Radioiodination of Quetiapine and Cyclobenzaprine as Brain Monitoring Agents: A Comparative Study on SPECT Imaging

H. A. El-Sabagh\textsuperscript{1*}, M.A. Mourad\textsuperscript{2}, A.M. Amin\textsuperscript{1} and S.A. Abo El-Enein\textsuperscript{3}

(\textsuperscript{1}Labeled Compounds Department, Hot Labs Center, Atomic Energy Authority, Cairo, Egypt
(\textsuperscript{2}Professor of radiochemistry, Labeled Compounds Department, Hot Labs Center, Atomic Energy Authority, Cairo, Egypt.
(\textsuperscript{3}Center of Radiation Oncology and Nuclear Medicine, Kasr Al-Ainy, Cairo, Egypt
(\textsuperscript{4}Chemistry Department, Faculty of Science, Ain Shams University, Cairo, Egypt

ABSTRACT

The aim of this study is to use drugs capable of crossing the blood-brain barrier (BBB) to develop new radiopharmaceuticals for non-invasive brain imaging. Quetiapine (QTP) and cyclobenzaprine (CBP), as two 5-HT2A receptor antagonists, were successfully labeled with radioactive iodine (125I) using Chloramine-T (CAT) as an oxidizing agent via electrophilic substitution reactions. After studying the parameters affecting the labeling yield, the highest radiochemical yields of 125I-QTP and 125I-CBP were found to be 94.5 \% \pm 1.0 and 91.7 \% \pm 0.6, respectively, at pH 2. The biodistribution and the SPECT/CT image showed that the maximum uptake of radioiodinated-QTP by the mouse brain was 10.2\% and 10.9\% at 120 minutes post-injection, while the uptake percentages of radioiodinated-CBP were 7.7\% and 12.4\% at 240 minutes post-injection. The results have shown that radioiodinated-QTP and radioiodinated-CBP are novel radiopharmaceuticals and may be used for brain imaging.

1. INTRODUCTION

In recent years, the development of new brain imaging radiopharmaceuticals for single-photon computed tomography / computed tomography (SPECT / CT) emission has rapidly progressed. SPECT / CT alone or combination with positron emission tomography (PET) and/or functional magnetic resonance imaging (FMRI) is used for the assessment of human cognition, the monitoring of neuroreceptor structures, the detection or evaluation of neurological disease development and following up responses to psychiatric treatments [1-11]. However, in comparison with PET, SPECT / CT has the advantage of being widely available worldwide. The physical properties of \textsuperscript{125}I (half-life \textit{t}_{1/2} = 59.4 \text{ d} and \textit{E}_{\gamma} = 35.5 \text{ keV}) allowed it to be used in \textit{in-vitro} and radiolabeling studies. Due to the similarities between different radioiodine isotopes (\textsuperscript{123}I, \textsuperscript{124}I, \textsuperscript{125}I and \textsuperscript{131}I) in their chemical properties, they can be used in the radiolabeling process [12].Because 10 \% of its energy is \textit{via} gamma rays, \textsuperscript{131}I radionuclide was used for the determination of the radiochemical purity, biodistribution and SPECT imaging[13].

Quetiapinefumarate (2-[2-(4-dibenzo[b,f] [1,4] thiazepine -11-yl)-1-piperazinyl]ethoxy]ethanol) is a typical antipsychotic agent used for the treatment of schizophrenia, bipolar disorder and major depressive disorder[14-15].Sometimes, it is also used as a sleep aid due to its sedating effect, but this use is not recommended [16].The antipsychotic activity of quetiapine may be due to a combination of antagonism in the frontal cortex at 5-HT2A receptors and D2 receptors in the mesolimbic pathway. 5-HT2A receptors antagonism relieves negative symptoms of schizophrenia, while antagonism at D\textsubscript{2} receptors relieves its positive symptoms.

Cyclobenzaprine hydrochloride (3-(5H-dibenzo[a,d] cyclohepten-5-ylidene)- N,N-dimethyl-1-propanamine) is a muscle relaxant used to relieve skeletal muscle spasms and associated pain in acute musculoskeletal conditions [17].CBP does not work directly on the muscle or the neuromuscular junction, but through central action, it relieves muscle spasms, likely at the level of the brain stem.
CBP binds to the serotonin receptor and is known to be a 5-HT2A receptor antagonist- that improves muscle tone by reducing serotonergic neuronal activity. Both QTP and CBP were reported to have a high penetration probability (about 0.9906 and 0.9512, respectively) via BBB[18]. The chemical structures of QTP and CBP are shown in Fig. (1).

