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NATURAL BIO- POLYMER: A REWARD FOR GASTRO RETENTIVE FLOATINGTABLET

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ABSTRACT

The global presence of diabetes has been rising day by day and it accounts for endangering 6.6% of the total population of the world. The increase in the blood glucose levels is the basic criterion of describing diabetes. It is also symptomized by glycosuria, hyperlipidemia, ketonemia, etc. Insulin and oral hypoglycaemics are the two most widely used categories of drugs utilized for treatment of diabetes. Oral hypoglycaemics is the class of drugs associated with lowering the glucose levels, but many of them suffer from the drawback of smaller half lives, short residence time. The gastroretentive dosage forms help in overcoming these drawbacks and also increase the bioavailability of the drug administered. The gastroretentive dosage form has shown a better potential keeping in mind the research aspect as well as the commercial aspect of the formulation. Gastroretentive formulations consisting of oral hypoglycaemics have found a vast market and have been formulated and marketed by various MNCs. The present article tries to describe all the recent advances made and the current market status of the aforesaid technology.

KEYWORDS: Gastroretentive; hypoglycemics; nateglinide; glinate; bio polymer chitosan.

INTRODUCTION

Diabetes mellitus (DM) is a term that refers to a variety of conditions defined by high blood glucose levels caused by an unbalanced oxidation and use of glucose, which is linked to the failure of insulin-producing pancreatic -cells. Diabetes is caused by a malfunction in insulin secretion (insufficient insulin synthesis), a decline in peripheral insulin response (insufficient

insulin sensitivity of cells), or both.[1] The intensity of diabetic symptoms is determined by the kind of diabetes and how long it has been present. The majority of patients, especially those with TIIDM, are asymptomatic in the early stages of the condition. Patients may develop polydypsia, polyphagia, polyuria, ketoacidosis, and weight loss in addition to hyperglycemia. The severity of hyperglycemia increases the risk of microvascular consequences like diabetic neuropathy, retinopathy, and nephropathy, as well as macrovascular problems like ischemic heart disease, peripheral vascular disease, and so on.[2,5]

In the previous 16 years, the global prevalence of diabetes has climbed by 211 million people at an alarming rate. In 2017, an estimated 425 million persons aged 20 to 79 were diagnosed with diabetes, with that number anticipated to rise to 629 million by 2045. Diabetes has evolved over the last 30 years from a minor ailment of the elderly to one of the leading causes of morbidity and mortality among the young and middle-aged.[6,7]

However, the medical community still has a significant difficulty in managing diabetes complications with minimum side effects. The use of plant-derived medicines for the safe and effective management of diabetes and its complications can help to reduce the dependency on synthetic pharmaceuticals.[8] In comparison to synthetic medications, which are known to pose hazards to both humans and the environment, herbal/natural products connote safety.[9,10] This problem has prompted substantial research into effective natural anti-diabetic medications that have fewer negative effects. Herbal medicinal agents' growing popularity has prompted numerous studies to examine the available sources for biological activity.[11] Synthetic medications used to treat diabetes have a slew of negative side effects.

Furthermore, they are widely and easily accessible.

Types of diabetes

The two main types of diabetes are:

- Type 1 Diabetes
- Type 2 Diabetes

Type 1 diabetes

Type 1 diabetes is believed to be an autoimmune condition. This means your immune system mistakenly attacks and destroys the beta cells in your pancreas that produce insulin. The

damage is permanent. What prompts the attacks isn't clear. There may be both genetic and environmental reasons. Lifestyle factors aren't thought to play a role.

Type 2 diabetes

Type 2 diabetes starts as insulin resistance. This means your body can't use insulin efficiently. That stimulates your pancreas to produce more insulin until it can no longer keep up with demand. Insulin production decreases, which leads to high blood sugar.

Epidemiology

Diabetes is the fourth leading cause of death by disease and a person dies from diabetes related causes in every 10 seconds. The International Diabetes Federation released figures according to which it is estimated that diabetes has affected 28.5 crore people worldwide in 2010, which is about 6.6 percent of the total adult population and it is expected to rise up to 43.8 crores by 2030.[4] The current number of people suffering from diabetes in India is 5.08 crore.[2] which were 1.9 crore in 1997 and it is expected to increase to 6.99 crore by 2025. Currently up to 11 percent of India's urban population and 3 percent of rural population above the age of 15 is suffering from diabetes.[4]

Physiology of Gastrointestinal Tract

One prerequisite for successful performance of oral controlled release drug delivery system is that drug should have good absorption throughout the gastrointestinal tract, preferably by passive diffusion [5]. The bioavailability of drugs with an absorption window in the upper small intestine is generally limited (6-8 hrs), Phenformin (8-12 hrs), Repaglinide (2-3 hrs), Nateglinide (2-3 hrs) are the most suitable candidates for the gastroretentive approach.[3]

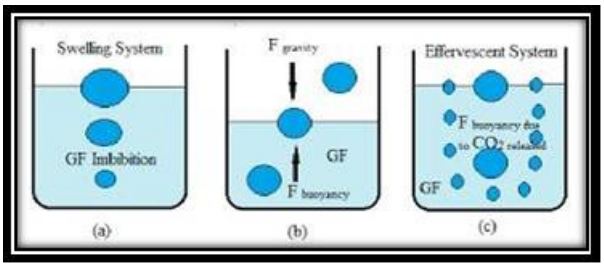
These drugs also have a suitable absorption in the stomach which is an essential characteristic required for gastroretentive approach.[2]

Floating Drug Delivery Systems

Floating Drug Delivery Systems (FDDS) are the reduced density systems having density lesser than that of the gastric fluid which impart buoyancy to the systems and due to the virtue of buoyant force these formulations float on the gastric fluid. Superficially the floating systems are of two different types i.e. Effervescent Systems and the Non Effervescent.

