EMERGING THERAPIES FOR DIABETES

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ABSTRACT

Diabetes is becoming a greater hazard to human health, especially in recently industrialized and densely populated nations. Although they have different aetiologies, type 1 and type 2 diabetes both cause similar metabolic disturbances by an absolute or relative insulin deficiency that causes high plasma glucose.

Diabetes mellitus is a group of metabolic disorders that affect protein, lipid, and carbohydrate metabolism. It is characterized by persistent hyperglycemia that results from deficiencies in insulin secretion, action, or both. Diabetes mellitus has been identified for thousands of years.

In the past three decades, a number of new medications have been developed to improve the clinical management of the condition and associated disorders. These medications are the result of a deeper understanding of physiology and diabetic pathology. A number of novel medicinal agents are currently being developed as a result of recent discoveries regarding insulin-dependent and insulin-independent molecular events. These drugs have the potential to further improve diabetes management. This chapter offers a background on the events that have occurred.

Keyword: *diabetes mellitus; blood glucose level; insulin; treatment strategies; nanocarrier*

1. Introduction

Almost 100 million people (6% of the world's population) globally are affected by diabetes mellitus (DM), the most prevalent endocrine illness. It is brought on by the pancreas' insufficient or inefficient secretion of insulin, which causes a spike or decrease in blood glucose levels. It is discovered to harm.

Various bodily organs, including the blood vessels, eyes, kidneys, heart, and nerves. Insulin-dependent diabetes mellitus (IDDM, Type I) and non-insulin-dependent diabetes mellitus are the two categories into which diabetes mellitus has been divided (NIDDM, Type II). In contrast to Type II diabetes, which is defined by peripheral insulin resistance and poor glucose tolerance, Type I diabetes is an autoimmune illness characterized by a local inflammatory response in and around the islets, followed by the selective death of insulin-secreting cells.

When diabetes is present, there is an increased risk of a variety of consequences, including heart disease, peripheral vascular disease, stroke, neuropathy, renal failure, retinopathy, blindness, and amputations, among others. This review emphasizes cutting-edge developments in the disciplines of GM, insulins, drug administration, data management, and decision analysis. Additionally, it will examine the value of linked care and the evolving responsibilities both the diabetic patient and the doctor who works to give their care must play.

The main purposes of drugs are to treat symptoms and prolong life. The prevention of long-term diabetic problems and an improvement in longevity through the removal of numerous risk factors are secondary goals. The cornerstone of treatment and management for type 2 DM is diet and lifestyle changes, while insulin replacement medication is the backbone for people with type 1 DM. There are numerous types of hypoglycemic medications, including biguanides and sulfonylureas, that can be used to treat diabetes. Unfortunately, none of these drugs is optimal due to their harmful side effects, and their continued usage might occasionally lead to a reduction in responsiveness.

2. Types of Diabetes

1. Type I Diabetes
2. Type II Diabetes
3. Gestational Diabetes

2.1Type I

Diabetes is a chronic autoimmune condition that selectively destroys pancreatic beta-cells that produce insulin. The development of massive insulitis by using infiltrating T lymphocytes, which measures an amnestic autoimmune reaction, occurs when the transplantation of pancreas from twin donors to chronically diabetic twin recipients occur in the absence of immune suppression because of the high heterogeneity of pancreatic lesions of -cells that are quickly destroyed. Insulin-dependent (IDDM) or juvenile-onset diabetes are other names for type 1 diabetes.

Symptoms: include frequent urination, thirst, excessive exhaustion, weight loss, acetone breath, nausea, vomiting, blurred eyesight, and itching in the genital region.

2.2Type II

Adult-onset diabetes is another name for type 2 diabetes mellitus. On a background of insulin resistance, the progressive insulin secretary malfunction. The action of insulin is frequently resistant in those with this kind of diabetes. Over the world, it has an impact on 5-7% of the population. The illness is typically under control with food therapy, physical activity, and hypoglycemic drugs. This is the most prevalent kind of diabetes mellitus, and it is strongly linked to having an older age, being obese, and not exercising.

