Evaluation of the Lyophilized MIBI Kit Fraction for ^{99m}Tc Labeling: A Cost-Effective Approach for Labeling Cold Kits in Nuclear Medicine Practice

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ABSTRACT

^{99m}-Technetium methoxy isobutyl isonitrile (MIBI) is one of the most commonly utilized radiopharmaceuticals for Myocardial Perfusion Imaging (MPI) and parathyroid scan. Typically MIBI kits contain substantial amounts of reagents suitable for labeling multiple doses of radiopharmaceuticals. The conventional practice of preparing only 1-2 doses from a single vial often results in significant wastage of the kit's contents. To mitigate this inefficiency, we explored the feasibility of fractionating cold kits. The MIBI kits underwent a systematic fractionation process, with precise ratios of 1:2 and 1:4. Total eight samples of each ratio were analyzed. The average percentage RCP for eight samples with a 1:2 ratio was determined to be approximately 93.87%, while for eight samples with a 1:4 ratio, it was found to be around 89.045%, as assessed using the TLC method. Normal biodistribution patterns were observed in imaging conducted with various samples of 1:2 ratio fractions. However, there were two reported cases of failure in biodistribution for a fraction with 1:4 ratio. Using this standardized technique for the fractionation of cold kits proves to be a cost-effective approach, minimizing the wastage of chemical components in cold kits.

Keywords: 99mTc-MIBI, Myocardial Perfusion Imaging, Cold kit fractionation, Radiochemical Purity, Biodistribution.

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INTRODUCTION

The radiopharmaceutical ^{99m}Tc-methoxy isobutyl isonitrile is a widely recognized cationic and hydrophobic compound utilized in myocardial perfusion imaging for routine diagnostic procedures or acute myocardial infarction diagnosis (1). It is also actively used for imaging parathyroid gland (2). According to the manufacturing guidelines, labeling can be performed by reconstitution of the cold kit with 2–5 ml of ^{99m}TcO4-, eluted from a ^{99m}Tc generator with a maximum TcO4-activity of 1000 mCi. For myocardial perfusion imaging (MPI), the typical administered dose of ^{99m}Tc (MIBI) [6] + can range from around 8 to 30 millicuries (mCi) (3), whereas for parathyroid imaging, the dose is generally in the range of 20 to 30 mCi (4).

In developing countries, it is a common practice to conduct organ scans or similar studies in a day, contingent on the number of patients and the available ^{99m}Tc activity. However, situations may arise where an unscheduled study for an emergency patient is needed. A lyophilized kit, specifically designed for multiple patients may need to be used for a single study. Occasionally, there may be a scarcity of cold kits in inventory due to unprecedented delay by the supplier. Therefore, ensuring both convenience and cost-effectiveness in the use of radiolabeling is crucial to the daily operations of nuclear medicine institutions. As a result, there should be a potential strategy of reconstituting a lyophilized kit in saline, dividing it into fractions, storing them at low temperatures, and labeling them when needed (5). To mitigate this inefficiency, we explored the feasibility of fractionating cold kits. In this study, we made a fraction of the MIBI kit using two possible dilution methods. The percentage (%) of radiochemical purity and quality of images of all the samples were analyzed.

MATERIALS AND METHODS

Materials: Free Technetium pertechnetate (TcO4-) was eluted from the ^{99m}Tc generator supplied from Radioisotope Production Division (RIPD) of Bangladesh Atomic Energy Commission (BAEC). MIBI Cold kit, used for the fraction, was imported and manufactured by Eczacibasi, Monrol. The labeling of ^{99m}Tc-MIBI was performed according to the standard procedure provided by the manufacturer.

Preparation of fractionated ^{99m}Tc-MIBI: The MIBI kits underwent a systematic fractionation process, with precise ratios of 1:2 and 1:4. This standardized procedure involved the addition of 2 and 4 ml of normal saline (0.91% NaCl) into individual cold kit vials. After the addition of saline, each vial underwent a further division into fractions, specifically into 2 and 4 equal parts, each containing 1 mL of the mixture. These fractions were transferred into separate vacuum vials. To facilitate organization and identification, labels were affixed to each of these vials. The fractions, after precise preparation, were promptly stored in a freezer. The duration of the fractionation process was carefully recorded for documentation.

