Biodistribution of intraperitoneally-administered ^{125}I-labeled IgG in Mouse

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1. Introduction

The use of radiolabeled antibodies is one of the most effective strategies to diagnose and treat cancers. However, it is hindered by the relatively low delivery to tumors following intravenous administration, in particular, cancers in peritoneal cavity [1]. Intraperitoneal administration of radiolabeled antibodies results in significantly higher exposure to the peritoneal cavity than does intravenous administration [2]. Therefore, intraperitoneal administration of the radiolabeled antibodies can be more effective to diagnose and treat cancers in peritoneal cavity such as ovarian and colonic cancers. This study was performed to determine the biodistribution pattern of intraperitoneally-administered radiolabeled antibodies.

2. Methods and Results

2.1 Preparation of ^{125}I-labeled IgG

^{125}I-labeled IgG was prepared using the IDOGEN method. IgG (from human serum, Sigma-Aldrich) was reacted with ^{125}I (Perkin Elmer) for 2 hours, and purified by gel filtration column chromatography using a PD-10 column (GE Healthcare).

Fig. 1 showed that the radiochemical purity of the prepared ^{125}I-labeled IgG was over 98%, and the specific activity was 123 MBq/mg.

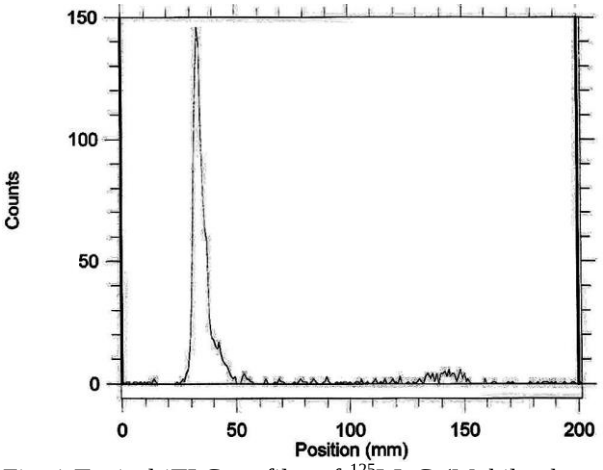


Fig. 1 Typical iTLC profiles of ^{125}I-IgG (Mobile phase: saline).

2.2 Biodistribution of ^{125}I-labeled IgG

Biodistributions were obtained from healthy ICR mice after a peritoneal administration of 185 kBq of ^{125}I-labeled IgG in 500 μl of saline (n=3~5). At the end of each residence interval, the mice were sacrificed, and the relevant organs and blood were assayed for residual radioactivity in a gamma counter (Perkin Elmer, Wallac-1470).

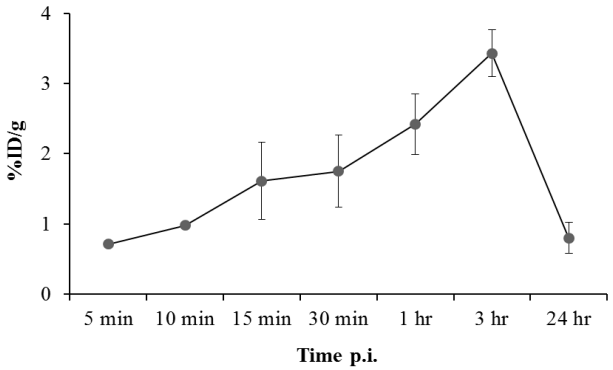


Fig. 2 Radioactivities in the blood after intraperitoneal administration of ^{125}I-labeled IgG.

As shown in Fig. 2, ^{125}I-labeled IgG was rapidly absorbed into the blood, and the radioactivities were increased in 3 hr p.i. It was also absorbed into the organs continuously, and most of the radioactivities were dropped and excreted within 24 hr p.i.

