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Review on diabetes mellitus type-2 in adults: Pathophysiology, prevention and medications

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Abstract
Type 2 diabetes is a chronic metabolic disorder affecting millions worldwide, and recent medical advancements have led to improved therapeutic options. This review provides an overview of current management strategies, focusing on modern treatments and emerging trends. It covers the biological basis, symptoms, and complications of the disease, along with new drug classes such as GLP-1 receptor agonists, DPP-4 inhibitors, and SGLT-2 inhibitors that enhance glycemic control and patient outcomes. The potential antidiabetic benefits of natural compounds like jamun, bitter melon, pterocarpus marsupium are also explored. Additionally, the review highlights the crucial role of physical activity in prevention and management. Ayurvedic herbs such as Gymnema Sylvester, Aegle marmelos, and Trigonella foenum-graecum are discussed for their ability to regulate blood sugar and improve insulin sensitivity. Overall, the review emphasizes a holistic approach combining medication, lifestyle modifications, and regular monitoring to optimize long-term diabetes management.

Keywords: SGLT-2, GLP-1 receptor agonists, DPP-4 inhibitors, human insulin, tpye-2 diabetes mellitus

1. Introduction
Type 2 diabetes mellitus (T2DM) is a chronic, progressive metabolic disorder characterized primarily by insulin resistance and a gradual decline in insulin secretion from pancreatic β-cells. Together, these abnormalities result in persistent hyperglycemia and a wide range of associated metabolic disturbances that affect nearly every organ system in the body [1]. In the early stages of the disease, peripheral tissues such as skeletal muscle, adipose tissue, and the liver become less responsive to the physiological actions of insulin. To compensate for this impaired insulin signaling, pancreatic β-cells initially increase insulin production and secretion [2]. However, over time, this compensatory mechanism becomes inadequate, eventually leading to decreased β-cell function and overt hyperglycemia. This dual process insulin resistance coupled with declining insulin output forms the central pathophysiological basis of type 2 diabetes [3].
Globally, type 2 diabetes accounts for nearly 90% of all diagnosed cases of diabetes, making it the most common and fastest-growing form of the disease. Its prevalence has reached epidemic proportions, driven by rapid urbanization, sedentary lifestyles, excessive caloric intake, and increasing rates of overweight and obesity [4]. According to international health organizations, the number of individuals affected by T2DM continues to rise annually, with alarming increases observed in both developed and developing regions [5] This trend is especially concerning because many low- and middle-income countries lack adequate healthcare infrastructure for early diagnosis, education, and long-term management [6]. As a result, the burden of complications such as cardiovascular disease, neuropathy, nephropathy, retinopathy, and peripheral vascular disease remains disproportionately high in these population. Insulin resistance and decreased insulin production are hallmarks of type 2 diabetes, a chronic metabolic disease that causes hyperglycemia and related metabolic problems. Type 2 diabetes is thought to account for 90% of all instances of diabetes worldwide, and its incidence is rising [7].

1.1 Human insulin
The pancreatic beta cells produce human insulin, a peptide hormone that is essential for energy regulation and glucose metabolism. With a molecular weight of roughly 5,808 Da, it is a complex molecule made up of 51 amino acids [8].

