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Synthesis, labeling and biodistribution of ^{99m}Tc-3-amino-2-quinoxalin-carbonitrile 1,4-dioxide in tumor bearing mice

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Abstract 3-Amino-2-quinoxalincarbonitrile 1,4-dioxide (AQCD) is a quinoxaline derivative, which was synthesized by condensation method. AQCD was labeled with ^{99m}Tc with labeling yield above 90% investigated by paper chromatography. ^{99m}Tc-AQCD was prepared using stannous chloride as reducing agent at pH 7 and 10 min reaction time. ^{99m}Tc-AQCD should be freshly prepared, otherwise the yield significantly decreased after 15 min post labeling. Stability study of ^{99m}Tc-AQCD reflected the short time stability of Biodistribution study of $^{99\ m}$Tc-AQCD in tumor bearing mice reflected that its uptake in tumor sites in both ascites and solid tumor sites. This uptake of ^{99m}Tc-AQCD in tumor sites was sufficient to radioimage the inoculated sites.

Keywords Quinoxaline · ^{99m}Tc · Labeling · Biodistribution · Ascites · Imaging

Introduction

Quinoxaline (benzopyrazine) is a heterocyclic compound containing a ring complex made up of a benzene ring and a pyrazine ring. They are isomeric with quinazolines. The synthesis and chemistry of quinoxalines have attracted considerable attention in the last years [1]. Some of them exhibit biological activities including anti-viral, anti-bacterial, anti-inflammatory, anti-protozoal anti-cancer (colon cancer therapies), anti-depressant, anti-HIV, and as kinase inhibitors [2]. They are also used in the agricultural field as fungicides, herbicides, and insecticides [3]. Also, quinoxaline moieties are present in the structure of various antibiotics such as echinomycin, levomycin and actinoleutin, which are known to inhibit the growth of gram positive bacteria and they are active against various transplantable tumors [4]. In addition, quinoxaline derivatives have also found applications in dyes [5], efficient electron luminescent materials [5], organic semiconductors [6], chemically controllable switches [7]. They also serve as useful rigid subunits in macrocyclic receptors in molecular recognition. They can be formed by condensing ortho-diamines with 1,2-diketones. The parent substance of the group, quinoxaline, results when glyoxal is condensed with 1,2-diaminobenzene. Substituted derivatives arise when α-ketonic acids, α-chlorketones, α-aldehyde alcohols and α-ketone alcohols are used in place of diketones [8–10].

Recently, radiolabeling of quinoxaline derivatives had been studied and biodistribution of the labeled quinoxaline in tumor bearing animals were investigated [11, 12]. This study was conducted to synthesize 3-amino-2-quinoxalincarbonitrile 1,4-dioxide (AQCD). It also, conducted to label 3-amino-2-quinoxalincarbonitrile 1,4-dioxide with ^{99m}Tc, studying factors affecting labeling yield, investigate the % labeling yield was the convenient chromatographic techniques and biodistribution of the labeled compound in normal and tumor bearing mice.

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Experimental

Drugs and chemicals

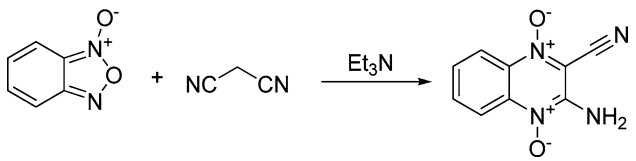
1 ^{99m}Tc was obtained as saline eluent of an expired Mo column.
2 Benzofurazan oxide, malononitrile, dimethyl formaldehyde (DMF), triethylamine and diethyl ether were supplied from ICN Chemical Company, USA.
3 Tin chloride was purchased from Sigma Chemical Company, USA.
4 All other chemical reagents were of analytical grade (AR), obtained from reputed manufacturers.
5 Ehrlich ascites carcinoma (EAC) was kindly supplied from National Cancer Institute, Cairo, Egypt.

Animals

Female Swiss Albino mice weighing 20–25 g were purchased from the Institute of Eye Research Cairo, Egypt. The animals were kept at constant environmental and nutritional conditions throughout the experimental period and kept at room temperature (22 ± 2) °C with a 12 h on/off light schedule. Female mice were used in this study due to their susceptibility to Ehrlich ascites carcinoma more than male mice [13]. Animals were kept with free access to food and water allover the experiment.