![Chemical structures of CBP and QTP](image)

This study focuses on factors affecting the radioiodination yield of $^{131}$I-QTP and $^{131}$I-CBP and the comparison between them as novel radiopharmaceuticals for SPECT / CT brain imaging. In addition, the biodistribution and localization efficacy of the labeled compounds were evaluated in laboratory animals and confirmed using SPECT/CT imaging.

2. EXPERIMENTAL

2.1. Materials

QTP and CBP were obtained as a gift from the National Organization for Drug Control and Research, Giza, Egypt. CAT was purchased from Aldrish Chemical Company, China. Radioactive iodine-125 (Na$^{125}$I) with 370 MBq (10 mCi) activity was purchased from Isotope Company, Budapest. Radioactive iodine-131 (Na$^{131}$I) with 1.85 GBq (50 mCi) activity was presented as a gift from the Radioisotope Production Facility, Egyptian Atomic Energy Authority, Egypt. All chemicals were used in analytical or clinical grades and were used without further purification. Silica gel thin-layer chromatography (SG-TLC) was purchased from Merck, Germany. The Hidex single detector gamma counter was used to measure the radioactivity and SPECT/CT model Syngo, Siemens AG.

3. METHOD

3.1. Radioiodination

$^{125}$I-QTP and $^{125}$I-CBP can be synthesized by direct electrophilic substitution reaction with $^{125}$I using CAT as a mild oxidizing agent [19-20]. In brief, an appropriate amount of CAT(25-250 µg) dissolved in water was added to the desired amount of QTP or CBP(25-200 µg). The pH of the reaction mixtures (pH 2-11) was adjusted using different buffer systems. Reactions were allowed to proceed at different time intervals (5-60 min) and at different temperatures (up to 100°C). To quench the reactions, a drop of sodium thiosulfate solution (20 mg/mL) was added to reduce the unreacted iodine to iodide completely.

3.2 Radiochemical analysis

Radiochemical yields of $^{125}$I-QTP and $^{125}$I-CBP were determined by SG-TLC. The sample was spotted at 2 cm above the lower edge of the strip (1.5 cm wide, 14 cm long), then TLC was developed with a mixture of chloroform to methanol (3:1 v / v). The radiolabeled compounds ($^{131}$I-QTP and $^{131}$I-CBP) migrated with a solvent front (Rf =0.9), whereas the free iodide remained near the spotting point at baseline (Rf =0-0.1). The strip was removed from the developer jar to dry and cut into segments of 1 cm and its activity was measured using the gamma counter. The radiochemical yield was determined using the following equation [21].

$$\text{% Radiochemical yield} = \frac{\text{Activity of labeled compound}}{\text{Total activity}} \times 100 \quad (1)$$

3.3. Radiochemical purity

The HPLC analysis of $^{131}$I-QTP and $^{131}$I-CBP was performed using NaI/Tl crystal gamma counter. Samples (5-10µL) of the reaction mixtures of both $^{131}$I-QTP and $^{131}$I-CBP were injected in a reversed phase column RP-C18. The elution process was carried out using methanol: acetonitrile: pH 6.6 phosphate buffer...
Radioiodination of Quetiapine and Cyclobenzaprine

(15:40:45 v/v) for $^{131}\text{I}$-QTP and methanol:0.02 mol/l KH$_2$PO$_4$ (75:25 v/v, pH 3 was adjusted using 1% orthophosphoric acid) for $^{131}\text{I}$-CBP as mobile phases at 1mL/min flow rate. The fractions were collected and counted using NaI/Tl crystal gamma counter [22-23].

3.4. Lipophilicity

A partition coefficient experiment was conducted with $^{125}\text{I}$-QTP and $^{125}\text{I}$-CBP for in vitro screening of their ability to pass through the BBB. This experiment was performed by mixing $^{125}\text{I}$-QTP or $^{125}\text{I}$-CBP with equal volumes of 1-octanol and phosphate buffer (0.025mol/L at pH 7.4) in a centrifuge tube. The mixture was vortexed at room temperature for 1 min, then centrifuged at 5,000 rpm for 5 min. Samples (100 μL) were pipetted into test tubes and counted for each phase. Measurements were made in triplicate and the values for the partition coefficient were expressed as log p [24].

