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DIRECTED SEARCH FOR NOVEL A-GLUCOSIDASE INHIBITORS USING STRUCTURE SIMILARITY WITH TESTED SUBSTANCES

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Type 2 diabetes mellitus is one of the most fast-spreading socially-important diseases of our days, so researches worldwide are oriented for antidiabetic drug discovery. One of the approaches to hyperglycemia pharmacocorrection is the inhibition of α-glucosidase.

In this regard, the target of the present study is computer-aided search for novel α glucosidase inhibitors by method of structure similarity with tested substances. The prediction was carried outusing the database containing the information about structure and α-glucosidase inhibition activity of 183 newly tested substances. The data about their maximum inhibiting activity (Δ%) in 1 mM concentration were subjected to clusterization by *k*-means method, and 3 classes of activity were defined: high (19 subst.), moderate (40 subst.), low (74 subst.).

In silico activity prediction for 695 new compounds was made with the program TestSim 17.01.28 from IT Microcosm software complex [1]. This utility employs the method of similarity with standards, based on calculation of QL-modified Tanimoto similarity index *T* [2]. For each substance *T* values were calculated for all tested substances from database. The maximum value T_{max} was determined, with the indication of code and activity level of the most structurally similar tested substance.

A total of 15 compounds with predicted high value and T_{max}>0,6 were tested in vitro by method[3] in 1 mM concentration. The reference drug was acarbose.

According to the experimental results, out of 15 promising predicted substances 10 were found to possess high α-glucosidase inhibition activity. Five compounds were more active than reference drug and another five have the same activity as acarbose. So, the prediction accuracy of the α-glucosidase inhibitory properties by structure similarity with tested substances was defined as 66,7%.

As a result, we can conclude, that this method can be used for *in silico* prediction of new α-glucosidase inhibitors per their structural similarity with earlier tested substances. The accuracy was 66,7%, and five newly identified active compounds were selected for the further detailed pharmacological evaluation.

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