in patients with type 2 diabetes

Adverse effect
Common side effect are nasopharyngitis & upper respiratory tract infections.

Sodium glucose co-transporter-2-inhibitors
Mechanism of action
GLP-1 is broken down by the DPP-4 enzyme, and by blocking DPP-4 from doing so, DPP-4 inhibitors, which are effective orally and used in type 2 diabetes patients, extend the effects of endogenous GLP-1.

Adverse effect
Nasopharyngitis and upper respiratory tract infections are frequent adverse effects.

Sodium glucose cotransporter-2 inhibitors
Mechanism of action
It is in charge of the PCT (renal tubules) reabsorbing glucose. These medications produce glucosuria in people with diabetes by blocking this transporter. When treating type 2 diabetes orally.

Adverse effect
Urinary tract infections, vaginal infections, and weight loss are the main adverse effects.

Ayurvedic plants used in treatment of diabetic mellitus

Fig 1. Turmeric [5-8]

Zingiberaceae, the turmeric plant (curcuma longa) family. It is the herbaceous rhizomatous plant. Ayurvedic and Traditional Chinese medicine both utilise it to treat diabetes. Acurcumin's structure, which reveals the diferuloylmethane, was figured out in 1910 by Lampe & Milobedeska. The 1972 publication Effect of curcumin in diabetic patients is reducing the blood glucose level. Curcumin improves insulin sensitivity and has antihyperglycemic properties. Additionally beneficial at reducing the elevated levels of fasting blood sugar and urine sugar was dietary curcumin.

Fig 1: Turmeric

Pharmacological action

Tumour necrosis factor-alpha (TNF-alpha) and plasma free fatty acids may be reduced by curcumin. The liver's enzymes involved in glycolysis, gluconeogenesis, and lipid metabolism are all activated by curcumin. Bone marrow transplantation and vitamin C-supplemented curcumin were successful in lowering levels of blood glucose, hb, HbA1c

Fig 2. Neem [9]

Neem is a natural material that has numerous medical uses. Neem is referred to by its scientific name, Azadicthta Indica, and is a member of the Meliaceae family. It has additional beneficial non-wood components, including fruit oil, flowers, leaves, neem cake, and leaves.

Fig 2: Neem

Pharmacological action

Neem has a wide range of medicinal effects, including anti-inflammatory, hypolipidemic, immunostimulant, hepatoprotective, and hypoglycemic effects. Neem is mostly helpful in the treatment and prevention of diabetes and obesity. Neem is rich in flavonoids, terpenoids, tannins, saponins, anthraquinones, sterols, and alkaloids, all of which are beneficial for managing diabetes. Rutin and quercitin, the primary chemical components of neem, have hypoglycemic or antihyperglycemic action. One of neem's chemical components, nimidin, also has the ability to help people manage their weight.

Fig 3. Coccinia indica [10-12]

In the Ayurvedic medical system, Coccinia Indica is well known for its hypoglycemic and anti-diabetic effects. Its family is Cucurbitaceae and its synonyms include Coccinia Grandis and Coccinia Cordifolia.In Hindi, it is known as Kandutikibel, while in Marathi, it is known as Gourd or Ranotandi. According to Mankil *et al*. (2006), many of them are effective in treating the relatively prevalent illness diabetes mellitus. Allium cepa, Allium satium, Aloe vera, Coccinia indica, Caesalpinia bonducella, Eugenia jambolana, Mucuna pruriens, Murraya koeingii, and others are a few of these typical examples.Tinospora cordifolia, Mormodica charantia, Swertia chirata, Syzigium cumini, Trigonella foenum-graecum, and Syzigium cumini. For the treatment of diabetes, fresh root juice is employed.

Fig 3: coccinia indica

Pharmacological action

Coccinia indica has saponins, flavonoids, sterols, and alkaloids among its chemical components. Flavonoids and saponins are in charge of the anti-diabetic activity. Effect of insulin on beta cells from C. indica leaves in diabetics. It has anti-diabetic and hypoglycemic properties.

Fig 4.Cinnamon [13]

Cassia cinnamon is a popular spice and flavouring ingredient. According to numerous stories, Egypt imported cinnamon from China in the year 2000 BC. The word “cinnamon” derives from a Greek word that means “sweet fruit.” Ceylon tea or real cinnamon the biological source of cinnamon is C. zeylanicum, or Cinnamomum verum. Cassia C. aromaticum, commonly referred to as Chinese cinnamonom, is the biological source of cinnamon. Belongs to the Lauraceae family.

Fig 4: Cinnamon

Pharmacological action

Cassia cinnamon contains methylhydroxychalcone (MHCP), an excellent insulin mimic. Studies conducted *in vivo* reveal that cassia cinnamon treatment increases insulin-stimulated IR-Beta and IRS-1 tyrosine phosphorylation. *In vivo*, cinnamon and insulin work together as a synergistic agonist to lower blood sugar levels.

