

Synthesis of ^{99m}Tc -N-clinafloxacin Dithiocarbamate Complex and Comparative Radiobiological Evaluation in *Staphylococcus aureus* Infected Mice

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Abstract

Clinafloxacin dithiocarbamate (CNND) preparation and radiolabeling through [$^{99m}\text{Tc} \equiv \text{N}$] $^{2+}$ core with the gamma (γ) emitter (^{99m}Tc) was assessed. The potentiality of the $^{99m}\text{Tc}^V \equiv \text{N}$ -CNND complex was investigated as perspective a *Staphylococcus aureus* (*S.a.*) *in vivo* infection radiotracer in terms of radiochemical stability in normal saline (n.s.), human serum (h.s.), binding efficacy with live and heat killed *S.a.* and biodistribution in female nude mice model (FNMD). More than 90% stability was observed in n.s. for 4 h with the highest yield of $98.70 \pm 0.26\%$ at 30 min after reconstitution. In h.s., the $^{99m}\text{Tc}^V \equiv \text{N}$ -CNND complex was found stable up to 16 h with 15.35% side products. Maximum *in vitro* binding ($68.75 \pm 0.80\%$, 90 min) with *S.a.* was observed after 90 min of incubation. In FNMD, (infected with live strain) approximately six-fold higher uptakes was noted in the infected to inflamed and normal muscles. The higher stability in n.s., h.s., higher *S.a.* (live) up take with specific and targeted *in vivo* distribution confirmed potentiality of the $^{99m}\text{Tc}^V \equiv \text{N}$ -CNND complex as perspective *S.a.* *in vivo* infection radiotracer.

Keywords: $^{99m}\text{Tc}^V \equiv \text{N}$ -clinafloxacin dithiocarbamate complex, *Staphylococcus aureus*, *in vivo* infection radiotracer

Introduction

Nuclear medicine technology (NMT) has gain popularity specifically in the accurate in time diagnosis of infection and its discrimination from inflammatory disease in early stages as the most sophisticated equipments such as ultrasound technology, computerized tomography, and the magnetic resonance imaging have shown insignificant precise information, especially in the initial stages of the disease. The significantly enhanced and accurate diagnostic results of the NMT had overcome the serious concerns of clinicians and substantially reduced the probability of wrong diagnosis.^[1]

Recently, a number of novel infection radiotracers have been reported including ours for the diagnosis of various

deep tissues infections using NMT. The promising diagnostic results using these novel agents encouraged the investigators to seek for more novel and better infection radiotracers.^[2-7]

Clinafloxacin (CNN) [7-(3-aminopyrrolidin-1-yl)-8-chloro-1-cyclopropyl-6-fluoro-4-oxoquinoline-3-carboxylic acid] is reported as a new fourth generation fluoroquinolone antibiotic with a better broad spectrum antibacterial activity against Gram-positive and -negative bacteria, aerobes, and anaerobes. It inhibits bacterial deoxyribonucleic acid (DNA) gyrase or topoisomerase intravenous enzyme thus effect DNA replication and transcription. In comparison with ciprofloxacin, the CNN has shown higher potency against a verity of pathogens.^[8,9]

It is observed that the compounds labeled with ^{99m}Tc through the [$^{99m}\text{Tc}^V \equiv \text{N}$] $^{2+}$ core has revealed higher and longer radiochemical stability both in saline and serum when compared to other methods. To exploit the superior antibacterial activity of the CNN for the diagnostic purpose, herein we investigated the radiolabeling of the CNN to develop more potent diagnostic agent. The

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labeling of the CNN involved the derivatization to its dithiocarbamate for so as to potentiate the labeling for higher and stable yield. The $^{99m}\text{Tc}^{\text{V}} \equiv \text{N-clinafloxacin dithiocarbamate (CNND)}$ complex was further characterized for radiochemical purity stability in normal saline (n.s.), human serum (h.s.), binding with *Staphylococcus aureus (S.a.)* and biodistribution in female nude mice (FNM) artificially infected with live and heat killed *S.a.* Further the radiobiological characteristics of the $^{99m}\text{Tc}^{\text{V}} \equiv \text{N-CNND}$ complex were compared with the ^{99m}Tc -CNN complex.

