Tytuł projektu

Badania oddziaływań białek surowicy krwi ludzkiej z wybranymi lekami w warunkach stresu.

Project title

Study of the interaction of human plasma proteins with selected drugs under stressful conditions.

Dyscyplina /Area of science

Nauki chemiczne

PROJECT DESCRIPTION

Project goals

- influence of stress factors on the degree of binding of selected OTC drugs to plasma proteins (human serum albumin HSA and acidic glycoprotein AGP)
- impact of the stress factors on the protein structure (HSA and AGP)
- determination of the drug binding to HSA and AGP in either free form or immobilized on the carrier surface
- application of the oxidative stress and the glycemic stress as stressors
- research will include the active substances available for OTC, in particular the non-steroidal anti-inflammatory drugs , as well as proton pump inhibitors (PPI)

Outline

Drugs distribution in body depends on the affinity of the drug for blood plasma proteins and tissues. The greatest clinical significance is the interaction with such proteins as human serum albumin (HSA) and acidic glycoprotein (AGP). This interaction is non-specific and is significant for the therapeutic effect. The drug molecule associated with the protein is pharmacologically inactive - it can't reach biophase, undergo metabolism and excretion. Therefore, determination of the degree of drug interaction with these biomacromolecules is one of the basic pharmacokinetic parameters for active substances. It is known that binding of a drug through proteins is influenced by many factors such as the structure of the active substance and protein, or the form of the drug. However, increasingly, oxidative and glycemic stress are mentioned as the most important factors affecting this parameter.

The aim of the project is to study the impact of selected drugs on plasma proteins and structural changes induced in the protein molecule by stress conditions and effects of free radical scavengers administration.

As part of the planned studies, the influence of stress factors on the degree of

binding of selected OTC drugs to plasma proteins (HSA and AGP) will be investigated. In addition, attempts will be made to determine the impact of these factors on the protein structure itself, which has not been described in the literature so far. HSA and AGP will be used to determine the degree of drug binding to proteins in either free form or immobilized on the carrier surface. For this purpose, one of the steps will be the synthesis of magnetic nanoparticles with a surface enriched with functional groups, what allows the effective immobilization of the protein. As stressors, the oxidative stress and, even more significant, the glycemic stress will be used. Among the active substances available for OTC, drugs from the group of non-steroidal anti-inflammatory drugs will be used initially because of their increasing use. In the next stage, the degree of binding of proton pump inhibitors (PPI) will be examined due to the fact that since their introduction as OTC they have been misused very often. The final stage of the work will be to examine the addition of free radical scavengers, reducing the effect of stress on the observed processes.

Modern analytical techniques such as surface plasmon resonance (SPR), capillary electrophoresis, LC-MS chromatography and crystallographic methods will be used to carry out the research. Magnetic nanoparticles obtained as carriers for the immobilization of plasma proteins will be fully characterized using ATR-FTIR, TEM, SEM, DLS and SQUIAD techniques.

In connection with the above research plan, a future PhD student is expected to know the methods of work with proteins, magnetic nanoparticles and determine the degree of binding active substances by the protein.

The above research is a part of the research plan proposed by the interdisciplinary BRAIN team (Biomedical & phaRmAceutical InterdyscipliNary group), which was awarded in the competition for the Priority Research Teams of the Nicolaus Copernicus University.

Work plan

1. Study of free protein interaction with selected drugs without a stress factor
2. Study of the interaction of free form protein with selected drugs in the presence of stressogenic agents.
3. Determination of the influence of stress factors on structural changes in the protein molecule.
4. Synthesis of magnetic nanoparticles as supports for protein immobilization.
5. Investigation of the interaction of protein immobilized on magnetic nanoparticles with selected drugs under non-stress conditions.
6. Investigation of the interaction of protein deposited on magnetic nanoparticles with selected drugs in the presence of the stress factors.
7. Study the effect of free radical scavengers on the interaction of the drug with proteins under stress conditions.

Literature

1. Lakshmi P., Mondal M., Ramadas K., Natarajan S. *Spectrochim Acta A Mol Biomol Spectrosc*., **183** (2017), 90-102
2. Joshi R., Jadhao M., Kumar H1.Ghosh S. *Bioorg Chem*. **75** (2017) 332-346
3. Ghuman J., Zzunszain P.A., Petipas I., Bhattacharya A.A., Otagirl M., Curry S. *J Mol Biol*. **14** (2005) 38-52.
4. Grzebyk E., Piwowar A. *Pol. Merk. Lek*., 2013, **32**, 239-242
5. Karpińska A., Gromadzka G. *Postepy Hig Med Dosw* **67** (2013) 43-53
6. Kawakami A., Kubota K., Yamada N. *FEBS J*. **273** (2006) 3346-3357
7. Dalle-Donnel I., Rossi R., Colombol G., Giustarini D., Milzani A. *Trends in Biochem. Sci*. **34** (2009) 85-96
8. Maciążek-Jurczyk M., Sułkowska A. *Mol. Biomol. Spectr*oscopy **136** (2015) 265-282
9. Johnson F., Giulivi C. *Mol Aspects Med*. **26** (2005) 340-352

Required initial knowledge and skills of the PhD candidate

- ➔ Knowledge of Polish
- ➔ Analytical thinking
- ➔ Eager to learn
- ➔ Knowledge of chemistry (including analytical and polymer chemistry),
- ➔ Knowledge and experience in methods of work with proteins and magnetic nanoparticles
- ➔ Knowledge on methods of the surface modification of magnetic nanoparticles
- ➔ Understanding analytical methods of chemistry and biology for determination the degree of binding active substances to the protein
- ➔ Eager to work hard

Zgłaszający projekt/ Author of the project	
prof. dr hab. Andrzej Wojtczak stopień/tytuł, imię, nazwisko	awojt@umk.pl e-mail
	Wydział Chemii UMK jednostka organizacyjna
Proponowani promotorzy i mentorzy/prospective supervisors	
1) promotor główny/ main supervisior	
prof. dr hab. Andrzej Wojtczak	e-mail: awojt@umk.pl

	Wydział Chemii UMK jednostka organizacyjna
2) promotor pomocniczy / co-supervisor	
Dr Marta Ziegler - Borowska e-mail	