E. Zmievskaya [1]
P. Vassiliev [1]
V. Kuznetsova [1]
E. Sokolova [1]
I. Egorova [1]

SEARCH FOR MAILLARD REACTION INHIBITORS BY THE SIMILARITY METHOD

[1] Chair of Pharmacology, Volgograd Medical State University, Pavshih bortsov Str., 1, Volgograd, Russia.

Eka-zmievskaya@yandex.ru

Maillard reaction initiates protein glycation leading to harmful outcomes of diabetes mellitus, such as an angiopathy, cardiopathy, retinopathy [1]. Its inhibitors would be a novel class of antidiabetic drugs, but no one has implemented in clinical practice yet. Search for them needs to be highly productive, so a virtual screening is essential. The aim of this work is comparison of two prediction methods based on structure similarity in application to antiglycation activity.

Data on 695 substanses with various structures was used. 303 of them were tested experimentally [2], and others were examined using a virtual screening by two structure similarity methods [3]. First one compared structure of new substances with standards known as proved active. Second one compared with already tested. The comparison was done by IT Microcosm software [4].

The similarity with standards. 13 substances were used as standards (substances researched in details and having activity as an aminoguanidine). 392 substances were compared. The prediction was based on a consensus between the coefficient of mean similarity with all standards and the coefficient of max similarity with one of them. 9 substances were predicted as active and tested with an experiment [2]. 5 found themselves glowing so whouldn't be tested correct with an applicable methodology. 2 were found as active (>15%). Ones activity was comparable with an aminoguanidine (standard, 50%) and ones was less. Hence a predictive efficiency of this method is about 50% (2 of 4).

The similarity with tested substances. 303 experimental tested substances were clustered to 3 classes of activity: high, moderate and low. Then 392 substances were compared with already tested. A substance was predicted as active if had the max coefficient of similarity to the tested substance clustered as 'high' (>35,5%). So 7 substances were predicted and tested with experiment [2], 2 of them were glowing. From 5 other 2 showed themselves active, one is as active as aminoguanidine, second is much more. Thus this method has a predictive efficiency of 40% (2 of 5).

Thereby both of this methods have a quite high predictive value. As predicted active substances had different structures, methods can't be considered as interchangable. The similarity with standards ought to be used at the beginning of a screening because doesn't need an experimental data, but predicted substances had a bit lower activity. The similarity with tested substances predicted more active substances, probably because it considers particularity of the methodology and has advantages at the next stage.

1. Ansari N.A. et al. *Biomedical Chemistry*, 2010, **56**: 168-178.
2. Jedsadayanmata A. *Naresuan University Journal*, 2005, **13(2)**: 35-41.
3. Vassiliev P.M. et al. *In: Target-oriented search for antidiabetic agents*, VSMU, 2016: 126-181.
4. Vassiliev P.M., Kochetkov A.N. *IT Microcosm. State Registration Certificate for software program 2011618547 (Russian)*, 2011, 31 Oct 2011.

Funding: grant RSF (project №14-25-00139)