Structure

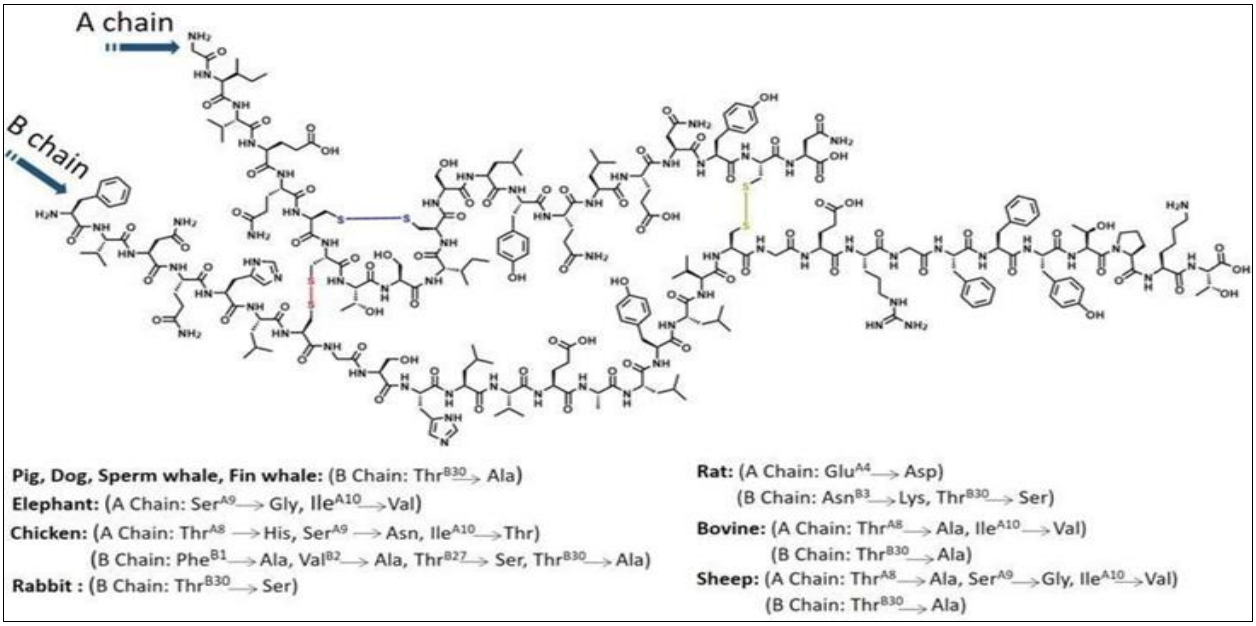

Fig 1: Chemical structure of Human Insulin

A Chain

Gly-Ile-Val-Glu-Gln-Cys-Cys-Ala-Ser-Val-Cys-Leu-Tyr-Gln-Leu-Glu- Assn-Tyr-Cys-As n

B Chain

Phe-Val-Asn-Gln-His-Leu-Cys-Gly-Ser-His-Leu-Val-Glu-Ala-Leu-Tyr-Leu- Val-Cys-Gly-Glu-Arg-Gly-Phe-Tyr-Thr-Pro-Lys-Thr

Function

1. Insulin is essential for controlling blood glucose levels.
2. It makes it easier for cells (muscle and adipose tissue) to absorb glucose.
3. Insulin encourages the synthesis of glycogen.
4. It prevents the liver from producing glucose.

Regulation

Numerous factors control insulin secretion, such as

1. **Glucose:** Insulin production is inhibited by low glucose levels and stimulated by high glucose levels.
2. **Hormones:** Insulin secretion is controlled by glucagon, somatostatin, and adrenaline.
3. **Neural signals:** Insulin secretion is influenced by the autonomic nerve system.
4. **Clinical significance:** Diabetes mellitus, a disorder marked by decreased insulin output or insulin resistance, is treated with insulin. Rapid-acting, short-acting, intermediate-acting, and long-acting insulin analogues are among the several types of human insulin.

Pathophysiology of Type 2 Diabetes

Diabetes type 2 is a complicated condition involving several physiological mechanisms. Type 2 diabetes is characterized by insulin resistance, which happens when the body's cells become less sensitive to insulin, making it more difficult for glucose to enter the cells.

Conversely, impaired insulin secretion happens when the pancreas cannot generate enough insulin to satisfy the body's requirements [9].

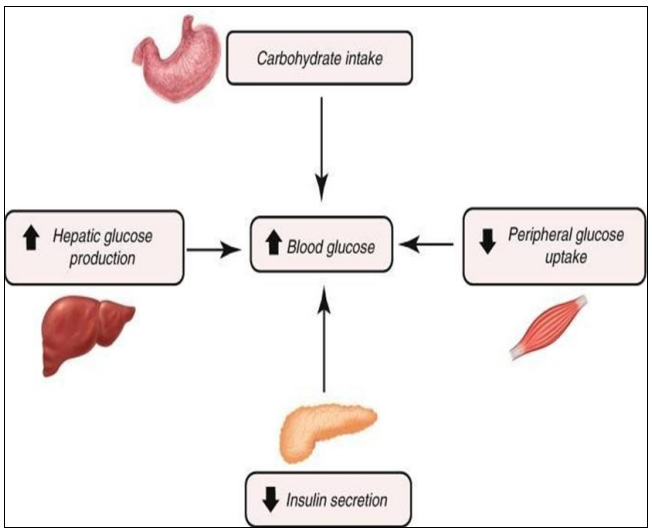

Fig 2: Pathophysiology of Type 2 Diabetes

3. Prevention

3.1. Healthy Dietary Habits

Adopting a balanced diet plays a fundamental role in diabetes prevention. Diets rich in whole grains, dietary fiber, fruits, vegetables, lean proteins, and unsaturated fats help improve insulin sensitivity and maintain normal glucose levels. Reducing intake of refined carbohydrates, sugary beverages, Tran's fats, and highly processed foods lowers the risk of metabolic disturbances that lead to diabetes.

