



Fund “Nauka” Project № 16021 Resume – Competition-Based Session 2016:

“Study of drug interactions at a biotransformation level”

Project leader: Prof. Kaloyan Dobrinov Georgiev, MScPharm, PhD

Introduction: Drug interactions are one of the main reasons for correction or discontinuation of drug therapy. The concomitant use of both drugs and plant extracts with drugs may lead to serious drug interactions or herb-drug interactions. The composition of foods and food supplements may significantly affect the pharmacokinetics and pharmacodynamics of some drugs, which may reduce their therapeutic effect or increase the risk of adverse reactions. In both cases, this is unfavorable for patients and requires more studies of the potential interactions between drugs and plant extracts that are part of nutritional supplements.

Objective: Assessment of potential drug interactions at the level of biotransformation in the simultaneous use of certain foods/ beverages and food supplements and certain drugs.

Materials and methods: Plant material, certain chemical compounds, nutritional supplements and cytochrome activity screening kits (Vivid® CYP450 Screening Kits) were needed to study possible drug interactions. The following tasks were set to carry out the study:

1. Literary review;
2. Isolation and analysis of methylxanthine fraction from *Pu-erh* and *Bancha* tea leaves;
3. Isolation and analysis of *Goji berry* fruit fractions;
4. *In vitro* study of the effect of methylxanthine fractions on the activity of CYP3A4 and CYP2C9 enzymes;
5. *In vitro* study of the effect of isolated *Goji berry* fractions on the activity of CYP3A4 and CYP2C9 enzymes;
6. *In vitro* study of the effect of probiotics (*Laktera Nature*®) on the activity of CYP3A4 enzyme;
7. *In vitro* study of the effect of *endomorphin-2* analogues, *RGD*- and *neurotensin* analogues on the activity of the CYP3A4 enzyme;
8. Presentation and publication of the obtained results.

Solid-liquid extraction and high-performance liquid chromatography (HPLC) were used for isolation and analysis of the listed plant extracts.

Results: It was observed *in vitro* inhibition of CYP3A4 by methylxanthine fractions, isolated from green tea, *endomorphin-2* analogues, *RGD*- and *neurotensin* analogues, while *Goji berry* extract showed inhibition of CYP3A4 and CYP2C9 enzymes. This may lead to

potential drug interactions when the listed extracts and compounds are co-administered with drugs, substrates of CYP3A4 and CYP2C9, resulting in an increased risk of adverse reactions.

Research significance: In the present project, it was first investigated the influence of an extract and individual fractions contained in green tea leaves and *Goji berry* fruits on the activity of cytochrome P450 enzymes. Data is available about the modulation of cytochromes from green tea and goji berry extracts, but the effect of the individual fractions obtained from these extracts on cytochromes have not been studied. The effect of *endomorphin-2* analogues, *RGD*- and *neurotensin* analogues and lactobacilli (*Laktera Nature*®) on the activity of CYP3A4 was also evaluated. The achieved results correspond to the established institutional priorities for scientific activity in the field of food and nutrition. The results from the present study were presented on 5 international scientific forums, published in 4 articles, one of which in a refereed journal with impact factor (IF: 4.011) and included in a dissertation work for obtaining Doctor of Science degree.

Conclusion: Conducting research to evaluate and detect potential drug interactions between plant extracts and drugs can significantly reduce the risk of drug therapy failure as well as the occurrence of side effects. Future studies are needed to demonstrate the observed interactions *in vivo*.