ABSTRACT

Charles University

Faculty of Pharmacy in Hradec Králové

Department of Biochemical Sciences

Author: Bc. Iva Kožená

Supervisor: RNDr. Miloslav Macháček, Ph.D.

Consultant: PharmDr. Jan Kollár, Ph.D.

Title of diploma thesis: Organ distribution of anionic phthalocyanine photosensitizers in a

mouse tumor model

Cancer treatment currently consists mainly of chemotherapy, radiotherapy, and surgery. As these treatments possess certain side effects, other ways of treating cancer are being explored. One of these modern approaches, which is the subject of intensive research around the world, is a non-invasive and minimally toxic method called photodynamic therapy (PDT). The PDT is based on the application of a light-sensitive substance called a photosensitiser (PS), which accumulates selectively in the tumour and, after exposure to a light of a suitable wavelength, a photochemical reaction occurs which leads to the production of reactive oxygen species. The result of this reaction is an oxidative stress in the tumour tissue together with cellular damage with subsequent cell death accompanied with vascular damage, and even stimulation of the immune response.

Due to their advantageous properties, the phthalocyanines (Pcs) are very promising PSs. They are usually prepared in the form of complexes with centrally bound metal cations such as zinc and aluminium. Selected anionic Pcs were first examined at the cellular level under in vitro conditions, and as their photodynamic activity was promising, they were selected for further in vivo experiments.

The aim of this work is to evaluate the organ distribution of selected PSs in a mouse model. Further, to determine in which organ these compounds accumulate most and at what time they reach their respective maximal concentrations. Also, the time profile of these substances in plasma and urine was investigated.

From the results of our experiments on the BALB/c mice, it can be concluded that amphiphilic compound P44 was present in the organs at higher concentrations than hydrophilic compound HK22. The studied PSs reached the highest concentration in the plasma immediately after administration and then they were gradually eliminated from this compartment. P44 was deposited most extensively in the liver without elimination from this organ within 24 h. It was present in low concentrations in other organs. HK22 could not be detected in muscle, tumour, and lungs at all. As both anionic compounds P44 and HK22 were not deposited in tumour tissue, they are not very suitable for utilization in PDT in terms of pharmacokinetics.