TRANSPORT STUDY OF KYNURENIC ACID AND ITS NEWEST DERIVATIVES THROUGH AN IN VITRO MODEL OF THE BLOOD-BRAIN BARRIER USING TARGETED UHPLC-MS\MS

Noémi Kmetykó[1], Imola Wilhelm[2], István Ilisz[1], Róbert Berkecz[1]

[1]*Institute of Pharmaceutical Analysis, University of Szeged, H-6720, Szeged, Somogyi u. 4, Hungary*
[2]*Institute of Biophysics, Biological Research Centre, H-6726, Szeged, Temesvári krt. 62, Hungary*
e-mail: berkecz.robert@pharm.u-szeged.hu

Abstract
We have developed a targeted UHPLC-ESI–MS/MS method for the quantification of kynurenic acid (KYNA) and its derivatives from biological samples. The samples were gained from in vitro permeability assay. We have found that the transportation of the derivatives through the blood-brain barrier is better than KYNA.

Introduction
Since kynurenic pathway has a great influence on the central nervous system, interruption of its chemical balance could lead to the development of neurodegenerative diseases. The kynurenics that have positive effect can get through the blood-brain barrier only in a very minimal rate, so restoring the balance is difficult. Nowadays best possible therapy seems to be the use of derivatives of **KYNA** as active ingredient.

Experimental
The method development and its application was preceded by an *in vitro* permeability assay using primary rat brain endothelial cells. The level of **KYNA** and its derivatives (**SZR104, SZR72**) that has passed through the assay was determined by a targeted ultra-high performance liquid chromatography combined with electrospray ionisation triple quadrupole tandem mass spectrometry (UHPLC-ESI-MS/MS) method. For quantitative analysis, external calibration was applied using **SZR73** as an internal standard.

Results and discussion
The main parameters of the sample preparation and the targeted UHPLC-ESI-MS/MS method were optimized. The developed procedures were successfully applied for quantification of **KYNA**, **SZR104** and **SZR72** in the biological samples. Overall, the derivatives **have** significantly better transportation through the blood-brain barrier than the **KYNA**. The amount of the transferred compounds was the following in descending order: **SZR104**, **SZR72** and **KYNA.**

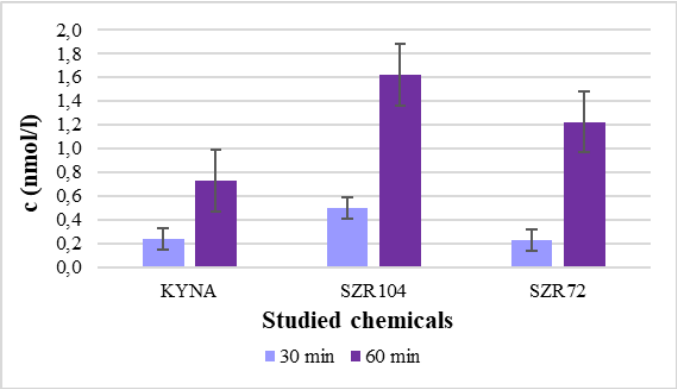

Figure 1. The amount of transferred chemicals *in vitro* permeability assay

Conclusion

Using the developed method on the biological samples, we have found that the amount of transported kynurenics is linked to the duration of the assay and the chemical modification of **KYNA** improved the permeability.

Acknowledgements

This research was supported by the EU-funded Hungarian grant EFOP-3.6.1-16-2016-00008 and GINOP-2.3.2-15-2016-00034 EU.