2.3Gestational Diabetes

Pregnant women often develop diabetes. During pregnancy large quantities of hormones are produced, these hormones may reduce insulin action in the mother’s body, causing insulin resistance. Women that develop diabetes mellitus during pregnancy and women with undiagnosed asymptomatic type 2 diabetes mellitus that is discovered during pregnancy are classified with gestational diabetes mellitus. The clinical importance of GDM lies in the fact that it is associated with significant maternal and fetal morbidity.

2. Pathophysiology

Type I Diabetes:

is an autoimmune illness in which autoreactive T lymphocytes specifically kill the pancreas' insulin-producing beta cells. It has been demonstrated that the autoreactive T lymphocytes can distinguish between islet autoantigens like insulin, glutamic acid decarboxylase (GAD), and zinc transporter 8 (ZnT8) (Blu. The patients eventually need insulin replacement medication because the diminished pancreatic beta-cell function can no longer sustain enough insulin to maintain euglycemia. Genetic and environmental variables work together to influence an etiology and pathophysiology of the autoimmunity prior to the diagnosis of T1D. The immunological responses coordinating the onslaught on the beta cells remain mysterious despite advances in our understanding of T1D pathophysiology. Before T1D develops into a clinical condition, autoantibodies can be found. The identification of causal environmental triggers is made more difficult by the delay between early biochemical changes and clinical presentation. Until recently, viruses, bacteria, and nutrition were among the environmental triggers thought to play a role in the etiology of the disease. To intervene as early as feasible and maintain functioning beta-cell mass, it is essential to unravel how these stimuli may interact with certain molecular targets to start the autoimmune cascade.

Type II

Any one or a combination of the "ominous octet" mechanisms shown in Fig. 1 and described below may contribute to the pathophysiology of type 2 diabetes (T2DM):

- Less insulin is secreted by islets of Langerhans cells.

- Increased glucagon secretion from the islets of Langerhans cells
- Increased glucose production in the liver
- Inability of neurotransmitters to function and insulin resistance in the brain
- Increased lipolysis vii) Increased glucose reabsorption by kidney
- The small intestine's incretin effect is diminished
- The liver, adipose tissue, and other peripheral tissues have a harder time absorbing glucose.

