IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 1, December 2023

Review on Oral Insulin for Diabetics Mellitus

Achal A. Kale, Bilal Sufi, Chandrashekhar M. Deotale, Vaibhav R. Urade
New Montfort Institute of Pharmacy, Wardha, Maharashtra, India
achalkale157@gmail.com

Abstract: *Oral insulin is one of the most exciting areas of diabetes therapy, due to the potential benefits of patient convenience, liver rapid insulination, appropriate insulin delivery to avoid hyperinsulin hypertension in the peripheral region, and the potential to avoid the harmful effects of weight gain and low blood sugar. Evidence is growing that early intensive insulin therapy leads to sustainable and tight blood glucose control and leads to serious complications, making effective oral insulin products even more important for the treatment of diabetic patients. Despite the knowledge of this medical need, insulin injections havefailed due to several obstacles. For decades, researchers have tried to develop oral insulin with various technologies, but have not succeeded in clinical and commercial studies. The review summarizes the development status of oral insulin and indicates that it is under clinical trial.*

Keywords: alternate routes of insulin delivery oral immunotherapy, diabetes

I. INTRODUCTION

Diabetes is a metabolic disorder caused by defects in insulin action or insulin secretion. Furthermore, insulin deficiency leads to long-term hyperglycemia and metabolic syndromes of carbohydrates, proteins and fats. Tissue and vascular damage is caused by the progression of the disease, resulting in major complications such as retinal, neurological, kidney, cardiovascular, and ulcer. Therefore, diabetes covers a wide range of heterogeneous diseases. The International Diabetes Association estimates that the total number of deaths from diabetes in 2011 was 366 million and is expected to reach 552 million in 2030. In the 21st century, diabetes was long considered a disease of little importance for global health, but today it is one of the most important threats to human health.

Asia is the main site of the rapidly developing diabetes epidemic. According to some estimates based on Asian population growth, ageing and urbanization, India and China will remain the two countries with the largest number of diabetic patients in 2030 (79.4 million and 43.23 million, respectively). In recent years, developing countries such as India have experienced the highest growth. The current prevalence of diabetes is 2.4% in rural areas and 11.6% in urban areas. India is expected to have the world's largest diabetes population by 2025. India is facing an uncertain future in terms of the possible burdens that diabetes could bear on it.

What is diabetes?

Diabetes is a metabolic disease that increases blood sugar over a long period of time. Untreated diabetes causes many complications. Acute complications include diabetic ketoacidosis and non-ketotic hyperosmolar coma. Long-term serious complications include heart disease, stroke, kidney failure, foot ulceration and eye damage.

Why is blood glucose level high?

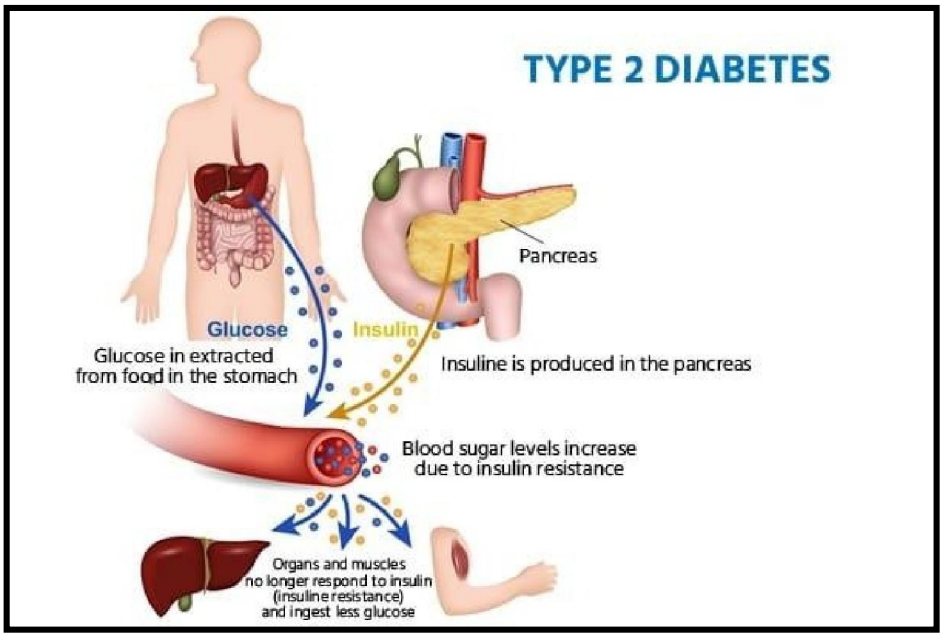
How does this happen? The digestive process includes the decomposition of foods you eat into various nutrients. When you eat carbohydrates (bread, rice, pasta, etc.), the body decomposes into sugar. When glucose is present in your bloodstream, you need help, and the "key" is used within the cell (the cell is the body's tissue and organs). This help is insulin or "key". Insulin is the hormone produced by the pancreas, an organ in the stomach. Your pancreas releases insulin into the bloodstream.

