

Development and Evaluation of a Single vial Cold Kit for Infection Imaging: Tc-99m Ciprofloxacin

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Abstract

Radiolabeled antibiotics have been used in nuclear medicine for the diagnosis of bacterial infection. They are used as specific infection-imaging agents because of their affinity to bind with bacteria. Tc-99m Ciprofloxacin is the most widely used infection-imaging agent. The aim of the present work is to increase the shelf life of an in house developed single vial kit for the preparation of Tc-99m Ciprofloxacin. Different methods were used to make the Ciprofloxacin kits. Kits were stored at a temperature of 4°C under nitrogen atmosphere and evaluated for stability by serially estimating the labeling efficiency using instant thin layer chromatography (ITLC) following reconstitution with Tc-99m pertechnetate at regular intervals of time up to 90 days after their preparation. The data were subjected to Sigmaplot software version 8.0 for shelf-life analysis. The kits were further evaluated for a number of standard quality control parameters. Kits containing sodium chloride-Ciprofloxacin pellets were found to have a shelf life of 7 months and constantly maintaining a labeling efficiency of 95% Tc-99m Ciprofloxacin. Biodistribution studies in balb/c mice showed significant levels in kidney, liver and intestine. Blood clearance studies showed a slow and biphasic clearance in rabbits. Gamma camera imaging of the rabbits bearing S.aureus infectious lesion confirmed the utility and specificity of the reconstituted kit in imaging infection. The final kit, which was recommended for clinical use was found to be stable for nine months with all its characteristics remaining unchanged from those of the freshly prepared Tc-99m Ciprofloxacin during the entire period of observation.

Keywords: Tc-99m Ciprofloxacin, Single vial kit, Excipients, Bacterial Infection, Radionuclide imaging

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Introduction

Diagnostic nuclear medicine involves in vivo administration of radiopharmaceuticals targeted to a particular organ, organ system or disease process. The radiopharmaceutical consists of tracer quantity of a drug or pharmaceutical agent bound chemically to a radionuclide. Tc-99m is one of the most commonly used radioisotopes in clinical imaging and has been extensively used in research for the development of new radiopharmaceuticals for imaging. It exists in eight oxidation states, namely, -1 to +7. It is generally supplied as Tc-99mO₄ (pertechnetate ion), in which it has +7 oxidation state. Tc-99m is chemically reactive at +4 and +5 oxidation states. Different reducing agents like stannous tartarate, stannous chloride, sodium borohydride, ferrous sulfate and dithionite are used to produce chemically reactive state of Tc-99m that results in radiolabeling of the ligand (1).

Developing appropriate radiopharmaceuticals for detection of occult infection at an early stage is one of the major challenges of current day research in the field of diagnostic imaging. Most of the existing radiopharmaceuticals are either nonspecific (e.g. radiolabeled white blood cells, Ga-67 citrate, human immunoglobulins etc) (2), or suffer from low sensitivity or are prohibitively expensive (e.g., radiolabeled monoclonal antibodies) (3). A few agents like radiolabeled dextran (4,5), citrate (6), hydroxy ethyl starch and peptides have also been introduced recently, but they also suffer from the above-cited problems. Thus, there is a need to develop safe, sensitive and cost-effective radiopharmaceuticals for specific bacterial infection imaging. The issue has gained global importance because of a growing geriatric and immuno-compromised population that are extremely vulnerable to infection, resurgence of resistant tuberculosis in the western world and continuing primacy of infective disorders in the tropical and developing countries.

Antibiotics have been labeled and used for imaging infectious lesions. Ciprofloxacin is a first generation fluoroquinolone antibiotic which is active against both gram-positive and gram-negative bacteria. It inhibits the "A" sub-unit of the DNA gyrase enzyme and thus interferes with the strand cutting and resealing function during DNA replication (7,8). Solanki et al labeled Ciprofloxacin with Tc-99m in 1993, supplied under the name of Infecton (9).

Initially they used formamidine sulphonic acid as the reducing agent that had to be boiled before use (10), an unwanted but necessary prerequisite. Later, the preparation was modified by using stannous tartarate reduction method that did not require boiling, but the pH of injectable radiopharmaceutical was quite low at 4 (11,12). Both these methods used two-vial kits for final preparation, whereas most of the clinically used radiopharmaceuticals in nuclear medicine imaging are single-vial kits. Besides, significant amount of colloid formation upon reconstitution with Tc-99mO₄ has also been reported with this kit (13).

It has been hypothesized that the unwanted colloid formation could be due to excess amount of reducing agent in the kit. After acquiring sufficient clinical experience with Infecton (14), we developed a single-vial kit for the preparation of Tc-99m Ciprofloxacin having high labeling efficiency, but with minimal colloid content (15). The kits contained lyophilized stannous tartarate and Ciprofloxacin. But they were not stable enough to produce acceptable labeling efficiency, as the percentage of the free Tc-99m started to rise within one week of preparation. The predicted cause of low shelf life was inefficiency of the reducing agent. Different approaches were subsequently tried, using physiologically acceptable excipients like sodium chloride, potassium chloride etc., to protect the interaction of Ciprofloxacin with stannous ions. Pellets of NaCl and KCl containing Ciprofloxacin were introduced to impart a physical barrier between Ciprofloxacin and stannous ions. This paper describes our efforts to increase the shelf life and the stability of the radiopharmaceutical after reconstitution to make it more useful for clinical use.

