Đanić *et al.: Intrinsic Activity*, 2018; **6**(Suppl.1):A5.7
doi:10.25006/IA.6.S1-A5.7
published online: 20 September 2018

INTRINSIC ACTIVITY

24th Scientific Symposium of the Austrian Pharmacological Society

Graz, 27–28 September 2018

MEETING ABSTRACT

A5.7

Preliminary study on gliclazide–probiotic bacteria interactions in *in vitro* conditions

Maja ĐANIĆ[1,*], Bojan STANIMIROV[2], Nebojša PAVLOVIĆ[3], Slavica LAZAREVIĆ[1], Svetlana GOLOČORBIN-KON[3] and Momir MIKOV[1]

[1]*Department of Pharmacology, Toxicology and Clinical Pharmacology, Faculty of Medicine, University of Novi Sad, Serbia;* [2]*Department of Biochemistry, Faculty of Medicine, University of Novi Sad, Serbia;* [3]*Department of Pharmacy, Faculty of Medicine, University of Novi Sad, Serbia*

Background: Recently, great attention has been paid to the implication of gut microflora composition in interindividual differences in drug metabolism and therapeutic response [1]. Gliclazide belongs to the sulfonylurea family of insulin secretagogues and is characterized by large interindividual differences in the therapeutic response. The origin of these variations is not fully understood and may be the consequence of different gut microflora profiles between patients. Therefore, the aim of this study was to make preliminary assumptions of gut microflora influence on interindividual differences in gliclazide response based on *in vitro* assessment of gliclazide transport and biotransformation in probiotic bacteria.

Methods: Samples of gliclazide with probiotic bacteria were incubated for 24 hours at 37 °C. After adequate sample preparation, intracellular and extracellular concentrations of gliclazide were determined at seven time points by high-performance liquid chromatography. Gliclazide biotransformation and potential metabolic products formed by enzymatic activity of probiotic bacteria were examined by appropriate software packages.

Results: During the twenty-four-hour incubation with probiotic bacteria, at all time points, statistically significantly lower concentrations of gliclazide in extracellular content were observed compared to controls. Accordingly, concentrations of gliclazide increased in probiotic cells over time. After 24 hours the total concentration of gliclazide, as the sum of intracellular and extracellular content, reached about 70 % of the concentration from the beginning of the experiment (from 209.16 ± 6.26 µg/ml to 131.21 ± 1.17 µg/ml, $p < 0.01$). Potential metabolic pathways of gliclazide biotransformation by enzymatic activity of probiotic bacteria involve reactions of hydrolysis and hydroxylations.

Discussion: Considering the fact that the total amount of gliclazide significantly decreased after the incubation period, it is assumed that one part of gliclazide is transformed to its metabolic products. It can be concluded that there are important interactions between gliclazide and probiotic bacteria, both at the level of active and passive transport into the cells, and at the level of drug biotransformation by enzymatic activity of probiotic bacteria. The effect of these interactions on the final therapeutic response of gliclazide should be further studied and confirmed in *in vivo* conditions.

Acknowledgements: This research was supported by HORIZON 2020 MEDLEM project no. 690876, Project for Scientific and Technological Develpment of Vojvodina no. 114-451-2072-/2016-02 and Project of Ministry of Education, Science and Technological Development of the Republic of Serbia, grant no. 173014.

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*Corresponding author e-mail: *maja.djanic@mf.uns.ac.rs*