Types of diabetes

Type 1 diabetes: Type 1 diabetes is usually caused by the destruction of the beta cells thatform insulin in the pancreas.

Type 2 diabetes (NIDDM): Type 2 diabetes occurs when insulin or low-circulatinginsulin circulating increases blood glucose levels, and because insulin manages glucoselevels, blood glucose levels can rise up to 6-20 times in normal range, changing the person's development or loss of function.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 1, December 2023



Prediabetes:
When blood sugar exceeds the normal range, it is not sufficient to diagnose type 2diabetes.

Gestational diabetes:
High blood sugar during pregnancy. Caused by insulin blocking hormone produced in the placenta. Get help from a doctor and take a simple step to manage blood sugar. After the birthof the baby, diabetes usually disappears.

5-Diabetes insipidus:
It is a very rare condition that causes a large amount of urine in the kidney.

Antidiabetic drug:
Antidepressants are drugs developed to stabilize and control blood sugar levels in diabetes patients. Antidepressants are usually used to treat diabetes.

Antidiabetic drug classification:
Sulphonylureas: EX. •Glibenclamide
Thiazolidinediones: EX. •Pioglitazone
Alpha-glucosidase inhibitors EX .•Acarbose, voglibose
Meglitinide analogues EX. • Nateglinide

Symptoms of diabetes:

- Increased heart rate;
- Frequent urinary tract;
- Extreme hunger;
- Weight loss;
- Fatigue;
- Polyuria;
- PLEASURES;
- Glycaemia;

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 1, December 2023

- Dry skin and mouth

Cause of diabetes:

Type 1 diabetes: Type 1 diabetes is usually caused by an abnormal immune system that destroys the beta cells of insulin in the pancreas, so insulin is not separated.

Type 2 diabetes: Type 2 M is a combination of genetic factors and lifestyle. Early or obese people also increase the risk.It is not possible to maintain blood sugar. Gestational diabetes is a type of diabetes that occurs during pregnancy due to certain hormonal changes. During pregnancy, the placenta produces other hormones that affect insulin.

Diagnosis:

In diabetic or pre-diabetic diagnosis, some tests are required, such as oral glucose tolerance tests, HbA1c tests, etc. The American Diabetes Association (ADA) recommends diagnosis of DM factors for high risk factors including obesity, high blood pressure and family history of diabetes. Focus on high-speed plasma glucose (FPG).

