Distribution Studies with ^{125}I -Labeled Synthetic Human Gastrin in Rats

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Although the role of gastrin is known to be related to gastric secretion, detail of its action as well as metabolic fate is poorly understood. In this report distribution of ^{125}I -labeled synthetic human gastrin (^{125}I -SHG) in rat organs is studied in order to clarify analogically its metabolic fate in human being.

Materials and Method

Synthetic human gastrin I was labeled with ^{125}I by the method of Hunter & Greenwood¹⁾, and the labeled product was purified with Sephadex G-10 and G-50 columns. Specific activity was $350 \mu\text{Ci}/\mu\text{g}$. The biological activity of ^{125}I -SHG was confirmed by the method of Lai²⁾.

Forty male Wister rats weighing 200 to 290 g were used and were divided into 8 groups including 5 rats respectively. Under urethane anesthesia the dose of $0.1 \mu\text{Ci}$ of ^{125}I -SHG was injected to the animals intravenously in a few seconds. They were killed by decapitation 2,5,15, and 30 minutes; 1, 3, 6, and 12 hours after the injection for each group. Tissues were removed, aliquots weighed, and their radioactivity was counted in a well-type gamma counter. The concentration of radioactivity in each tissue was calculated as the per cent dose per gram.

For comparison, an experiment was carried out in the same manner as described above, by using $0.1 \mu\text{Ci}$ of ^{125}I -Na solution

instead of ^{125}I -SHG.

Result

The time courses of the concentration of ^{125}I -SHG in each organs of principal interest, which include the glandular stomach, squamous stomach, kidney, liver, heart and small intestine, are shown in Figure 1.

Fig. 1 Time course of concentration of radioactivity of organs. (^{125}I -labeled synthetic human gastrin)

A peak concentration is observed in the kidney, liver, heart and small intestine from 5 to 15 minutes, which followed by rapid decrease. A markedly high concentration was noticed in the kidney. Hepatic concentration was next high to the kidney although there was a significant gap between both of these. In contrast to these organs,

a gradual increase of radioactivity was observed in the granular stomach during 12 hours following the injection.

The data of the distribution of $^{125}\text{I-Na}$ are shown in Figure 2. In this series a peak concentration is observed already at 2 minutes following the injection in the organs other than the stomach. The renal concentration was less than that in the series of $^{125}\text{I-SHG}$ injection and the difference between the two series was markedly significant ($p < 0.001$). In the granular stomach, when $^{125}\text{I-Na}$ was injected, the radioactivity reached a peak at 15 minutes and fell to the lowest at 1 hour and then again increased gradually. The difference of the concentration in this organ between both series of $^{125}\text{I-SHG}$ and $^{125}\text{I-Na}$ injection was not significant during the first 3 hours. In the other organs including the liver and small intestine, no significant differences were found between both series.

Fig. 2 Time course of concentration of radioactivity of organs. ($^{125}\text{I-Na}$)

Discussion

Any specific affinity of a hormone to an organ means that the organ has a large significance in reference to the action site and the metabolic site of the hormone. Various organs, such as the kidney, liver and small intestine, are regarded as the metabolic sites of gastrin. Newton³⁾ reported that, in his distribution studies with

$^{125}\text{I-SHG}$ in dogs, a significantly high concentrations of radioactivity was observed in only the kidney. Clendinnen⁴⁾ found the high degree of extraction of gastrin by the kidney during gastrin loading in dogs. On the other hand, Temperly⁵⁾ regarded the small intestine as a site of inactivation of gastrin. In rats, Wada⁶⁾ reported that the granular stomach had an affinity to gastrin. Furthermore, in a study with *t*-amyloxycarbonyl tetrapeptide of gastrin Ishimori⁷⁾ found that this peptide was inactivated by the liver.

The results of the present study demonstrated that the kidney of rat took high concentration of radioactivity specifically in the series of $^{125}\text{I-SHG}$ injection and that no specific accumulation of radioactivity was shown in any other organ. A gradual increase of the concentration of radioactivity following the injection was observed in the granular stomach, but it seems to be mainly degradation products of $^{125}\text{I-SHG}$, since no significant difference was found between both series of $^{125}\text{I-SHG}$ and $^{125}\text{I-Na}$. In the rat the kidney is presumed to be a site of metabolism of gastrin.

Summary

Distribution studies with ^{125}I -labeled synthetic human gastrin in rats were described. A significant concentration of radioactivity was noticed in the kidney, while in the other organs any specific accumulation of radioactivity was not demonstrated.

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