3rd National Congress on Physical Sciences, 29 Sep. – 2 Oct. 2016, Sofia
Section: Physics of Living and Soft Matter. Physics in Medicine

In vitro and *in silico* Studies of the Membrane Transport of Selected Flavonoids

A. Diukendjieva, P. Alov, I. Tsakovska, F. Fratev, M. Al Sharif, T. Pencheva, I. Pajeva

Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences, Acad. G. Bonchev Str., Block 105, 1113 Sofia, Bulgaria

Abstract. In the recent years the number of natural products (NPs) used as components in dietary supplements, cosmetics and pharmaceuticals has tremendously increased. The broad application of NPs requires a more extensive evaluation of their ADME/Tox (Absorption, Distribution, Metabolism, Excretion, and Toxicity) properties.

In the present study we used both *in vitro* and *in silico* methods to evaluate bioavailability after oral administration (gastrointestinal absorption) of selected natural flavonoids and their derivatives, with a particular focus on flavonolignans that are the main components of *Silybum marianum* L. (milk thistle). A parallel artificial membrane permeability assay (PAMPA) [1] was used for transcellular permeation evaluation since PAMPA permeability has been shown to correlate with passive human intestinal absorption. Additionally, an in house developed QSAR (Quantitative Structure-Activity Relationship) model [2] predicting PAMPA permeabilities from calculated physico-chemical molecular descriptors was used for estimation of permeability and it was shown that the derived predictions correlate well with obtained *in vitro* results.

The active transcellular transport of flavonolignans and co-administered drugs depends on their effect on the function of the multidrug resistant transporter P-glycoprotein (P-gp) [3]. Therefore, *in silico* models of P-gp were developed to explore the interactions of the compounds with P-gp at a molecular level.

Acknowledgements: Support from ESF COST Action CM1407 and the matching project of the National Science Fund of Bulgaria (grant DCOST 01/11/16.08.2016) is acknowledged.

References

1. Kansy M, Senner F, Gubernator K (1998) Physicochemical high throughput screening: parallel artificial membrane permeation assay in the description of passive absorption processes. *Journal of medicinal chemistry 41* 1007-10.

2. Diukendjieva A, Marinov L, Alov P, Tsakovska P, Pajeva I (2015) *In silico* modelling to predict transcellular permeability of bioactive compounds. *Series G. Medicine, Pharmacy and Dental medicine, Union of Scientists in Bulgaria, 18* 187-190.
3. Dzubák P, Hajdúch M, Gazák R, Svobodová A, Psotová J, Walterová D, Sedmera P, Kren V. (2006) New derivatives of silybin and 2,3-dehydrosilybin and their cytotoxic and P-glycoprotein modulatory activity. *Bioorganic & medicinal chemistry 14* 3793-3810.