Experimental

Materials

CNN was purchased from Laiwu Hehui Chemical Co., Ltd. Shandong, China, thin layer chromatography (TLC) from Merck, Germany, succinic dihydrazide (SDH), propylenediamine tetra-acetic acid (PDTA) and all the other chemicals and solvents of analytical grade (Sigma). Reversed-phase high-performance liquid chromatography (HPLC) (Shimadzu, Japan) well counter and scalar count rate meter (Ludlum, USA) Dose calibrator (Capintech, USA) and Gamma camera GKS-1000 (GEADE Nuclearmedicine system, Germany).

Methods

Synthesis clinafloxacin dithiocarbamate

Clinafloxacin dithiocarbamate was prepared using the method previously reported.^[5] The CNND was re-crystallized from methanol/diethyl ether and characterized by Fourier transform infrared spectroscopy (FT-IR), ^1H nuclear magnetic resonance (NMR), ^{13}C NMR, electrospray ionization mass spectrometry (ESI-MS) and elemental analysis.

FT-IR/ ν : 3400-3250/cm (b.s OH), 1680/cm (C = O), 1620 $^{-1}$ (C = N). ^1H NMR (400 MHz, DMSO) δ 9.9 (s, OH), δ 7.93 (d, J = 12.8 Hz, 1H, -HC = C-COOH), δ 7.12 (s, 1H, Ar-H), δ 3.48 (dd, J = 12.8 Hz, 2.8 Hz, 1H, CH-C = C-COOH), δ 0.90 (td, 11.0 Hz, 3.2 Hz, 1H -CH₂CH-CH), δ 0.42 (dt, 4H, CH₂-CH₂-CH-), δ 2.98 (d, J = 7.5 Hz, 2H, N-CH₂), δ 2.86 (t, J = 7.2, 2H, N-CH₂-CH₂), δ 1.8 (dt, 9.8 Hz, 2.2 Hz, 2H, CH-CH₂-CH₂), δ 1.6 (td, 9.8 Hz, 7.5 Hz, 1H, =N-CH-CH₂). ^{13}C NMR (400 MHz, DMSO): δ 164.3 (NaS-C = N-), δ 178.2 (Ar-CO-C = C), δ 158.0 (CH-CH = C-COOH), δ 155.2 (F-C = C (Ar)), δ 137.8 (N-C = C (Ar)), δ 138.0 (C = C (Ar)), δ 130.1 (Cl-C = C (Ar)), δ 125 (C = C (Ar)), δ 114.5 (C = C (Ar)), δ 170 (-COOH), 131.0 (CO-C = C-COOH), δ 61.5 (N-CH₂), δ 58.8 (=N-CH), δ 50.0 (N-CH₂-CH₂-), δ 47.5 (Ar-CH-CH (Cyclic)), δ 27.6 (-CH-CH₂-CH₂), δ 16.2 (CH₂-CH-CH (Cyclic)), δ 5.3 (CH₂-CH-CH₂). EIMS: M/Z = 484, ESI: 485.0180 (M + H). Elemental analysis: % C, 47.06; % H, 3.33; % Cl, 7.31; % F, 3.92; % N, 5.78; % Na, 9.48.

Radiolabeling of clinafloxacin dithiocarbamate

2.0 mg of the CNND was taken in nitrogen filled vial followed by the addition of 2 mCi of the sodium pertechnetate ($\text{Na}^{99m}\text{TcO}_4^-$), 120 μg stannous chloride, 5.0 mg of PDTA and 5.0 mg of SDH. Thereafter, the reaction mixture was incubated for 15 min at 27°C and then it was filtered through Millipore filter.

Determination of partition coefficient (P)

Partition coefficient (P) was determined using the previously reported method.^[6] Briefly, equimolar amount of the $^{99m}\text{Tc}^{\text{V}} \equiv \text{N-CNND}$ complex, phosphate buffer and octanol were vortexed at room temperature for 5 min. The reaction mixture was then centrifuged at 4000 rpm/min for 10 min. Thereafter, aliquots at different intervals were withdrawn and calculated for activity using single well counter interface with scalar count rate meter using the formula: $P = (\text{counts/min in octanol} - \text{counts/min in background}) / (\text{counts/min in buffer} - \text{counts/min in background})$.

