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Pancreatic Fate of 6-Deoxy-6-[^{125}I]Iodo-D-Glucose

In Vitro Experiments

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The apparent distribution space of 6-deoxy-6-[^{125}I]iodo-D-glucose, recently proposed as a tracer of D-glucose transport, was measured in rat isolated islets, acinar tissue, and pieces of pancreas. While such a space reached a steady-state value corresponding to the ^{3}HOH volume in pancreatic islets within 5 min, it slowly increased in pieces of pancreas and, even after 60-min incubation, remained lower than the ^{3}HOH volume. Moreover, the net uptake of 6-deoxy-6-[^{125}I]iodo-D-glucose by pancreatic pieces was inhibited by unlabeled 6-deoxy-6-iodo-D-glucose, D-glucose, and cytochalasin B, while being less or not affected by these agents in isolated islets. A preferential labeling of the endocrine, relative to exocrine, moiety of the pancreas was documented both by comparing, after 2 min incubation, the uptake of 6-deoxy-6-[^{125}I]iodo-D-glucose by pieces of pancreas from normal vs streptozotocin-injected rats and by comparing the radioactive content of pancreatic islets and acinar tissue obtained from normal rats injected intravenously 3 min before sacrifice with 6-deoxy-6-[^{125}I]iodo-D-glucose. It is proposed, therefore, that advantage could conceivably be taken from the vastly different time course for the uptake of selected monosaccharides by pancreatic islets vs acinar cells in the perspective of imaging of the endocrine pancreas by a non invasive method.

Key Words: Pancreatic gland; pancreatic islets; 6-deoxy-6-iodo-D-glucose.

Introduction

The D-glucose analog 6-deoxy-6-[^{125}I]iodo-D-glucose was recently proposed as a potential tracer for the in vivo determination of cellular D-glucose transport by single-photon emission computer tomography *(1)*. No information was so far available, however, on the uptake of the D-glucose analog by the pancreas. The major aim of the present study is to characterize in vitro the pancreatic uptake of 6-deoxy-6-[^{125}I]iodo-D-glucose, with emphasis on comparison between the exocrine and endocrine moieties of the pancreatic gland.

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Results

Effect of 6-DIG upon Glucose-Stimulated Insulin Release

When groups of eight islets each were incubated for 30 min at 37°C in 1.0 mL of medium, the release of insulin increased from a basal value of 15.9 ± 2.5 to 186.8 ± 5.3 μU/islet per 90 min in the presence of 11.1 m*M* D-glucose (n = 60 in both cases; $p < 0.001$). In the presence of the hexose, unlabeled 6-DIG failed to affect significantly insulin output when tested at concentrations of 1.0 μ*M* (186.0 ± 7.1 μU/islet per 90 min; n = 30), 10.0 μ*M* (190.7 ± 6.5 μU/islet per 90 min; n = 30), or 0.1 m*M* (175.4 ± 9.9 μU/islet per 90 min; n = 30). A modest, but significant ($p < 0.005$), decrease in glucose-stimulated insulin release to 153.3 ± 11.0 μU/islet per 90 min (n = 30) was only recorded in the presence of 1.0 m*M* 6-DIG.

Effect of 6-DIG upon D-glucose Metabolism in Pancreatic Islets

As shown in Table 1, unlabeled 6-DIG (1.0 μ*M* to 1.0 m*M*) failed to affect significantly the utilization of D-[5-^{3}H]glucose, the oxidation of D-[U-^{14}C]glucose and its conversion to either ^{14}C-labeled acidic metabolites or amino acids in islets exposed for 120 min to 11.1 m*M* D-glucose. The paired ratio between D-[U-^{14}C]glucose oxidation and D-[5-^{3}H]glucose utilization was also not significantly affected by 6-DIG.

Distribution Space of 6-D^{125}IG

The third series of experiments was conducted in isolated islets and pieces of pancreas separated, after incubation, from their surrounding medium by centrifugation through a layer of oil into a solution of CsCl in HCl.