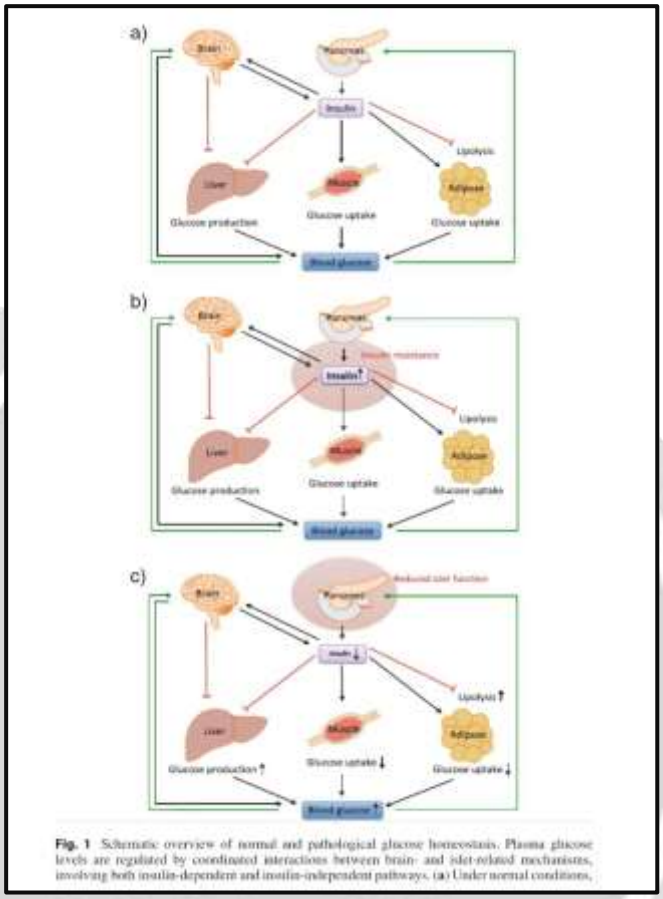

Fig.1 Diagrammatic representation of Diabetes

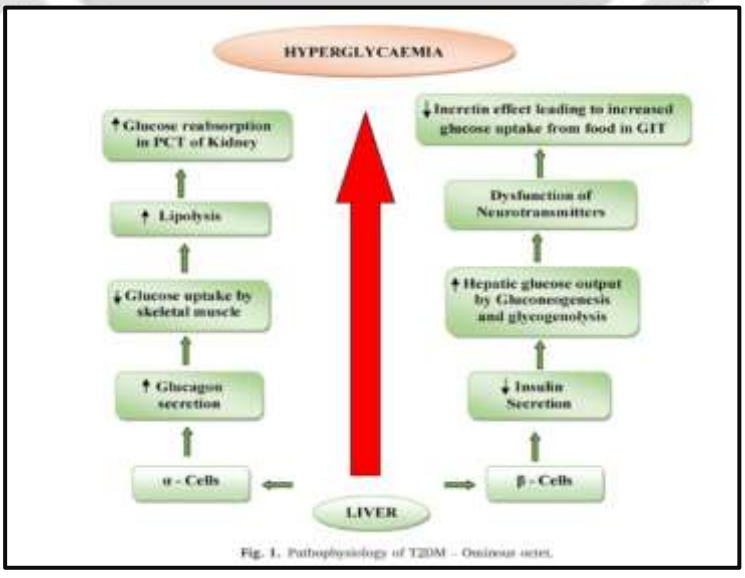

Fig.2: Pathophysiology of T2DM-Ominous octet

The hormonal changes that occur during pregnancy are the cause of gestational diabetes. Hormones produced by the placenta decrease the sensitivity of cells to the effects of insulin.

• Just as gene mutations in a single gene cause monogenic diabetes, genetic changes can result in diabetes mellitus. Neonatal diabetes and maturity-onset diabetes of the young are the two most prevalent types of monogenic diabetes.

• Due to the thick mucus produced by cystic fibrosis, the pancreas becomes scarred from not producing enough insulin.

• Hemochromatosis results in excessive iron storage in the body. Iron can accumulate in the body and harm the pancreas and other organs if the disease is left untreated.

• Certain hormonal conditions cause the body to produce excessive amounts of hormones, which can

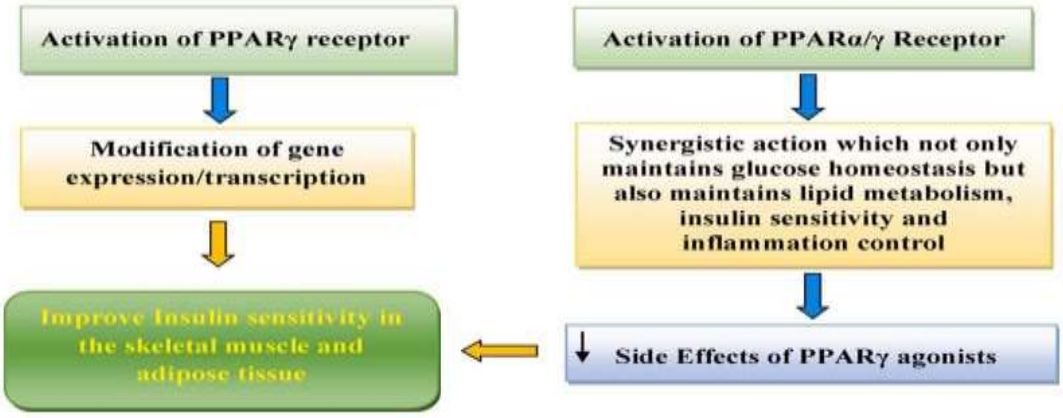

Fig.3: Pathogenesis of Diabetes

3.Treatment

Diabetes treatments vary depending on the patient and the kind of diabetes.