3.2. Regular Physical Activity

Engaging in routine physical activity enhances glucose uptake by skeletal muscles and improves overall metabolic function. At least 150 minutes of moderate-intensity aerobic exercise per week, along with resistance training, can significantly decrease insulin resistance. Additionally, minimizing sedentary behavior helps maintain a healthy metabolic profile.

3.3. Weight Management

Obesity particularly central obesity is a primary risk factor for Type 2 Diabetes. Maintaining a healthy weight through calorie control, portion management, and regular physical activity reduces the risk of developing insulin resistance. Even a 5-10% reduction in body weight can markedly lower diabetes risk in high-risk individuals.

3.4. Stress Reduction and Adequate Sleep

Chronic stress and poor sleep contribute to abnormal cortisol release and impaired glucose metabolism. Stress-management techniques such as yoga, meditation, and mindfulness, along with 7-9 hours of quality sleep, help maintain hormonal balance and support glucose regulation.

3.5. Avoidance of Tobacco and Excessive Alcohol

Smoking increases inflammation and alters glucose metabolism, significantly raising diabetes risk. Limiting or avoiding alcohol consumption also supports metabolic health, as excessive intake contributes to weight gain and impaired liver function.

3.6. Regular Monitoring in High-Risk Individuals:-

People with prediabetes, family history of diabetes, obesity, or metabolic syndrome benefit from regular screening of fasting glucose, HbA1c levels, and lipid profiles. Early detection allows for immediate lifestyle intervention to prevent progression to Type 2 Diabetes.

3.7. Dietary Supplements and Functional Foods:-

Certain naturally occurring substances such as omega-3 fatty acids, polyphenols, curcumin, and dietary fiber have demonstrated beneficial effects on insulin sensitivity and inflammation. Including these in the diet may offer additional preventive benefits when combined with a healthy lifestyle.

Risk Factors for Type 2 Diabetes

Type 2 diabetes is caused by a number of risk factors, such as: -

1. Obesity.
2. Physical inactivity.
3. Heredity.
4. Poor diet.

An individual's risk of type 2 diabetes is also influenced by their age, ethnicity, and family history [10].

Fig 3: Risk Factors for Type 2 Diabetes.

Complications of Type 2 Diabetes

Numerous acute and long-term consequences, including microvascular ones like kidney disease and retinopathy and macrovascular ones like cardiovascular disease and stroke, can result from type 2 diabetes. Additionally, diabetes is linked to a higher risk of infections, skin disorders, and cognitive decline [11].

Fig 4: Complications of Type 2 Diabetes

Symptoms

1. Increased urination.
2. Increase thirst.
3. Fatigue.
4. Blurred vision.
5. Slow healing of cuts and wounds.
6. Tingling or numbness in hands and feet.
7. Recurring skin, gum, or bladder infections.
8. Increased hunger.
9. Unexplained weight loss.
10. Darkened skin patches.
11. Frequent infections

Causes

1. Insulin Resistance.
2. Obesity and increased body fat.
3. Physical inactivity.
4. Genetic Predisposition.
5. Unhealthy Diet.
6. Ageing.
7. Metabolic Syndrome components.
8. Gastrolienal Diabetes History.
9. Polycystic Ovary Syndrome.
10. Sleep Disorder.
11. Chronic Stress and Cortisol Excess.
12. Certain Medications.

Dietary Plan for Diabetes Mellitus Type 2

A dietary plan for Type 2 Diabetes aims to control blood glucose, manage weight, and prevent complications such as heart disease, kidney the diet focuses on balanced nutrition, low glycemic index foods, and controlled carbohydrate issues, and neuropathy. The diet focuses on balanced nutrition, low glycemic index foods, and controlled carbohydrate intake [15].