Materials and Method

Ciprofloxacin Hydrochloride, Torrent Labs (P) Ltd, Ahmedabad, was used for the study. Stannous tartarate, potassium chloride and sodium chloride of Sigma Chemicals, USA, and acetone, ammonia and ethanol of Qualigen, Mumbai, were used. ITLC-SG strips of Gelman Sciences, USA were used. Other chemical reagents of analytical grade were purchased from the local suppliers.

Labeling efficiency of sodium chloride, glucose and potassium chloride was studied using stannous tartarate, similar to the protocol developed by Singh et al (15) for the radiolabeling of the Ciprofloxacin. Approximately 70 MBq of Tc-99m pertechnetate was added to 1 ml solution (4 mg/ml) of excipient containing 400µg of stannous tartarate. After an incubation period of 30 min, the percentage of the labeled excipient was estimated by instant thin layer chromatography (ITLC).

Different concentrations of stannous tartarate, i.e., 400 to 800µg were lyophilized in neutral glass vials. 70 MBq of sodium pertechnetate and 1ml of Ciprofloxacin solution (2 mg/ml) were added. The percentage of the radiolabeled Ciprofloxacin, reduced/hydrolyzed (R/H) and free pertechnetate were estimated by ITLC. Stannous tartarate

concentration of 600µgm was found to give the best labeling efficiency.

Subsequently three different types of Kits, each containing 600µgm of lyophilized stannous tartarate and varying concentrations of Ciprofloxacin and excipients were prepared under aseptic conditions as follows: Kit-A: containing 600µgm lyophilized stannous tartarate and 2 mg lyophilized Ciprofloxacin; Kit-B: containing 600µgm lyophilized stannous tartarate, 8 mg pellet of NaCl and Ciprofloxacin in a ratio of 3:1 and Kit-C: containing 600 µgm lyophilized stannous tartarate, 4 mg pellet of KCl and Ciprofloxacin in a ratio of 1:1. The kits were prepared in triplicate and stored at 4°C. The labeling efficiency of the Ciprofloxacin with Tc-99m in each kit was checked at different time intervals up to 90 days (0, 1, 3, 6, 10, 15, 20, 30, 45, 60, 75, and 90). The kits were reconstituted with 70 MBq of sodium pertechnetate and the percentage of the radiolabeled drug was determined by ITLC. The data obtained was subjected to Sigmaplot software version 8.0 for shelf life analysis accepting 90% of Tc-99m Ciprofloxacin as optimum labeling efficiency. The kit, which was found to have the maximum shelf life results, was further standardized by comparing its in vitro and in vivo quality control parameters with established radiopharmaceuticals (15).

The kits were reconstituted by adding sodium pertechnetate solution. Radiochemical purity of the kits was ascertained by instant thin layer chromatography (ITLC). Silica Gel (SG) impregnated fiber glass strips were used as stationary and acetone as mobile phase. In this solvent system free Tc-99m moved with solvent front leaving labeled and R/H Tc-99m at the point of application. Reduced/hydrolyzed Tc-99m was separated by using human serum albumin coated SG strips as stationary phase, and solvent mixture ethanol: ammonia: water: : 2:1:5, as mobile phase (1). In this system free Tc-99m and labeled compound moved with the solvent front whereas R/H Tc-99m remained at the point of application.

In vitro stability of the radiolabelled products was also carried out. The reconstituted kit preparation was incubated in rabbit serum. A spot of 2µl of the preparation was placed on a 1 cm wide and 10 cm long silica gel strip previously incubated at a temperature of 110°C for 30 min. The chromatogram was run in the mobile phase as mentioned before up to 8 cm. After that the strip was dried and divided into several 1 cm sections. The counts in each centimeter were measured in polystyrene test tubes by well type gamma ray spectrometer (Electronics Corporation India Limited, ECIL). In vitro stability of Tc-99m Ciprofloxacin was studied by estimating radiochemical purity for 24 hrs at room temperature.

In vivo quality control procedures were carried out. This was done following intravenous administration of reconstituted Tc-99m Ciprofloxacin (37 MBq/Kg of body weight) through the dorsal vein of New Zealand White Rabbit weighing about 2.5 kgs. Blood samples were

withdrawn at various time intervals up to 24 hrs. Radioactivity was measured in blood samples using a well-type counter attached to a gamma ray spectrometer (Electronics Corporation India Limited, ECIL) and the results were expressed as percent administered dose in whole body blood that was considered to be 7% of the body weight.

