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# Morning glory resin glycosides as α-glucosidase inhibitors: In vitro and in silico analysis

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ABSTRACT

Twenty-seven individual resin glycosides from the morning glory family (Convolvulaceae) were evaluated for their α-glucosidase inhibitory potential. Four of these compounds displayed an inhibitory activity comparable to acarbose, which was used as a positive control. Molecular modeling studies performed by docking analysis were accomplished to predict that the active compounds and acarbose bind to the α-1,4-glucosidase enzyme catalytic site of MAL12 from the yeast *Saccharomyces cerevisiae* through stable hydrogen bonds primarily with the amino acid residues HIS279 and GLN322. Docking studies with the human maltase-glucoamylase (MGAM) also identified binding modes for resin glycosides inside the catalytic site in the proximity of TYR1251. These results postulate that resin glycosides may be a source of phytotherapeutic agents with antihyperglycemic properties for the prophylaxis and treatment of non-insulin-dependent type 2 diabetes mellitus.



## 1. Introduction

Currently, non-insulin-dependent type 2 diabetes mellitus (T2DM) is considered the third most serious public health problem worldwide. In Mexico, this chronic metabolic disease is the second leading cause of death with approximately 9.2% of the population suffering the disorder or a prediabetic condition (Jiménez-Corona et al., 2013). Therefore, there is an imperative demand for the discovery of novel antihyperglycemic agents from natural sources that could be used as prototypes for developing new alternative therapies. Herbal remedies have gained wide acceptance for treating this disorder in countries like Mexico with a rich tradition of ethnomedical records, which provided more that 380 plant species employed for the treatment of T2DM (Andrade-Cetto et al., 2008; Mata et al., 2013). In recent years, many efforts have been made to identify effective inhibitors of α-glucosidases from plants traditionally used as hypoglycemic remedies (Mata et al., 2013). These chemical studies have provided an abundant variety of secondary metabolites like flavonoids (Vinayagam and Xu, 2015), alkaloids (Sharma et al., 2010), 4-phenylcoumarins (Andrade-Cetto et al., 2008), chromenes (Escandón-Rivera et al., 2012), and sesquiterpene lactones (Qian-Qian et al., 2013), among others, but the best known α-glucosidase inhibitor of natural origin is acarbose (Fig. 1), a pseudo-tetrasaccharide that is composed of an acarviosine group α-(1–4) linked to a maltose, obtained commercially from fermentation cultures of selected strains of an unidentified species of *Actinoplanes* (Wehmeier and Piepersberg, 2004). This potent antihyperglycemic drug is used worldwide in the treatment of T2DM and, in some countries, prediabetes; and it is being an option as monotherapy and as an add-on to other hypoglycemic drug treatments (e.g., metformin and glybenclamide), especially when postprandial hyperglycemia is the main concern (Derosa and Maffioli, 2012). Unfortunately, it produces gastrointestinal complaints. As the incidence of T2DM is increasingly expanding, a demand for antihyperglycemic drugs, such as acarbose, needs to be anticipated. Recently, plants from the morning glory family (Convolvulaceae) have been reported for the treatment of diabetes. For example, in India, the juice of the aerial parts of sweet potato (*Ipomoea batatas*) is taken for its hypoglycemic properties (Chhetri et al., 2005). Also, members of the convolvulaceae have been described as a source of potent α-glucosidase inhibitors (Anis et al., 2002). Cairicosides I–IV and two related oligosaccharides from *Ipomoea cairica*, resembling the pseudotetrasaccharide structure of acarbose, exhibited a stronger α-glucosidase inhibitory activity when compared to this therapeutic positive control (Jie-Hong et al.,

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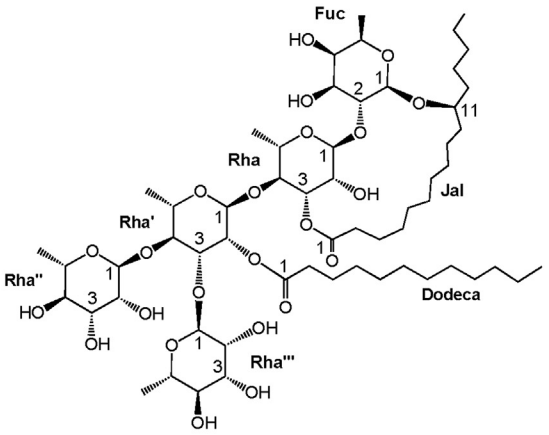