Methods

Synthesis of 3-Amino-2-quinoxalincarbonitrile 1,4-dioxide



Benzofurazan oxide **A** (1.36 g, 0.01 mol) and malononitrile (0.7 g, 0.016 mol) were dissolved in DMF (4 mL). The reaction mixture was cooled in an ice bath, and a solution of triethylamine (0.2 mL) in DMF (3 mL) was added. The temperature of the mixture was kept below 25 °C and it was maintained under these conditions for 1.5 h. The precipitate was filtered under suction and washed with diethyl ether to give compound **B** (1.51 g, 75% yield), m.p. 238–240 °C, (lit. 240–242 °C) [14, 15].

Labeling procedure and requirement

^{99m}Tc(AQCD) was prepared by the following procedures [15]. A total of 1 mg AQCD was dissolved in 3 mL purged distilled water with stirring. Tin chloride was added to AQCD solution in evacuated vial with Hamilton syringe and approximately 200–400 MBq ^{99m}Tc at room temperature. After a specified interval of time, chromatographic analysis was developed using paper chromatography ascending techniques [16]. The yield of the reaction and the radiochemical purity were determined by paper chromatography using acetone as mobile phase to distinguish between free at the top and both complex and reduced colloids near the point of spotting. On the other hand, 4 N NaoH as a mobile phase differentiate between reduced colloids which persist near the point of spotting and both complex and free, which move towards the front of chromatogram.

Factors affecting % labeling yield

This experiment was conducted to study the different factors that affect labeling yield such as: (1) Tin content, (2) Substrate content, (3) pH of the reaction and (4) Reaction time.

In the process of labeling, trials and errors were performed for each factor under investigations till obtains the optimum value. The experiment was repeated with all factors kept at optimum changing except the factor under study, till the optimal conditions achieved [17].

Paper chromatography

Paper chromatography was achieved using two mobile phases acetone and 4 N NaoH with ascending technique [18].

$$\mathrm{RF} = \frac{\text{Distance traveled by } ^{99m}\text{Tc} - \text{AQCD}}{\text{Distance traveled by solvent}}$$

In vitro stability

This experiment was conducted to determine the stability of ^{99m}Tc-AQCD after labeling and the impact of time on that compound. The yield was measured at different time intervals (1, 2, 4 6 and 12 h) after labeling [19].

Tumor transplantation in mice

The parent tumor line (Ehrlich Ascites Carcinoma) was withdrawn from 7 days old downer female Swiss albino mice and diluted with sterile physiological saline solution to give 12.5 × 10^6 cells/mL. A total of 0.2 mL solution

was then injected in mice intraperitoneally to produce ascites, or intramuscularly in the right thigh to produce solid tumor. The animals were maintained till the tumor development was apparent for about 10–15 days [20].

In vivo biodistribution

In normal mice

In vivo biodistribution studies were performed using four groups each comprise six mice. Each animal was injected in the tail vein with 0.2 mL solution containing 200–400 KBq of ^{99m}Tc-AQCD freshly prepared. The mice were kept in metabolic cages for the required time. Each group was subjected to scarification by cervical dislocation at the recommended time (15 min, 1 h, 6 h or 12 h) after injection. Organs or tissues of interest were removed, washed with saline, weighted and counted. Correction was made for background radiation and physical decay during the experiment. The weights of blood, bone and muscles were assumed to be 7, 10 and 40% of the total body weight, respectively [21].

In tumor bearing mice

Biodistribution of ^{99m}Tc-AQCD was carried out in two groups of animals each group consists of 24 mice, one ascites bearing group and the other solid tumor bearing mice. Each animal was injected in the tail vein with 0.2 mL solution containing 200–400 KBq of freshly prepared ^{99m}Tc-AQCD 2 weeks post inoculation. Each group subdivided to four subgroups of six mice each. Animals in each group were kept in metabolic cages for scarification at its required time, after 15 min, 1 h, 6 h or 12 h post injection of the labeled drug. Sacrification of mice was done by cervical dislocation and the organs or tissues of interest were isolated, weighted and counted for its uptake of radioactivity. Ascites fluid was drained and counted as a whole. The counting tubes, including a standard equivalent to 1% of the injected dose, were assayed in a well type NaI (TI) gamma counter and the results were calculated as percentages of injected dose (I.D) per gram tissue. The final results were expressed as mean ± one standard error [22].

