^{18}F-Labelling of Organic Compounds and Their Application to Scintigraphy

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Benzotrifluoride, sodium m-trifluoro-methylbenzene sulfonate, sodium p-fluorobenzoate and cholesteryl fluoride were labelled with ^{18}F produced by the cyclotron at the Institute of Physical and Chemical Research, Saitama, and tested the possibility to apply to scintigraphy by animal experiments. Fluorine-18 was produced from oxygen gas using ^{16}O (^{3}He,p) ^{18}F reaction with the yield of 20 to 30 mCi per 1 hour bombardment. Produced ^{18}F was trapped in the target box by $NaBF_4$, KF, SbF^3 or AgF with isotopic exchange and used as the labelling material. As the indirect chemical labelling methods were employed, the specific activity of the labelled compounds was low with the order of 1 mCi per gram. Ten to twenty microcurie of the compounds were intra-venously injected to each of ICR mice. The dose of the compounds were, however, lethally toxic except for sodium p-fluorobenzoate. The organ distribution of sodium p-fluorobenzoate was measured at 10, 30 and 60 minutes following injection. No significant concentration of activity was shown in any organ and then failed to reveal organ image on the scintigram. Activity in the inplanted Ehrlich ascitic tumor was also failed to be concentrated.

Incorporation of ^{75}Se-Selenomethionine into Acid-soluble and Protein Fractions of Mouse Pancreatic Cells

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To obtain fundamental knowledges for the development of new pancreas-scanning agent, certain experiments were conducted in the following way.

In general, ^{75}Se-Met is understood to be highly incorporated into enzyme proteins produced in the pancreas. In some clinical applications, the scanning is carried out within very short time (5–10 min.) after administration of it. However, as it has been generally recognized that protein synthesis comes to a maximum after one or two hours after beginning of the reaction in vitro, it was thought that such ^{75}Se-Met incorporation into the pancreas within short time might be owing to the incorporation into acid-soluble fraction rather than into protein one.

The radioactivity of in vitro ^{75}Se-Met incorporated into the acid-soluble fraction of pancreatic cells was 2–3 times higher than into that of protein fraction. Saturation of the incorporation into acid-soluble fraction of both pancreatic and liver cells was observed after about 30 min. and the incorporation into protein fraction of both cells increased gradually with increasing incubation period. In the case of mouse fasted for 24 hours, the simillar feature of incorporation was also obtained. There was observed no effect of energy sources on the in vitro incorporation into the two fractions of both tissues. The single or mixed presence of amino acid inhibited considerably the incorporation of ^{75}Se-Met and the incorporation of ^{75}Se-Met into the two fractions of pancreas and liver roughly competited with methionine on the basis of Lineweaver-Burk plot. Several inhibitors

had no effect on incorporation into acid-soluble fraction of both tissues. DNP and PCMB, however, inhibited considerably the incorporation into protein of pancreas.

From the results mentioned above, it was suggested that ^{75}Se-Met incorporation after very short time was owing to that into acid-soluble fraction of pancreas rather than into protein fraction, and furthermore, the measurement of an incorporation of test compound into the acid-soluble fraction of pancreas might be usefull for the search for new pancreatic scanning agents.

On the accumulation into mouse pancreas of new two tritiated compounds for the development of pancreatic scanning agents

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^{75}Se-Selenomethionine (^{75}Se-Met) are often utilized as a pancreatic scanning agent. However, it is difficult for doctors to obtain a effective scanning profile with use of ^{75}Se-Met. From a point of this view, more excellent scanning agents are desired together with the development of better scanning systems or instruments. Hence, there are many reports on the development of new pancreatic scanning agents along with this line.

It is well-known that a certain group of compound cause a experimental *Diabetes Mellitus* because of a blocking effect against Zinc in the B-cells of islets of Langerhans in the pancreatic tissue. Amoung such a group, 2-methyl-8-hydroxy-quinoline was used for this experiment. The compounds was tritiated by Wilzbach's method, and purified by repeated paperchromatographic method. After *per os* administration of 10 and 100 μ gram of the $_3$H-compound a mouse, the pancreas, liver, spleen etc. were taken out at several interval of time, liophilized, subjected to combustion in a flask filled with oxygen, and $_3$H radioactivity in the tissues was measured with use of a liquid scintillation counter.

As another compound to test was tried to use rutin and its diglycerol ether (a water-soluble derivative of it), because the vitamin is detected in pancreatic tissue. This compound also was tritiated, purified, and administered in the same was mentioned above. Fianlly, the accumulation were determined as radioactivity in the pancreas. In addition to the above experiment, the *in vitro* incorporation into acid-soluble fraction of these compounds was measured on both pancreatic and liver cells.

As a result, these compounds gave no superior accumulation in the pancreatic tissue in comparison with liver tissue. We are now conducting a study on new derivatives of amino acids.