When a specific fraction was scheduled for use, the vial was thawed to room temperature on the designated day. To initiate the radiopharmaceutical formulation process, freshly eluted ^{99m}Tc pertechnetate was introduced with a minimal volume into the vial containing the fraction. Thorough mixing ensued. The quantities of ^{99m}Tc pertechnetate added varied according to the type of vial fraction. A maximum of 500 mCi was added to each vial for 1:2 fractions and 250 mCi was added to each vial for 1:4 fractions. This controlled addition ensured precise dosages and consistency in the radiopharmaceutical preparations. After mixing, the fraction was kept in hot water bath for 10 minutes. After 10 minutes, the vials were pulled out from the water bath and then kept it at room temperature to cool down.

Radiochemical Purity:

The radiochemical purity test was performed by Instant Thin Layer Chromatography (ITLC) and solvent extraction technique. To Determine percentage (%) of Radiochemical Purity (RCP)

thin layer chromatography was preformed using ITLC-SG as stationary phase and solvent mixture of Chloroform (CHCl3) and Methanol (MeOH) in ratio of 9:1 (CHCL3: MeOH), as mobile phase. A small drop of sample was placed in the strip then dried and placed in the TLC chamber. Subsequently, the dried strip was scanned using a TLC scanner (Elysia Raytest miniGita TLC scanner). Radiochemical purity was calculated based on the results obtained from the TLC scan.

Solvent Extraction Method: A small quantity of ^{99m}Tc-MIBI was added to a tube containing a mixture of water and chloroform in a 1:1 ratio. The tube was then subjected to vortexing for 1 minute and left to stand for phase separation. Subsequently, the upper phase was transferred into a separate tube. The activity in each phase was measured using a dose calibrator. The percentage bound was determined by dividing the activity in the organic phase by the total activity in both phases.

RESULT

Eight samples of each fractionated MIBI at ratios of 1:2 and 1:4 were analyzed. The average radiochemical purity, indicating labeling efficiency, was determined as approximately as ~ 93.87% for 8 samples of 1:2 ratio and 89.045 % for 8 samples of 1:4 ratio respectively (Figure I, 2) respectively. The mean of % of RCP for 1:2 fractionated samples was approximately 97.028 & that of 1:4 fractionated samples was found 95.09 (Figure 3) as assed by solvent extraction method. Bio distribution of the radiopharmaceutical during imaging was deemed appropriate across all samples based on (Figure 4,5).

