

Radiochemical Purity of New Radiopharmaceuticals

Because of the carrier-free nature of the popular radionuclides, most radiopharmaceuticals cannot be studied by ultraviolet or infrared spectroscopy, nuclear magnetic resonance, or elemental analysis. Accordingly, chromatography has become the major analytic tool for determining the radiochemical purity of a radiopharmaceutical. However, the term "radiochemical purity" is much abused. The strict definition is the percentage of the radionuclide in question in the desired chemical form. The common mistake is to use a chromatographic system which can only separate one radiochemical impurity and then to report the radiochemical impurity on that basis. This is especially evident for ^{99m}Tc radiopharmaceuticals, which are often stated to be pure after analysis for pertechnetate. The cause of this misinterpretation is not clear: certainly pertechnetate is the obvious impurity in ^{99m}Tc radiopharmaceuticals, but as early as 1967 another impurity, variously called reduced unbound ^{99m}Tc or reduced hydrolyzed ^{99m}Tc , had been identified.

Because of the loose interpretation of "radiochemical purity," the conclusions of many articles have been difficult to interpret. Therefore, a set of guidelines are proposed to bring uniformity to the articles on new radiopharmaceuticals published in the *Journal*. To be reasonably sure that a radiopharmaceutical contains only the desired species, at least two chromatographic systems should be used, with either different solvents, different solid-phase supports, or both. The two systems used to assay for radiochemical impurity should show a single band of radioactivity and possess a partition coefficient such that the compound is neither freely eluted nor strongly adsorbed. Requiring this sort of information for each new radiopharmaceutical will provide a rational basis for judging the usefulness of the radiopharmaceutical. It is always judicious to note that radiochemical purity is not an absolute but is based rather on the known impurities. Still another radiochemical impurity might be detected in a radiopharmaceutical thought to be pure by using a more sophisticated separation technique, but two appropriate systems are usually sufficient. These guidelines will only apply to the radiopharmaceutical *in vitro*, although pertinent *in vivo* data on radiochemical purity are certainly needed for a full explanation of the mechanism of action and will be strongly encouraged.

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