Floating systems are low-density systems with enough buoyancy to float above gastric contents and remain buoyant in the stomach for an extended length of time without altering

the gastric emptying rate. The medicine is slowly released at the desired pace from the system while it is floating on the stomach contents. The residual system in the stomach is emptied once the medicine is released. As a result, GRT is raised, and variations in plasma drug concentrations are better controlled.[23]



Gastro retentive drug delivery system

Gastro retentive drug delivery is a method of extending the time a medication spends in the stomach, allowing for site-specific drug release in the upper gastrointestinal tract (GIT) for local or systemic effects. Gastro retentive dosage forms can stay in the gastrointestinal area for a long time, extending the gastric retention time (GRT) of medications substantially. As a result, they not only extend dose intervals but also improve patient compliance beyond what is now possible with controlled release dosage forms. This technique is very useful for delivering insoluble and sparingly soluble medicines.[18] It is well recognised that when a medication's solubility declines, the amount of time available for dissolution reduces, and therefore transit time becomes a critical factor impacting drug absorption. The capacity to prolong and regulate the emptying time of dose forms that stay in the stomach for a longer duration of time than normal dosage forms is a key advantage for dosage forms that stay in the stomach for a longer period of time than conventional dosage forms. Designing controlled release systems for improved absorption and bioavailability presents a number of challenges. The difficulty to contain the dose form in the desired location of the gastrointestinal system is one of these challenges.[19] Drug absorption from the gastrointestinal system is a complicated process that is influenced by a number of factors. Gastro retentive systems can stay in the gastric area for several hours, considerably extending the duration medications spend in the stomach. Prolonged stomach retention enhances bioavailability, minimises drug waste, and improves solubility for medicines that are less soluble at high pH. It can also be used to deliver drugs to the stomach and proximal small intestine. Gastro retention aids in the provision of innovative drugs with novel treatment potential and significant patient advantages.[20,21]

The following drugs must be made into gastro-retentive dose forms

- Drugs acting locally in the stomach.
- Drugs that are primarily absorbed in the stomach.
- Drugs that is poorly soluble at alkaline pH.
- Drugs with a narrow window of absorption.
- Drugs rapidly absorbed from the GI tract
- Drugs that degrade in the colon.

Treatment of Diabetes

A number of dosage forms and novel systems are present for the administration of the Oral hypoglycaemic drugs like tablets, combination products, hydrogels, osmotic systems, aerosols, transdermal patches, implants, microspheres, implants and vesicular systems (liposomes, niosomes and transferosomes). The conventional tablets have a drawback that they have a short duration of action and require repeated administration. The current therapies of diabetes include the conventional single dose tablets, combination products like metaglip (glipizide/metformin combination), Glucovance (glyburide/metformin combination), avandamet (rosiglitazone/metformin combination), actoplus Met (pioglitazon/metformin combination),[60] etc. When the combination products are implied these have a better applicability over the conventional tablets but there are just a few combination products with very few dosage regimens and moreover the dose administered in the combination products is very low and requires frequent administration and are also costlier than the conventional tablets [60]. Some Sustained release marketed preperations are also available in the market such as Glucotrol XL, Glucophage XR.[61] The sustained release products have their effect for a longer period but the plasma drug concentration keeps on changing as the absorption index of the drug from the dosage form keeps on changing all over the GIT tract with the change in pH.

Antidiabetic agents

Antidiabetic agents refer to all the different types of medicine involved in the treatment of diabetes. All these agents aim to reduce blood sugar levels to an acceptable range (called achieving normoglycemia) and relieve symptoms of diabetes such as thirst, excessive urination, and ketoacidosis (a serious complication of diabetes that occurs when the body cannot use glucose as a fuel source). Antidiabetic agents also prevent the development of, or slow the progression of, long-term complications of the disease, such as nephropathy (kidney

disease), neuropathy (nerve damage), and retinopathy (damage to the retina of the eye).

Common antidiabetic agents include

- Alpha-glucosidase inhibitors (acarbose, miglitol)
- Amylin analogs (pramlintide)
- Dipeptidyl peptidase 4 inhibitors (alogliptan, linagliptan, saxagliptin, sitagliptin)
- Incretin mimetics (albiglutide, dulaglutide, exenatide, liraglutide, lixisenatide)
- Insulin
- Meglitinides (nateglinide, repaglinide)
- Non-sulfonylureas (metformin)
- SGLT-2 inhibitors (canagliflozin, dapagliflozin, empagliflozin)
- Sulfonylureas (chlorpropamide, glimepiride, glipizide, glyburide, tolazamide, tolbutamide) and thiazolidinediones (rosiglitazone, pioglitazone).

CONCLUSION

The gastroretentive dosage forms are used for drugs which have a short half life and require repetitive dosing at shorter intervals. These are helpful in reducing the dosing interval and also reduce the amount of drug to be administered on overall basis. All the approaches of the gastroretentive drug delivery had shown promising role for the sustained effect of the drug on the body.

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