Statistical analysis

The results are expressed as means ± SEM for the indicated number of different experiments. The statistical significance of differences was assessed by unpaired Student's *t*-test $P < 0.05$.

Results and discussion

Synthesis of AQCD

The precipitate was filtered under suction and washed with diethyl ether to give compound **B** (1.51 g, 75% yield), m.p. 238–240 °C, (lit. 240–242 °C) [1, 2].

Paper chromatography

The analysis of chromatographic data revealed the high percentage labeling yield of ^{99m}Tc-AQCD. Free ^{99m}Tc was obtained from paper acetone chromatogram. Colloid was obtained from 4 N NaoH chromatogram. Complex ^{99m}Tc-AQCD was obtained by subtracting % colloid from % activity obtained near the spotting in acetone chromatogram.

Factors affecting labeling yield

Tin content

Results obtained in this study showed the high yield obtained for ^{99m}Tc-AQCD using tin chloride as reducing agent (Table 1). It was observed that the radiochemical yield significantly increased by increasing the amount of tin from 10 to 75 µg (optimum content) at which maximum labeling yield was obtained. By increasing the amount of tin to 100 µg, the yield showed significant decrease in % complex ^{99m}Tc-AQCD. A significant reduction in the labeling yield was noted by decreasing the concentration of tin below 75 µg may be explained as at low concentrations of tin, not all ^{99m}Tc-was reduced. While by increase the tin content to 100 µg colloid may be increased and hence, % labeled complex decreased [23].

Table 1 Effect of Tin chloride content on the radiochemical yield ^{99m}Tc AQCD

Tin (µg)	% Labeled compound	% Free ^{99m}Tc	% Colloid
10	63.0 ± 0.25	36.0 ± 0.1	1.0 ± 0.03
25	64.1 ± 0.35*	32.5 ± 0.5	3.4 ± 0.17
50	92.25 ± 0.4*†	5.75 ± 0.06	2.0 ± 0.06
75	97.2 ± 0.32*†	1.80 ± 0.05	1.0 ± 0.05
100	90.0 ± 0.2*†	7.1 ± 0.5	1.90 ± 0.05

Values represent the mean ± SEM $n = 6$

* Significantly different from the initial values using Student's *t*-test ($P < 0.05$)

† Significantly different from the previous values using Student's *t*-test ($P < 0.05$)

Effect of substrate content

The influence of AQCD content as a substrate on the labeling yield using tin chloride was shown in Table 2. The increase of the concentration of AQCD was accompanied by a significant increase in the labeling yield, where it reached above 90% at 500 µg of AQCD. Increasing the amount of AQCD above 500 µg produced significant decrease in the labeling yield. Increasing the concentration of starting material is usually increases the total incorporation of ^{99m}Tc-AQCD since there is a minimum limit to the volume used [24]. A total of 500 µg AQCD was required to obtain maximum labeling yield, below this concentration significant decrease in the yield.

Effect of pH

In order to reach the suitable pH value for maximum radiochemical yield, labeling of AQCD with ^{99m}Tc- was carried out at different pH ranging from 2 to 12. The test was performed using 500 µg of AQCD, 100 µL of 0.5 M phosphate buffer of pH7 at 30-min reaction time. The experiment was repeated using 100 µL of each buffer at different pH values. As shown in Table 3, pH 7 is the optimum pH at which the maximum yield was obtained (97.5%). Also, it was observed that at pH 2 or 4, the yield was 98%, while at pH values 9 and 12; the yield was 79.0, 50%, respectively. There was significant difference between all pH values of the reaction mediums. The observation of this study that the optimum pH is 7, using phosphate buffers is constant with other previous work [25] (Table 3).

Effect of reaction time

Table 4 shows the relationship between the reaction time and the yield of ^{99m}Tc-AQCD. Radiochemical yield was significantly increased from 89 to 97.5% with increasing reaction time from 1 min to 10 min. Extending the reaction time more than 10 min produced significant decrease in the radiochemical yield. Extending the reaction time to 15, 30 and 1 h results in decreases the labeling yield to 90, 87.5 and 79% respectively. The efficiency of reducing agent may be affected by time and thus yield decreased [26].