Bio-distribution of reconstituted kit preparation was studied in balb/c mice after intravenous injection of 3.7 MBq of the radio tracer through the tail vein. The animals were sacrificed (by cervical dislocation) at 1, 4 and 24 h post injection. Different organs were removed in quick succession, washed in saline, dried on filter paper and then weighed. The radioactivity in the organs was counted using well-type gamma ray spectrometer (Electronics Corporation India Limited, ECIL). The results were expressed as percent administered dose per gram of tissue.

Sterile inflammatory lesions were developed by injecting 100 μ l of autoclaved turpentine oil in the thigh muscle of three healthy New Zealand White rabbits each weighing about 2 kg. Infectious lesions were also developed on the contra-lateral thighs of the same rabbits by giving intramuscular injection of 10⁷ live *S. aureus* bacteria in growing phase in a volume of 100 μ l. Swelling, redness and hyperthermia were evident in sterile as well as infectious inflammatory lesions after 48 hrs. The aspiration cytology of the lesions revealed presence of inflammatory cells in sterile lesion and live *S.aureus* in infectious lesion, thereby confirming the pathologies.

Scintigraphy in animal models was performed following intravenous administration of radiotracer (37 MBq/Kg body weight) in the ear vein of New Zealand White rabbits. Imaging was performed at different time intervals post-administration till 24 hrs. The rabbits were sedated with intravenous diazepam, 0.75 ml/kg body weight (Calmpose , Ranbaxy Laboratories Limited); and intramuscular Ketamine, 1 mg/Kg body weight (AneketTM, Neon Laboratories) as muscle relaxant 15 min before imaging under the ECIL Gamma Camera. Differential accumulation of the tracer in the lesions with time was studied.

Results

The labeling efficiency of various excipients like sodium chloride, potassium chloride and glucose with Tc-99m was studied as per the radio-labeling protocol of Ciprofloxacin. This was done to prove that the excipients do not participate in the labeling of Tc-99m pertechnetate. Free Tc-99m and R/H Tc-99m were determined by ITLC. In the formulation with sodium chloride as excipient, the labeling efficiency of Tc-99m with sodium chloride was found to be 6.25% with 88.4% free Technetium pertechnetate and 5.35% R/H Tc-99m. On the other hand the labeling efficiency of potassium chloride was found to be 21.93% with 73.7% free pertechnetate and 4.37% R/H Tc-99m, while the labeling efficiency of glucose was found to be 62% with 33.1% free pertechnetate and 4.9% R/H Tc-99m (Table 1). The results revealed that addition of excipient NaCl and KCl is least

