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Editorial

Crucial Role of Radio-Chromatography in Clinical Chemistry of Nuclear Medicine and Radiopharmaceutical Research

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Editorial

During the last centuries, world has been facing with various fatal diseases such as cancer and neurodegenerative diseases. Despite of the technology developing in crescendo, these diseases have adverse effects with a wide audience. Due to this unfavorable situation, there are a many attempt to prevent, diagnose and treat in early stage of disease. Molecular imaging utilizing radiopharmaceuticals or radiotherapy are frequently employed techniques for diagnosis or therapy of cancer, neurodegenerative diseases etc. In addition to clinical applications, great numbers of scientists have been focusing on investigation of novel targeted radiopharmaceuticals.

Chromatography comes first among the most applicable methods for the purification, separation and identification of organic compounds [1]. Thin Layer Chromatography (TLC) and High Performance Liquid Chromatography (HPLC) are the most essential and widely utilized chromatographic and analytical methods for several objectives within the clinical applications, pharmaceutical research and development laboratory [1–10]. Besides, radio-chromatography is the most often utilized method to determine the purity and identity of radioactive materials [2,11]. Recently, Thin Layer Radio-Chromatography (TLRC) and High Performance Liquid Radio-Chromatography (HPLRC) methods have been the common trend in the clinical chemistry of nuclear medicine, radiopharmaceutical research and development laboratory.

Furthermore, paper electrophoresis is another type of radio-chromatography methods which is particularly used in pharmaceutical research and development laboratory. This method is utilized in wide range to determine the charge of radio labeled compounds or kits [11]. One of the important parameters of radio labeled compounds or kits is charge. Permeability of complex within the membranes depends on the charge of a compound. Brain Blood Barrier (BBB) has a critical role for brain cancer and neurodegenerative diseases. Promising agents or brain kits have to cross the BBB. The ability to cross the BBB is determined by charge. Charge is obtained by utilizing paper electrophoresis. Uncharged structures have ability to cross the BBB [10,12].

In nuclear medicine, various commercial kits are carried out to diagnose or therapy. These kits are radio labeled with radioisotopes such as Technetium-99m (^{99m}Tc) or Iodine-131 (^{131}I). Then, these radio labeled kits (radiopharmaceuticals) are administered to patients. However, it is mandatory to make quality control of the radio labeled kits prior to administration of radiopharmaceuticals to patients. The radiochemical purity of the final product should be minimum 95 %, otherwise it is not allowed to administration. To fulfill quality expectations, radio-chromatographic techniques such as TLRC, HPLRC and paper electrophoresis are most widely utilized for estimation of the radiochemical purity of the final product. Similar situation is valid for radiopharmaceutical research and development laboratory.

Thin Layer Radio-Chromatography is a cheap, fast solid-liquid adsorption chromatography method. It is used for identifying compounds and determining their purity. This method was used for testing radiopharmaceuticals since 1967 [11]. In this method, TLC scanner equipped with a radioactivity detector (for example; Bioscan AR2000) is utilized to determine the relative front (R_f) values of radioactive compounds. In the absence of TLC scanner equipped with a radioactivity detector, TLC plates should be covered by a cello-band after its development in solvent and cut into 0.5 cm widths. Then, the slices should be counted with a radioactivity detector (such as Cd (Te), Na (I) detector) and TLRC chromatograms should be obtained by plotting counts versus distance. TLRC is the most used, practical and cheapest method utilized in clinical chemistry of nuclear medicine. Unfortunately, resolution and sensitivity of this method are lower than HPLRC method. Additionally, there are situations that R_f value of radio labeled compound is closely with R_f values of other radiochemical impurities. In those cases, HPLRC is preferred. During the radiopharmaceutical research and development laboratories, various combinations of TLC plate type and mobile phase mixtures are tested.

HPLC system is called as High Performance Liquid Radio-Chromatography (HPLRC) such cases in which detection is performed utilizing radioactivity detectors such as Cd (Te), Na (I) detector. HPLC and HPLRC have gained its popularity mainly due to its reliability (use of pressure driven liquid support) and versatility (possibility of adjusting the composition of both mobile and stationary phases) [13,14].The chromatographic mode or separation mechanism depends on the overall interactive interactions between the stationary phase, the mobile phase and the analytes.

In radiopharmaceutical research and development laboratories it is important to investigate specific targeted agents and to radiolabel agents in high yields with appropriate radioisotope. Radio labeled agents should be contained impurities like unlabeled radioisotope

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used for radio labeling, with degradation products formed during oxidation or reduction of radioisotope and secondary complexes which should be formed during radio labeling reaction. Thus the estimation of impurities in the radio labeled compounds is important. Besides, the methods used to determine the identity of the radio labeled agent would give valuable information about the purity and radio labeling yield of the radioactive product. Radio labeling yield of agent should be minimum % 95 to continue the pre-clinical investigation with that agent. During the research experiments, radio labeling reaction parameters would be optimized. Mainly, all of these optimization studies and quality control studies are carried out by utilizing TLRC, HPLRC and paper electrophoresis methods. Similarly, the radiochemical purity of the radio labeled agent is generally measured by radio-chromatographic methods such as TLRC or HPLRC. These radio-chromatographic methods have been used in laboratories worldwide over the past 40 years for radiopharmaceutical sciences [2,11].

HPLRC is the most commonly used method for estimating radiochemical impurities. HPLRC method is practical and ideal technique for determination of impurities in radio labeled compounds, whereas TLRC method is cheaper and easier. After all, HPLRC method is more sensitive with higher resolution. Similarly, HPLC is one of the most popular and mature analytical methods and by far the most widely used separation method; however, HPLRC is less commonly used in clinical chemistry of nuclear medicine than TLRC. On the other hand, HPLRC method is one of the most widely used methods for quality control in radiopharmaceutical research and development laboratories.

HPLRC is a very sensitive system for separation of a sample's components based on different physic-chemical characteristics. The components are separated from the chromatographic columns by elution at different retention times. A variety of columns, as well as by the choice of an appropriate solvent system is utilized for the separation. In HPLRC method, analysis is made by comparison of Ultraviolet (UV) or Diode Array Detector (DAD) and radioactivity detector (such as Cd (Te) and NaI) signals. Occasionally, the analyzed compounds should be identical to each other. In those cases, combinations of solvents with different polarities and of gradient elution are applied.

There are several studies in the literature about determining the radiochemical purity utilizing TLRC and HPLRC methods [1–10]. Many of the procedures have employed TLRC in combination with HLPRC. Additionally, there are a great amount of studies which paper electrophoresis is preferred to determine charge of radio labeled compounds [9,15–17]. A large number of radio-chromatographic method procedures have been flourishing gradually year by year in the scientific literature. It's important to determine radiochemical purity easily. Thus radio-chromatographic methods in particular; paper electrophoresis, TLRC and HPLRC have a crucial role in the survey of radio labeled agents' investigation.

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