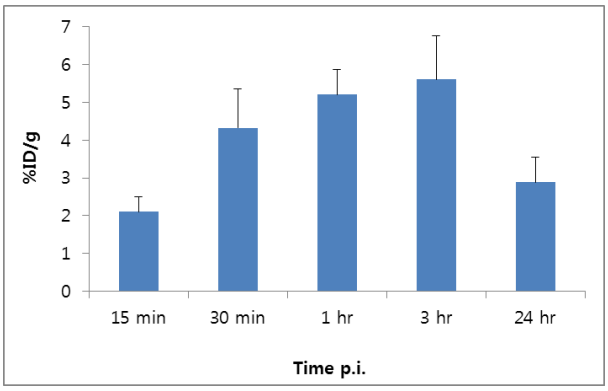
Table I. Biodistribution of ^{125}I-IgG in healthy ICR mice at Different Times p.i.[a]

Organ	15 min	30 min	1 h	3 h	24 h
Blood	1.61 ± 0.55	1.75 ± 0.51	2.42 ± 0.43	3.43 ± 0.33	0.80 ± 0.22
Liver	2.11 ± 0.38	4.32 ± 1.02	5.20 ± 0.66	5.60 ± 1.16	2.88 ± 0.67
Kidney	2.85 ± 0.34	5.10 ± 0.81	8.58 ± 0.43	13.32 ± 1.16	8.09 ± 1.70
Spleen	2.62 ± 1.01	4.63 ± 1.84	4.89 ± 1.26	4.22 ± 0.58	2.38 ± 0.78
Heart	0.44 ± 0.03	0.67 ± 0.24	0.77 ± 0.11	0.90 ± 0.07	0.29 ± 0.06
Small Intestine	1.90 ± 0.40	2.74 ± 0.37	2.70 ± 0.48	4.69 ± 0.61	1.10 ± 0.19

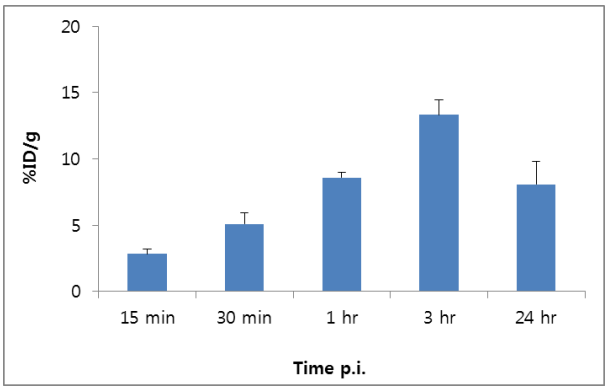
Large Intestine	2.55 ± 0.97	2.56 ± 0.69	1.77 ± 0.41	2.00 ± 0.68	3.53 ± 0.70
Lung	2.31 ± 1.43	6.20 ± 3.67	5.21 ± 3.48	6.43 ± 3.73	1.64 ± 1.01
Stomach	5.92 ± 0.47	12.43 ± 3.90	12.48 ± 4.54	22.56 ± 0.79	7.26 ± 2.61

[a]Results are expressed as % ID/g ± SD (*n*=3).

The ^{125}I-labeled IgG was excreted via renal-urinary pathway, and %ID/g in the kidney was 13.32 ± 1.16 at 3 hr p.i. As other reports using antibodies, ^{125}I-labeled IgG was uptaked in the liver. In particular, the stomach has the highest %ID/g among the organs.



(A)



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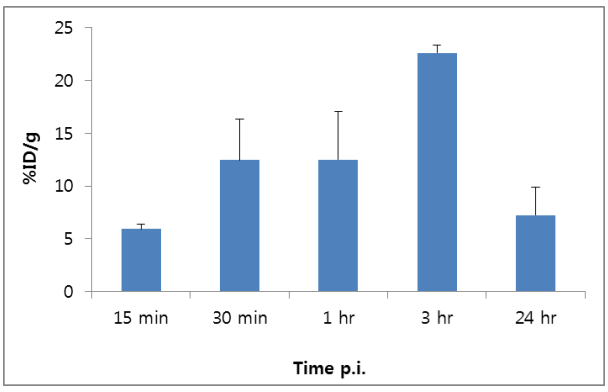

(C)

Fig. 3 %ID/g of the ^{125}I-labeled IgG in the organs; liver (A), kidney (B) and stomach (C) at Different Times p.i.

3. Conclusions

Our experiments show the absorption and distribution of intraperitoneally-administered ^{125}I-labeled IgG. The ^{125}I-labeled IgG was rapidly absorbed into the blood and organs, and the radioactivities were dropped in 24 hr p.i. These results suggest that the intraperitoneal administration of the radiolabeled antibodies can be an effective way to treat diseases in the peritoneal cavity.

Acknowledgement

This study was supported by the KAREI Major Project, Development of Radioisotope Production and Application Technology (525140-15).

REFERENCES

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[2] Wahl RL et al. Intraperitoneal delivery of monoclonal antibodies: influence of class and fragmentation on kinetics and intraperitoneal dosing advantage. J Nucl Med 1985;26:P114