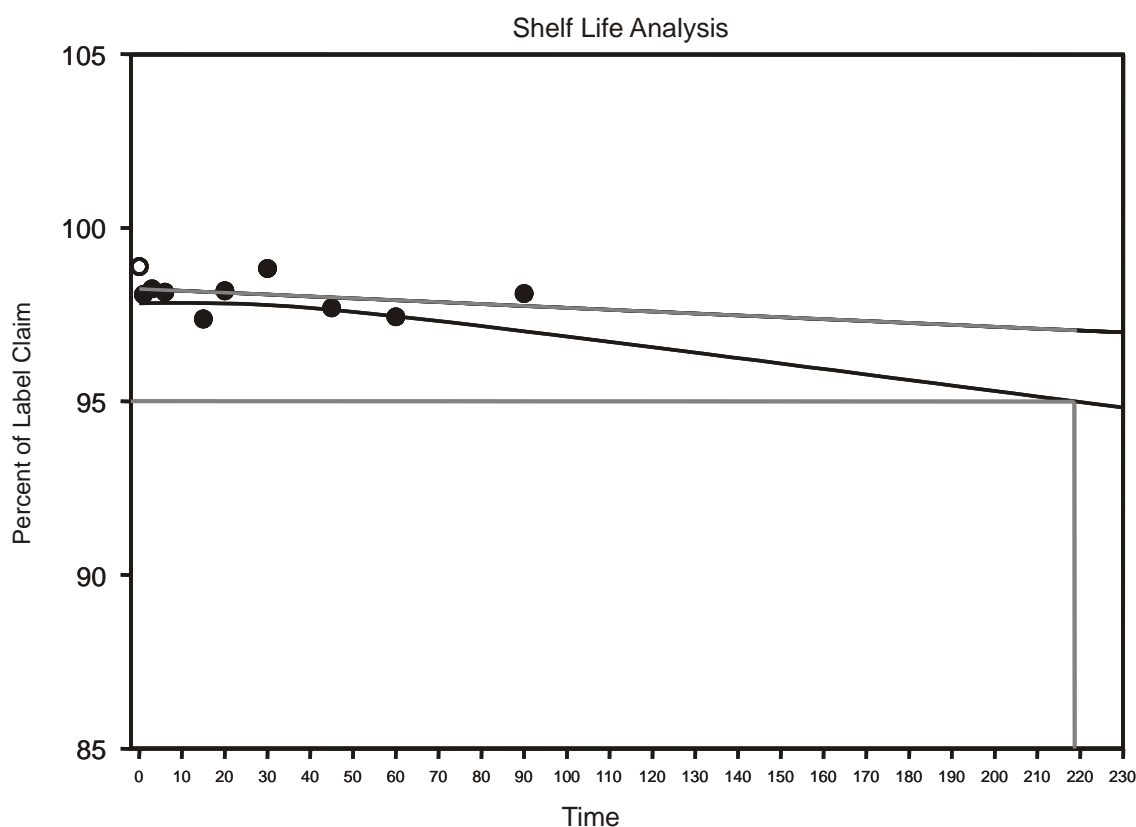


Figure 1. Shelf life analysis of Kit-B using Sigmaplot Software Version 8.0

| Excipient | pH | Percentage Free pertechnetate | Percentage Colloids |
|--------------------|----|-------------------------------|---------------------|
| Glucose | 7 | 33.1 | 4.9 |
| Sodium chloride | 7 | 88.4 | 5.35 |
| Potassium chloride | 7 | 73.7 | 4.37 |

Table 1. Labeling efficiency of the excipients.

likely to affect the labeling efficiency of Tc-99m with Ciprofloxacin. Hence, NaCl and KCl were used in the preparation of pellets. From out of the various concentrations of lyophilized stannous tartarate, which were used to label fixed amounts (2 mg) of Ciprofloxacin, 600 μ g was found to result in the best labeling efficiency. Table 2 summarizes the percentage of the free; R/H and drug bound Tc-99m with different amounts of lyophilized reducing agent.

Kits-A (control), 'B', and 'C' as described before were prepared and stored at 4°C. From time to time they were taken out of the shelves and labeled with Tc-99m pertechnetate. Table 3 shows the estimated serial labeling efficiency of Ciprofloxacin over a period of 90 days. Kits containing excipients like NaCl (Kit-B) and KCl (Kit-C) revealed 98.10 and 96.25% labeling efficiency respectively at day-90. The labeling efficiency of Ciprofloxacin in Kit-A started decreasing with time and reduced to 80.92% at day 60. The shelf life of the Kit-B and Kit-C was further analyzed by using Sigmaplot software version 8.0 (Figure 1). A shelf life of 219 days, when 95% labeling efficiency can be obtained successfully, was assigned to Kit-B and 101 days to Kit-C. The shelf life of the Kit-A was found to be only 1 day. Out of the three Kit types, Kit-B was found to possess the longest shelf life. However, in clinical

practice a kit producing 90% labeling efficiency has also been accepted. Hence, keeping in view 90% labeling efficiency as the acceptable limit, the shelf life of Kit-B was calculated to be 530 days (i.e. approximately 1.5 years) and that of Kits-A and C were 24 and 276 days respectively. Hence Kit-B was designated as the "best" product and subsequently it was subjected to a series of *in vivo* and *in vitro* quality control assessments. The radiopharmaceutical in the reconstituted kit remained fairly stable *in vitro* up to 24 hrs. Percentage of the labeled Ciprofloxacin was found to be around 94.85% at 24 hrs as determined by ITLC (Figure 2). *In vivo*, the radiolabelled compound was also found to be sufficiently stable up to 24 hrs, as no stomach or thyroid uptake was seen in the whole body scans of rabbits (Figure 5).

The blood clearance data in rabbits after intravenous administration of 37 MBq/Kg body weight of formulated Tc-99m Ciprofloxacin exhibited a slow and biphasic pattern (Figure 3). At 1 hr post-administration 16% of the injected radioactivity was present in the blood, which reduced to 3% by 24 hrs.

Biodistribution data of radiotracer in 2-3 month old balb/c mice is summarized in figure 4. Based on the percentage-injected dose per whole organ, the highest uptake of Tc-99m Ciprofloxacin was found in kidneys, intestine, liver and bone, averaging 9.95, 6.32, 4.67 and 5.54%

