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Short Research Article

Production and biological evaluation of [^{201}Tl(III)]bleomycin

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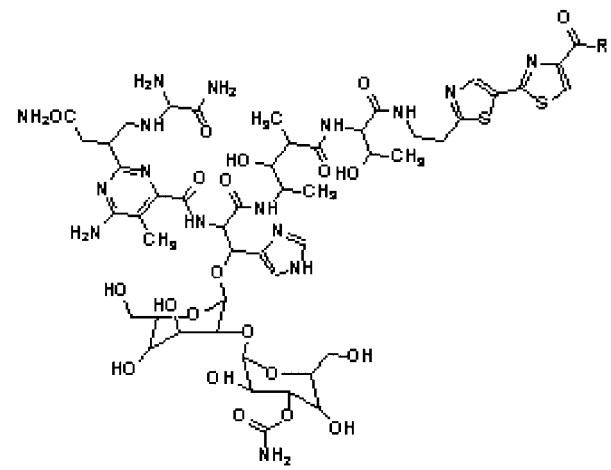
Introduction

The development of ^{201}Tl(III)radiopharmaceuticals could provide many advantages: (a) the physical properties of ^{201}Tl are interesting; (b) the chemistry of ^{201}Tl(III) complexation molecule is simple; (c) the complexation constant for most of Tl(III) complexes are among the highest (for instance, Tl(III)-DTPA at 25°C, $\log K = 46$) for all metal–chelator complexes; (d) high specific activity radiopharmaceuticals can be synthesized in kit formulations; (e) ^{201}Tl is available in many parts of the developed and developing world and can offer alternatives for other metallic radioisotopes including [^{111}In]In^{3+}. Despite the above advantages, ^{201}Tl labeled compounds are rare in the literature.[1–3] We optimized ^{201}Tl complex formation conditions (Figure 1). The stability of [^{201}Tl]bleomycin complex in presence of human serum and final preparation was determined for 72 h according to our recent works.[4] Finally, the optimized tracer was administered to normal rats for biodistribution and preliminary SPECT studies. The accumulation of the tracer in fibrosarcoma-bearing rats is under investigation (Table 1).

Results and discussion

In order to obtain the best labeling reaction conditions, the complex formation was optimized for pH,



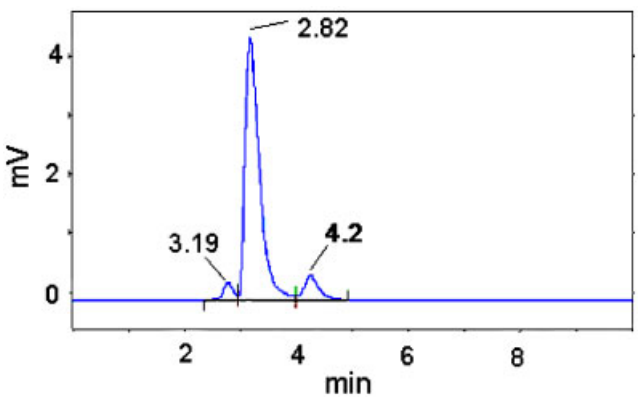


Figure 1 HPLC radiochromatogram of [^{201}Tl]bleomycin, flow rate; 2 ml/min, mobile phase; 10% ammonium acetate:methanol (1:1), Si Kromasil, flow scintillation detector. Figure available in colour online at www.interscience.wiley.com

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Table 1 Biodistribution of ^{201}Tl-BLM in normal rats at 1,3,4,24,48 and 72 h post i.v. injection

Tissues	ID/g %					
	1 h	3 h	4 h	24 h	48 h	72 h
Blood	0.76	0.39	0.73	0.58	0.17	0.35
Lung	4.53	3.85	4.62	2.96	1.67	2.34
Kidney	49.66	58.09	47.23	54.61	51.93	53.22
Skin	1.63	1.56	1.40	2.12	2.20	2.41
Muscle	4.51	2.73	2.80	4.39	4.72	4.72
Bone	3.68	2.91	3.25	0.97	0.63	1.43
Intestine	5.31	4.72	6.52	4.23	4.39	4.22
Colon content	3.61	4.04	6.64	3.47	3.56	4.53
Heart	12.41	12.25	19.96	16.79	20.08	14.44
Brain	0.54	0.00	0.00	0.00	0.00	0.00
Liver	7.70	7.74	6.12	8.80	9.52	11.12
Stomach	5.60	1.66	0.73	1.02	1.10	1.21

temperature, time, and the amount of bleomycin. At a random temperature (room temperature for instance), at neutral pH the labeling occurred successfully. This is different from what had been previously reported for [^{111}In]bleomycin. At higher pHs (>8), the radiochemical yield dropped due to the degradation of bleomycin to less-soluble compounds. At the pH6–7, the yield reached a maximum within 30 min, and stayed constant for longer reaction times (see Figure 1 and Table 1).

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