After 5 min incubation, the ^{3}HOH and L-[1-^{14}C]glucose distribution space averaged, respectively 4.40 ± 0.21 and 1.58 ± 0.05 nL/islet, yielding an extracellular space that represented 36.5 ± 1.5% of the paired ^{3}HOH space (n = 4 in

Table 1
Effect of 6-DIG Upon the Metabolism of D-glucose (11.1 m*M*) in Isolated Islets

6-DIG	Nil	1.0 μ*M*	10.0 μ*M*	0.1 m*M*	1.0 m*M*
D-[5-^{3}H]glucose utilization[a]	216.8 ± 32.0 (16)	206.2 ± 12.2 (16)	219.5 ± 22.5 (15)	258.3 ± 34.6 (16)	223.0 ± 22.0 (16)
D-[U-^{14}C]glucose oxidation[a]	49.0 ± 5.6 (16)	53.0 ± 2.8 (16)	50.8 ± 4.1 (16)	60.8 ± 4.1 (16)	58.9 ± 3.8 (16)
D-[U-^{14}C]glucose conversion to acidic metabolites[a]	56.2 ± 6.9 (16)	40.8 ± 3.8 (16)	42.9 ± 4.0 (16)	46.9 ± 5.8 (16)	45.1 ± 4.8 (16)
D-[U-^{14}C]glucose conversion to amino acids[a]	18.7 ± 2.4 (16)	17.8 ± 0.9 (16)	18.2 ± 1.1 (16)	19.2 ± 1.0 (16)	18.9 ± 1.3 (16)
D-[U-^{14}C]glucose oxidation/ D-[5-^{3}H]glucose utilization[b]	23.7 ± 1.7 (16)	26.2 ± 1.2 (16)	25.1 ± 1.6 (15)	25.8 ± 1.8 (16)	28.1 ± 1.7 (16)

[a]Results expressed as pmol of D-glucose equivalent per islet and 120 min incubation.
[b]Paired ratio expressed as a percentage.

all cases). The apparent distribution space of 6-D^{125}IG (10.0 μ*M*) averaged, after 15, 30, and 60 min incubation, respectively, 4.35 ± 0.47 (n = 12), 4.19 ± 0.32 (n = 8), and 5.21 ± 0.37 (n = 11) nL/islet. None of the latter three values were significantly different from one another or from the ^{3}HOH distribution space.

The situation found in isolated islets differed from that found in pieces of pancreas (14.2 ± 1.1 mg wet wt; n = 132) in three respects.

First, the measurements of the ^{3}HOH distribution space (835 ± 36 nL/mg wet wt after 5 min incubation, n = 5; 850 ± 49 nL/mg wet wt after 15 min incubation, n = 12; and 855 ± 115 nL/mg wet wt after 60 min incubation; n = 4) and L-[1-^{14}C]glucose distribution space (170 ± 25 nL/mg wet wt after 5 min incubation, n = 5; 177 ± 15 nL/mg wet wt after 15 min incubation, n = 12; and 178 ± 25 nL/mg wet wt after 60 min incubation, n = 4) yielded mean respective values of 847 ± 38 and 176 ± 11 nL/mg wet wt, indicating that the extracellular space represented only 20.6 ± 0.7% of the paired ^{3}HOH space (n = 21 in all cases), a value significantly lower ($p < 0.001$) than that found in islets (*see above*).

Second, in pieces of pancreatic tissue, the apparent distribution space of 6-D^{125}IG (10.0 μ*M*) progressively increased ($p < 0.02$ or less) from 361 ± 25 nL/mg wet wt (n = 17) after 15 min incubation to 458 ± 30 (n = 17) and 649 ± 55 (n = 18) nL/mg wet wt after 30 and 60 min incubation, respectively (Fig. 1). Moreover, even the latter value remained significantly lower ($p < 0.005$) than the ^{3}HOH distribution space.

Last, where cytochalasin B (0.02 m*M*) decreased ($p < 0.005$ or less) to a comparable relative extent ($p > 0.25$), the apparent distribution space of 6-D^{125}IG (10.0 μ*M*) in isolated islets and pancreas pieces, unlabeled 6-DIG or D-glucose (1.0 m*M* each) decreased such a space only in pancreas pieces ($p < 0.01$ or less) and failed to do so in isolated islets (Table 2). Incidentally, if allowance is made for the presence of 6-D^{125}IG in the extracellular space, the inhibitory action of cytochalasin B upon the net uptake of the iodinated hexose was also much more pronounced in pancreas pieces than isolated islets. Indeed, the ratio for such an uptake in the presence/absence of cytochalasin B was about one order of magnitude lower in pancreas pieces (approx 6.2%) than isolated islets (approx 49.9%).