Table 2 Effect of AQCD content on the labeling yield

Substrate (µg)	% Labeled compound	% Free ^{99m}Tc	% Colloid
50	82.5 ± 0.4	16.20 ± 0.15	1.3 ± 0.03
100	85.1 ± 0.50*	12.0 ± 0.3	3.0 ± 0.1
200	87.8 ± 0.25*†	9.5 ± 0.5	2.7 ± 0.05
500	97.1 ± 0.30*†	1.90 ± 0.02	1.0 ± 0.05
1000	94.3 ± 0. 2*†	2.20 ± 0.05	3.5 ± 0.45

Values represent the mean ± SEM $n = 6$

* Significantly different from the initial values using unpaired Student's t-test ($P < 0.05$)

† Significantly different from the previous values using unpaired Student's t-test ($P < 0.05$)

Table 3 Effect of pH of the reaction medium on the labeling yield of ^{99m}Tc AQCD

Ph value	% Labeled compound	% Free ^{99m}Tc	% Colloid
2	98.0 ± 0.40	1.50 ± 0.03	1.0 ± 0.02
4	98.5 ± 0.50*	1.0 ± 0.05	0.50 ± 0.02
7	97.5 ± 0.5 2*†	1.00 ± 0.05	1.5 ± 0.05
9	79.3 ± 0. 25*	11.0 ± 0.25	9.7 ± 0.45
12	50.5 ± 0.3*†	24.2 ± 0.15	25.3 ± 0.35

Values represent the mean ± SEM $n = 6$

* Significantly different from the initial values using unpaired Student's t-test ($P < 0.05$)

† Significantly different from the previous values using unpaired Student's t-test ($P < 0.05$)

Table 4 Effect of reaction time on the % labeling yield of ^{99m}Tc-AQCD

Time of reaction (min)	% Labeled compound	% Free ^{99m}Tc	% Colloid
1	89.10 ± 0.40	9.0 ± 0.3	1.90 ± 0.02
5	97.5 ± 0.5 2*†	1.00 ± 0.05	1.5 ± 0.05
10	97.6 ± 0.72*	1.00 ± 0.05	1.4 ± 0.05
15	89.0 ± 0.32*†	7.4 ± 0.35	3.6 ± 0.25
30	87.3 ± 0. 25*	8.0 ± 0.25	4.7 ± 0.05
60	79.3 ± 0. 25*	11.0 ± 0.25	9.7 ± 0.45

Values represent the mean ± SEM $n = 6$

* Significantly different from the initial values using unpaired Student's t-test ($P < 0.05$)

† Significantly different from the previous values using unpaired Student's t-test ($P < 0.05$)

In vitro stability of ^{99m}Tc-AQCD

In the present experiment, a significant decrease in the stability of ^{99m}Tc-AQCD from 97.5 to 50% at 6 h post labeling was observed. Significant reduction was observed at all time intervals post labeling, as the yield was 87, 79, 69 and 50% at 1/2 h, 1 h, 2 h and 6 h, respectively (Table 5).

Biodistribution of ^{99m}Tc-AQCD

In normal mice

Biodistribution study of ^{99m}Tc-AQCD in normal mice showed that ^{99m}Tc-AQCD was distributed rapidly in blood,

Table 5 Effect of time on the stability of ^{99m}Tc-AQCD

Time post labeling (h)	% Labeled compound	% Free ^{99m}Tc	% Colloid
10 min	97.5 ± 0.5 2*†	1.00 ± 0.05	1.5 ± 0.05
1/2 h	87.3 ± 0. 25*	8.0 ± 0.25	4.7 ± 0.05
1 h	79.3 ± 0. 25*	11.0 ± 0.25	9.7 ± 0.45
2 h	69.1 ± 0. 50*	20.2 ± 0.25	10.7 ± 0.50
6 h	50.1 ± 0.3*†	24.6 ± 0.15	25.3 ± 0.35

Values represent the mean ± SEM $n = 6$

* Significantly different from the initial values using unpaired Student's t-test ($P < 0.05$)

† Significantly different from the previous values using unpaired Student's t-test ($P < 0.05$)

stomach, heart and kidney at 15 min post injection. After 1 h, ^{99m}Tc-AQCD uptake was significantly decreased in organs like blood, heart, liver and intestine. However, ^{99m}Tc-AQCD uptake was significantly increased in bone and muscle after 1 h. At 4 h and 6 h post injection, the majority of tissues showed significant decrease in ^{99m}Tc-AQCD uptake (Table 6).

