Abstract

Nuclear medicine and imaging are currently one of the most dynamically developing directions in medical sciences. The outcome is the strong development of research on new radiopharmaceuticals, which was the inspiration for the research presented in this dissertation.

The aim of this dissertation was to collect information on the current state of knowledge about the latest radiopharmaceuticals, to develop methods to obtain data on the physicochemical parameters and stability of biologically active 1,2,3,4-tetrahydroacridine derivatives that are carriers of non-radioactive isotopes of elements used in nuclear imaging, as well as streamlining the process of designing and obtaining new medicinal substances using chromatographic techniques, which in the future can be successfully applied in research on new radiopharmaceuticals.

The study results provided information on the physicochemical properties of 1,2,3,4-tetrahydroacridine iodine derivatives, which are "cold" radiopharmaceuticals. The developed derivatives contained in their structure the iodine element, which will be finally replaced by a radioactive isotope. The obtained data concerned log P and pKa values for 2-iodo-N-[4-(1,2,3,4-tetrahydroacridine-9-amino)butyl]benzamide, 3-iodo-N-[4-(1,2,3,4-tetrahydroacridine-9-amino)butyl] benzamide and 4-iodo-N-[4-(1,2,3,4-tetrahydroacridine-9-amino)butyl]benzamide, which allowed to assess the effect of iodine substituent placement in the aromatic ring on the crucial physicochemical properties of the compound in terms of pharmacokinetics. 3-iodo-N-[4-(1,2,3,4-tetrahydroacridine-9-amino)butyl]benzamide was also subjected to a chemical stability test. The samples were analyzed by HPLC using a fully validated method according to report Q2 issued by the International Council for Harmonization. The results of the research provided valuable information on the photolabile of the structure, and allowed for the development of the proper method of storage and transport of the tested analogues of this compound. One of the most important element in the development of new medicinal substances is their correct purification after the synthesis process. This process was optimized, the result of which was the development of a TLC optimization strategy for the separation of FLASH chromatography. This strategy allows for precise determination of the gradient separation conditions, which is aimed at eliminating the unfavorable effects of wet load technique and obtaining pure fractions of the tested compound within a specified retention time, regardless of the scale of the procedure. The developed strategy significantly improves and accelerates the purification process of biologically active substances, which is important in the purification process of radiopharmaceuticals, which, due to the specific half-life of radioactive isotopes, require fast, repeatable and efficient procedures.