Current Treatment Options: Type 2 diabetes is currently treated with drugs including Metformin, sulfonylureas, and insulin therapy as well as lifestyle changes like diet and exercise. These medicines have drawbacks, too, and more potent and long-lasting treatments are required [12].

Medications

SGLT-2 inhibitors: SGLT2 inhibitors (Sodium-Glucose Cotransporter-2 inhibitors) are a newer class of oral anti-diabetic medicines mainly in Type 2 Diabetes Mellitus.

Common example

1. Dapagliflozin
2. Empagliflozin
3. Canagliflozin
4. Ertugliflozin [13]

This lower blood sugar levels by preventing the kidneys from reabsorbing glucose.

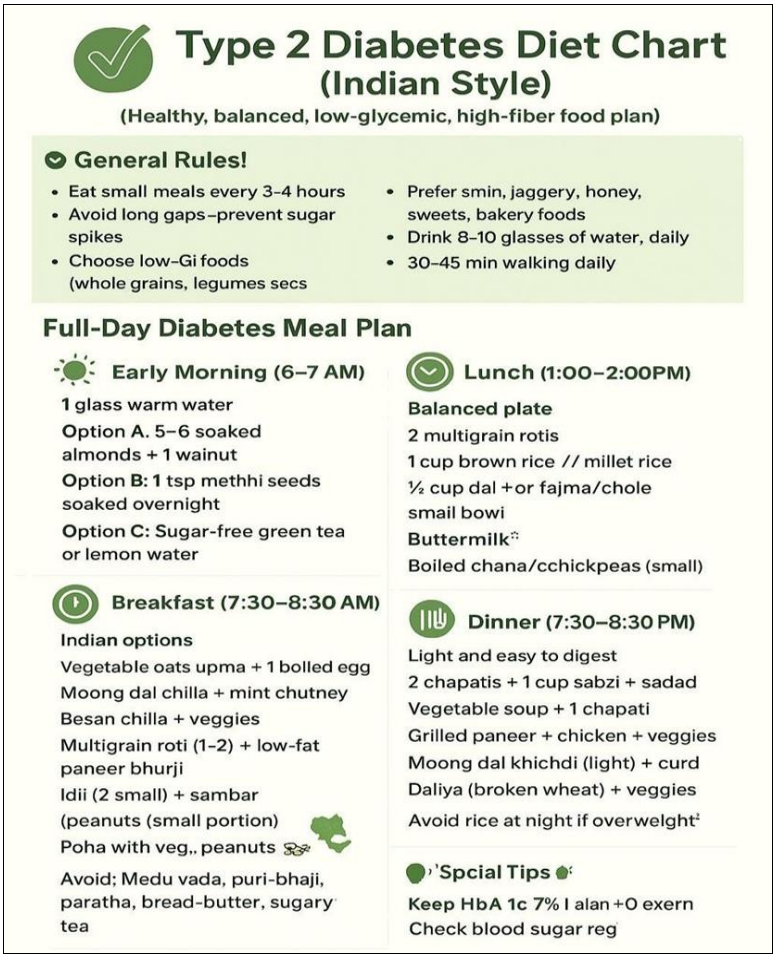

Fig 5: Dietary Plan for Diabetes Mellitus Type 2

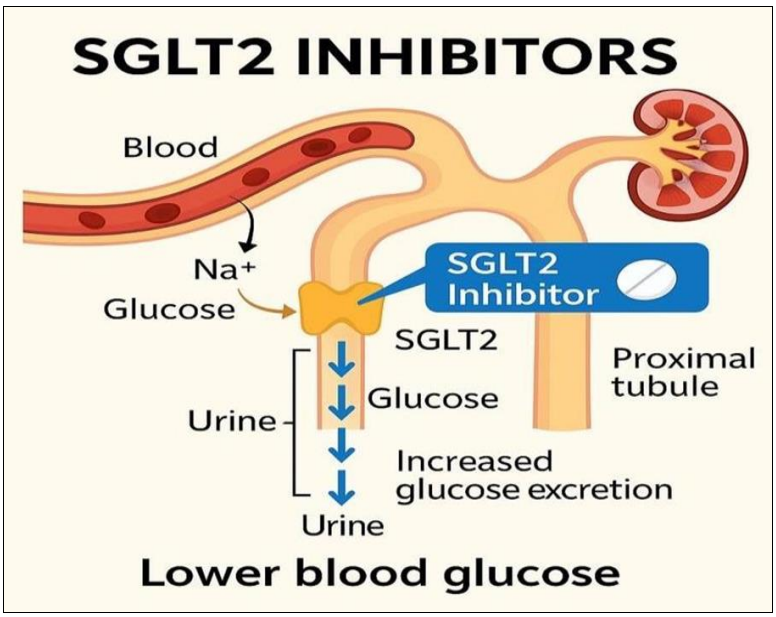

Fig 6: SGLT-2 inhibitors

GLP-1 receptor agonists

GLP-1 receptor agonists (Glucagon-like peptide-1), a hormone your body releases after eating. They are widely used for type 2 diabetes and, more recently, for weight management.

