

## Recent trends in therapeutic approach of type 2 diabetes mellitus

### ABSTRACT –

Diabetes Mellitus is a metabolic condition that causes blood glucose levels to rise (hyperglycemia). Type 2 diabetes mellitus, often known as NIDDM (non-insulin dependent diabetes mellitus), is a disease in which cells do not adequately utilise insulin. Adult-onset diabetes is another name for it. It has become a major health concern all over the world, but thanks to advancements in the medical sector and growing developments in treatment, diabetes may now be managed. The progress and treatment of diabetes mellitus help to lower the health risks and complications associated with the disease. It is vital to undertake lifestyle modifications in addition to therapy to ensure long-term diabetes control. Sulphonyl ureas, biguanides, and alpha glucosidase inhibitors are among the latest generation of medications used to prevent blood glucose levels from rising too high. Patients who do not react to a single pharmacological therapy are given dual drug regimens. Nanotechnology, microtechnology, and statin therapy are some of the more recent treatments that are now commonly employed to treat Diabetes Mellitus. This article examines the most recent trends or the advancements in therapeutic approaches for type 2 diabetes, with a focus on progress over the last 10-15 years. The goal of this study is to find out about the latest developments in the treatment of type 2 diabetes mellitus and to examine the merits and drawbacks of each option for DM management and find a better cure for the disease. It will help to decrease the mortality rate due to the growing rise of the diabetes mellitus.

**KEYWORDS-** Type 2 DM, Treatment, antidiabetic, Insulin, Nanotechnology, advance therapy

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## Introduction –

Diabetes mellitus has recently become a common metabolic condition. Diabetes has developed into an important medical issue around the life, affecting individuals over all ages, genders, culture, and races, and its frequency has been increasing at an alarming rate. Over the next few years, the prevalence of type II Diabetes Mellitus is expected to skyrocket. By 2025, the number of people infected by Diabetes Mellitus is predicted to climb to 35 percent worldwide.<sup>[1]</sup>

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The word diabetes is derived from original Greek word siphon which literally means that individuals with diabetes "passed water". There are various varieties of diabetes, each with its own cause. Types of diabetes are:

1. TYPE 1 DIABETES MELLITUS- This is caused to the loss of beta cells in the islets of Langerhans, which results in a shortage of insulin. Insulin-dependent diabetic mellitus (IDDM) is another name for it. Degeneration of beta cells, viral infection, congenital abnormality of beta cells, and auto immune disorders are all causes of type 1 diabetes mellitus.
2. TYPE 2 DIABETES MELLITUS- Insulin resistance, or the inability of insulin receptors to give a response to insulin, is the cause. It is a type of diabetes mellitus that is more common. NIDDM stands for Non-insulin-dependent Diabetes Mellitus. Genetic abnormalities, stress, and lifestyle changes such as poor eating habits and physical inactivity are all factors that contribute to type 2 diabetes mellitus.

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The three main relapses of insulin deficiency lead to various symptoms of diabetes.

1. Increased blood glucose levels due to decreased tissue utilization
2. Fat from adipose tissue is mobilised for energy reasons. As a result, the amount of fatty acids in the body increases.
3. Recovery of protein from tissues

### WAYS TO KEEP BLOOD GLUCOSE IN CHECK

- i. Blood glucose testing: Because structural components of blood cells are lacking, glucose concentrations in plasma or serum are 10-15% greater than in whole blood.
- ii. Venous blood sample: Enzymatic, colorimetric, and automated methods are routinely used in laboratories to determine plasma glucose levels.

iii. Capillary blood samples: Several strip-based portable, battery-operated metres use the glucose oxidase method to test capillary blood samples. The latest gadgets use infrared absorption spectra to provide a non-invasive technique.<sup>[2]</sup>

**Comment [ME6]:** The write-up under this heading is not in consonant with the headline.

Diabetes mellitus is a disease that can lead to a variety of consequences, such as coronary heart disease, retinopathy, and neuropathy. It is now evident that maintaining tight blood glucose control lowers the risk of diabetes complications.

Type II diabetes mellitus can be treated by oral hypoglycemic drugs.

The medications used to treat Type 2 Diabetes mellitus fall into three categories:

**Comment [ME7]:** Be consistent in the use of either type II diabetes or type 2 diabetes.

1. Insulin secretagogues are treatments that primarily stimulate insulin secretion.
2. Insulin sensitizers are drugs that make tissues (mainly the liver and adipose tissue) more sensitive to the action of insulin.
3. There are medications that primarily impact glucose absorption.