3.5. In vivo biodistribution study

Biological research experiments were carried out in accordance with the guidelines laid down by the Egyptian Atomic Energy Authority and approved by the Labeled Compounds Department. Swiss albino male mice weighing between 25-30 g were selected for biodistribution studies. Three mice were used for each radio-compound at each time point. Mice were injected with $^{131}\text{I}$-QTP or $^{131}\text{I}$-CBP compounds via the caudal (tail) vein. Animals were humanely killed at different time intervals and the blood was collected by cardiac puncture. Subsequently, the brain and other organs were dissected and washed twice with normal saline to remove adhesive tissue/fluid. The radioactivity percentage in each tissue/organ was measured using a gamma scintillation counter.

3.6. In vivo SPECT/CT imaging

Mice were anesthetized by intravenous diazepam injection (5 μL / g) and then injected $^{131}\text{I}$-QTP or $^{131}\text{I}$-CBP via the caudal vein containing about 37 MBq (1 mCi) radioactive iodine-131. Each mouse was positioned at the chosen time intervals (10, 60, 120 and 240 min) for imaging. The mice were imaged in prone and feet first position using a pinhole collimator with a configuration of 180 head for 10 min acquisition duration. The images obtained were a planner with matrix 512x512 and an optical zoom 3.

4. RESULTS AND DISCUSSION

The structure of $^{125}\text{I}$-CBP and $^{125}\text{I}$-QTP via reaction of CBP and QTP with iodine-$^{125}$I in the presence of CAT at pH =2 is shown in Eq. (2) and (3) respectively. Preparation and confirmation structure of the iodo-CBP and iodo-QTP were investigated using stable iodine for the preparation of large amounts to enable their separations for characterization, and prepared under the same conditions as those used for the preparation of $^{125}\text{I}$-CBP and $^{125}\text{I}$-QTP. The iodo-CBP and iodo-QTP were characterized by proton NMR.

The $^1\text{HNMR}$ spectrum of iodo-CBP in (Acetone-d6) revealed signals at:

2.0-2.4(t.q-4H-2methylene aliphatic) 2.9-2.9(s.s-6H-2 methyl) 5.9(t.1H methane -C=C-H aliphatic) 6.9-6.9(d.d2H H-C=C-H aliphatic) 7.2-7.3(m.4H benzene) 7.5-7.7(m.3H-benzene).

Fig. (2): HNMR spectrum of iodo-CBP

![HNMR spectrum of iodo-CBP](image)

The $^1$HNMR spectrum of iodo- QTP in (DMSO-d6) revealed signals at: 2.2-2.2(t.t-4H.2 methylene aliphatic) 2.3-2.6(t.t-4H-2 methylene aliphatic) 2.8-2.9(t.t-4H -2 methylene cyclic) 2.8-2.9(4H-2 methylene cyclic aliphatic) 5.6(1H-OH alcohol) 6.1-7.2(m-3H-benzene)7.2-7.6(m-4H-benzene).

Fig. (3): HNMR spectrum of iodo-QTP

![HNMR spectrum of iodo-QTP](image)

4.1. Optimization of the radiolabeling process

4.1.1. Effect of substrate amount

The radiochemical yield depends on the quantity of $^{125}$I-QTP or $^{125}$I-CBP as shown in Fig. (4), where reactions were performed at different substrate quantities (25-200 μg) while the other parameters (CAT, pH reaction, reaction time and temperature) remained constant. Radiolabeling yields of $^{125}$I-QTP and $^{125}$I-CBP were at a maximum of 100 μg of substrate, which may be attributed to the fact that this substrate quantity is sufficient to capture the entire iodonium ion produced [21]. By increasing the amount of substrate above the optimum value, the yields for radiolabeling were reduced because the molarity of both of CBP and QTP exceeded the molarity of iodonium ions presented in the solution [25].