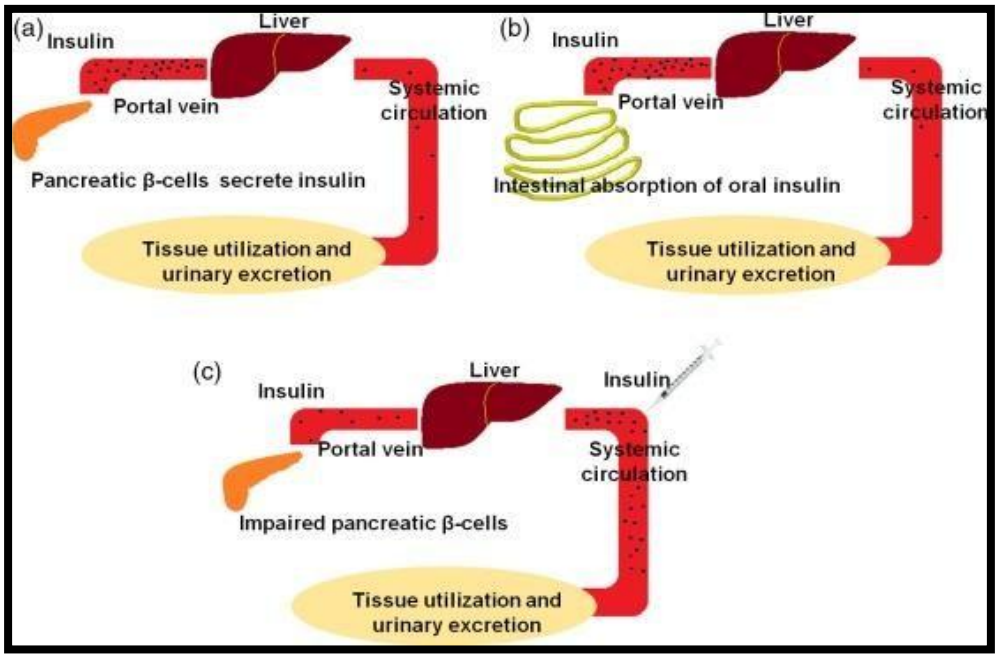
Prevention:

Type 1 diabetes cannot be prevented because it is caused by autoimmune diseases, and must be controlled by the use of certain medications (oral hypoglycemia drugs).Type 2 diabetes can also be prevented or delayed by maintaining normal weight, physical activity, a healthy diet.Limited consumption, less red meat, and other saturated fats can also help prevent diabetes.

II. ORAL INSULIN

The oral insulin delivery system can be the most patient-friendly way to administer insulin, more likely to mimic insulin's physiological delivery (more portal insulin concentrations than peripheral insulin concentrations)[45], but the challenges of oral insulin manufacturing include the inactivation of digestive enzymes and the low permeability of intestinal membranes due to insulin size and hydrophobia, which leads to low bioavailability. Several pharmaceutical companies are developing carriers to protect insulin from GI damage and promote the transport of insulin in the intestinal tract in order to provide sufficient bioavailability for insulin in circulation

Mechanism of oral Insulin :



IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 1, December 2023

III. NEED OF ORAL INSULIN

Insulin resistance is the main cause of clinical inertia and the lack of achievement of the goal glycemic target. Patients and doctors fear the complexity of insulin treatment, the risk of diabetes, weight gain, and the need for needles during insulin treatment. Insulin is considered to have a high invasive index because conventional insulin must be taken before meals. Patients expect oral insulin to develop early because it is easy to administer, low intake, practical, patient-oriented, adherence, and ultimately leads to better control of glucose, thus preventing diabetes complications.

Current Development

Reviewing the current status of oral insulin development in 2014 is a very difficult task, asonly six of the 13 companies have claimed to have published the results of new clinical trials over the past five years. The focus will then be on the progress of companies (alphabetically) publishing new clinical trials reports. Compared to five years ago, four new companies announced that they would implement a clinical development program for oral insulin. Only Apollo Life Sciences seems to have officially stopped its development. However, in some cases, there is no published evidence of clinical efforts

Advantages Associated with Oral Insulin Delivery

1] However, oral administration is regarded as a better route due to its cost-effectiveness.2] This is especially effective in avoiding the use of needles and other injection materials.

Several attempts have been made to develop oral carriers that provide insulincontinuously and effectively

Thereby avoiding the risks of contamination, local pain and immune reactions - andovercoming patient compliance problems.

In addition, the administration of oral insulin improves the normal insulin pathways inthe body after endogenous secretion, thus improving glucose homeostasis.