Radiochemical stability in normal saline

To characterize and determine the radiochemical stability of the $^{99m}\text{Tc}^{\text{V}} \equiv \text{N-CNND}$ complex in n.s. HPLC radiochromatography was employed. The main HPLC system was from Shimadzu (SCL-10 AVP) interface with SDP-10 AVP, UV detector (254 nm), Packard 500 TR, flow scintillation analyzer, 4.6 \times 150 mm C-18 column, binary pump and online degasser. Water: Methanol was used as mobile phase to characterize various components of the $^{99m}\text{Tc}^{\text{V}} \equiv \text{N-CNND}$ complex. In the instant characterization 10 μL of the $^{99m}\text{Tc}^{\text{V}} \equiv \text{N-CNND}$ complex was injected to the HPLC system followed by elution with water: Methanol mobile phase for a period of 15 min with a flow rate of 1 mL/min. The elution parameters were 0-2 min (100:00), 2-5 min (70:30), 5-7 min (60:40), 7-10 (40:60), 10-12 (30:70) and 12-15 (50:50), respectively. The radio-eluent (1 mL/min) was collected separately in different vials and counted for activity in single well counter interface with scalar count rate meter. The process was repeated for ^{99m}Tc -CNN complex for comparison. The overall scheme was repeated at 30, 60, 90, 120, and 240 min after reconstitution for determination of radiochemical stability of the complexes.

Stability in human serum

The stability of the $^{99m}\text{Tc}^{\text{V}} \equiv \text{N-CNND}$ complex at different intervals at 37°C up to 16 h of incubation in h.s. was assessed using TLC technique using the reported method.^[7] Briefly, for 16 h at 37°C, 1.8 mL of fresh h.s. was incubated with 0.2 mL of the freshly prepared $^{99m}\text{Tc}^{\text{V}} \equiv \text{N-CNND}$ complex. In incubation aliquots were withdrawn at 0, 2, 4, 6, 8, 10, 12, 14, and 16 h and spotted on the TLC strips. After drying in oven the strips were developed in n.s. and $\text{CH}_2\text{Cl}_2:\text{CH}_3\text{OH}$ (9:1) (v/v). In equal parts, the developed strips were divided and counted for

activity in single well counter interface with scalar count rate meter. The process was repeated for ^{99m}Tc -CNN complex for comparison.

Binding with *Staphylococcus aureus*

Binding of the *S.a.* live and heat killed strains with $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex was investigated using the reported method.^[10] Briefly, 10 MBq of the freshly prepared $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex was mixed with 0.1 mL sodium phosphate buffer in a clean sterilized pyrogen free test tube. Then, 0.01 M (0.8 mL 50%, v/v) acetic acid including 1×10^8 CFU of *S.a.* was added it. The mixture was incubated under sterile condition for 1 h at 4°C at a pH 5 followed by centrifugation at 2000 rpm for 10 min. Subsequently, the supernatant from the centrifuged mixture was removed followed by another centrifugation at 2000 rpm for 10 min. Thereafter, the pellets were removed and their activity was counted using in single well counter interface with scalar count rate meter. For comparison the process was repeated for ^{99m}Tc -CNN complex.

Biodistribution in rats

Biodistribution profile of the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex was investigated in FNM artificially infected with live and heat killed *S. a.* Twenty-four typical FNM were selected for this experiment with weight between 30 and 40 g. The selected FNM were divided equally into two groups (Group A and B). For the conception of inflammation, 0.2 mL sterilized turpentine oil was injected to the left thigh of each FNM and for conception of infection 0.2 mL of live *S.a.* was injected to the right thigh of the Group A and heat killed to the Group B, FNM. After 24 h, 10 MBq of the freshly prepared $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex was intravenously injected to each FNM of Group A and B. The female nude mice model was sacrificed in accord in accordance with the rules stipulated in the manual of Nuclear Medicine Research Laboratory University of Peshawar part-I and II. After that accurately, 1 g each of the blood, liver, spleen, stomach, intestines, kidneys, infected, inflamed, and normal muscles of the Group A and B, FNM were weight and placed in separated counting vials and counted for percent uptake using single well counter fitted with scalar count rate meter. The process was repeated for ^{99m}Tc -CNN complex for comparison.

