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Alpha-Glucosidase Inhibitors (AGIs): A New Class of Oral Medication for Treatment of Type 2 Diabetes Patients

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Abstract

α-Glucosidase inhibitors (AGIs) are a new class of antidiabetic drug that inhibits the absorption of carbohydrates from the gut and is exclusively used for the treatment of T2D. This group lowers blood glucose in a dose-dependent fashion by modifying the intestinal absorption of carbohydrates and fat. For T2D patients, postprandial hyperglycaemia control is essential for the maintaining recommended HbA1c goals, and AGIs are used as monotherapy or in combination with other antidiabetic medications to achieve normal glucose level. Acarbose, Miglitole, 1-deoxynojirimycin, and Voglibose are four AGIs, and among these; Acarbose has been shown to decrease the risk of progressing to diabetes in subjects with impaired glucose tolerance. In this mini review an attempt has been taken to discuss the aspects of AGIs with their efficacy and safety when a T2D patient uses these.

Keywords: α-Glucosidase inhibitors, α-glucosidase enzyme, hyperglycaemia

1. Introduction

Diabetes mellitus (DM) is an endocrine metabolic disorder characterized by chronic hyperglycaemia, and treatments for DM are the use of insulin and oral hypoglycaemic drugs, changes in lifestyle, biotechnology products, and pancreatic transplants. Some of the risk factors for T2D are obesity, sedentary lifestyle, and eating habits (Fauci et al., 2009). It is one of the most prevalent diseases seriously threatening the health of T2D patients. It is associated with damage, dysfunction and failure of various organs. It increases the risk of microvascular complications, such as retinopathy, nephropathy, and neuropathy; and macrovascular complications, such as ischaemic heart disease, of blindness, kidney failure, stroke, lower limb amputation, and peripheral vascular disease (Lawal, 2022). The World Health Organisation (WHO) has observed that every year about 50% of diabetes patients die due to heart disease and stroke (Morrish et al., 2001).

Alpha-glucosidase inhibitors (AGIs) are not technically hypoglycaemic agents, simply diabetes pills. These reduce blood sugar level and are used to treat diabetes. These do not have a direct effect on insulin secretion or sensitivity. These work on the brush border of the intestine and cause cirrhosis, inflammatory bowel disease, predisposition to bowel obstruction, and carbohydrate mal-absorption syndromes (Yee & Fong, 1996). Actually, these delay the breakdown of carbohydrates in the gut, and consequently slow down the absorption of sugars. Of all available antidiabetic drugs, AGIs seem to be the most effective in reducing post-prandial hyperglycaemia (Derosa & Maffioli, 2012). These break down and absorb carbohydrates, such as dextrins, maltose, sucrose and starch, and no effect on glucose. Four alpha-glucosidase inhibitors generics are Acarbose, 1-deoxynojirimycin, Miglitole, and Voglibose (Chiasson et al., 1994). These are pseudo-carbohydrates that competitively inhibit α-glucosidase enzymes located in the brush border of enterocytes that hydrolyze non-absorbable

oligosaccharides and polysaccharides into absorbable monosaccharaides (Derosa & Maffioli, 2012). These four AGIs do not increase insulin output potentially leading to hypoglycaemia. These are very safe and are nontoxic drugs (Godbout & Chiasson, 2007). Among these, Acarbose is the most prescribed and most effective drug against glucoamylase, often use as insulin and OAD combinations to achieve better glycemic control. It was isolated by Schmidt from cultures of actinoplanes in 1977. It is effective, safe and well tolerated. From many studies it is found that it could decrease the risk of cardiovascular disease (Krause & Ahr, 1996).

These slow the digestion of starch in the small intestine. Consequently, glucose from the starch of a meal enters the bloodstream more slowly. These reduce glycated hemoglobin (HbA1c) values up to 0.5–1.0% (Chiasson et al., 1994). These are selective for postprandial hyperglycaemia and no hypoglycaemic symptoms are seen. Doses are for Acarbose 25–50 mg thrice a day, for Miglitol 25–100 mg thrice a day, and for Voglibose 0.2–0.3 mg thrice a day. These can be used as monotherapy and in combination with the Sulfonylureas or insulin for T2D (Yee & Fong, 1996).

