UNIWERSYTET MEDYCZNY W ŁODZI
WYDZIAŁ FARMACEUTYCZNY

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NR ALBUMU:15/U3-B/2014

Nowe pochodne kumaryn o potencjalnej aktywności antykoagulacyjnej

(The new coumarin derivatives as novel anticoagulant drugs)

Rozprawa doktorska na stopień doktora nauk farmaceutycznych

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Łódź 2018

Summary

Nowadays, the scientists are looking for new drugs to create an alternative drugs, which are already on the market. These "older" drugs cause many side effects, very often. Therefore, in the development of modern organic synthesis, it is possible to synthesize new chemical compounds which, after examination, may constitute potential drugs. Studying a specific disease, scientists can find out what causes it and which cells and receptors are responsible for it. Researchers are looking for potential ingredients that will interact with the target to overcome the activity associated with the disease. The most frequent diseases in Europe and in the world are cardiovascular diseases. There are many cardiac drugs on the market, however, they cause frequent side effects. In clinical situations antithrombotic treatment is very important. Among the various anticoagulants, coumarins, which are the basis of oral anticoagulation, deserve attention. However, they cause many side effects, which let scientists discovering new drugs with potential anti-coagulation effects.

Coumarins are an interesting group of natural compounds with diverse properties. First step of my study was about design and synthesis of new coumarin derivatives with potential anticoagulant properties. The study was based on the following steps: chemical (synthetic), theoretical and biological. The chemical part included the synthesis of substrates and products, i.e. new coumarin derivatives. In the theoretical part, the binding of the new coumarin derivatives to human serum albumin (HSA) and vitamin K reductase subunit 1 (VKORC1) was determined using molecular modeling.

The biological part involved the examination of fluorescence quenching of human serum albumin in binding to new organic compounds - coumarin derivatives, and key element of this study was about determination of cytotoxic activity of the new compounds, which are candidates for potential drugs.

The results obtained by me allowed to conclude that I achieved the intended goal in the form of confirming the similarity between the new coumarin compounds and warfarin enantiomers, of which compound **3b** have the most attractive properties (two binding sites to HSA, maximum value of lipophilicity). However, in order to become a future anticoagulant drug which has been introduced to the pharmaceutical market, many further studies are needed.