Fig 5. Aloe vera [14-15]

It is a natural chemical that has been employed in medicinal biology for over 4,000 years. Aloe is a genus of succulent, perennial xerophytes. It is African in origin.

Fig 5: Aloe vera

Pharmacological action

Aloe vera, also known as Aloe berberidansis, is a member of the Asphodelaceae family. Aloe vera has the capacity to lower blood sugar levels. The separation of the mucilaginous layer from the anthraquinones provides the basis for the results. It also lowers hepatic transaminases, plasma & cholesterol, triglycerides, free fatty acids, and phospholipids in addition to blood glucose levels. The process of reducing blood sugar by accelerating glucose metabolism. Additionally, it demonstrates the antioxidant function, which lowers peroxide levels and, consequently, oxidative damage. Additionally, aloe vera exhibits lowering triglyceride levels with hypolipidemic and hypoglycemic effects.

Effect of yoga in patients with type 2 diabetes mellitus [16-19]

Suryanamaskar

Surya namaskar, also known as the sun salutation, is a vigorous yoga method. It is the most effective strategy to raise cellular needs for oxygen and glucose. These methods encourage the synthesis of insulin Surya namaskar and other yoga poses were found to dramatically lower diastolic blood pressure and improve glycemic control in perimenopausal women after 25 minutes of practise.

Asanas (yoga postures)

Asanas involved relaxing and doing stretches or twists. Asanas that promote pancreatic function include ardhamatsyendrasan, yoga mudra, and mandukasan. The pancreas can be massaged and squeezed in the asanas to encourage the release of insulin. According to a study, people with type 2 diabetes' glucose utilisation and fat distribution were both improved by yoga poses.

Bandha (Lock)

Bandha refers to holding, tightening, or locking particular body parts and rerouting blood and lymph flow to other body areas. Bandhas are paired with asanas or pranayama. Uddiyan Bandha, also known as abdominal lock, is used in the treatment of diabetes to lock the negative abdominal pressure and compress the abdominal region. It has been demonstrated that negative abdominal pressure enhances pancreatic function.

Pranayam

Yogic breathing is practised through a process called pranayama, or "yogic breathing." Pranayama alters the autonomic nerve system in a complete way, regulating the heart rate and its variability as well as the rate and pattern of breathing.Alternate nostril breathing is known as Anulom Vilom, whereas left nostril breathing is known as Chandranadi, cooling breaths are known as Sitkari, and humming bee breath is known as Bhramari. Bhastrika breathing exercises are described as being strong and energising. As breathing fire.

Dhyan (meditation)

Diabetes patients who practice meditation can gain mental steadiness. An improvement in diabetes management can be shown after six weeks of sahaja and meditation. Blood pressure control, anxiety reduction, and quality of life. It is also advised to visualise and focus on the pancreas during meditation to help control diabetes and lower blood sugar levels

Mechanism of action

Yoga's ability to efficiently relieve stress aids in the management of diabetes. According to research, doing yoga enhances wellness while lowering stress, anxiety, and depressive symptoms in healthy volunteers.

The pancreas cells regenerate as a result of abdominal stretching workouts. Many of the poses used in yoga practise can increase beta cells' sensitivity to glucose and their ability to secrete insulin.

Additionally, it might enhance the blood flow to the muscles and provide muscle relaxation. The process of glucose uptake is also improved by yoga postures. Improvement in hormonal homeostasis and glycemic control in diabetes

mellitus patients. Additionally strengthening the immune system is yoga therapy. In diabetic patients, yoga therapy enhances the proportion of receptors that bind to insulin as well as their quantity. By enhancing the insulin kinetics by lowering fasting insulin levels, yoga therapy normalises the insulin-to-glucose ratio. Additionally, it lowers levels of free fatty acids either reduced insulin resistance or increased insulin sensitivity. Through improvements in the lymphocyte migration test, yoga helps persons with type 2 diabetes' cell-mediated immunity.

Conclusion

In this way, it has become clear that diabetes mellitus is a chronic, widespread, and treatable illness. Although diabetes mellitus is a schedule J disease, there are numerous anti-diabetic medications accessible in india's allopathy and ayurveda medical systems to treat it. using these medications any diabetic can simply beat their condition and lead to a fulfilling life in this world, just like healthy volunteers. This teaches us that a prediabetic patient can safeguard himself from an incurable illness like diabetes mellitus by maintaining a balanced diet. The goal is to raise or improve blood levels of insulin, which lowers blood glucose levels through increasing insulin receptors. additionally we know that only increased blood sugar levels can issue significant result from it, including hypertension, nerve damage, eyesight loss, kidney damage, tjerefore bringing the blood glucose level back to normal should be crucial. we have seen that ayurveda and yoga have a significant impact on blood glucose level regulation.