Results and Discussion

Radiochemistry of the $^{99m}\text{Tc}^V \equiv \text{N-clinafloxacin}$ dithiocarbamate complex

CNN [Figure 1a] was converted to its dithiocarbamate derivative (CNND) [Figure 1b] followed by tagging with ^{99m}Tc through [$^{99m}\text{Tc} \equiv \text{N}$] $^{2+}$ core to give $^{99m}\text{Tc}^V \equiv \text{N-CNND}$

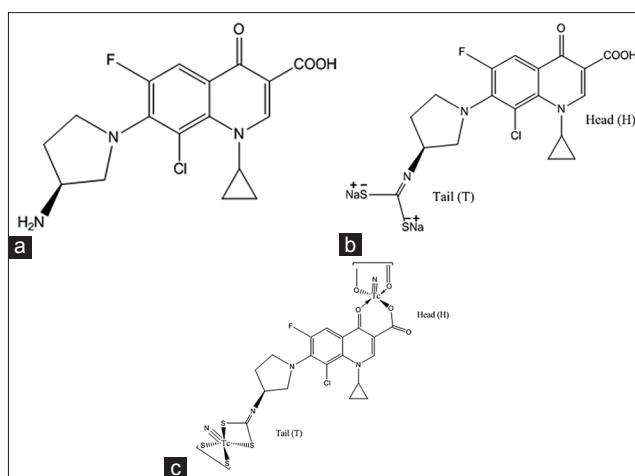


Figure 1: (a) Structure of the clinafloxacin (b) Derivatized clinafloxacin dithiocarbamate (c) Proposed structure of the ^{99m}TcN -clinafloxacin dithiocarbamate radiocomplex

complex as shown in Figure 1c using the reported scheme.^[11]

Although technetium can subsist in a number of oxidation states but +V state is the most general in TcN complexes. The two molecular orbitals involved will be the highest occupied nonbonding molecular orbitals (HOMO) and the lowest two unoccupied degenerate π^* antibonding orbitals (lowest unoccupied molecular orbital), the arrangement of these will account for the square pyramidal (sp) structure of the TcN complexes.

The crystal structural studies on TcN complexes, have shown that when the four coordinated atoms are π -donor Lewis bases, then sp structure is more likely.^[12,13] The speculated structure of $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ [Figure 1c] with tetradentate (two bidentate sites) ligand will have a sp structure with ^{99m}TcN -CNND: Ligand ratio of 1:1 with HH, TT, HT possible complexation.

Partition coefficient of the $^{99m}\text{Tc}^V \equiv \text{N-clinafloxacin}$ dithiocarbamate complex

The Partition coefficient (P) value of the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex observed was 1.09 ± 0.02 and for ^{99m}Tc -CNN was -1.04 ± 0.01 ^[9] respectively. The P values of the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ suggested lipophilic and that of ^{99m}Tc -CNN complex, a hydrophilic nature respectively.

High-performance liquid chromatography characterization and stability in saline

The HPLC radio chromatogram of the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex using C-18 column as stationary phase and water: Methanol as mobile phase is given in Figure 2. Two distinctly variable signals at 5.1 and 12.9 min were noted. The signal at 5.1 min of retention represented the

intermediate fraction ($[^{99m}\text{Tc}^V \equiv \text{N}]^{2+}$) and the 12.9 min the bound fraction ($^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex).

The $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex was found stable in n.s. up to 240 min after reconstitution as shown in Figure 3. The stability of the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex was decreased with time from a maximum value of $98.70 \pm 0.26\%$ to $91.20 \pm 0.30\%$ within 240 min. However, in case of the ^{99m}Tc -CNN, a lower stability ($97.55 \pm 0.22\%$ to $90.50 \pm 0.18\%$) with 240 min was seen than $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex.^[9] The combined radiochemical stability profile of the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ and ^{99m}Tc -CNN is shown in Figure 3.