GLP-1 receptor agonists that increase insulin secretion and lower glucagon levels include

1. Liraglutide
2. Exenatide
3. Dulaglutide

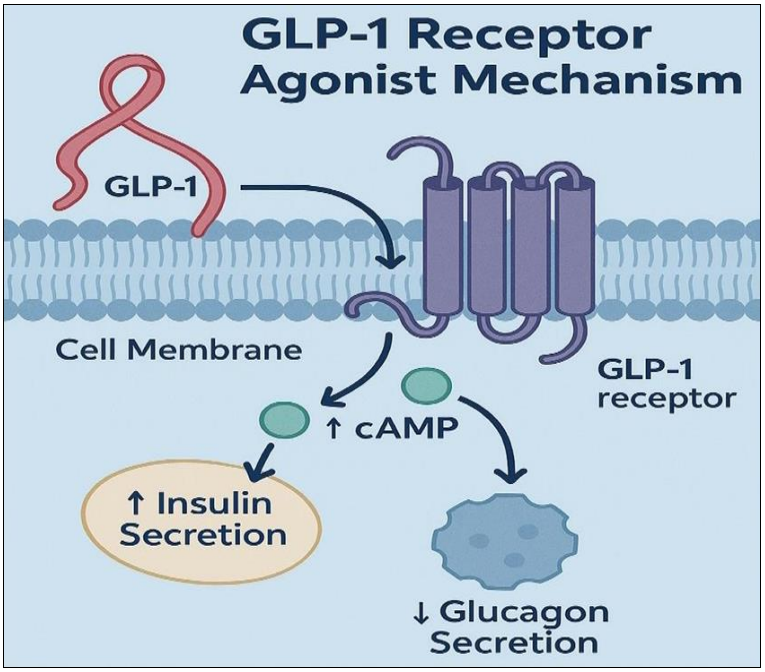

Fig 7: GLP-1 Receptor agonist mechanism.)

DPP-4 inhibitors

They inhibit DPP-4 (Dipeptidyl peptidase-4) an enzyme that rapidly breaks down incretin hormones (GLP-1 and GIP).
By blocking DPP-4, these hormones last longer and help: Increase insulin secretion when blood sugar is high.

By blocking DPP-4, these hormones last longer and help

1. Increase insulin secretion when blood sugar is high.
2. Reduce glucagon, lowering liver glucose production.
3. Improve post-meal glucose control.

DPP-4 inhibitors do not cause significant weight loss and are generally weight-neutral- 4 inhibitors, such as

1. Sitagliptin.
2. Sax gliptin.
3. Linagliptin.

And it increases insulin production and decrease glucagon levels by blocking the enzyme DPP-4 [14].