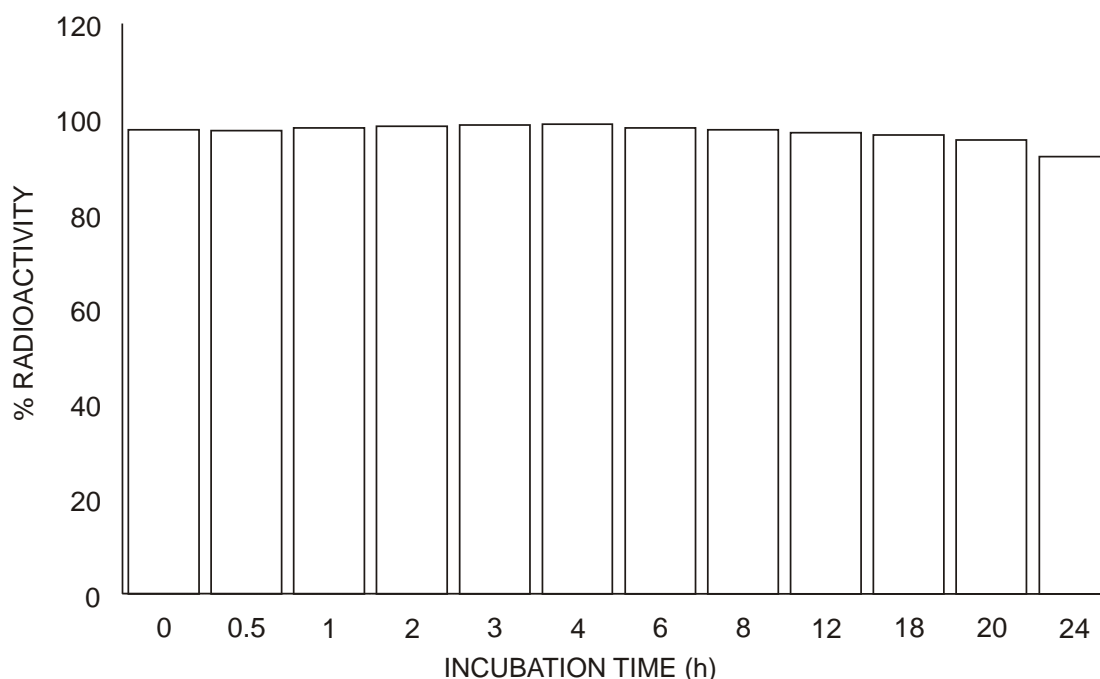


Figure 2. *In vitro* stability of Tc-99m Ciprofloxacin at room temperature up to 24 hrs.

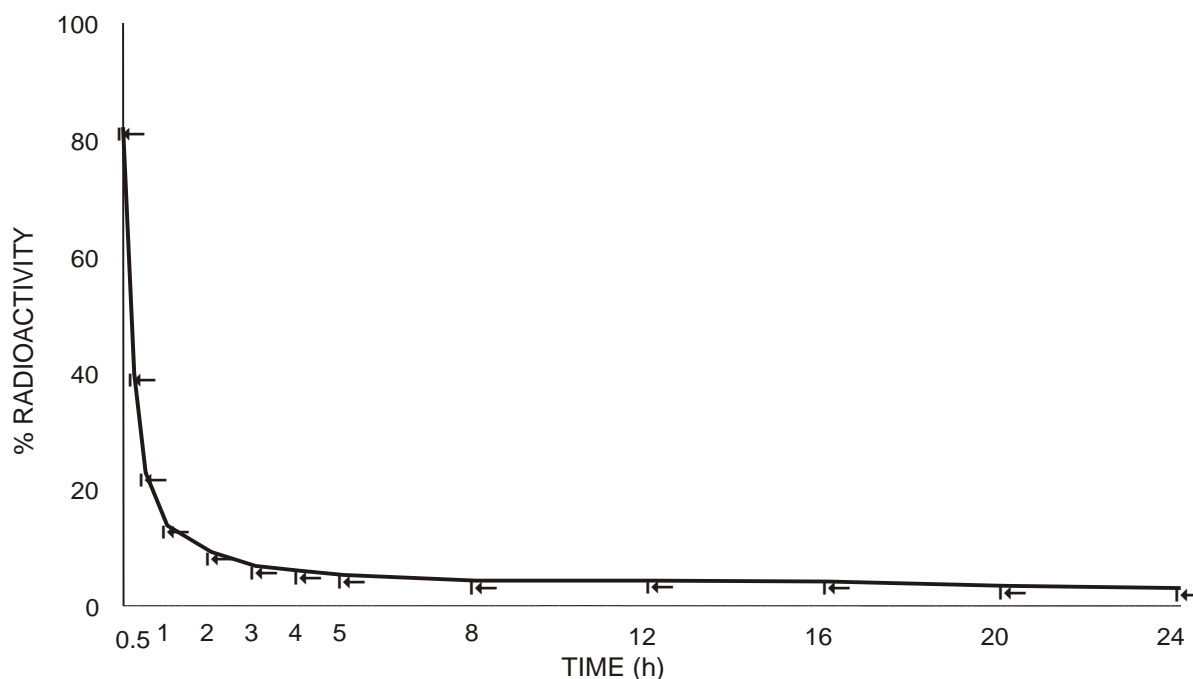


Figure 3. Blood clearance of Tc-99m Ciprofloxacin in rabbits

| Lyophilized stannous tartarate (μg) | Percentage Free pertechnetate | Percentage Colloid | Percentage Tc-99m Ciprofloxacin |
|--|-------------------------------|--------------------|---------------------------------|
| 400 | 4 | 2 | 94 |
| 500 | 4 | 4 | 92 |
| 600 | 2 | 3 | 95 |
| 700 | 2 | 5 | 93 |
| 800 | 2.15 | 6 | 91 |

Table 2. Reducing efficiency of lyophilized stannous tartarate.