Radiochemical stability in serum

In serum at 37°C the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex showed stability up to 4 h. However, the stability went down with the appearance of undesirable side products by 15.35% within 16 of incubation which is lower (18.15%)^[7] than

the ^{99m}Tc -CNN complex. The overall stability profile of the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ and ^{99m}Tc -CNN in serum at 37°C up to 16 h is given in Figure 4.

Binding with *Staphylococcus aureus*

Binding affinity of the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ and ^{99m}Tc -CNN with live and heat killed *S.a.* is given in Figure 5. The $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex showed maximum *in vitro* binding of $68.75 \pm 0.80\%$ within 90 min of incubation with live strain of *S.a.* It was observed that the binding affinity of the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex was higher from the ^{99m}Tc -CNN complex.

Biodistribution in rats

Distribution of the $^{99m}\text{Tc}^V \equiv \text{N-CNND}$ complex in the blood, liver, spleen, stomach, intestines, kidneys, infected, inflamed, and normal muscles of the Group A and B (FNM) is given in Table 1. In Group A and B FNM, it was

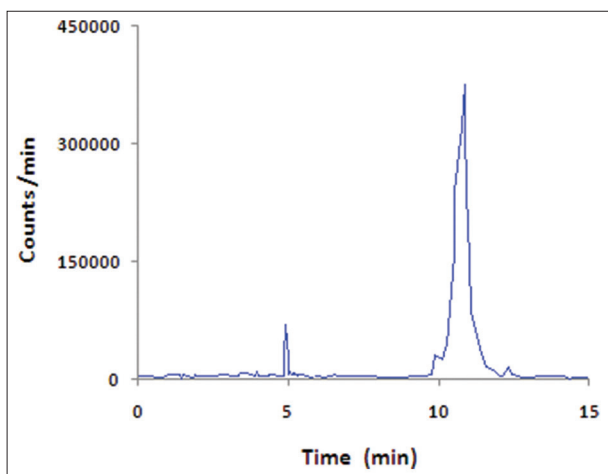


Figure 2: High-perman ce liquid chromatography radiochromatogram of the $^{99m}\text{Tc}^V \equiv \text{N}$ -clinafloxacin dithiocarbamate complex

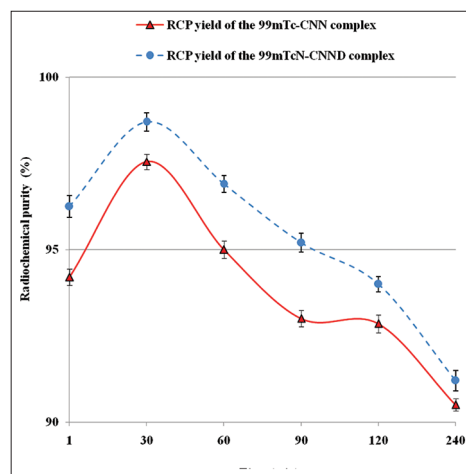


Figure 3: In normal saline radio-stability of the ^{99m}TcN -clinafloxacin dithiocarbamate complex within 240 min after reconstitution

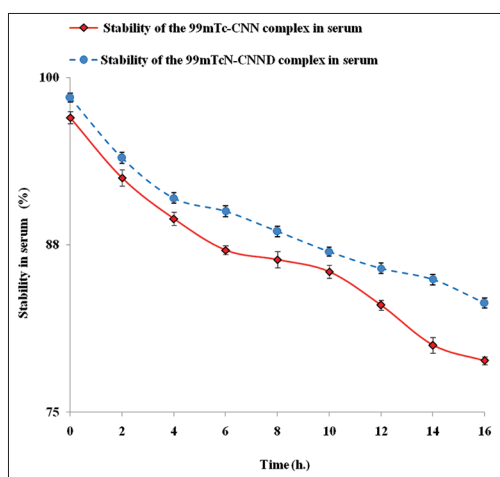


Figure 4: Stability of the ^{99m}TcN -clinafloxacin dithiocarbamate complex in serum at 37°C up to 16 h