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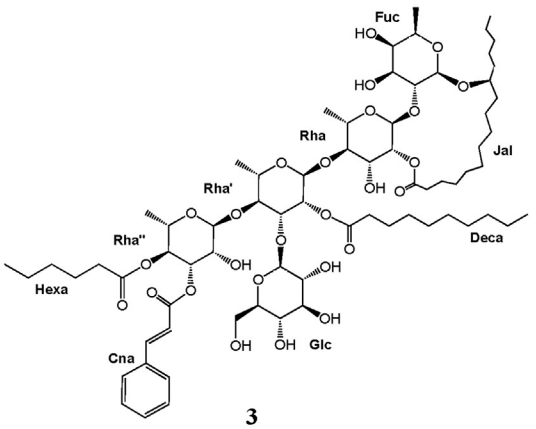


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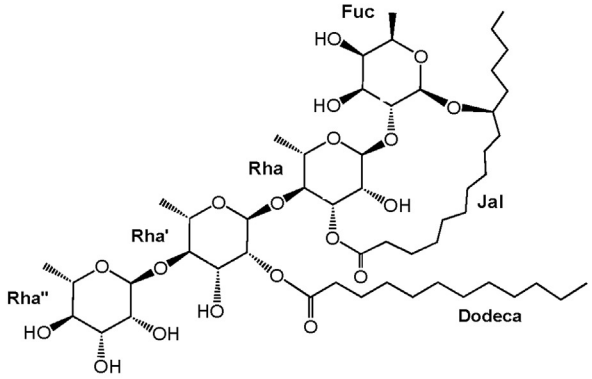


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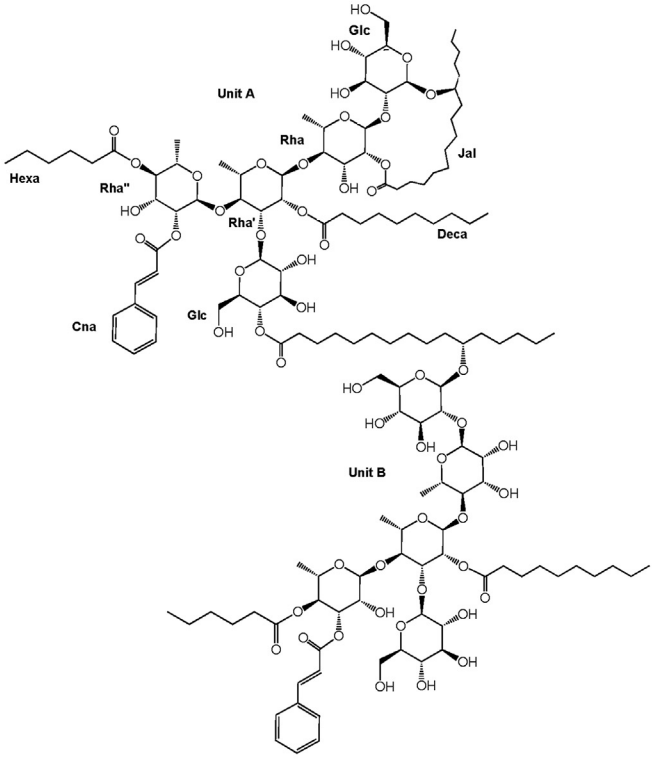


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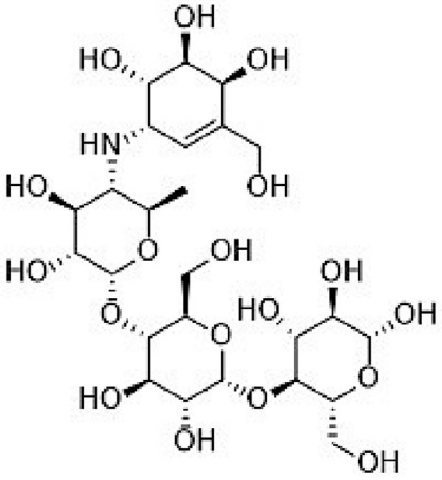

**Fig. 1.** Structure of acarbose, an oral antihyperglycemic medicine currently in use.