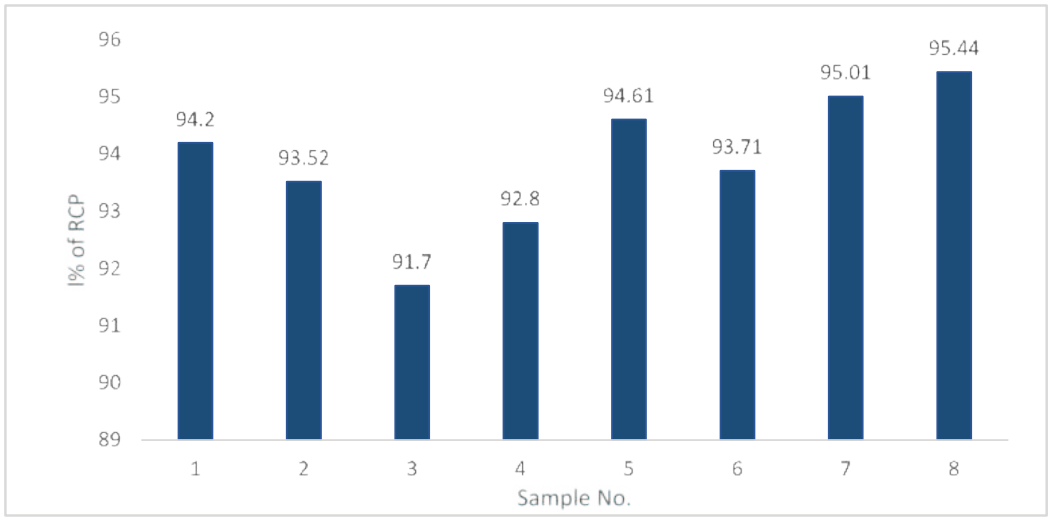

Figure 1: Radiochemical purity of 1:2 ratio samples of MIBI

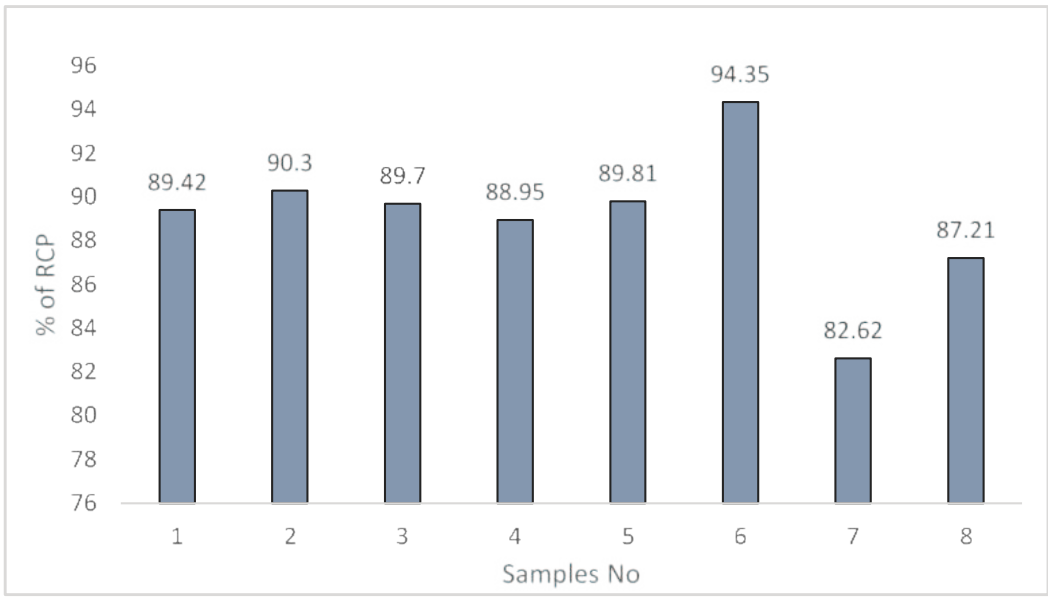

Figure 2: Radiochemical purity of 1:4 ratio samples of MIBI

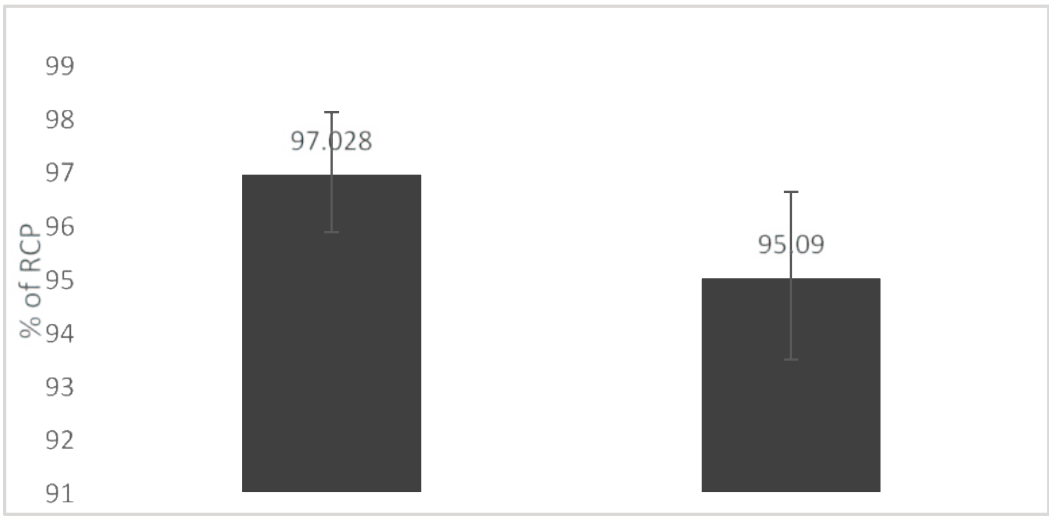