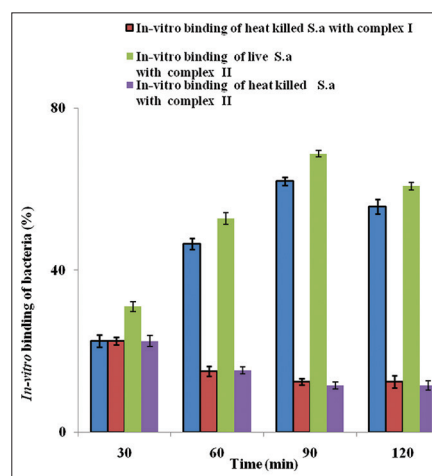


Figure 5: Binding profile of the ^{99m}TcN -clinafloxacin dithiocarbamate complex with live and heat killed *Staphylococcus aureus* at different intervals

Table 1: Percent uptake of the ^{99m}Tc -VN-clinafloxacin dithiocarbamate complex per gram of blood, liver, spleen, stomach, intestines, kidneys, infected, inflamed, and normal muscles of the female nude mice model

Organ/tissues (gm)	Up take of the of the ^{99m}Tc -CNND complex at different time							
	Group A, FNM				Group B, FNM			
	30	60	90	120	30	60	90	120
Infected muscle	6.20 ± 0.18	10.55 ± 0.20	14.20 ± 0.16	12.15 ± 0.00	2.50 ± 0.18	3.50 ± 0.14	3.50 ± 0.00	3.00 ± 0.18
Inflamed muscle	4.50 ± 0.18	3.50 ± 0.14	3.50 ± 0.20	3.00 ± 0.14	4.00 ± 0.14	3.50 ± 0.18	3.50 ± 0.12	3.00 ± 0.16
Normal muscle	2.50 ± 0.10	3.50 ± 0.18	3.00 ± 0.14	3.00 ± 0.12	2.50 ± 0.14	3.50 ± 0.16	3.50 ± 0.10	3.00 ± 0.12
Blood	18.45 ± 0.14	10.20 ± 0.18	9.05 ± 0.20	4.40 ± 0.14	18.75 ± 0.20	10.00 ± 0.14	9.25 ± 0.10	4.50 ± 0.20
Liver	17.75 ± 0.20	12.60 ± 0.14	10.20 ± 0.10	6.25 ± 0.22	18.15 ± 0.22	12.30 ± 0.10	9.95 ± 0.14	6.00 ± 0.12
Spleen	10.35 ± 0.14	8.40 ± 0.14	7.40 ± 0.14	4.30 ± 0.12	10.15 ± 0.22	8.75 ± 0.18	7.75 ± 0.18	4.25 ± 0.22
Kidney	9.40 ± 0.18	16.35 ± 0.20	19.80 ± 0.12	24.20 ± 0.16	10.00 ± 0.20	14.95 ± 0.14	20.15 ± 0.10	24.00 ± 0.20
Stomach & intestines	8.10 ± 0.16	7.50 ± 0.10	6.20 ± 0.22	4.15 ± 0.10	8.35 ± 0.12	7.15 ± 0.22	6.05 ± 0.12	4.00 ± 0.18

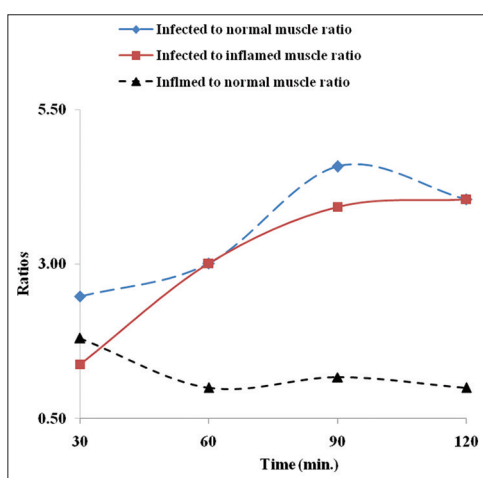


Figure 6: Ratio wise uptake in different organs of female nude mice model at different intervals