Acknowledgement

With lots of respect to my family and my college, I would like to thanks to my college B.C.O.P college of pharmacy for permitting me to do this review article.special thanks to my friends, respected teachers to give me lots of information and valuable time, thank you for support. I am also thankful of this International journal of research pharmacy and pharmaceutical science journal who give me the opportunity to publish this review article.

Objectives

- To study effect of allopathic -ayurvedic drug combination in controlling diabetes mellitus
- To estimate the effect of buddhisht walking meditation on glycemic control in patients with type 2 diabetes mellitus.
- To study effect of SGLT2 inhibitors and GLPI receptor agonists in diabetes mellitus patients.

References

1. Ayurvedic, Allopathic & Integrated Treatment of Diabetes in Northern India: Practitioner Perceptions. Camile M. Clancy, University of Vermont, 2015, 9-57.
2. Management of diabetes mellitus in individuals with chronic kidney disease:therapeutic perspectives and glycemic control. Carolina C.R.Betonico,silvia M.O.Titan,Maria Lucia C.Correa-Giannella, Marcia nery,Marcia Quiroz,2016:(1):47-53.
3. Oral hypoglycemic Medications.kavitha Ganesan,Muhammad Burhan Majeed Rana,Sultan, 2022.
4. Wang Y, Perri MA. systemic Review of patient reported satisfaction with oral Medication Therapy in Patients with type 2 Diabetes.value Health,2018:(11):1346-1353.
5. Role of medicinal Plants in the management of Diabetes mellitus: A Review,Bindu Jacob. Narendhirakannan R.T, 2018, 1-17.
6. Curcumin And Diabetes: A Systematic Review. Dong-wei zhang, Min Fu,Si-Hua Gao,and Jun li-liu volume, 2013, 1-16.
7. Shehzad A, Ha T, Subhan F, Lee YS. New mechanism and the anti-inflammatory role of curcumin in obesity and obesity related metabolic diseases,2011:50(3):151-161.
8. Goel A, Kunnumakkara AB, Aggarwal BB." Curcumin as curecumin:from kitchen to clinic,biochemical pharmacology,2008:75(4):787-809.
9. Satyanarayana K, sravanthi K, Anand shaker I, Ponnulakshmi R. Molecular approach to identify antidiabetic potential of Azadirachta indica.,2015:6(3):165-174.
10. Deokate UA, Khadabadi SS. Review Pharmacology and Phytochemistry of Coccinia indica,2011:3(11)155-159.
11. Ajay SS. Bhaskar VH. Teotia D. Quality standardization of coccinia indica fruit. Asian J. Chem,2009:21(7):5351-5354.
12. Azad KAK,Akhtar S,mahtab H (1979) coccinia indica in the treatment of patients with diabetes mellitus.bangladesh Med.Res.council Bull,.5(2)60-66
13. Jean-Jacque Dugoua, Dugald Seely, Dan Perri, Kieran Cooley, Taryn Forelli, *et al*. Critical Review / Synthese Critique. From type 2 diabetes to antioxidant activity:a Systematic review of the safety & efficacy of common & cassia cinnamon bark, 2007, 837-47.
14. A Review on Pharmacological Properties of Aloe vera. By Priyanka Sharma, International Journal of Pharmaceutical Scientific Review and Research,2014:29(2):31-37.
15. Hypoglycemic and hypolipidemic effect of aloe vera L. in non- insulin dependent diabetics.monica choudhary,Anika kocchar,jaswinder sangha,2014:51(1):90-96.
16. Therapeutic Role of Yoga in Type 2 diabetes, by Arkiath Veettil Raveendran, AnjaliDeshpandae and Shashank R. Joshi,2018:33:307-317.
17. Thangasami SR, Chandini AL, Thangaswami S. Emphasis of yoga in the management of diabetes.J Diabetes Metab,2015:6:613.
18. Jyotsna VP. Prediabetes and type 2 diabetes mellitus:evidence for effect of yoga.indian J Endocrinol Metab,2014:18:745-9.
19. Mullur RS, Ames D. Impact of a 10 minute seated yoga practice in the management of diabetes.J yoga phys Ther,2016:6:1000224.
20. Diagnosis and classification of Diabetes By American diabetis association,2010:33:s62-69.
21. Significance of HbA1c test in the diagnosis and prognosis of Diabetic patients by shariq I, sherwani, haseeb A, khan aishah ekhzaimy, afshan Masood, meena k sakharkar,2016:11:95-104.