2. Literature Review

The literature is an introductory section of research, which exhibits the works of previous researchers in the same field within the existing knowledge (Polit & Hungler, 2013). It is a hard-working search, scholarly inquiry, and investigation that aim for the discovery of new facts and findings (Adams et al., 2007). Floris Alexander van de Laar has reviewed the use of AGIs as initial treatment for patients with T2D, or as treatment for patients with impaired glucose tolerance (IGT) and impaired fasting blood glucose (IFBG) in case of elevated fasting blood glucose (van de Laar, 2008). Giuseppe Derosa and Pamela Maffioli have conducted a review analyzing the clinical efficacy and safety of AGIs, both monotherapy and in combination with other anti-diabetic drugs, with respect to glycemic control, inflammation and atherosclerosis. They have realized that AGIs proved to be effective and safe in both cases (Derosa & Maffioli, 2012). Giuseppe Derosa and his coauthors have compared Acarbose and Repaglinide in T2D patients treated with a sulfonylurea-metformin combination therapy (Derosa et al., 2009).

Peter S. Johnston and his coworkers have tried to determine the safety, efficacy, and tolerability of the α-glucosidase inhibitor Miglitol vs. the Sulfonylurea Glyburide in the treatment of elderly patients with T2D, inadequately controlled by diet alone. They have observed that AGIs are useful and relatively safe therapeutic options in the elderly T2D patients (Johnston et al., 1998).

Ariane Godbout and Jean-Louis Chiasson have found that AGIs are designed to specifically delay the digestion of complex carbohydrates, thus significantly reducing postprandial glycemic and insulinemic excursions (Godbout & Chiasson, 2007). Teni Ernawati and her coworkers have tried to observe molecular interactions between α-glucosidase inhibitor (IAG) and α-glucosidase enzymes derived from Saccharomyces cerevisiae, Rattus norvegicus, and GANC-human (Ernawati et al., 2018).

Devajit Mohajan and Haradhan Kumar Mohajan have studied diabetes mellitus, eating disorders, and various anthropometric indices. They have also studied on insulin and various oral medications for the treatment of T2D. They have stressed that overweight and obesity are the roots of many non-communicable diseases (Mohajan & Mohajan, 2023a-z). Pornthep Temrangsee and his coworkers have found that Acarbose Thai traditional medicine considered it as an imbalance of body functions, as α-glucosidase inhibitor reduces blood sugar level and are used to treat diabetes. Benjakul (B) and Soros Benjakul (SB) are formulas used for correcting the imbalance. These are comprised of five plants in different ratios: fruit of *Piper retrofractum* Linn. (PR), root of *Piper sarmentosum* Roxb. (PS), stem of *Piper interruptum* Opiz. (PI), root of *Plumbago indica* Linn. (PL) and rhizome of *Zingiber officinale* Rosc. (ZO) (Temrangsee et al., 2019).

3. Research Methodology

Research is the procedures of systematic investigations that requires collection, interpretation and refinement of data, and ultimately prepares an acceptable article, working paper, book chapter or a thesis by the appropriate use of human knowledge (Pandey & Pandey, 2015). It serves as an indicator of the subject that has been carried out previously (Creswell, 2007). Methodology is a guideline of any research, which is considered as an organized procedure that follows scientific methods efficiently (Kothari, 2008). It provides the research design and analysis procedures to perform a good research (Hallberg, 2006). Research methodology provides the principles to the researchers for organizing, planning, designing and conducting a good research (Legesse, 2014). To prepare this article we have dependent on the secondary data sources. We have used books of famous authors, research articles, handbooks, and theses related to our research area. We have also collected valuable information from websites and internets to enrich this paper.

