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The Role of Chemistry in the Development of the Radiosynthesis Methods for Fluorine-18 Radiopharmaceuticals

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Fluorine-18 radiopharmaceuticals are drug molecules that contain the positron-emitting (β+) radioisotope [18F] F. As a favorable halogen atom in radiopharmaceutical chemistry, [18F] F is suitable for the development of many radiopharmaceuticals, intended for investigating tumors by positron emission tomography (PET).

The utilization of nucleophilic [18F]F−ions in the fluorine-18 radiopharmaceutical synthesis processhas many advantages over fluorine gas[18F]F2. The radiosynthesisis fully automated using a chemical synthesizer in a lead-shielded hot cell because of handling with radioisotopes. Therefore, during the radiosynthesis method development, sampling at different reaction steps to follow reaction progress can be a challenge. Finding a solution may demand the efforts of many research experiments wherefore operator radiation exposure increases, so applications of [19F]F− chemistry would be practical.

This study aimed to discuss [19F]F− chemistry practices in developing of radiosynthesis method and to adapt suitable reaction conditions with the most common radioisotope used in PET, short-lived fluorine-18 (t1/2 = 109.77 min). The experiments were carried out using the stable isotope, [19F]F−or radioisotope [18F]F−in an aqueous solution. Analysis of the reaction mixture at different steps of synthesis (before/after fluorination reaction, unhydrolyzed/hydrolyzed intermediate mixture, unpurified product mixture) as well as in the final purified product were performed. The samples were analyzed with HPLC method.

The radiosynthesis development was facilitated by using this experimental chemistry approach. Also, the results obtained can help overcome the challenges, which can impede the reactions or lead to unwanted chemical impurities during radiosynthesis.

Keywords: Radiopharmaceutical, ^{18}F-chemistry, radiosynthesis, developing, analysis