3.1Treatment of patients with type 1 diabetes

Patients with type 1 diabetes are dependent on highly supplied insulin since they are no longer able to make insulin on their own and would otherwise die.

3.2Insulin therapy

Managing the variables that affect the insulin dose on a daily basis is necessary for persons who use insulin. You can provide rapid-acting insulin prior to, during, or right after a meal.

1. conventional therapy - two mixed insulin shots every day. administered before breakfast, combined insulin contains both short- and long-acting forms of the after-dinner.

2. Conventional therapy with a split nighttime dose- Before breakfast, 1 injection of mixed insulin (rapid, short-acting, and intermediate-acting), 1 injection of During the evening meal, administer rapid- or short-acting insulin, and before the night snack, administer one injection of intermediate-acting insulin.

3. Multiple daily injections (MDI) of intermediate- or long-acting insulin given once or twice a day with rapid- or short-acting insulin before each meal.

4. Intensive therapy with a continuous subcutaneous insulin infusion (CSII or insulin pump)- Based on the number of carbohydrates consumed and the measured blood glucose level, an insulin bolus dose is administered prior to meals and snacks.

In therapy for type 2 diabetic patients in this treatment, a variety of variables play a role.

1. Body mass

2. Current dietary practices

3. Your level of exercise right now

4. Symptom severity

5. Blood sugar amounts

6. Diabetes onset time

Treatment options include insulin therapy, medication, food, and exercise.

Exercise, stopping smoking, weight loss, nutritional advice, a diabetic diet, and dietary fiber are all examples of self-care.

Medication: Blood thinners, statins, and anti-diabetic drugs both insulin

Pneumococcal and influenza vaccines are preventative measures.

4. Novel Technology

4.1Painless Smart Patch:

An insulin administration system based on microneedle array patches has been developed by North Carolina State University. It has been merged with hypoxia-sensitive hyaluronic acid (HSHA) vesicles that carry glucose oxidase (GOx) and insulin. It contains functioning beta cells and releases insulin as blood glucose levels rise. The combination of HS-HA 2-amino imidazoles results in the formation of glucose-responsive vesicles (GRVs), which are then created by the GRVs. The vesicles include insulin and glucose oxidase. In hyperglycaemic situations, glucose undergoes oxidation that is catalyzed by GOx, creating a milieu of hypoxia that causes the vesicles to separate and release insulin.

Advantages:

1. Quick response and close pharmacokinetic similarities to pancreatic
2. Convenience of administration
3. Biocompatibility

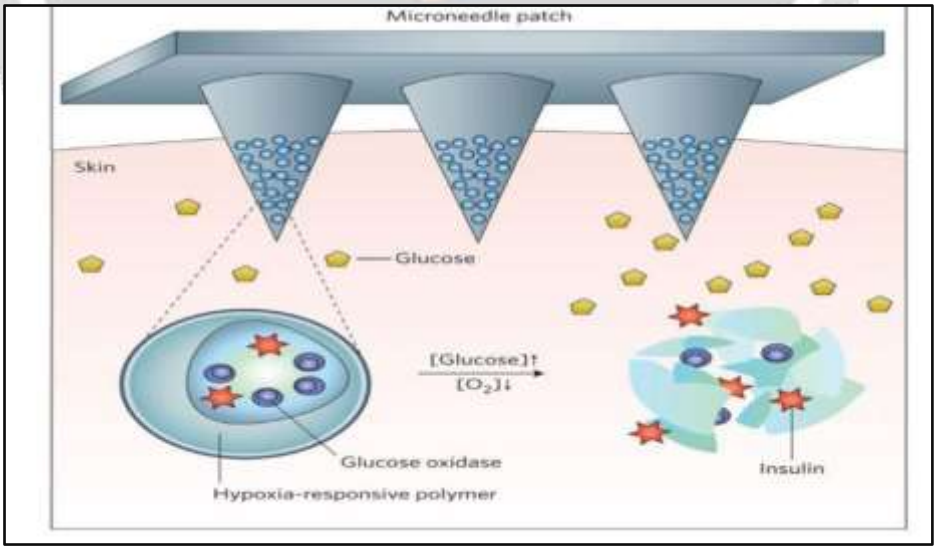

Fig.3: Schematic of the glucose-responsive insulin delivery system using hypoxia-sensitive vesicle loading MN array patches