respectively at 1 hr post-administration. Very little uptake of the radiotracer was seen in lungs, stomach and heart. Scintigraphy in rabbits bearing simultaneously the infectious and sterile lesions over the thighs showed very good early uptake at 2 hrs by the infectious lesion. Reasonably good uptake was also noted in the sterile lesion on the contralateral thigh. However the radioactivity levels in the sterile lesion declined significantly with time, with very little tracer retention in the lesion at 24hrs. On the other hand the infectious lesion continued to be seen prominently even in the 24hrs scan (Figure 5). Lesion to background ratio in case of infectious lesion increased from 2.7:1 at 2 hrs to 3.5: 1 at 24 hrs, while that of non-infectious (sterile) lesion reduced from 1.5:1 at 2 hrs to 1.1:1 at 24 hrs creating an appreciable contrast.

Discussion

The results obtained in the present study show that the shelf life of Ciprofloxacin kit can be enhanced significantly by addition of a small quantity of NaCl. The kits prepared with lyophilized stannous tartarate and Ciprofloxacin-sodium chloride pellets have a shelf life of 219 days as compared to

the conventional kits containing lyophilized stannous tartarate and Ciprofloxacin, reported earlier by Singh et al in 2001 (15). Other parameters of the new product like blood clearance, bio-distribution, in vitro stability and scintigraphic pattern remained essentially the same. The blood clearance and bio-distribution of the radiolabelled product were also found to be similar to those reported with the unlabeled drug (16,17). The kit upon reconstitution was found to produce higher labeling efficiency with minimal amounts of R/H and free pertechnetate. The radiopharmaceutical was also found to be stable for a longer period of time in comparison to the original Infecton (10). Until now there has been no published data with regard to the shelf life of the kits made for the preparation of Tc-99m Ciprofloxacin. However, our manufacturer's instruction for Infecton clearly indicates that the kit could be used up to one year from the date of manufacture.

Ciprofloxacin is a broad-spectrum antibiotic active against most of the gram positive and gram-negative bacteria. Tc-99m Ciprofloxacin is a specific infection-imaging agent by virtue of its (Ciprofloxacin's) specific binding to bacterial DNA gyrase (7). Tc-99m Ciprofloxacin has been in use for the past several years and it is now a well-established

| Day | Percentage of Tc-99m Ciprofloxacin | | |
|-----|------------------------------------|----------------|---------------|
| | Kit-A | Kit-B | Kit-C |
| 0 | 95.35 ± 0.367 | 98.88 ± 1.064 | 98.34 ± 0.739 |
| 1 | 95.19 ± 0.742 | 98.073 ± 0.753 | 97.83 ± 0.836 |
| 3 | 95.3 ± 0.785 | 98.24 ± 0.398 | 97.81 ± 0.542 |
| 6 | 94.16 ± 0.942 | 98.14 ± 0.983 | 97.27 ± 1.106 |
| 15 | 93.61 ± 1.037 | 97.37 ± 0.527 | 96.93 ± 0.582 |
| 20 | 92.2 ± 0.453 | 98.18 ± 0.672 | 97.36 ± 0.866 |
| 30 | 91.905 ± 0.93 | 98.82 ± 0.491 | 96.76 ± 0.386 |
| 45 | 86.92 ± 0.342 | 97.69 ± 0.753 | 95.97 ± 0.643 |
| 60 | 80.92 ± 0.846 | 97.43 ± 0.382 | 97.32 ± 0.774 |
| 90 | - | 98.10 ± 0.284 | 96.25 ± 0.399 |

Table 3. Labeling efficiency of different types of kits over time duration of 90 days. Data are presented as mean ± standard deviation (n = 3).

radiotracer, used for infection imaging. A two-vial kit, Infecton, developed at St. Bartholmew's Hospital, London in early 1990s (9), has been used for the localization of bacterial infections. The preparation of Tc-99m Ciprofloxacin using Infecton involved boiling at 100°C for 10 min and the radiopharmaceutical was found to be stable only for 8 hrs (10). We at INMAS have subsequently developed a single vial kit for the radiocomplexation of Ciprofloxacin with Tc-99m (15). However, the shelf life of the kit developed, was very short as evident from the results (1 day shelf life of Kit-A). The percentage of free Tc-99m started increasing in the

conventional kit within the first week itself beyond the acceptable limits. The plausible causes of this could be as follows: (1) lyophilization may decrease the reducing efficiency of the stannous tartarate and (2) stannous tartarate could be incompatible with Ciprofloxacin. It may be noted that stannous tartarate is a reducing agent that should be freshly prepared before use. However, in the preparation of the kit the aqueous solution of stannous tartarate (1 mg/ml) is used and then lyophilized after being dispensed (400µg) in vials. This entire processing of stannous tartarate affects its reducing efficiency. We studied the labeling efficiency of Ciprofloxacin using