4. Objective of the Study

The leading objective of this study is to consult aspects of α-Glucosidase inhibitors (AGIs) and their importance for the treatment of type 2 diabetes (T2D) patients. These are effective in decreasing glycosylated hemoglobin

(HbA1c) and postprandial glucose levels in patients with T2D when administered as monotherapy or in combination with other antidiabetic agents. Some other trivial objectives of this study are as follows:

- to show the activities of AGIs, and
- to provide the side-effects of AGIs.

5. AGIs Rich Plants

AGIs delay the absorption of ingested carbohydrates by reducing the postprandial glycemia and insulin peaks. With the rejection of the α-glucosidase enzyme, glucose levels in the blood could be returned within the normal limits (Stuart et al., 2004). *Physalis peruviana* is Andean specie whose fruits are rich in phenolic compounds and are eaten as food and also has been reported in Colombian folk medicine for DM. The plant was identified and classified at the Herbario Nacional Colombiano, Universidad Nacional de Colombia and a voucher specimen was deposited in his collection under the code number (COL-574701). The fruits of *Physalis peruviana* inhibited the alpha amylase and alpha glucosidase enzymes (Rey et al., 2015). Five plants in different ratios are used in Thailand for the treatment of DM. These are; the fruits of *Piper retrofractum* Linn. (PR), the root of *Piper sarmentosum* Roxb. (PS), the stem of *Piper interruptum* Opiz. (PI), the root of *Plumbago indica* Linn. (PL) and the rhizome of *Zingiber officinale* Rosc. (ZO) (Temrangsee et al., 2019). *Merremia peltata* is ethnomedicine plant used as traditional medicine that is used for the treatment of diabetic in Sulawesi, Sumatra, Maluku, and Papua (Af-idah et al., 2021).

6. Activities of AGIs

Alpha-Glucosidase enzyme is a type of hydrolase enzyme that catalyzes the hydrolysis of non-reducing terminal carbohydrates into α-glucose. When α-glucosidase enzyme, such as maltase, isomaltase, and glucomaltase that serve to hydrolyze the oligosaccharides is rejected in the body, glucose levels in the blood could be returned within the normal limits (Nashiru et al., 2001). Postprandial hyperglycaemia is a diabetes complication. If it is not properly controlled, it might progress to DM, a metabolic syndrome. AGIs can be used as a first-line drug in newly diagnosed T2D insufficiently treated with diet and exercise alone. Also, these can be used as in combination with all other oral antidiabetics and insulin if first-line therapy fails (Derosa & Maffioli, 2012). Usually, the ingested polymeric sugar chain is broken down into monosaccharides by the action of AGIs absorbed in the proximal part of the small intestine and released into the bloodstream. Consequently, the postprandial rise in plasma glucose is blunted and prolonged (Godbout & Chiasson, 2007).

7. Side-Effects of AGIs

AGIs cause the weight loss by lowering the amount of sugar metabolized. These prevent the degradation of complex carbohydrates into glucose, some carbohydrate will remain in the intestine and be delivered to the colon (Derosa & Maffioli, 2012). Consequently, bacteria digest the complex carbohydrates, causing gastrointestinal severe side-effects, such as flatulence, bloating, diarrhea, and abdominal pain (Spiller, 1998). These are only effective in mild hyperglycaemia. Side-effects may decrease in 1 to 2 months, and gradual escalation from low to higher doses may weaken the adverse effects. Also, these have no severe toxicity (Hanefeld, 1998).

8. Conclusions

A new class of oral glucose lowering drugs, AGIs is used for the prevention and management of T2D. It decreases postprandial plasma glucose and insulin and improves insulin sensitivity. It does not cause hypoglycaemia among elderly T2D patients. This class alters the intestinal absorption of carbohydrates by inhibiting their conversion into simple sugars. It improves glycemic control and HbA1c in patients with diabetes. As a result, it is associated with a decreased risk of microvascular complications. For the safety and tolerability, it becomes an attractive choice to the T2D patients and is used as monotherapy or in combination with other oral drugs or with insulin as second-line therapy. Among AGIs, Acarbose has to be the best studied among all oral antidiabetic agents and is an effective agent in preventing diabetes.

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