Disadvantage Associated With Oral Insulin Delivery:

Includes low bioavailability due to insulin degradation in the intestine by proteolyticenzymes.

High pH physiological conditions and low permeability through the intestinalepithelium

High molecular weight and water-soluble proteins reduce their intestinal absorption andcause low oral bioavailability, low plasma concentration and high variability.

Approaches to oral insulin:

Various workers have tried to overcome the above obstacles in different ways. Insulin is absorbed by mucous adhesion polymers such as chitosan, lactic glycolic acid (PLGA), and alginate, preventing enzyme degradation and allowing absorption through the Ping epithelial layer. This approach depends on the absorption of insulin in the intestine, and it is too late to correct the first phase's insulin secretion deficit. Insulin is also injected with protease inhibitors such as Bacitracin, Natriumglucoside, and Camostat Mesilate, improving absorption rate.

III. CONCLUSION

Alternatives to insulin injection are on the horizon. By reproducing the physiological pathways of insulin secretion and absorption, oral insulin may have some advantages that cannot be achieved by systemic insulin administration, but may raise new concerns inherentin oral medicines that must be addressed. Patients and doctors have many expectations that insulin will be administered in a different way to replace injections. Such insulin is a practical method of implementing insulin much earlier than currently practiced and can promote longer-term compliance and compliance, resulting in better control of blood sugar levels among the population. Thus, the most promising strategy for obtaining oral insulin may bethe use of microsphere systems, which is basically a combination strategy. Microspheres are an inhibitor of proteins that protects insulin absorbed from the degradation of enzymes in the matrix and increases permeation by effectively crossing the epithelial layer after oral administration. More research is needed, especially in combination with the identification of polymer spheres that demonstrate greater absorption in the intestinal tract, and may integrate insulin with gentle methods to overcome absorption and enzyme barriers and ultimately develop safe and effective means of completely or partially replacing oral insulin development. Research on oral insulin delivery focuses

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 1, December 2023

mainly on overcoming insulin degradation and improving insulin absorption in GIT. Other challenges, such as insulin degradation by receptors, dose stability, and dose stability of insulin, are also addressed. To better manage patient compliance with oral insulin, Novo Nordisk, Oramed, Emisphere and Biocon have been attracting companies to take measures to market it in the future.

REFERENCES

[1]. Bearse MA, Han Y, Schneck ME, Barez S, Jacobsen C, Adams AJ. Local multifocal oscillatory potential abnormalities in diabetes and early diabetic retinopathy. Investig Ophthalmol Vis Sci. 2004;45(9):3259–6

[2]. Hove MN, Kristensen JK, Lauritzen T, Bek T. The prevalence of retinopathy in an unselected population of type 2 diabetes patients from Århus County, Denmark. Acta Ophthalmol Scand. 2004;82(4):443–8.

[3]. Seki M, Tanaka T, Nawa H, Usui T, Fukuchi T, Ikeda K, et al. Early Retinal Neuropathy of Streptozotocin-Induced. Am Diabetes Assoc. 2004;53(September):1–8.

[4]. Huang C, Kim Y, Caramori MLA, Fish AJ, Rich SS, Miller ME, et al. Cellular basis of diabetic nephropathy: II. The transforming growth factor-β system and diabetic nephropathy lesions in type 1 diabetes. Diabetes. 2002;51(12):3577–81.

[5]. Saely CH, Aczel S, Marte T, Langer P, Drexel H. Cardiovascular complications in Type 2 diabetes mellitus depend on the coronary angiographic state rather than on the diabetic state [5]. Diabetologia. 2004;47(1):145–6.

[6]. J, Smith DG, Sullivan K, Hayes S, et al. Incidence of falls, risk factors for falls, and fallrelated fractures in individuals with diabetes and a prior foot ulcer. Diabetes Care. 2002;25(11):1983–6

[7]. Bastaki S. Diabetes mellitus and its treatment. Int J Diabetes Metab. 2005;13(3):111– 34.