In ascites bearing mice

The results of this experiment showed that the sites of greatest uptake of ^{99m}Tc-AQCD after 15 minutes post injection were the blood, heart and lung (1.65, 8 and 7.5), respectively. Table 7 shows that the concentration of ^{99m}Tc- AQCD was the lowest in muscle and spleen at 15 min post injection. The uptake of ^{99m}Tc-AQCD in ascitic fluid was rapidly take place as each mL of ascitic fluid received 4.5% of total activity. The uptake of ascitic fluid was significantly increased after 1 h and 12 h to reach 6.5 and 6.2% per 1 mL, respectively. No significant change in the uptake of ^{99m}Tc-AQCD at 24 h post injection was observed when compared to its previous value. The data also showed that some organs exhibit significant increase of uptake at 1 h post injection like stomach, ascitic fluid, bone and thyroid. On the other hand, significant decrease in ^{99m}Tc-AQCD uptake was observed in blood, heart, kidney and lung at the same time. At 12 h post injection, the majority of organs showed significant decrease in uptake of ^{99m}Tc-AQCD. No significant increase was observed in ascitic fluid and thyroid at 4 h post injection. Similarly, at 6 h post injection, the majority of organs showed additional significant decrease in ^{99m}Tc-AQCD uptake. The results of biodistribution study of ^{99m}Tc-AQCD in ascites bearing animal revealed that ascites was one of the most site of uptake of ^{99m}Tc-AQCD and this was clear at l h and lasted to 6 h post injection. ^{99m}Tc-AQCD uptake in ascites was about 25% of the injected dose at 12 h post injection before reflecting the uptake per gram tissue. The uptake of each mL of ascites was 4.5, 6.5 and 6.2 at 1, 4 and 6 h, respectively. It was also observed that ascites was the site of highest uptake considering the average volume of ascites (4.3 ± 0.7). This result suggests the use ^{99m}Tc-AQCD in imaging of tumor. The high uptake of ^{99m}Tc-AQCD in kidney may reflect the excretion of the drug via urine [27] (Tables 6, 7).

In solid tumor bearing mice

Biodistribution of ^{99m}Tc-AQCD in solid tumor bearing mice was found to be greatest in heart, liver and stomach (8, 8.5 and 12, respectively) at 15 min post injection and lowest in left leg, blood and bone (1.3, 1.7 and 2.2, respectively) (Table 8). The biodistribution of ^{99m}Tc-AQCD in the right thigh (inoculated) was greater than that of left one. The uptake of ^{99m}Tc-AQCD in right thigh was significantly increased with time at 1 h and 4 h post injection, as it was 4.4 and 6.1% per g, respectively.

Table 6 Biodistribution of ^{99m}Tc-AQCD in normal mice

Organs and body fluids	Percent I.D./gram organ			
	Time post injection			
	15 min	1 h	4 h	6 h
Blood	16.90 ± 1.10	14.8 ± 0.20*	7.7 ± 0.04*	4.3 ± 0.30*
Bone	2.5 ± 0.05	3.30 ± 0.10*	2.4 ± 0.10*	2.4 ± 0.2
Muscle	0.75 ± 0.01	1.90 ± 0.02*	1.8 ± 0.10	1.0 ± 0.02*
Liver	7.10 ± 0.05	8.50 ± 0.15*	4.25 ± 0.16*	2.5 ± 0.02*
Lung	2.90 ± 0.10	6.10 ± 0.12*	4.1 ± 0.20*	3.1 ± 0.01*
Heart	3.0 ± 0.50	5.2 ± 0.50*	4.0 ± 0.01*	1.2 ± 0.04*
Stomach	8.2 ± 0.90	12.2 ± 0.600	8.3 ± 0.16*	6.7 ± 0.2*
Intestine	8.40 ± 0.50	8.5 ± 0.30*	4.5 ± 0.10*	1.6 ± 0.03*
Kidney	4.90 ± 0.40	7.30 ± 0.600	3.9 ± 0.30*	2.2 ± 0.06*
Spleen	2.70 ± 0.02	3.50 ± 0.24*	3.4 ± 0.2	1.4 ± 0.250*

Values represent mean ± SEM. $n = 10$

* Significantly different from the previous value of each organ using unpaired Student's t-test ($P < 0.05$)