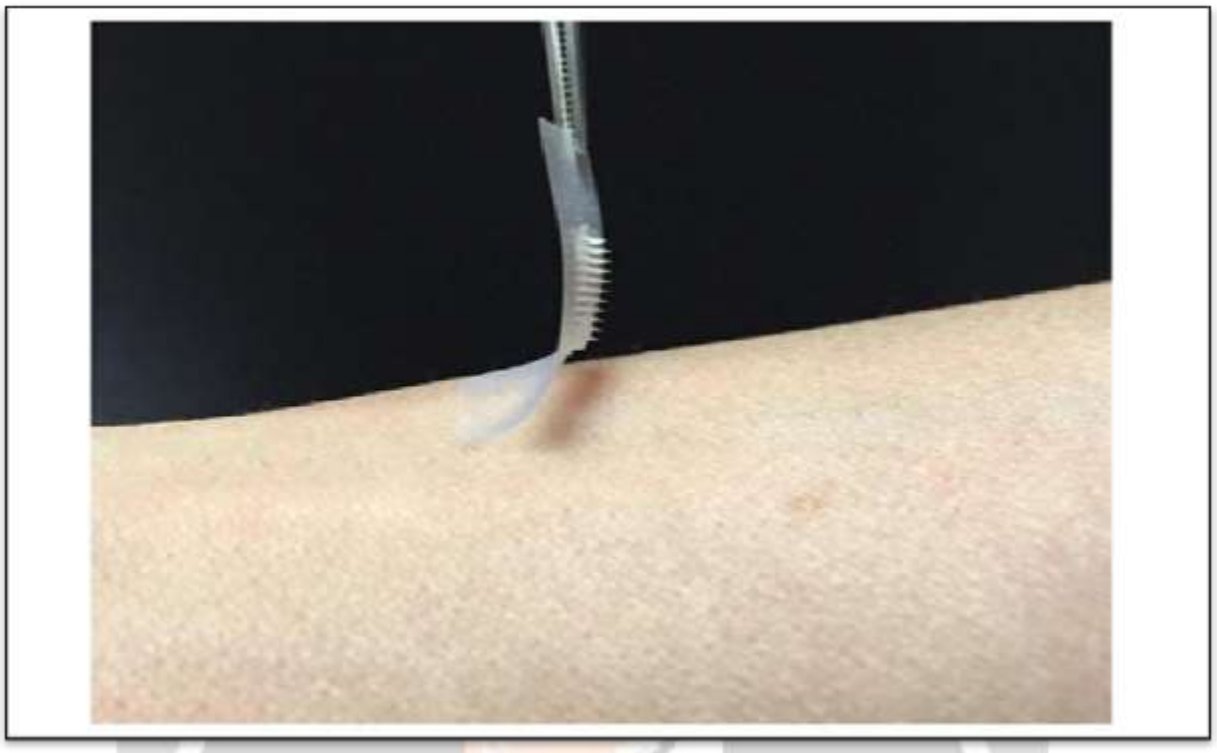

Fig.5: Photograph with smart insulin patch an MN array

4.2 Click Soft micro-injections:

It is an intradermal microneedle injection system with a spring load. While delivering insulin via this device, the patient feels no pain. The device's microneedles stick out and penetrate the patient's skin while an ultrafine needle delivers a fine stream of liquid medication from the drug chamber into the skin's layers.

