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INSULIN PILLS – A NOVEL APPROACH IN DIABETES MANAGEMENT

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ABSTRACT

Insulin pills is also known as insulin tablets, remained at an early stage of clinical trials with several companies racing to establish this pill as an alternative to insulin injections to avoid the pain of needles which is the main goal of many pharmaceutical companies. However, a drug maker is yet to get succeed in encapsulating insulin into a one-off dose, easily swallowed like any other tablet. Insulin is difficult to ingest orally as it is a protein which gets degraded in the stomach and small intestine, making it almost impossible to design as oral drug delivery. The past has seen massive oral insulin efforts flop, including the inhalable insulin Exubera. However, major drug makers are thought to be working on the insulin pill, Novo Nordisk is amongst them. The theory behind this concept is Insulin delivery via the stomach which would transport the much needed hormone directly to the liver, where it could mimic the action of endogenous insulin. Infact, the future could see insulin pills making diabetes management considerably more safe and convenient for the people with diabetes.

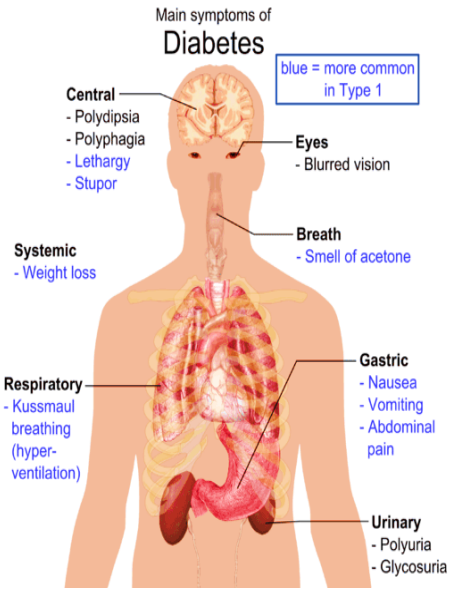
INTRODUCTION

Diabetes is defined as a group of metabolic diseases in which the person has high blood glucose (blood sugar), either because of inadequate insulin production, or because the body's cells do not respond properly to insulin, or both. Patients with high blood sugar levels will typically experience polydipsia (excess thirst),frequent urination (polyuria) and polyphagia (excessive hunger). There are different types of diabetes: Type 1 Diabetes – It is referred to the condition where the body does not produce insulin,so replacement insulin must be delivered in the form of insulin injections, pump or by inhalation. Approximately 10% of diabetes cases are type 1. Type 2 Diabetes –It is referred to the condition where the body makes too little insulin or the B-cells do not respond to insulin that is produced ("insulin resistance"). Approximately 90% of all diabetes cases are of this type. Gestational Diabetes - This type of diabetes affects females mainly during pregnancy. Type 2 diabetic's struggles to regulate their own blood glucose levels because the beta cells in their pancreas slowly stop producing enough insulin following meals. This condition can be due to lifestyle, genetic factors, obesity etc..and it can often be managed by using oral hypoglycaemic without the need for insulin injections. But currently around 90 percent of worldwide population have type 2 diabetes, and many of them rely on injections to avoid dangerously high blood sugar levels.

BLOOD SUGAR LEVEL CHART

	FASTING	JUST ATE	3 HOURS AFTER EATING
NORMAL	80-100	170-200	120-140
PRE-DIABETIC	101-125	190-230	140-160
DIABETIC	126+	220-300	200+

DIABETES SYMPTOMS:-



TREATMENT:

- Different kinds of conventional dosage forms work in different ways to control your blood sugar (blood glucose).
- Combining two different kinds of diabetes tablets can work better to lower your blood sugar than a does a single medicine.
- But combining two kinds of diabetes tablets can make it more likely that your blood sugar will drop too low (hypoglycemia).
- Most diabetes tablets can cause weight gain. One kind, metformin (Glucophage), does not make you gain weight.

ORAL HYPOGLYCEMICS (OHA'S):-

Oral hypoglycemics are classified into Seven different classes for the treatment of type 2 diabetes as well as combinations of drugs from different classes:

- ✓ Sulphonylureas
- ✓ Biguanides
- ✓ Meglitinides
- ✓ Alpha Glucosidase Inhibitors
- ✓ Thiazolidinediones
- ✓ D-Phenylalanine Derivatives
- ✓ Dpp-Iv Inhibitors

INSULIN INJECTIONS: There are several types of insulin. These types are classified according to their quick action and how long it remains active:

- ✓ Rapid acting (eg, insulin lispro [brand name: Humalog], insulin aspart [brand name: NovoLog], and insulin glulisine [brand name: Apidra])
- ✓ Short acting (eg, insulin regular)
- ✓ Intermediate acting (eg, insulin NPH, NPL [neutral protamine lispro])
- ✓ Long acting (eg, insulin glargine [brand name: Lantus], insulin detemir [brand name: Levemir])
- ✓ Very long acting (eg, insulin degludec [brand name Tresiba])

These insulins can be used in combination to achieve around-the-clock blood sugar control.

NOVEL APPROACHES: US scientists has developed a method of administering insulin orally that can be a less painful and can be a alternative to many people worldwide with diabetes who have to take insulin injections themselves with the drug to manage their blood-sugar levels. In this method,the insulin has been encapsulated using Cholestosomes – a neutral, lipid-based particle – that can be administered orally with tiny vesicles that can deliver insulin where it needs to go without injecting. The Computer modelling of this showed that once the lipids are assembled into spheres, they form neutral particles resistant to attack from stomach acids. Drugs can be easily loaded inside, and the tiny packages can pass through the stomach without getting degraded.When cholestosomes reach the intestines, the body recognises them as something to be absorbed. These vesicles pass through the intestines into the bloodstream, and then the

cells take them in and break them apart, releasing insulin. The insulin pills work by using a protective coating and a high-enough dose of insulin so that most of it can get destroyed in the digestive tract,but it will still deliver a beneficial amount of the hormone into the bloodstream.

