Purification System of ^{131}I-Metaiodobenzylguanidine

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1. Introduction

^{131}I-metaiodobenzylguanidine (mIBG) is used as a radiopharmaceutical for the diagnosis and therapy of neuroendocrine tumors, especially adrenal medullary tumors. A structural similarity between mIBG and neuroendocrine allows ^{131}I-mIBG to enter the cell of neuroendocrine tumors and get localized.

^{131}I-mIBG is mainly prepared by isotope exchange of cold mIBG ligand for clinical application. Among several exchange labeling methods, the in-situ copper(I) catalyzed reaction leads to the product with high radiolabeling yield and high specific activity. Radioiodination of mIBG proceeds by reduction of copper sulfate (converts Cu^{2+} to Cu^{+}) by ascorbic acid, followed by the formation of an organo-Cu complex. Radioactive iodine is inserted at the meta-position of the benzylguanidine precursor to react to break the covalent bond between copper and the phenyl ring to form the ^{131}I-mIBG. After the isotope exchange is completed, purification is required to remove the unlabeled iodide ions using an anion exchange resin.

In the purification process, unfortunately, I-131 emits high-energy beta radiation, which causes corrosion of the connection tubing and the radiation effects of electronic equipment, making it difficult to introduce automated equipment. Therefore, since the operator has to proceed manually, there is a problem that the operator is excessively exposed to radiation and thus the ^{131}I-mIBG production yield is limited.

Currently, ^{131}I-mIBG purification process has been performed by mixing the resin, Sephadex, with the reaction solution and then filtering it using membrane filter. This process not only requires a large amount of Sephadex, but also has a large amount of unextracted ^{131}I-mIBG. Thus, we used Sephadex filled in solid-phase extraction (SPE) tube to reduce the amount Sephadex and increase the recovery of unextracted ^{131}I-mIBG. Furthermore, our division has considered methods to reduce operator exposure to radiation. In this presentation, we have developed a semi-automatic device of ^{131}I-mIBG purification that is not affected by beta rays.

2. Methods and Results

2.1. Materials

All reagents and materials were of analytical grade. Polymer reversible SPE tubes were purchased in 0.5, 1 and 2 ml volumes. Each volume of SPE tube was filled with 50, 100 and 200 mg of Sephadex and conditioned with distilled water.

2.2. Pre-separation test in cold condition

In cold conditions, an experiment was performed to determine that the SPE tube containing Sephadex adsorbed iodide ion sufficiently and not mIBG. The iodine and the mIBG solutions were confirmed by passing each volume of SPE tube using a syringe. UV absorption spectra were used to identify iodide ion and mIBG containing aromatic compounds. As a result, it was confirmed that mIBG was not adsorbed by Sephadex and almost passed. In addition, it was shown that most of the iodide ions were adsorbed to 100 mg of Sephadex in 1 ml of SPE tube.

2.3. Purification test

To separate the ^{131}I-mIBG, the procedure was as shown below (Fig. 1). The separating product was confirmed by HPLC equipped with radioactivity detector. In this condition, 200 mg of Sephadex (2 ml of SPE tube) should be used to sufficiently separate ^{131}I-mIBG that can be satisfied as a radiopharmaceutical.

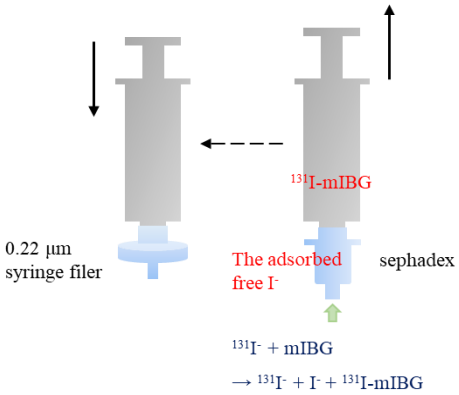

Fig. 1. Schematic representation of the purification concept of ^{131}I-mIBG using SPE tube.

The semi-automatic system of purification consists of stages, supporters for SPE tube and membrane filter, and a weight connected pulley, etc., as shown in Fig. 2. This device was developed to work with manipulators in hot cell.

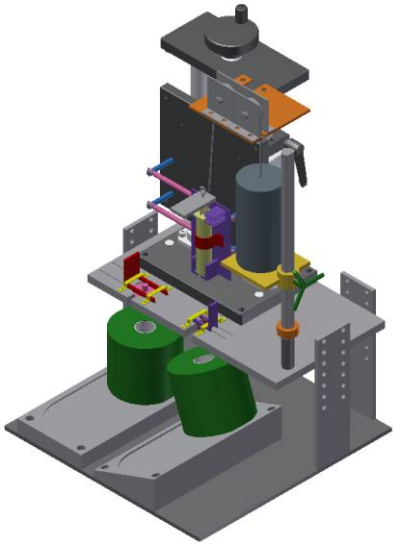

Fig. 2. Semi-automatic system for ^{131}I-mIBG purification not affected by beta rays.

3. Conclusion

This system was designed for semi-automated separation of ^{131}I-mIBG, which reduces operator exposure to radiation. In particular, it was confirmed that 200 mg of Sephadex can separated the unlabeled I-131 in an amount less than the amount of Sephadex used in the conventional method. As a result, purification by a semi-automatic system can increase production and significantly reduce the exposure of operator to radiation.

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