Advantage

1. It is capable of delivering more than 100 units of insulin in a single dose.

2. Compared to other rapid acting insulin that is currently on the market, it acts more quickly.

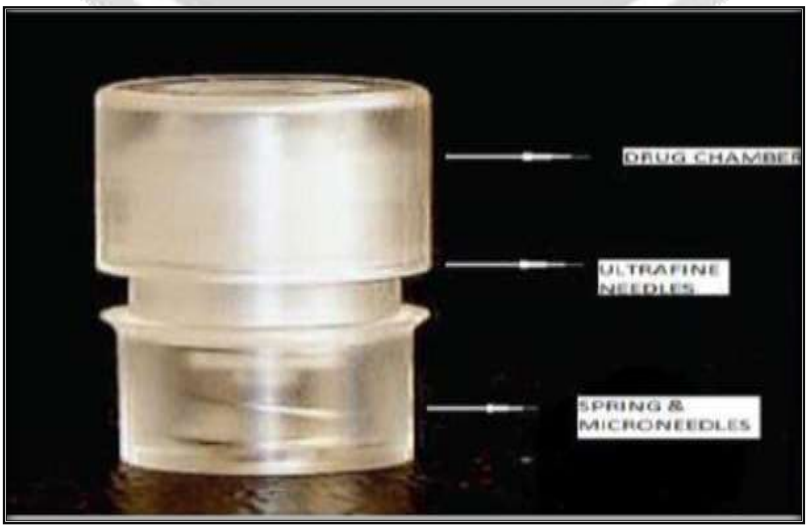

Fig.6: Click soft microinjection device with drug chamber

4.3 V-go:

It is an FDA-approved gadget that releases insulin hourly over the course of 24 hours. This non-electric device, which employs the patch technology, operates without batteries or pipes. Rapid-acting analogue insulin is used by Vgo. It's water-resistant. A fresh insulin cartridge needs to be inserted into the device once every 24 hours.

Advantage:

1. The fear of needles is vanquished.

2. decreases infusion of numerous doses.

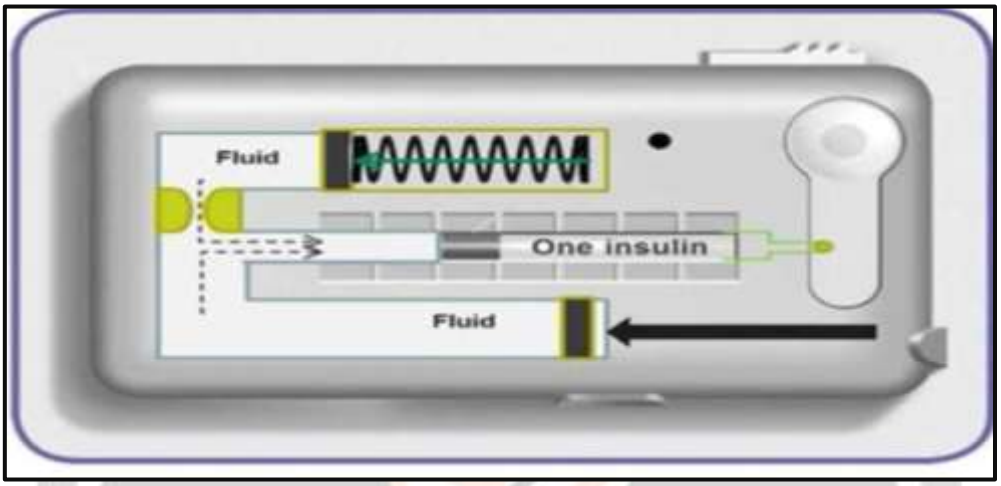

Fig.7: V-Go device

4.4 Conclusion

Intensive insulin therapy has been demonstrated to postpone and lower the risk of T1D and T2D complications. The aim of all new technologies is to reduce A1c to the lowest value while still reducing the danger of hypoglycemia. CSII and pen-based insulin delivery technological advancements have greatly increased patient acceptance of intense therapy, glycemic control, and quality of life.

Moat of the use of emerging therapy of diabetes is the smart insulin patch.