![Graph showing radiochemical yield vs. substrate amount](image1)

Fig. (4): Radiochemical yields of $^{125}$I-QTP and $^{125}$I-CBP as a function of substrate amount

4.1.2. Effect of CAT amount

The effect of the amount of oxidizing agent on the radiochemical yields of $^{125}$I-QTP and $^{125}$I-CBP is shown in Fig. (5). The radiochemical yield of $^{125}$I-CBP increased to 91.7 % at a CAT amount of 150 μg, whereas the $^{125}$I-QTP yield reached a maximum of 94.5% at a CAT amount of 50 μg. A further increase in the amount of CAT led to a decrease in the radiochemical yields and this may be due to the formation of undesirable by-products resulted from oxidative side reactions [12, 21].

![Graph showing radiochemical yield vs. CAT amount](image2)

Fig. (5): Radiochemical yields of $^{125}$I-QTP and $^{125}$I-CBP as a function of CAT amount

4.1.3. Effect of temperature

The binding of iodonium ion to the molecule of substrate is energy-dependent. As shown in Fig. (6), the maximum radiochemical yields of $^{125}$I-QTP and $^{125}$I-CBP were obtained at 60°C and 70°C, respectively, and radiochemical yields decreased gradually as temperatures increased to 100°C, probably due to the thermal decomposition of radiolabeled compound.

![Graph showing radiochemical yield vs. temperature](image3)

Fig. (6): Radiochemical yields of $^{125}$I-QTP and $^{125}$I-CBP as a function of reaction temperature

4.1.4. Effect of pH of reaction medium

The oxidizing CAT species are dependent on the pH of the medium and the condition of the reaction [26]. The pH of the reaction medium was studied at a pH range from 2 to 11, as shown in Fig. (7). At pH 2, the yields of $^{125}$I-QTP and $^{125}$I-CBP exceeded the maximum (94.5% and 91.7%, respectively) due to an increase in benzene ring protonation. When the pH of the reaction mixtures shifted to the alkaline medium, the yield dropped sharply to 30.4% and 41.9% at pH 11 for $^{125}$I-QTP and $^{125}$I-CBP, respectively, due to the formation of hypoiodite ion (IO$^-$) and iodate (IO$_3^-$) which are not suitable for iodinated process [27, 28].

![Graph showing radiochemical yield vs. pH](image4)

Fig. (7): Radiochemical yields of $^{125}$I-QTP and $^{125}$I-CBP as a function of pH
4.1.5. Effect of reaction time

The radiochemical yields of $^{125}$I-QTP and $^{125}$I-CBP were determined at different time intervals ranging from 5 to 60 min, as shown in Fig. (8). The radiolabeling yield of $^{125}$I-QTP increased to 94.5% in 30 min. It appears that short reaction time is not sufficient for CAT to fully react with iodide ions and to generate iodonium ions. It is also evident from the Figure that the radiochemical yield of $^{125}$I-CBP is substantially increased to maximum (93.4%) at 45 min, but this is considered time consuming, because 30 min produces a very good yield on labeling (91.7%).

![Fig. (8): The radiochemical yields of $^{125}$I-QTP and $^{125}$I-CBP as reaction time function](image)

4.2. In vitro stability

The in vitro stability of $^{125}$I-QTP and $^{125}$I-CBP was studied in order to evaluate the time that they could be safely injected. It was determined along 24h and the data are listed in Table (1). The data clearly confirmed that the $^{125}$I-QTP tracer was stable for 4h without a sufficient identification of by-products in the reaction mixture. The stability results also showed that $^{125}$I-CBP was stable up to 4 h with a radiochemical yield of 89.0%.

<table>
<thead>
<tr>
<th>Time post labeling (h)</th>
<th>$^{125}$I-QTP labeling yield (%)</th>
<th>$^{125}$I-CBP labeling yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>93.4 ± 1.1</td>
<td>90.1 ± 1.3</td>
</tr>
<tr>
<td>2</td>
<td>92.3 ± 1.0</td>
<td>89.7 ± 1.7</td>
</tr>
<tr>
<td>4</td>
<td>91.0 ± 0.5</td>
<td>89.0 ± 1.4</td>
</tr>
<tr>
<td>8</td>
<td>87.8 ± 2.1</td>
<td>80.1 ± 1.9</td>
</tr>
<tr>
<td>24</td>
<td>86.9 ± 2.7</td>
<td>77.6 ± 2.7</td>
</tr>
</tbody>
</table>

![Fig. (9): HPLC elution profile of QTP, Peaks: (1) free $^{131}$I and (2) $^{131}$I-QTP](image)

4.3. Lipophilicity

The partition coefficient values of $^{125}$I-QTP and $^{125}$I-CBP were 1.97 ± 0.01 and 1.76 ± 0.03, respectively, indicated that $^{125}$I-QTP and $^{125}$I-CBP are very lipophilic and can easily cross the BBB.