Figure 3: Radiochemical purity by solvent extraction method

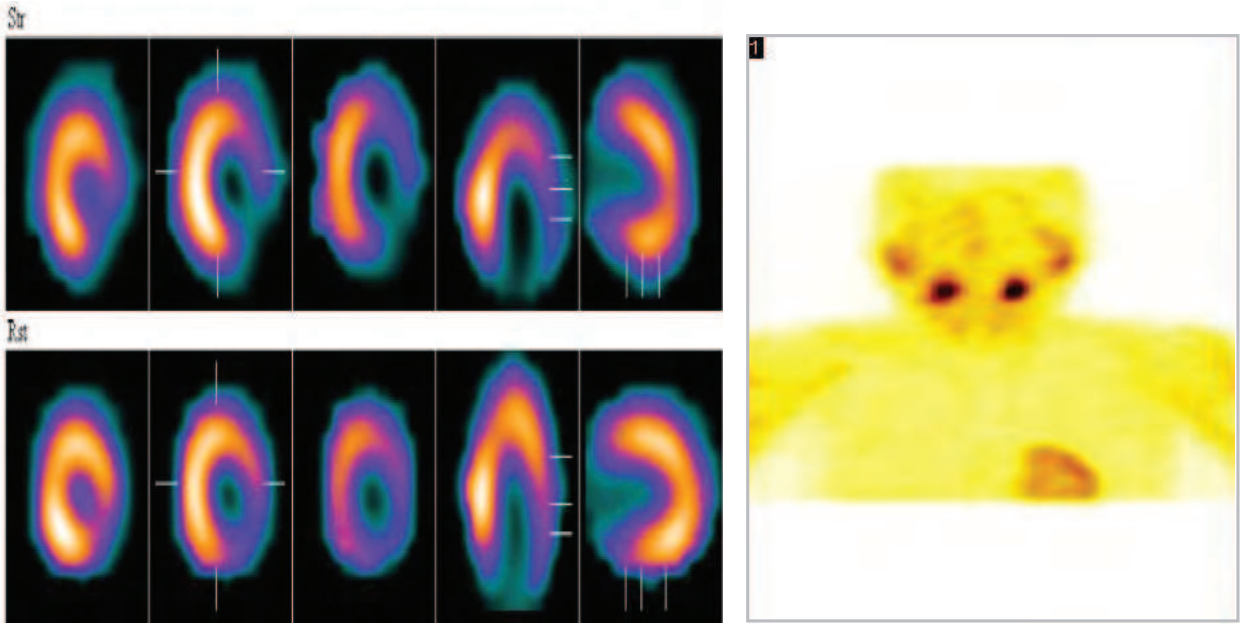

Figure 4: ^{99m}Tc-sestaMIBI scan of a) Myocardial Perfusion Imaging and b) Parathyroid Imaging with a fractionated sample of 1:2 ratio