Table 7 Biodistribution of ^{99m}Tc-AQCD in ascites bearing mice

Organs and body fluids	Percent I.D./gram organ			
	Time post injection			
	15 min	1 h	4 h	6 h
Blood	1.82 ± 1.00	2.30 ± 0.50*	0.590 ± 0.10*	0.40 ± 0.15*
Bone	3.70 ± 0.15	2.20 ± 0.150	2.30 ± 0.15*	1.6 ± 0.10*
Muscle	2.20 ± 0.09	1.3 ± 0.020*	1.6 ± 0.01*	0.9 ± 0.04*
Liver	8.40 ± 0.25	7.10 ± 0.20	4.60 ± 0.06*	2.3 ± 0.07*
Lung	7.20 ± 0.10	9.40 ± 0.04	2.20 ± 0.10*	1.5 ± 0.01*
Heart	10.00 ± 0.30	5.40 ± 0.30*	4.80 ± 0.10*	2.1 ± 0.02*
Stomach	12. 0 ± 0.30	13.4 ± 0.60*	10.7 ± 0.60*	7.1 ± 0.50*
Intestine	6.40 ± 0.50	3.60 ± 0.07*	3.20 ± 0.10*	2.1 ± 0.20*
Kidney	7.00 ± 0.40	10.20 ± 0.10*	4.01 ± 0.10*	2.1 ± 0.06*
Spleen	3.30 ± 0.10	4.35 ± 0.01*	1.70 ± 0.01*	0.9 ± 0.01*
Ascitic fluid	4.50 ± 0.30	6.50 ± 0.40*	6.20 ± 0.10*	4.2 ± 0.500

Values represent mean ± SEM. $n = 6$

* Significantly different from the previous value of each organ using unpaired Student's t-test ($P < 0.05$)

Table 8 Biodistribution of ^{99m}Tc-AQCD in solid tumor bearing mice

Organs and body fluids	Percent I.D./gram organ			
	Time post injection			
	15 min	1 h	4 h	6 h
Blood	1.70 ± 0.15	1.20 ± 0.06*	0.67 ± 0.02*	0.42 ± 0.04 *
Bone	2.20 ± 0.15	2.4 ± 0.10	1.4 ± 0.1*	1.3 ± 0.10
Liver	8.50 ± 0.40	6.70 ± 0.2	4.1 ± 0.1*	3.7 ± 0.10
Lung	5.50 ± 0.50	8.10 ± 0.30*	4.9 ± 0.2*	3.2 ± 0.15*
Heart	8.00 ± 0.40	6.21 ± 0.10*	3.8 ± 0.05*	3.5 ± 0.200
Stomach	12.0 ± 0.75	14.6 ± 1.1*	8.76 ± 0.25*	6.2 ± 0.26*
Intestine	5.10 ± 0.20	.70 ± 0.1*8	4.1 ± 0.3*	2.6 ± 0.250
Kidney	5.50 ± 0.70	7.60 ± 0.2*	3.7 ± 0.3*	2.0 ± 0.20*
Spleen	6.51 ± 0.50	8.7 ± 0.4*	4.9 ± 0.5*	3.3 ± 0.25*
Left leg	1.30 ± 0.05	1.70 ± 0.10	1.5 ± 0.10	1.2 ± 0.03*
Right leg	2.5 ± 0.30	4.4 ± 0.5*	6.1 ± 0.8*	4.2 ± 0.3*

Values represent mean ± SEM. $n = 6$

* Significantly different from previous value of each organ using unpaired Student's t-test ($P < 0.05$)

Liver showed significant increase in % ^{99m}Tc-AQCD uptake at 15 min, 1 h and 12 h post injection, when compared to ascetic bearing animals. In addition, ^{99m}Tc-AQCD uptake in the stomach of solid tumor mice was significantly increased at 15 min, 1 h and 4 h post injection when compared to ascetic bearing mice.

Conclusion

Incorporation of ^{99m}Tc-AQCD to a tumor site was achieved by labeling of AQCD with ^{99m}Tc. The appropriate conditions for labeling of 500 µg ^{99m}Tc-AQCD (97% yield) were 75 µg tin as reducing agent, at pH 7, at room temperature and 10 min reaction time. The great incorporation of ^{99m}Tc-AQCD in tumor sites (ascites or solid tumor) facilitates tumor imaging. ^{99m}Tc-AQCD was found to be highly localized in tumor sites which considered an ideal victor to carry energy to the nucleus of tumor cells [28]. In conclusion, this study demonstrates a hopeful approach for cancer imaging.