4.4. HPLC analysis

The HPLC analysis showed that the retention times for iodide and $^{131}$I-QTP (Rt) were 3 and 9 min, respectively, as shown in Fig. 9. In the case of CBP, as shown in Figure (10), the Rt of iodide and $^{131}$I-CBP were found to be 5 and 9 min respectively. The eluted fractions of $^{131}$I-QTP and $^{131}$I-CBP that contain the labeled compounds were collected individually. Those pooled fractions were evaporated into dryness. The traces were then dissolved in the physiological saline and sterilized using a filter of 0.22-μm Millipore. The $^{131}$I-QTP and $^{131}$I-CBP were then appropriate for biodistribution and imaging.
4.5. In vivo biodistribution study

Table (2) shows the biodistribution pattern of $^{131}$I-QTP and $^{131}$I-CBP in normal albino mice. Because the elimination of QTP is mainly due to hepatic metabolism [29], the tracer passes to the small intestine through the liver, which holds an early uptake of the tracer reaching 5.8 % at 10 min and increased to 10.7% at 120 min post injection. The data also showed that $^{131}$I-QTP remained in the intestine at 7.8% after 10 min and increased to 22.3% after 240 min from the injection. Because CPB is excreted by the kidney [30], $^{131}$I-CBP removed from circulation primarily via urine is approximately 28.9 % at 240 min after injection of the tracer. The low activity in the thyroid gland is representative $^{131}$I-QTP and $^{131}$I-CBP is stable in vivo against biological decomposition.

With respect to brain radioactivity and that in the blood per gram of tissue(target to non-target), the ratio is concluded to have increased over time and reached its maximum value of 1.2 and 1.9at 120 min and 240 min post injection for $^{131}$I-QTP and $^{131}$I-CBP, respectively. This was due to high bloodstream clearance of the tracer, although low brain tissue washes-out.

<table>
<thead>
<tr>
<th>Organ or body fluid</th>
<th>$^{125}$I-QTP</th>
<th>$^{125}$I-CBP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10 min</td>
<td>60 min</td>
</tr>
<tr>
<td>Brain</td>
<td>0.5 ± 0.1</td>
<td>2.3 ± 0.1</td>
</tr>
<tr>
<td>Blood</td>
<td>21.1 ± 1.2</td>
<td>16.6 ± 0.5</td>
</tr>
<tr>
<td>Liver</td>
<td>5.8 ± 0.2</td>
<td>8.6 ± 0.3</td>
</tr>
<tr>
<td>Intestine</td>
<td>7.8 ± 0.4</td>
<td>14.4 ± 0.5</td>
</tr>
<tr>
<td>Stomach</td>
<td>4.8 ± 0.1</td>
<td>7.3 ± 0.4</td>
</tr>
<tr>
<td>Lungs</td>
<td>1.3 ± 0.1</td>
<td>1.3 ± 0.2</td>
</tr>
<tr>
<td>Heart</td>
<td>1.0 ± 0.1</td>
<td>0.9 ± 0.1</td>
</tr>
<tr>
<td>Kidneys</td>
<td>6.8 ± 0.2</td>
<td>2.9 ± 0.4</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.9 ± 0.1</td>
<td>0.9 ± 0.1</td>
</tr>
<tr>
<td>Muscles</td>
<td>41.8 ± 0.3</td>
<td>12.1 ± 0.4</td>
</tr>
<tr>
<td>Bones</td>
<td>2.4 ± 0.2</td>
<td>15.5 ± 0.3</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.4 ± 0.2</td>
<td>0.2 ± 0.1</td>
</tr>
<tr>
<td>Urine</td>
<td>5.3 ± 0.2</td>
<td>17.0 ± 0.3</td>
</tr>
<tr>
<td>Brain*</td>
<td>1.4 ± 0.1</td>
<td>7.3 ± 0.1</td>
</tr>
<tr>
<td>Blood*</td>
<td>11.8 ± 1.2</td>
<td>12.1 ± 0.5</td>
</tr>
<tr>
<td>(Br/Bl)*</td>
<td>0.1</td>
<td>0.6</td>
</tr>
</tbody>
</table>