Oral drugs and insulin work in one of the following ways to treat diabetes:

1. Stimulates the pancreas to produce and secrete more insulin.
2. Slows the release of glucose from the liver (excess glucose accumulates in the liver).
3. Blocks carbohydrate digestion in the stomach or intestines, which makes tissues more insulin sensitive (and responsive).
4. Aids remove glucose from the body by increasing urination.

Recent developments in new drugs such as sulfonylureas, biguanides and alpha-glucosidase inhibitors are used to lower blood sugar levels. Recent advances in drug led discovery have led to the development of new classes of drugs, such as incretin mimetics, amylin analogues, GIP analogues, and dipeptide peptidase 4 inhibitors, that can potentially reduce diabetes.

**Comment [ME8]:** reference

Major drugs developed are (1) boosters of insulin release, (2) augmenters of insulin action, (3) inhibitors of glucose production in liver, and (4) inhibitors of glucose uptake from the gut.

An effective new drug has been developed that potentially reduces the risk of heart and kidney failure. Advances in technologies such as continuous blood glucose monitoring (CGM) systems and continuous subcutaneous insulin infusion are opening up new possibilities for improving blood glucose control. The number of new drugs available for diabetes has exploded over the past decade, and notable new drugs are being developed to

achieve this. 4,444 technological solutions target delivery of insulin plus other hormone glucagon via 4,444 artificial pancreas, with system components already in use, with 4,444 suggesting that the above alternative may become available in the upcoming decade. The goal of this article is to give a quick rundown of the most recent developments in diabetes treatment for therapeutic application. <sup>[3]</sup>

**Comment [ME9]:** is not ideal to start a sentence with number.

**Objective-** The focus of this review is on substantial advancements in the treatment of blood glucose in people with type 2 diabetes. The purpose of this paper is to offer a quick summary of recent DM management developments for clinical use.

### **Main text-**

The recent therapies used in the treatment of Diabetes mellitus are

1. **Nanotechnology** New glucose estimation and insulin delivery methods have resulted from the application of nanotechnology to diabetes management.

Nanotechnology is shown useful in the treatment of diabetes mellitus by expanding the accessible surface area of the sensor-receptor complex as well as boosting the catalytic characteristics of electrodes. Improved oral formulations and islet encapsulation might transform insulin administration. Clinical nanotools are pore-encrusted microcapsules that might be used to administer medications. The holes that are present are so big that it lets small atoms like oxygen, glucose, and insulin to flow via, but small enough that larger and safer skeleton atoms proliferate. Diabetic patients can have microcapsules implanted beneath their skin with replacement islets of Langerhans cells, which are generally supplied from pigs. This might temporarily correct the body's defective glucose feedback loop without the need of harsh immunosuppressive drugs, which could put the patient at danger of infection. Nanoparticle targeted drug delivery has the benefit of increasing medication bioavailability by targeting specific tissues, organs, and tumours, as well as providing maximal doses of medicines directly to the target location.

**Comment [ME10]:** ??

Insulin is a critical component of type 1 and type 2 diabetes progression, and traditional insulin administration systems have been associated with infection, unpleasant dosing, and low patient compliance. Recent micro and nanotechnology, on the other hand, has made insulin administration easier by altering insulin delivery methods, such as pulmonary, nasal, transdermal, and closed-loop delivery. <sup>[3]</sup>

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2. **Gene therapy** The most significant aspect of treatment is blood sugar control, which **minimises** the number of problems connected with diabetes. For somatic cell gene therapy, there are two techniques of gene delivery that use the body's somatic cells. Ex vivo gene therapy is the initial procedure, and it is defined as removing tissue from the body. Therapeutic genes are introduced in vitro and subsequently put back into the body, whereas in vivo treatment entails immediately providing a gene therapy vector to the patient via subcutaneous, intravenous, or bronchial channels, or with the help of local injection. Ex vivo therapy is used to produce cells that have beta-cell characteristics, such as insulin-producing cells. This technique has also been utilised to generate transplantable cells.