observed that the level of activity in the blood decreased from $18.45 \pm 0.14\%$ to $4.40 \pm 0.14\%$ within 120 min of p.i. Similar profile was seen in the liver, spleen, stomach, and intestines where the activity decreased to $6.25 \pm 0.22\%$, $4.30 \pm 0.12\%$, and $4.15 \pm 0.10\%$ respectively within 120 min. However, reciprocal behavior was noted in kidneys where the uptake increased from $9.40 \pm 0.18\%$ to $24.20 \pm 0.16\%$ within 120 min. In Group A, FNM the uptake of the $^{99m}\text{Tc}^V \equiv \text{N}$ -CNND complex in the infected muscle of the FNM was almost five-fold higher than the inflamed and normal muscle. However, no significant difference was seen in the uptake of the complex in the infected, inflamed and normal muscles of the Group B, FNM. No significant difference in the uptake of the $^{99m}\text{Tc}^V \equiv \text{N}$ -CNND and ^{99m}Tc -CNN complex was seen. Ratio-wise uptake of the complex in the infected, inflamed and normal muscles of the FNM is shown in Figure 6. The appearance of activity in the urinary system and disappearance from the circulatory system confirm the normal route of excretion.

Conclusion

CNND was labeled through $[^{99m}\text{Tc} \equiv \text{N}]^{2+}$ core and its potentiality as a perspective *S.a. in vivo* infection radiotracer was assessed. The higher stability in n.s., h.s., higher *S.a.*(live) up take and specific and targeted *in vivo* distribution confirmed potentiality of the $^{99m}\text{Tc}^V \equiv \text{N}$ -CNND complex as perspective *S.a. in vivo* infection radiotracer.

References

- Stumpe KD, Dazzi H, Schaffner A, von Schulthess GK. Infection imaging using whole-body FDG-PET. *Eur J Nucl Med* 2000;27:822-32.
- Zhang J, Guo H, Zhang S, Lin Y, Wang X. Synthesis and biodistribution of a novel (^{99m}Tc) TcN complex of ciprofloxacin dithiocarbamate as a potential agent for infection imaging. *Bioorg Med Chem Lett* 2008;18:5168-70.
- Shah SQ, Khan AU, Khan MR. ^{99m}Tc -novobiocin: A novel radiotracer for infection imaging. *Radiochimica Acta* 2011;99:53.
- Zhang J, Zhang S, Guo H, Wang X. Synthesis and biological evaluation of a novel ^{99m}Tc (CO)₃ complex of ciprofloxacin dithiocarbamate as a potential agent to target infection. *Bioorg Med Chem Lett* 2010;20:3781-4.
- Motaleb MA. Preparation and biodistribution of ^{99m}Tc -lomefloxacin and ^{99m}Tc -ofloxacin complexes. *J Radioanal Nucl Chem* 2007;272:95-9.
- Shah SQ, Khan AU, Khan MR. (^{99m}Tc) Tc-prulifloxacin in artificially infected animals. *Radiosynthesis and biological evaluation*. *Nuklearmedizin* 2011;50:134-40.
- Shah SQ, Khan MR. Synthesis of technetium-99m labeled clinafloxacin (^{99m}Tc -CNN) complex and biological evaluation as a potential *Staphylococcus aureus* infection imaging agent. *J Radioanal Nucl Chem* 2011;288:423-8.
- Shah P, Trostmann U, Tack K. Open-label, multicentre, emergency-use study of clinafloxacin (CI-960) in the treatment of patients with serious life-threatening infections. *Int J Antimicrob Agents* 2002;19:245-8.
- Bulera SJ, Theiss JC, Festerling TA, de la Iglesia FA. *In vitro* photogenotoxic activity of clinafloxacin: A paradigm predicting photocarcinogenicity. *Toxicol Appl Pharmacol* 1999;156:222-30.
- Welling MM, Paulusma-Annema A, Balter HS, Pauwels EK, Nibbering PH. Technetium-99m labelled antimicrobial peptides discriminate between bacterial infections and sterile inflammations. *Eur J Nucl Med* 2000;27:292-301.
- Boschi A, Duatti A, Uccelli L. Development of technetium-99m and rhenium-188 radiopharmaceuticals containing a terminal metal-nitrido multiple bond for diagnosis and therapy. *Top Curr Chem* 2005;252:85.
- Bandoli G, Dolmella A, Porchia M, Tisato E, Refosco P. Structural overview of technetium compounds (1993-1999). *Coord Chem Rev* 2001;214:43.
- Schwochau K. *Technetium Chemistry and Radiopharmaceutical Applications*, Weinheim, Germany: Wiley-VCH; 2001.

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