* % Injected dose / g tissue; Br: Brain; Bl: Blood
Fig. (11): Pinhole SPECT/CT brain scans of two mice injected with $^{131}$I-QTP (a-d) and $^{131}$I-CBP (e-h) at several periods of time (10, 60, 120 and 240 min from left to right)

Table (3): The percentage of doses injected of $^{131}$I-QTP in some organs as per SPECT/CT imaging

<table>
<thead>
<tr>
<th>Organs</th>
<th>Time post injection (min)</th>
<th>10</th>
<th>60</th>
<th>120</th>
<th>240</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td></td>
<td>0.4 %</td>
<td>9.2 %</td>
<td>10.9 %</td>
<td>10.7 %</td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td>1.5 %</td>
<td>7.6 %</td>
<td>10.9 %</td>
<td>13.4 %</td>
</tr>
<tr>
<td>Bladder</td>
<td></td>
<td>1.2 %</td>
<td>1.5 %</td>
<td>4.2 %</td>
<td>5.4 %</td>
</tr>
</tbody>
</table>

Table (4): The percentage of doses injected of $^{131}$I-CBP in certain organs as per SPECT/CT imaging

<table>
<thead>
<tr>
<th>Organs</th>
<th>Time post injection (min)</th>
<th>10</th>
<th>60</th>
<th>120</th>
<th>240</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td></td>
<td>3.5 %</td>
<td>8.1 %</td>
<td>10.3 %</td>
<td>12.4 %</td>
</tr>
<tr>
<td>Liver or GIT</td>
<td></td>
<td>7.2 %</td>
<td>10.2 %</td>
<td>16.0 %</td>
<td>12.3 %</td>
</tr>
<tr>
<td>Bladder</td>
<td></td>
<td>3.6 %</td>
<td>6.1 %</td>
<td>11.9 %</td>
<td>7.6 %</td>
</tr>
</tbody>
</table>

4.6. SPECT/CT imaging

Pinhole SPECT/CT brain scans of two mice, one of them injected with $^{131}$I-QTP and the other one injected with $^{131}$I-CBP are shown in Fig.(11) To explore where each drug is located in the brain at several intervals of time (10, 60, 120 and 240 min post intravenous injection), the images were taken. In the case of QTP, there was no significant $^{131}$I-QTP percentage reaching the brain after 10 min of injection (0.4%), but after 120 min of injection, it increased to its maximum value (10.9 %) as shown in Table (3). Table (4) shows that about 3.5 % of $^{131}$I-CBP dose reached the brain after 10 min of injection and increased gradually with time till reaching 12.4 % after 240 min of injection. The scintigraphy images were consistent with the findings of the biodistribution studies.
CONCLUSION
Radiolabeling of both QTP and CBP were conducted through an electrophilic substitution reaction with high radiolabeling yields of 94.5±1.0% and 91.7±0.6%, respectively. The in vivo biodistribution results showed a higher brain uptake of $^{125}$I-QTP (10.2 ± 0.3%) than that of $^{125}$I-CBP (7.7 ± 0.2%) after 120 and 240 min, respectively, post injection. This uptake was greater than $^{125}$I-sibutramine and $^{125}$I-fluoxetine (5.7 ± 0.19 and 6.14 ± 0.26%, respectively) [26]. Also, the uptake results in this study were higher than those of the commercially available agents namely, $^{99m}$Tc-ECD and $^{99m}$Tc-HMPAO (4.7 and 2.25%, respectively) [31, 32]. These results were confirmed by SPECT/CT brain scans, where the maximum uptake percentages for $^{131}$I-QTP and $^{131}$I-CBP were 10.9 % and 12.4 % after 120 and 240 min post injection respectively. Thus, radioiodinated QTP and CBP are prospective novel radiopharmaceuticals for brain imaging.

REFERENCES