References

1. Clarke ED, Greenhow DT (1995) J Med Chem 38:1786
2. Islami MR, Hassani Z (2008) ARKIVOC 15:280
3. Monge A, Martinez-Crespo FJ, López de Cerain A, Palop JA, Narro S, Senador V, Martin A, Sainz Y, Gonzalez M, Hamilton E, Barker AJ (1995) J Med Chem 38:4488
4. Monge A, Palop JA, López de Cerain A, Senador V, Martinez-Crespo FJ, Sainz Y, Narro S, Garcia E, De Miguel C, Gonzalez M, Hamilton E, Stock WB, Undevia SD, Bivins C, Ravandi F, Odenike O, Faderl S, Rich E, Borthakur G, Godley L, Verstovsek S, Artz A, Wierda W, Larson RA, Zhang Y, Cortes J, Ratain MJ, Giles FJ (2008) Invest New Drugs 26:331
5. Katritzky AR, Rees CW (1984) Comprehensive heterocyclic chemistry, 2B, Part 3. Pergamon, Oxford, p 157

6. Sherman D, Kawakami J, He HY, Dhun F, Rios R, Liu H, Pan W, Xu YJ, Hong SP, Arbour M, Labelle M, Duncton MAJ (2007) Tetrahedron Lett 48:8943
7. Sakata G, Makino K, Karasawa Y (1988) Heterocycles 27:2481
8. Dell A, William DH, Morris HR, Smith GA, Feeney J, Roberts GCK (1975) J Am Chem Soc 97:2497
9. Heravi MM, Bakhtiari K, Tehrani MH, Javadi NM, Oskooie HA (2006) ARKIVOC 16:16
10. Raw SA, Wilfred CD, Taylor RJK (2003) Chem Commun 18:2286
11. Kumar A, Kumar S, Saxena A, De A, Mozumdar S (2008) Catal Commun 778
12. Jaung JY (2006) Dye Pigment 71:45
13. Ametamey MSM, Kokic M, Carrey-Rémy N, Bläuenstein P, Willmann M, Bischoff S, Schmutz M, Schubiger PA, Auberson YP (2000) Bioorg Med Chem Lett 10(1):75
14. Davison A (1983) In: Deutsch E, Nicolini M, Wagner HN (eds) Technetium in chemistry and nuclear medicine. Cortina International, Verona, Italy, pp 3–14
15. Rbbbins PJ (1984) Chromatography of ^{99m}Tc-radiopharmaceuticals, Practical guide
16. Motaleb MA (2001) Ph.D Thesis, Faculty of Science, Ain-Shams University
17. Boyd RE (1973) In: Proceedings of the symposium on new developments in radiopharmaceuticals and labeled compounds, vol 1, Combenhagen, (1973), STI/Pub/344, IAEA, Vienna, p 3
18. Talaat HM (1997) M.Sc. Thesis, Chemical Dept. University College for Girls, Ain Shams University
19. Svoboda K, Lezama J, Melichor F (1985) J Radioanal Nucl Chem Lett 96:403
20. El-Kolaly MT (1993) J Radioanal Nucl Chem Lett 170:393
21. Johannsen B, Spies H (1991) Workshop on generator and cyclotron produced radiopharmaceuticals, Riyad, Saudi Arabia, Oct
22. Abd El-Ghany EA (1998) Preparation and evaluation of freeze dried Kits for ^{99m}Tc labeling, M.Sc. Thesis, Faculty of Pharmacy, Cairo University
23. Cheng CH, Meares CF, Goodwin DA (1983) In: Lambrecht RM, Morcos N (eds) Application of nuclear and radiochemistry. Pergman, New York
24. Thorell JO, Stone-Elander S, Ingvar M, Eriksson L (1994) J Labelled Comp Radiopharm 36:251
25. El-Asrag HA, El-Kolaly MT (1988) 4th Conf Nucl Sci Appl 2 (3.1/1) 565
26. Proulx A, Ballinger JR, Galenchyn KY (1989) Int J Appl Radiat Isot Isot 40:95
27. Ballinger RJ (2001) Imaging hypoxia in tumors, seminars in nuclear medicine 31(4), 321
28. Kenji Y, Hideo K, Kazuki F (1999) J Nucl Med 40:5