Radiopharmaceutical purity for nuclear medicine verified by thin layer chromatography

Mark Moskovitz, PhD
Gary Witman, MD

Radiopharmaceuticals are defined as pharmaceuticals incorporating one or more radioactive isotopes (i.e.radionuclides). The radiochemical purity of a radiopharmaceutical preparation represents that fraction of the radionuclide present in its stated chemical form. It is essential for technologists working in nuclear medicine to know precise drug purity in order to accurately determine the actual radiation dose being administered to a patient.

Radiopharmaceuticals in the hospital setting may be administered either orally or intravenously, and are useful for both diagnostic and therapeutic applications. Diagnostic studies include routinely performed clinical procedures such as bone scans, kidney scans, thyroid scans, PET scans, etc. In more than 90% of instances the radioactive compounds are utilized for diagnostic purposes. An example for the therapeutic use of a radiopharmaceutical would include the treatment of a hyperactive goiter of the thyroid gland by administering radioactive iodine. In this instance the radiation administered as properly dosed provides the desired therapeutic benefit.

A radiopharmaceutical contains at least two major components:

1. a radionuclide that produces the desired radiation characteristics
2. a chemical compound with structural or chemical properties that determines the in vivo distribution and physiological behavior of the radiopharmaceutical

Impurities may alter the biodistribution of radiopharmaceuticals, resulting in distorted scintigraphic images. As a consequence there may be either major diagnostic or therapeutic failures using the radiopharmaceutical agent. Adequate quality control should detect both radiochemical purities as well as the stability of the bound compound.

The purity of a radiopharmaceutical agent is essential for estimating the administered radiation dosage. Impurities may arise from radionuclide production, subsequent chemical procedures, incomplete preparative separation or chemical changes during storage. Radiochemical impurities in radiopharmaceuticals may result from decomposition and from improper preparative procedures. Radiation causes decomposition of water, a main ingredient of most radiopharmaceuticals. This leads to the production of reactive hydrogen atoms and hydroxyl radicals, hydrated electrons, hydrogen, hydrogen ions and hydrogen peroxide.

Radiopharmaceuticals are usually used in tracer quantities, and as such there is none of the dose response relationships associated with conventional drug administration.

In the hospital setting the radiochemical purity of radiopharmaceuticals is best determined by thin layer chromatography. Of the many procedures used in nuclear medicine for performing purity analysis planar chromatography is the preferred procedure. Radiopharmaceuticals have short half lives and speed is an essential element for quality control. Besides speed and convenience, the other major advantage of planar chromatography over column and elution methods is that the total amount of applied radioactivity remains on the chromatoplate (TLC plate). This enables quantification of various segments using a suitable collimated counter under standard conditions.

The common procedural characteristic for all forms of planar chromatography requires that the sample be applied to a stationary medium with an appropriate mobile phase. What is becoming commonplace is the use of instant TLC (ITLC), a process which increases the migration speed of the mobile phase.

Multiple studies published in the literature demonstrate that TLC chromatography is now the standard for the evaluation of radiopharmaceutical purity. With SPECT and PET scanning complimenting fast speed CT scan imaging in both the outpatient as well as hospital setting, the role of diagnostic radiopharmaceutical evaluation using TLC techniques will continue to take on a much more significant role in health care delivery.