[8]. Whiting DR, Guariguata L, Weil C, Shaw J. IDF Diabetes Atlas: Global estimates of the prevalence of diabetes for 2011 and 2030.

[9]. Diabetes DOF. General aspects of diabetes mellitus. 2014;126.

[10]. Zimmet P. Globalization, coca-colonization and the chronic disease epidemic: Can the Doomsday scenario be averted? J Intern Med Suppl. 2001;249(741):301–10

[11]. Estimates for the year 2000 and projections for 2030. 2004;27(5)

[12]. 12. Ramachandran A, Wan Ma RC, Snehalatha C. Diabetes in Asia. Lancet [Internet]. 2010;375(9712):408–18. Available from: http://dx.doi.org/10.1016/S0140- 6736(09)60937-5

[13]. . Aubert RE. Prevalence, numerical estimates, and projections. 2000;21(9):1414–31.

[14]. Srivastava AK. Diabetes mellitus : Complications and therapeutics Diabetes mellitus : Complications and therapeutics. 2014;(August 2006).

[15]. Kaveeshwar SA, Cornwall J. The current state of diabetes mellitus in India. Australas Med J. 2014;7(1):45–8.

[16]. Giriraj KG, Giriraj KT. Oral Insulin-Fact or Fiction. Resonance 38–43 (2003). Gowthamarajan K, Kulkarni GT. Oral Insulin – Fact or Fiction

[17]. Gemmil CL. The Greek concept of diabetes. Bull N Y Acad Med. 1972;48:1033-6.

[18]. Bliss M. The history of insulin. Diabetes Care. 1993;16(3):4-7

[19]. Uianzon CC, Cheikh I. History of Insulin. J Commu Hospital Internal Med Pers 2012;2(2):1-3

[20]. Joshi SR, Parikh RM, Das AK. Insulin History, Biochemistry, Physiology and Pharmacology. Supplement Japi. 2007;55:19-21

[21]. Meier JJ, Holst JJ, Schmidt WE, Nauck MA. Reduction of hepatic insulin clearance after oral glucose ingestion is not mediated by glucagon-like peptide 1 or gastric inhibitory polypeptide in humans. Am J Physiol Endocrinol Metab. 2007

[22]. Eaton RP, Allen RC, Schade DS. Hepatic removal of insulin in normal man: dose response to endogenous insulin secretion. J Clin Endocrinol Metab 1983

[23]. Meistas MT, Rendell M, Margolis S, Kowarski AA. Estimation of the secretion rate of insulin from the urinary excretion rate of C-peptide. Study in obese and diabetic subjects.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 1, December 2023

[24]. Satake S, Moore MC, Igawa K, Converse M, Farmer B, Neal DW, Cherrington AD. Direct and indirect effects of insulin on glucose uptake and storage by the liver. Diabetes. 2002

[25]. Curtis ,L.T, Charles A.R, 2ND ,William, pharmacotherapy: A pathophysiology

[26]. Approach 7 th edtion , Mc Graw Hill -2009

[27]. Baynest HW. Classification, Pathophysiology, Diagnosis and Management of Diabetes Mellitus. J Diabetes Metab. 2015;06(05):1–10.

[28]. Katsarou A, Gudbjörnsdottir S, Rawshani A, Dabelea D, Bonifacio E, Anderson BJ, et al. Type 1 diabetes mellitus. Nat Rev Dis Prim [Internet]. 2017;3:1–18. Available from: http://dx.doi.org/10.1038/nrdp.2017.16

[29]. Leslie RD. Predicting adult-onset autoimmune diabetes clarity from complexity. Diabetes. 2010;59(2):330–1.

[30]. Atkinson MA, Eisenbarth GS, Michels AW. Type 1 diabetes. Lancet [Internet]. 2014;383(9911):69–82. Available from: http://dx.doi.org/10.1016/S0140-6736(13)60591-7

[31]. Buzzetti R, Quattrocchi CC, Nisticò L. Dissecting the genetics of type 1 diabetes: Relevance for familial clustering and differences in incidence. Diabetes Metab Rev. 1998;14(2):111–28.