- Insulin pills and insulin inhalers both have been developed. Each has it's own level of effectiveness. Insulin inhalers are still far from perfect.
- The oral insulin could be developed that would get absorbed through buccal mucosa (through the walls of the cheeks). This method of delivering could see insulin reaching the bloodstream intact.
- At this stage, insulin remains too complex protein to survive within the environment of the body. Many of the leading pharmaceutical companies are thinking to use protein engineering to bring the insulin pill one step closer.

The following are the companies leading in the marketing of oral insulin:

CLINICAL TRIALS:

Oral Insulin Testing On Animals:

- The data obtained after testing oral insulin on animals has yielded extremely positive results.
- In 2003, Case studies from Diabetes Care reported that a small study appeared to find oral insulin as effective as injectable insulin for type 2 diabetics.
- Experimental studies done by researchers announced that an insulin pill has successfully reduced night-time blood glucose levels in 180 patients with type 2 diabetes.
- Previously, it was assumed that insulin wouldn't survive the digestive juices of the stomach, so it couldn't be delivered orally - hence the dependence on insulin injections. But this new mid-stage trial suggests for the first time that if the right dose is given, insulin tablets could really work.
- If these findings are verified and repeated in additional trials, it would mean that the insulin tablets could replace injections for patients with type 2 diabetes.
- This new insulin tablets work by using a protective coating and a high-enough dose of insulin so that most of it can get destroyed in the digestive tract, and it will still deliver a required amount of the hormone to decrease the blood sugar levels in the bloodstream.

Oral Insulin Testing On Humans:

- The Oramed researchers did a 28-day trial and took 180 patients with type 2 diabetes who were no longer responding adequately to metformin - a first-line medication given to people when they're diagnosed with the condition.
- Ante lectum (before bed), they were either given the insulin pill - which has been called ORMD-0801 - or a placebo, and their overnight glucose levels were monitored.
- The patients who were given oral insulin had a mean night-time glucose reduction of nearly 6.5% compared to the placebo group.
- The results were find to be effective as there weren't any serious side effects reported, and no issues with the blood sugar levels dropping too low.
- Phase III clinical trials are expected to begin shortly, by the Oramed researchers and if those results are positive, we might finally have an alternative to insulin injections available to those with advanced type 2 diabetes.
- The researchers believe that the insulin pills might actually be better for patients,as they mimic the pathway of natural insulin, which goes directly to the liver once it's produced, before being circulated into the blood stream.

S.No	Companies Name	Research Work
1.	Generex Biotechnology	They have developed rapid mist delivery system (an oral insulin spray) approved for use in Ecuador. This oral insulin spray is absorbed by the buccal mucosa. They have developed this system to avoid the pain of needles.
2.	Coromed	Coromed is a privately funded biotechnology company started in 1994. They developed a product called Alveair, and offers a 'needleless' alternative for insulin users. This device delivers a regulated blast of insulin and it has lower side-effect levels than injectable insulin.
3.	Nektar	The Nektar company have developed a Pulmonary delivery system, Exubera-fast-acting dry powder insulin designed for inhalation.
4.	Aradigm Corporation	Aradigm Corporation aims to develop and manufacture innovative drug solutions: they are back by another insulin market leader called Novo Nordisk.
5.	Wockhardt	Wockhardt, a giant Indian company that acquired UK insulin supplier CP pharmaceuticals, has recently launched a cartridge and pen system into the Indian market that it claims is almost painless.

CONCLUSION:

Insulin is difficult to ingest orally as it is a protein which gets degraded in the stomach and small intestine, making it almost impossible to design as oral drug delivery. The past has seen massive oral insulin efforts flop, including the inhalable insulin Exubera. However, major drugmakers are thought to be working on the insulin pill, Novo Nordisk is amongst them. In 2003, Case studies from Diabetes Care reported that a small study appeared to find oral insulin as effective as injectable insulin for type 2 diabetics. The results were finding to be effective as there weren't any serious side effects reported, and no issues with the blood sugar levels dropping too low. Phase III clinical trials are expected to begin shortly, by the Oramed researchers and if those results are positive, we might finally have an alternative to insulin injections available to those with advanced type 2 diabetes. These pills mimic the pathway of natural insulin, which goes directly to the liver once it's produced, before being circulated through the blood stream.

"The beauty of this insulin pill is that it mimics the natural production of insulin by delivering insulin to the liver. But despite of the effective results for type 2 diabetics, there's no word as yet on whether something similar would work for patients with type 1 diabetes. The difference between type 1 and type 2 is that type 1 diabetes is a condition, which means the immune system is attacking patients' beta cells. Because of which, their blood glucose levels rise and fall unpredictably - and it isn't always as simple as just needing to pop a pill to lower blood sugar levels. But research is going on for type 1 diabetics too and recently they developed a tiny patch that works like artificial pancreas, and can simply be stuck onto the arm to regulate blood sugar levels painlessly, without injections. The patch is still in the early phases of its development, but with research moving along pretty quickly on both of these fronts; the future is looking pretty bright for diabetics.

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