Prague, August 24, 2022

Review on thesis „Carriers of Therapeutic and Diagnostic Radionuclides for Nuclear Medicine“ by Ing. Ekaterina Kukleva

The thesis „Carriers of Therapeutic and Diagnostic Radionuclides for Nuclear Medicine“ submitted by Ing. Ekaterina Kukleva considers highly actual topic of radiolabeling nanoparticles for medicine. It is focused to synthesis, characterization and radiolabeling of hydroxyapatite nanoparticles (HAp) with several medically used radionuclides (^{99m}Tc, ^{223}Ra, ^{18}F, ^{68}Ga). The thesis is logically organized and highly consistent in content. It uses fully appropriate up to date methodology. Results from the thesis were published in 8 articles in peer-reviewed impacted scientific journals (of which 2 are first author papers of E. Kukleva), 4 patents and multiple functional samples and conference contributions, which is highly appretiable. I have only few minor objections to the thesis, which however do not devalve generally excellent level of the thesis:

1) The language quality is sometimes not perfect.
2) Page 14: It is not very suitable to call a PEGylated protein (Neulasta®) by a term „nanoparticle“.
3) In charts showing stability of radiolabeling in different environments (e.g., Fig. 17 on page 53), the y-axis should be better called „Stability“ than „Radiolabeling yield“.
4) Page 72: Perhaps the correlation of radionuclide decay half-life with radiolabeling kinetics is a random coincidence.

I have also few questions:

1) Page 10: Not only nanoparticles, but also low-molecular-weight vectors can target radionuclides. Will you provide some examples, please?
2) Generally, would you comment the biodegradability of HAp in the organism, please?
3) Page 13: Would you comment the influence of zeta potential of nanoparticles on their colloidal stability, biodistribution and biokompatibility, please?
4) Page 76, Tab. 10: How the time points were selected? As multiples of half-lifes of the corresponding radionuclides?
5) There was a mention of another uses of HAp as radionuclide binders. What do you think about the use of HAp as a ^{90}Sr binder (or Bi^{3+}-doped HAp as a ^{131}I binder) after nuclear accidents for oral, dermal or soil (in agriculture) immobilization of these radionuclides to prevent their uptake? Prussian blue is orally used to prevent bioavailability of ^{137}Cs in such cases in a similar way.

The thesis has very high quality fully achieving its aims and **I recommend it for defense** as a base of awarding the Ph.D. title to Ekaterina Kukleva with ranking A-excellent.

doc. Mgr. Martin Hrubý, Ph.D., DSc.