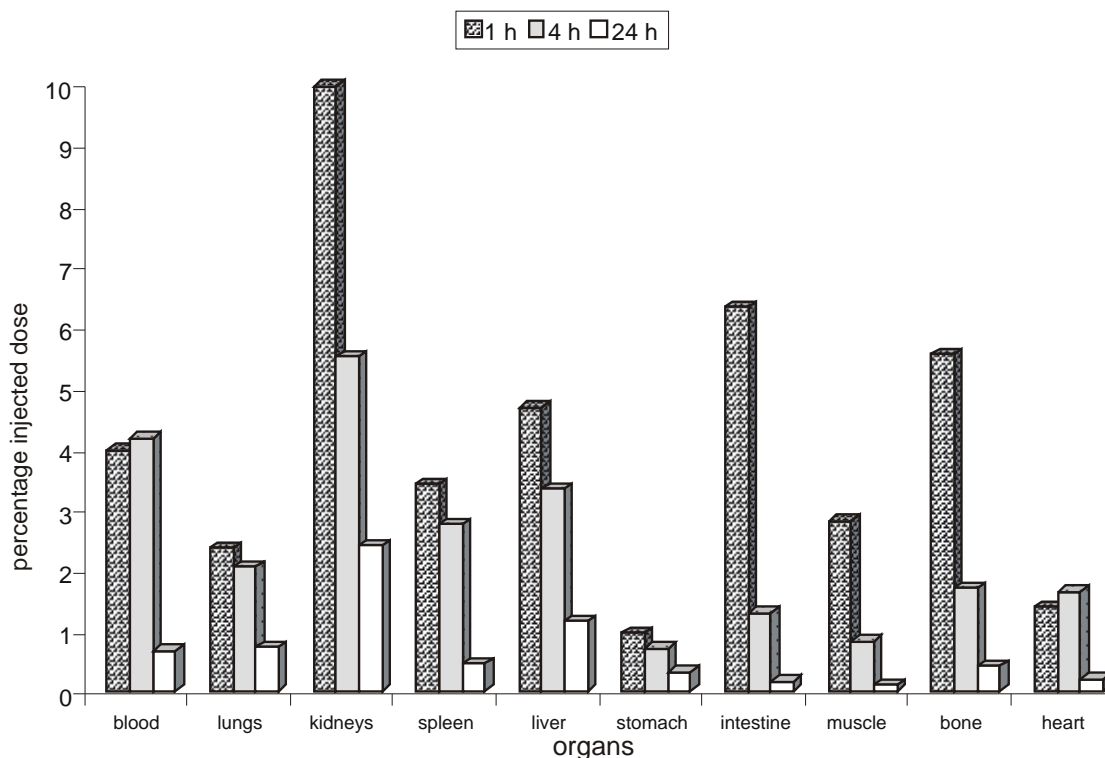


Figure 4. Bio-distribution of Tc-99m Ciprofloxacin in balb/c mice

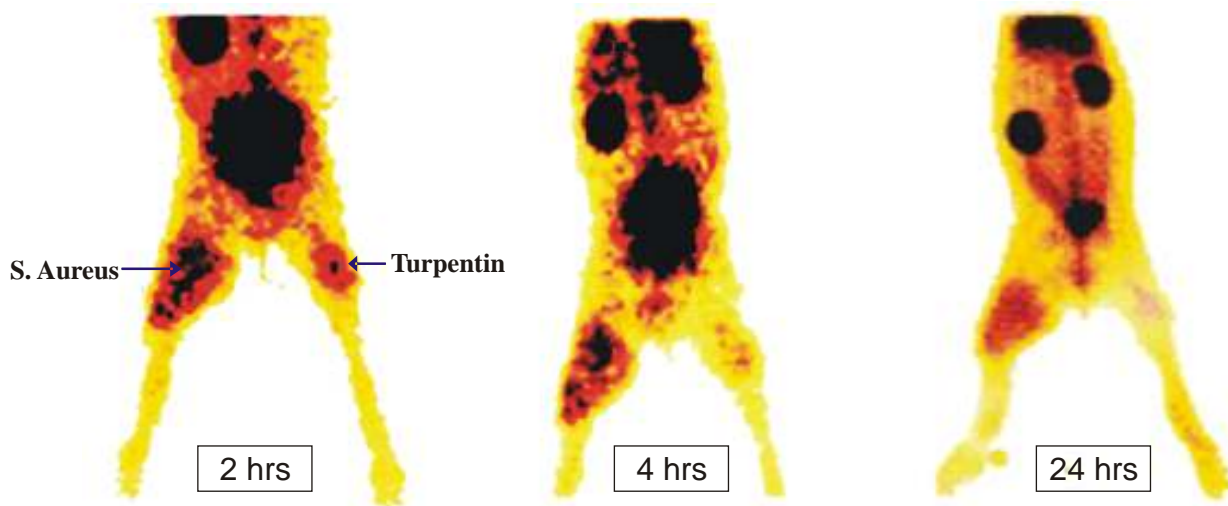


Figure 5. Tc-99m Ciprofloxacin imaging in an animal model (Rabbit) having an infective inflammation (*S. Aureus*) over right and a sterile inflammation (Turpentine oil injection) over left thigh. Scintigrams obtained at 2, 4 and 24 hrs (from left to right) following intravenous administration of 37 MBq of Tc-99m Ciprofloxacin reveal both lesions in the two hour scan (Left). The delayed 4 (Middle) and 24 hr (Right) scans reveal gradual disappearance of radioactivity from the sterile lesion, while the abnormality persists over the infective lesion even in the delayed 24 hr scan.