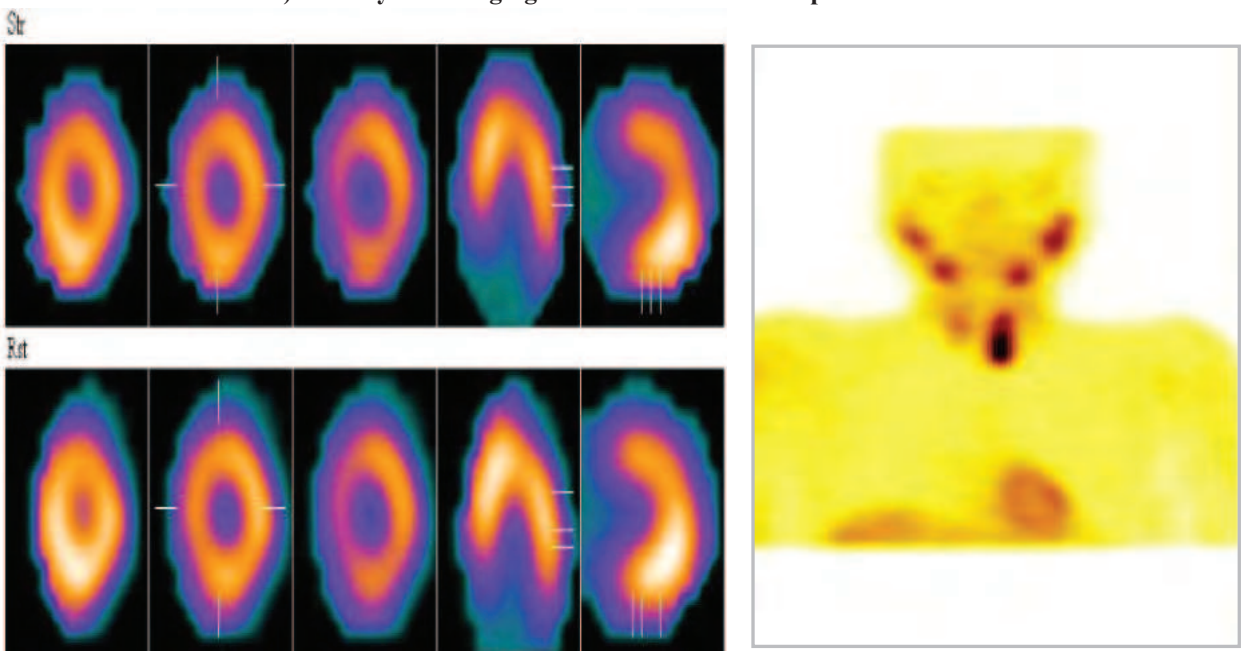

Figure 5: ^{99m}Tc-sestaMIBI scan of a) Myocardial Perfusion Imaging and b) Parathyroid Imaging with a fractionated sample of 1:4 ratio

DISCUSSION

Several facilities adopt fractionation techniques, particularly for costly kits, although there is limited literature on this subject (6, 7). Few studies show different approaches of MIBI kit fractionation. In those studies researchers have investigated variations in the radiolabeling conditions, such as temperature, pH, and reaction time or addition of antioxidant agent during storage of fractionated MIBI kits to enhance the efficiency and stability of ^{99m}Tc-MIBI complexes (8, 9). This study aimed to investigate the impact of fractionating a lyophilized MIBI kit on the radiochemical purity and biodistribution of the resulting labeled preparation. Two different aliquots of MIBI kits were prepared in this study. The mean value of the radiochemical

purity of the fractions was calculated as ~ 93.87% for 8 samples of a 1:2 ratio and 89.045% for 8 samples of a 1:4 ratio by the TLC method, respectively. The mean of the RCP for 1:2 samples was approximately 97.028 and 95.09 for 1:4 samples, as assessed by the solvent extraction method.

The biodistribution of these fractions was found normal during imaging with different samples except two cases from samples of 1:4 ratio. The potential reasons for the observed failures might be due to the introduction of an excessive amount of ^{99m}TcO4- activity, increased saline volume, and the assimilation of oxygen during storage. So, care should be taken during the fractionation and radiolabeling procedures.

All the fractions were utilized within a span of 7 days, storing them in a freezer. The average time taken for the fractionation procedure was 5 minutes. Overall, the process of preparing the aliquot and reconstituting the radiopharmaceutical dose with the fraction did not present any time-related issues, such as additional decay of the radiopharmaceutical, injection delays, or extra loss of gamma camera acquisition time.

CONCLUSION

Employing this standardized technique for the fractionation of cold kits proves to be a cost-effective approach, minimizing the wastage of chemical components in cold kits. Our practical experience indicates that this process yields clinically useful labeling efficiency for the studied radiopharmaceuticals. The time required for aliquot preparation and reconstitution, even with quality control procedures, is manageable within routine practice.

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