The main reason why new diabetes tools are not being used to their fullest potential in the US is economics. For patients to accept rigorous insulin therapy and achieve their target A1c, high-cost hurdles must be removed. Rules that prohibit healthcare providers and residents from meeting with pharmaceutical representatives are another hurdle. Many clinicians, therefore, miss out on the opportunity to learn about innovative diabetic technologies. Non-specialists find it very challenging to keep up with all the developments in diabetes therapy; as a result, they seldom recommend new diabetic technologies. In a 2009 survey of insulin pump users, endocrinologists made up 81% of their providers, compared to >90% of patients with diabetes who saw non-endocrinologists. The time spent by the staff.

Reference

1. Emerging treatment strategies for diabetes mellitus and associated complications , MDPI, vijay Mishra, Pallavi Nayak,2019.

2.karamanau ,M.;Protogerau,A.;Tsoucalas, G.;Paulakau-Rebelakau,E.Milstones in the history of diabetes mallitus: The main contributor.World J.diabetes 2016

3.Current emerging treatment option in diabetes care, Handbook of experimental pharmacology ,Christoffer Clemmensen,Timo D.Muller,april2015.

4.Diabetes mellitus review, international journal of pure and applied bioscience , ISSN:2320-7051,Chinmay D.deshmukh, Anurekha jain,june2015.

5. Diabetes mellitus, international journal of research and development in pharmacy and life science, ISSN(p):2393-932X,ISSN(E):2278-0238.

6.Neww Frontier in the Treatment of Diabetes,Journal of drug delivery and therapeutics,ISSN:2250-1177,Bhat Abhishekh Jayesh *;Vyas Arya Sudhanshu,15 oct 2019.

7.Emerging technology of diabetes care, Diabetes Technology and therapeutics Volume 20,Timothy S .Bailey, MD ,FACE, FACP ,CPI, John walsh,2018.

8. IDF. The Diabetes Atlas. IDF (3rd). 2006.2 Diabetes UK. Diabetes: State of the Nations. Diabetes UK.2006.

9. de Groot M, Anderson R, Freedland KE, Clouse RE,Lustman PJ. Association of depression and diabetes complications: a meta-analysis. Psychosom Med 2001; 63:

619–30.

10. Wanless D. Securing our future health: taking a long-termview. HM Treasury. 2002.

11.Jacobson AM. Impact of improved glycemic control on quality of life in patients with diabetes. Endocr Pract 2004;10: 502–8.

12. Muller WA, Faloona GR, Guilar-Parada E, Unger RH.Abnormal alpha-cell function in diabetes. Response tocarbohydrate and protein ingestion. N Engl J Med 1970;283: 109–15.

13.Harris MI, Klein R, Welborn TA, Knuiman MW. Onset ofNIDDM occurs at least 4–7 years before clinical diagnosis.Diabetes Care 1992; 15: 815–9. 1.

14.Karamanou, M.; Protogerou, A.; Tsoucalas, G.; Androutsos, G.; Poulakou-Rebelakou, E. Milestones in the history of diabetesmellitus: The main contributors. World J. Diabetes 2016.

15. Simos, Y.V.; Spyrou, K.; Patila, M.; Karouta, N.; Stamatis, H.; Gournis, D.; Dounousi, E.; Peschos, D. Trends of nanotechnology in type 2 diabetes mellitus treatment. Asian J. Pharm. Sci. 2021.

16. New frontier in the treatment of diabetes, journal of drug delivery and therapeutics, Bhat Abhishekh Jayesh; Vyas Arya Sudhanshu,2019.

17. Akram T Khorrubi and Hisham M Darwish; "Diabetes Mellitus:the epidemic of century"; World journal of diabetes; 2015,June 25, 6(6), page no 850-867.

18. Kenneth S Polonsky; "The past 200 yeasr in diabetes"; TheNew England Journal of Medicine.3.

19.SamreenRiaz; "Diabetes Mellitus"; Scientific Research andEssay; Vol 4(5); May 2009; page no. 367-373.4.

20.Anees A Siddiqul, et al; "Diabetes: Mechanism,Pathophysiology and Management: A Review"; InternationalJournal of drug development and research.