different amounts of stannous tartarate and observed best results with 600 μ g of lyophilized stannous tartarate (Table-2)

Metals like zinc, calcium and iron and antacids containing magnesium or aluminum have been reported to reduce the absorption of Ciprofloxacin due to the formation of metal-ion-Ciprofloxacin complexes (18,19,20). In the present case, there is a high probability that Ciprofloxacin could complex with stannous ions, and because of this the percentage of free Tc-99m increases in the Tc-99m Ciprofloxacin complex within one week. In order to obviate the interaction of Ciprofloxacin with stannous tartarate, pellets of Ciprofloxacin with NaCl and KCl were used in the preparation of kit. Sodium chloride and potassium chloride were used in the minimum amounts for the preparation of the pellets. These excipients, being physiological electrolytes, can be used in higher quantities but we did not use higher amounts as the results achieved with this amount were sufficient for nuclear medicine requirements. The labeling efficiency of the NaCl: Ciprofloxacin pellets containing kit was found to be stable till 90 days with the labeling efficiency of 98%. The data were subjected to Sigmaplot software version 2.0 for shelf life analysis and a shelf life of 219 days i.e. approximately 7 months was observed. The kit thus established was evaluated for all the in vitro and in vivo quality control parameters. The radiotracer was prepared by reconstituting the kit with 37-1000 MBq of sodium pertechnetate. It gives a labeling efficiency of 95% till the end of 7 months. It has the advantage of being a single vial kit, which in turn leads to simple handling protocol and lower radiation exposure.

In the present study, we evaluated the stability of the radiopharmaceutical, its blood kinetics, its bio-distribution,

and its infection imaging specificity. The in vitro stability of the Tc-99m Ciprofloxacin was assessed by ITLC and the radioactive contaminants were identified as R/H and free pertechnetate. The use of two solvent systems as described before was found to be an accurate method to clearly distinguish and quantitate the relative amounts of free Tc-99m, R/H Tc-99m and Tc-99m Ciprofloxacin. The radiotracer was stable up to 24 hrs with the labeling efficiency of 94.85%.

It may be noted that George in 1987 first studied the pharmacokinetics of Ciprofloxacin in human volunteers and had reported the mean terminal excretion half-life of Ciprofloxacin in normal volunteers as approximately 4 hrs (16). The blood clearance studies of Tc-99m Ciprofloxacin in rabbits exhibited slow and biphasic distribution similar to the unlabeled Ciprofloxacin (16). The first phase belongs to the distribution and elimination of the radiotracer and the second phase is due to its elimination from the blood. The average clearance half time of Tc-99m Ciprofloxacin is approximately 3-4 hrs. There was no evidence of in vivo dissociation of the complex. The scintigraphic studies and the biodistribution data confirm stability of the radiotracer. Hoffkenh et al in 1985 (21) and Hooper et al in 1985 (22) had described the phenomenon of entero-hepatic recirculation of the Ciprofloxacin (21,22). In our study the bio-distribution studies of Tc-99m Ciprofloxacin in mice have shown higher levels of radioactivity in the intestine and kidney, thereby indicating that the major route of excretion of the radiopharmaceutical is through the kidneys and hepato-biliary system. The bio-distribution studies also revealed high radiotracer concentration in the bones. The percentage uptake calculated in the bones exceeded that of the serum levels by over 50%. This is consistent with what has already been reported in literature (17). Tc-99m

Ciprofloxacin retains the pharmacological properties of the native drug. Our experience with both Infecton and the in house Tc-99m Ciprofloxacin confirm the excretion of the radiotracer by gall bladder and uptake in growing bones and osteoblastic lesions. The scintigraphic studies of the Tc-99m Ciprofloxacin in animal models confirmed the specificity of the radiopharmaceutical for the infectious lesion. It clears out with time from the sterile inflammatory lesion, while its uptake increases with time, up to 24 hrs, in the infectious lesion.

All studies carried out to evaluate the radiopharmaceutical formed by reconstitution of Kit-B suggest that the complex formed is a specific infection-imaging agent. The kit has been approved for human use and multi-center trials are planned.

Conclusion

The single vial cold kit based on Ciprofloxacin has been developed and evaluated. The kit appears to have better shelf life and stability as compared to the available alternatives with no change in pharmacokinetic and dynamic parameters. It is a stable, reproducible and safe preparation with high labeling efficiency, having specific accumulation in bacteria.

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