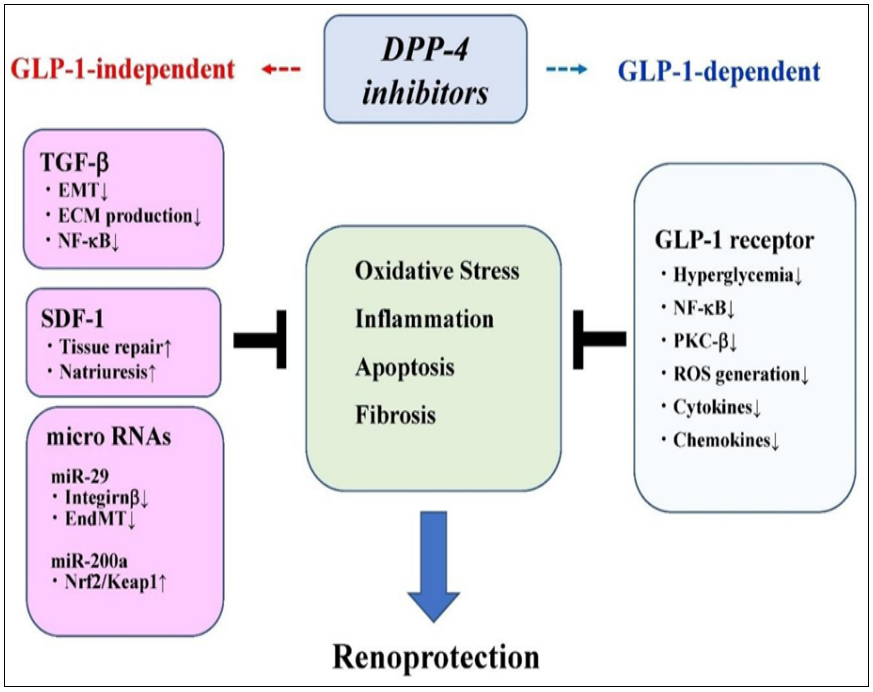

Fig 8: Reno protective effect of DPP-4 inhibitor.

Ayurvedic medication: An all-encompassing method of treating type 2 diabetes is provided by the Indian Traditional medical system known as Ayurveda. Here are typical commonly used Ayurvedic medicines for Type 2 Diabetes Mellitus, include the following [16]: -

Gymnemate Sylvester
This herb, sometimes called Gurman, is well-known for lowering blood sugar and enhancing insulin sensitivity.

Fig 9: Introduction of Gymnemate Sylvestre

Synonyms
Gurmar/Gudmar, Australian cow plant and periplocin of the woods.

Biological Source
Gymnemate Sylvestre consists of dried leaves of the plant Gymnemate Sylvestre (Retz.) R. Br. ex Sm. It is a woody climbing shrub.

Family
A polynucleate (previously Asclepiadaceae)
Chemical Constituents
The main chemical constituents of Gymnemate Sylvestre are gym emic acids and gymnasaponins, which are oleanane-type triterpene saponins. Other important components include gurami, stigmasterol, flavonoids, anthraquinones, and various organic acids such as tartaric, formic, and butyric acid.

Uses
1. Anti-diabetic: Reduces blood glucose levels and improves insulin activity.
2. Sugar taste suppression: Temporarily blocks sweet taste receptors.
3. Hypolipidemic: Lowers cholesterol and triglycerides.
4. Weight management: Reduces sugar cravings and supports metabolism.
5. Anti-inflammatory and antioxidant.

Aegle Markellos
This plant, sometimes called Bael, is well-known for its anti-inflammatory and antioxidant qualities, which can help control blood sugar levels and avoid problems.

Fig 10: Aegle Markellos

Synonyms
Bael, Bengal quince, golden apple, stone apple, and wood apple.

Biological Source
The biological source of Aegle mamelons is the unripe or half-ripe fruits, as well as the leaves, roots, bark, and seeds, of the Aegle mamelons tree. This tree is commonly known as bale and is native to the Indian subcontinent, growing wild in regions like India, Bangladesh, and Sri Lanka.

Family
Rutaceous.

Chemical Constituents
Aegle mamelons (bale) is rich in various chemical compounds, including alkaloids, coumarins, terpenoids, and flavonoids, with specific constituents differing by plant part. For example, leaves contain compounds like Marceline, rutin, and phenylethyl Cinna amides, while. Fruits contain mamelons and tannins, and seeds are a source of essential oils like limonene and phellandrene.

Uses
1. Helps control blood sugar levels.
2. Improves insulin function.
3. Often used in traditional medicine for Diabetes Mellitus.
4. Reduces kidney damage.
5. Improves lipid profile [18].

Trigonella Frenum-Graecum
This herb, often called fenugreek, is well-known for its capacity to increase insulin sensitivity and reduce the rate at which sugar enters the bloodstream.

Fig 11: Trigonella Frenum-Graecum.

Synonyms
Fenugreek, Methi and Greek clover.

Biological Source
Fenugreek consists of the dried ripe seeds of Trigonella Foenum-graecum Linn.

Family
Fabaceae (Leguminosae)

Chemical Constituents
Trigonella frenum-graecum contains a wide range of chemical constituents, including carbohydrates, proteins, lipids, alkaloids (like trigonelline), flavonoids (like

quercetin and vitexin), and saponins (Including steroidal sapogenins like diosgenin).