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Transgenes like glucokinase, for example, impact the liver by reducing glucose levels. The insulin gene can be altered to produce a single-chain insulin with 20-40 times the activity of mature insulin. The delivery of genes that signify a glucose response and the use of gene therapy to boost  $\beta$ -cell formation in the liver are two more fields of genetic engineering. The stimulation of cell production in the liver was also investigated. Endocrine cells can be induced to create  $\beta$ -cells by delivering islet-specific transcription factors, according to Kojima et al. [3]

3. **Statin therapy** Statins are blockers of 3-hydroxy-3-methylglutaryl coenzyme A, which block a crucial process of LDL cholesterol in the liver, decreasing blood cholesterol levels and improving blood vessel lining health. Statins (HMG Co A reductase inhibitors) are crucial medications for persons with type 2 diabetes who really want to diminish their risk of heart disease. Statins are significantly efficient in lowering cardiovascular disease in those with moderate serum cholesterol and no prior history of cardiovascular disease. HMG-CoA reductase inhibitors or statin therapy, on the other hand, may cause side effects such as renal failure. **Young and disease-free persons were found to be inefficient or poorly adherent to statin prescription in a trial of 6422 patients, according to Journal of Diabetes research**, however treatment should focus on older patients considering younger patients are less compliant. Patients with high risk factors and evidence of heart disease should also be given statins. [4,5]

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4. **Medical Nutrition Therapy** Numerous improvements in clinical research aimed at using the diet to treat illnesses and diseases have led to nutritional therapy in the prevention and treatment of diabetes. Sustaining optimal blood lipid levels, appropriate body weight, and normoglycemic levels are the goals of a diabetic diet. Nutritional therapy as a diabetes

treatment will be determined by the patient's age-related nutritional requirements, along with specific factors such as food preferences, other medical conditions, exercise regimen, and recommended nutritional requirements based on the patient's ability and health status. [5]

5. **Stem cell technology** Researchers may use stem cell research to generate certain types of human cells in the lab and study how they behave and interact under various settings. DM can be prevented by either eliminating abnormalities in pancreatic beta cells or enhancing the sensitivity of the body's cells to insulin action. While B-cell replacement procedures provide unique sources, existing islet and pancreatic transplantation strategies are constrained by a scarcity of donor organs. Because of its immunosuppressive qualities, soluble Mesenchymal stem cell (MSC) therapy has become a preferred treatment for type 1 DM. Because of the direct contact and generation of markers, MSCs have been reported to exert immunomodulatory effects both in vitro and in vivo. For type 1 DM patients with poor glycemic control, clinical pancreatic or islet transplantation has been regarded a viable therapy option. Researchers gathered and evaluated 13 papers published between 2006 and 2016 that included 342 patients who got stem cells similar to those found in cord blood and another 111 who received stem cells similar to those found in cord tissue to treat their diabetes.

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6. **Herbal therapy** For a lengthy moment, researchers have advocated for the use of tiny dosages of insulin and non-insulin dependent diabetic mellitus in locally generated prescriptions to treat diabetes. Plants having anti-diabetic qualities could be used as a supplement to current medications or as a proposed source for new hypoglycemic mixes. Researchers have long advocated for the use of small insulin and non-insulin secondary diabetes for the treatment of locally created diabetes mellitus using local prescriptions. Plants having anti-diabetic qualities could be used as a supplement to current medications or as a proposed source for new hypoglycemic mixes. For insulin-dependent and non-insulin-dependent diabetic mellitus, researchers have long proposed running-home recipes. Plants having anti-diabetic qualities could be used as a supplement to current medications or as a proposed source for new hypoglycemic mixes. Herbal medicines are extremely popular among the general public due to their low cost and lack of controversy. The stimulation of cell production in the liver was also investigated. Endocrine cells can be induced to create  $\beta$ -cells by delivering islet-specific transcription factors, according to Kojima et al. [6]

**Comment [ME15]:** this sentence is not clear

**Comment [ME16]:** it will be nice if some of these herbal medications be mentioned here with references

**Comment [ME17]:** should this be found under this heading?

- 7. Leptin Therapy** Leptin is a hormone produced by fat cells that affects central nervous system neurons. It prevents overeating by reducing food intake and raising energy expenditure. By activating leptin receptors, it lowers blood sugar levels.

