EFFECT OF MILKING EFFICIENCY ON ^{99}Tc CONTENT OF ^{99m}Tc DERIVED FROM ^{99m}Tc - GENERATORS

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INTRODUCTION

Technetium-99m has found widespread use in nuclear medicine because of its physical properties and the readiness with which it can form chelates. ^{99m}Tc obtained by separation from its parent ^{99}Mo always contains ^{99}Tc produced by decay of ^{99m}Tc and also by decay of ^{99}Mo. The presence of ^{99}Tc in ^{99m}Tc - pertechnetate has usually been ignored since the ^{99}Tc calculated to be present was thought to lead to an insignificant increase in radiation dose and to be present at a molar concentration far below that of the reducing agents and chelating agents present.

However, increased levels of ^{99}Tc have been shown to have an adverse effect on some radiopharmaceutical preparations. Smith[1,2] found that the presence of 25 ng ^{99}Tc would lead to reduced labelling with his blood cell labelling technique, whereas Srivastava[3] and Porter[4] found the presence of 100 ng and 500 ng ^{99}Tc respectively would produce reduced labelling efficiency with a ^{99m}Tc-lung kit and a ^{99m}Tc-HSA preparation.

The $^{99}Tc/^{99m}Tc$ ratio of ^{99m}Tc-sodium pertechnetate at milking depends chiefly on the time between milkings of a ^{99m}Tc generator but can be influenced by the milking efficiency of the generator. Lamson et al.[5] calculated the specific activity of ^{99m}Tc milked from a generator but ignored the effect of generator milking efficiency. In their calculations, Husak and Vlcek[6] considered the effect of milking efficiency but assumed that ^{99}Tc and ^{99m}Tc present were extracted with equal efficiency. The validity of this assumption may be questioned. The other factor which effects the $^{99}Tc/^{99m}Tc$ ratio is the time between milking of the generator and the time at which the ^{99m}Tc-pertechnetate is used to prepare a ^{99m}Tc-radiopharmaceutical. This is particularly significant in the use of "instant pertechnetate" where users obtain bulk ^{99m}Tc-pertechnetate from a central supplier. These suppliers normally use either a methyl ethyl ketone (MEK) extraction process or a sublimation process to separate the ^{99m}Tc from parent ^{99}Mo. The time of separation may be of the order of 24 hours before use leading to an increase in the $^{99}Tc/^{99m}Tc$ ratio by a factor of more than 16 to that obtained at milking.

Several reports have been made of measurements of the ^{99}Tc content of $^{99m}TcO_4^-$ in generator eluates. Srivastava[3] determined ^{99}Tc levels by liquid scintillation counting of decayed $^{99m}TcO_4^-$ samples, while Mattson[7] prepared a thin solid source and determined the ^{99}Tc level by beta counting the decayed source with and without a 4.2 mm perspex absorber between the source and detector. Both methods are subject to error due to long lived beta emitting impurities present in the original $^{99m}TcO_4^-$, particularly in the case of $^{99m}TcO_4^-$ produced from fission produced ^{99}Mo. Zodda et al.[8] recently described a HPLC method for the determination of ^{99}Tc in $^{99m}TcO_4^-$. $^{99}TcO_4^-$ was separated by isocratic elution of an amino bonded phase column with acetate buffer and subsequent u.v. detection of $^{99}TcO_4^-$. This method is not subject to the interferences above although the sensitivity of detection is not as high.

In the present study[9] a HPLC method has been developed to measure the $^{99}TcO_4^-$ content of sodium pertechnetate (^{99m}Tc) from generators with a detection limit of 0.9 ng ^{99}Tc for a 500 µl aliquot of $^{99m}TcO_4^-$. Using this method the ^{99}Tc content of a number of $^{99m}TcO_4^-$ samples was measured and compared to that calculated for the milking efficiency of the generator used.

RESULTS AND DISCUSSION

First eluates of 10 chromatographic generators gave $^{99}Tc/^{99m}Tc$ ratios ranging from 3.5 - 46 ng Tc/mCi ^{99m}Tc measured at the time of milking. In all cases the initial $^{99}Tc/^{99m}Tc$ ratio was of the order of that expected for the time that had elapsed between generator production and first milking of the generator. The $^{99}Tc/^{99m}Tc$ ratio of the first generator eluate was higher with imported generators reflecting the longer elapsed time between production and first use of the generator. The value of 46 ng ^{99}Tc/mCi ^{99m}Tc was obtained for a generator that had suffered shipping delays in transit.

The mean value of the ^{99}Tc content of 36 "instant pertechnetate" samples received during 1981 was 13.6 ng ^{99}Tc/mCi ^{99m}Tc at calibration time (standard deviation 9.8). These samples were produced using a MEK extraction process. The range in ^{99}Tc content measured was 3.4 - 51 ng ^{99}Tc/mCi ^{99m}Tc and is similar to that reported by Srivastava[3] for U.S.A. producers but is less than that reported by Mattsson[7] (2.9 - 290 ng ^{99}Tc/mCi ^{99m}Tc). As the samples measured in this study were prepared approximately 12-18 hours before calibration time, the values reported correspond to a

^{99}Tc content ranging from 0.4 - 6.5 ng ^{99}Tc/mCi ^{99m}Tc at milking. Calculation of the effect of milking efficiency on $^{99}Tc/^{99m}Tc$ ratio[9] shows that the higher values observed could be explained by the incomplete milking of the generator at times when generator capacity exceeded demand.

The above measurements indicate that $^{99}Tc/^{99m}Tc$ ratios high enough to cause adverse labelling effects could be found in "instant pertechnetate" and in the first eluate from ^{99m}Tc-generators for the activities normally used in radiopharmaceutical production.

Results[9] also demonstrate the need for producers of "instant pertechnetate" and users of MEK systems to milk generators fully each day to minimise build-up of ^{99}Tc in the system. If this precaution is taken, it should be possible to maintain ^{99}Tc levels below 10 ng/mCi ^{99m}Tc for $^{99m}TcO_4^-$ prepared 18-24 hours before calibration.

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