Uses
1. Help lower blood glucose levels by slowing carbohydrate digestion.
2. Improving insulin sensitivity.
3. Stimulating glucose uptake.
4. High soluble fiber slows glucose absorption [19].

Momordica Charantia
This herb, often called bitter melon, is well-known for its capacity to enhance insulin sensitivity and reduce blood sugar levels [4].

Fig 12: Momordica Charantia

Synonyms
Bitter melon, bitter gourd, and balsam pear, and karela.

Biological Source
Momordica Charantia is the herbaceous vine itself, commonly known as bitter melon or karela. Bitter melon is consist of fresh or dried fruits of the plant.

Family
Cucurbitaceae.

Chemical Constituents
Momordica Charania (bitter melon) contains a variety of chemical compounds, including the hypoglycemic agents Charan tin, vicine, and polypeptide-p (plant insulin), along with triterpenoids, saponins, and flavonoids**.**

Uses
1. Improves insulin sensitivity.
2. Increases glucose uptake.
3. Reduces glucose production.
4. Inhibits glucose absorption.
5. Stimulates insulin secretion [20].

Pterocarpus Marsupium
This herb, sometimes called Vijaya Sar, is well-known for its capacity to lower blood sugar levels and increase insulin sensitive.

Fig 13: Pterocarpus Marsupium

Synonyms
Kino tree, Malabar Kino tree, and Vijaya Sar.

Biological Source
The biological source for Pterocarpus is the Indian Kino tree (Pterocarpus marsupium), a deciduous tree.

Family
Fabaceae (also known as Leguminosae).

Chemical Constituents
It includes a variety of flavonoids, such as liquiritigenin, is liquiritigenin, and pterostilbene, as well as tannins like Kino tannic acid and kino-red.

Uses
1. Reduces blood glucose levels.
2. Regenerates pancreatic β-cells.
3. Improves insulin sensitivity.
4. Helps in reducing body weight and improving lipid metabolism.

Jamun
Jamun, also known as Indian blackberry, is a tropical fruit known for its sweet-astringent taste and strong medicinal value, especially in Ayurveda.

Fig 14: Jamun Seeds.

Synonyms: Java plum, Indian blackberry, Malabar Plum, and Black plum.

Biological Source
Jamun consists of the fruits and seeds obtained from the plant *Syzygies cumin* (L.) Skeels.

Family
Myrtaceous.

Chemical Constituents

Jamun contains a wide array of chemical constituents, including flavonoids (like quercetin and myricetin), phenolic acids (such as gallian ellagic acid), and tannins. It is also rich in essential nutrients like vitamin C and minerals like potassium, along with alkaloids (like Jambo sine) and glycosides.

Uses

1. Seeds contain Jambo line, which helps reduce the conversion of starch into sugar.
2. Helps improve insulin sensitivity.
3. Reduce post-meal blood glucose spikes.
4. Improve glycemic control.
5. Utilization of glucose by tissues.
6. Protect and repair beta cells of the pancreas.
7. Help improve natural insulin production.
8. Helps in management of dehydration and tiredness in diabetics [22].

Lifestyle Modifications

Type 2 diabetes can be well managed with lifestyle changes including diet and exercise in addition to Ayurvedic drugs. Regular exercise, like yoga or walking, and a nutritious diet low in sugar and saturated fats will help control blood sugar levels and enhance insulin sensitivity [23].

Exercises and Physical Activity

Frequent physical activity and exercise can enhance insulin sensitivity and help control blood sugar levels. Walking and cycling are examples of aerobic activity that can lower HbA1c levels and enhance cardiovascular health [24].

Activity

By promoting cell uptake of glucose and preventing the liver from producing glucose, insulin controls blood sugar levels.

Conclusion

A thorough strategy to managing type 2 diabetes is necessary due to its complexity and multifactorial nature. Novel therapeutic techniques that improve patient outcomes and quality of life have been developed as a result of recent developments in medical research. The significance of a comprehensive management strategy that incorporates medication, lifestyle modifications, and regular monitoring is emphasized in this review.

Healthcare practitioners can deliver efficient care and enhance patient outcomes by comprehending the pathophysiology, risk factors, and complications of type 2 diabetes.

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