#### RECENT DRUGS-

Sulfonylureas (SU) of the first generation were launched to successfully replace oral insulin in the majority of patients with type 2 diabetes at the time. A ten-year research by a university group (comparing tolbutamide to insulin or a single diet) found that glucocorticoids may increase cardiovascular disease mortality, but the findings were extensively contested and subsequently dismissed. The second generation of sulfonylureas is still widely used. Since the emergence of thiazolidinediones as the primary real insulin sensitizer around the turn of the century, insulin occlusion has steadily dominated a "pancreatic-centric" strategy as a focus for type 2 diabetes mellitus. To avoid lipotoxicity, the main MOA concept is to "eat up" free. They are agonists of the peroxisomal proliferation receptor (PPAR) gamma receptors, which are found largely in adipose tissue. <sup>[7]</sup>

#### COUNTER REGULATORY HORMONES

By promoting liver glycogenolysis and also gluconeogenesis, these compounds raise blood sugar levels. From a therapeutic aspect, specialists who interfere with the release or countermeasures of control substances can be advantageous. Glucocorticoids' worst enemy: Body bloating, insulin blockage, and hyperglycemia can all be caused by an increase in glucocorticoid concentrations, and any treatment that reduces glucocorticoid activity will lessen these antagonistic effects. <sup>[8]</sup> In big diabetic rodents, specific inhibitors of 11 HSD1 have been demonstrated to increase insulin-dependent capacity, glycemic control, and subsequent development of plasma lipids. Insulin is necessary for persons with type 2 diabetes who have had poor results with sulfonylureas.

SGLT2 (sodium glucose transporter 2) inhibitors, which block glucose and sodium reabsorption in the proximal tubule, are the last class of drugs proposed for diabetes. Up to 60 g of glucose is excreted per day, resulting in a drop in blood sugar without the use of insulin and calorie loss, resulting in weight loss. The inhibition of SGLT2 is insufficient and is somewhat compensated by the prolongation of SGLT1 tubular movement. Despite the fact that the number of SGLT2 and SGLT1 inhibitors is

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growing, equilibrium remains a problem. Endogenous gluconeogenesis is also increased, most likely due to glucagon stimulation, which can be avoided by connecting glucagon to incretinized GLDs. Cyclic stress is similarly reduced by SGLT2 inhibitors, but the composition is unknown. Inhibitors of 11B-selective hydroxysteroid dehydrogenase type 1 (11BHSD1) 11BHSD1 inhibitors show a lot of promise for treating osteoporosis and metabolic syndrome, which includes type 2 diabetes. Anti-diabetic, anti-adipogenic, and anti-lipogenic characteristics of BHSD1 inhibitors, as well as anti-osteoporotic activity.<sup>[9]</sup>

Mimic Amylin, a glucose regulator produced by islet beta cells, released alongside insulin, and deposited in the islets of diabetes patients. It appears to play a role in promoting satiety, slowing stomach emptying, and suppressing glucagon secretion. It also activates G protein-coupled receptors and activates a variety of common intracellular signal transduction pathways, ultimately leading to cell death.<sup>[10-16]</sup>

## Conclusion

In most countries, preventing type 2 diabetes mellitus is a top priority in order to stem the expanding epidemic. In the twenty-first century, the treatment of type 2 diabetes mellitus has progressed toward safer and maybe more effective medications, which in some situations can also minimise the risk of cardiovascular and renal complications. Over the past two decades, research of the pathohistology of DM has progressed at an alarming rate. The development of medication classes that target specific metabolic pathways has been aided by a better knowledge of diabetes. Significant advances in blood sugar management in type 2 diabetes have led to control of diabetes and potentially reduced mortality. Over the past decade, the incidence of kidney and heart related diseases in people with DM disease has decreased significantly. Treating the DM disorder is multifactorial. The development of strategies like as PCR, DNA microarrays, and qualitative knockout via sedation has opened up another realm of striking validation of imperfect traits/changes in the genome of living things. Diet, exercise, and diabetes education are still important components of diabetes management. Obesity should be approached aggressively and emphasize lifestyle changes. There is hope for a better future for diabetes as a variety of new and effective technologies for the treatment of diabetes emerge.

**NOTE:**

**Comment [ME19]:** there are so many strong statements you make without backing them up with references?

The study highlights the efficacy of "Herbal medicines" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable

**Comment [ME20]:** The author has failed to achieve this in the write-up

#### COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors

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**Comment [ME21]:** Some of the references were not well written. Some journal names appeared in capital letters while others in small letters???

**Comment [ME22]:** ???

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