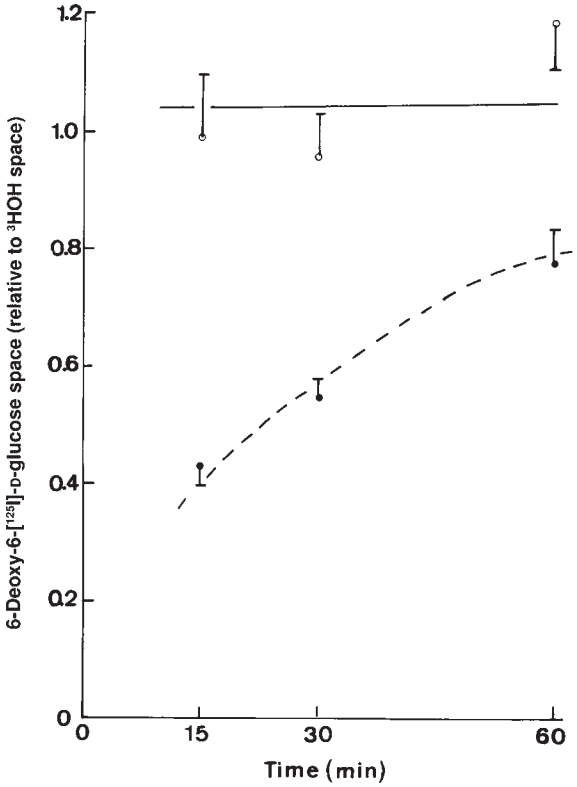

Fig. 1. Apparent distribution space of 6-D^{125}IG (10.0 μ*M*) in isolated islets (open circles and solid line) and pancreas pieces (closed circles and dashed line). Mean values (± SEM) refer to 8–12 (islets) and 17–18 (pieces) individual observations and are expressed relative to the mean ^{3}HOH space found within the same experiment(s).

In the last set of experiments in this series, we have compared the distribution space of 6-D^{125}IG and 3-*O*-[^{14}C-methyl]-D-glucose by isolated islets incubated in the absence or presence of cytochalasin B (0.04 m*M*). The

Table 2
Apparent Distribution Space of 6-D^{125}IG and 3-*O*-[^{14}C-Methyl]-D-Glucose in Isolated Islets and 6-D^{125}IG in Pancreas Pieces after 15 min Incubation

Experiment	Radioactive dose (μ*M*)	Unlabeled agent (m*M*)	Apparent distribution space (% of control 6-D^{125}IG space)	
			Isolated islets	Pancreas pieces
1	6-D^{125}IG (10.0)	Nil	100.0 ± 8.1 (12)	100.0 ± 5.3 (17)
		6-DIG (1.0)	98.9 ± 4.1 (11)	80.9 ± 3.8 (18)
		D-glucose (1.0)	99.2 ± 4.1 (12)	76.2 ± 4.7 (18)
		Cytochalasin B (0.02)	68.2 ± 4.1 (12)	60.0 ± 4.2 (16)
2	6-D^{125}IG (50.0)	Nil	100.0 ± 7.1 (8)	
		Cytochalasin B (0.04)	73.4 ± 3.7 (8)	
	3-*O*-[^{14}C-methyl]-D-glucose (50.0)	Nil	85.5 ± 5.6 (8)	
		Cytochalasin B (0.04)	60.6 ± 5.6 (8)	

concentration of the two monosaccharides amounted to 50.0 μ*M*, in order to reach a sufficient radioactivity in the incubation medium containing the ^{14}C-labeled compound. In these experiments, the distribution space of 6-D^{125}IG, in the absence of cytochalasin B, was again not significantly different ($p > 0.7$) from the ^{3}HOH space (4.17 ± 0.15 nL/islet; $n = 8$). It was decreased to 73.4 ± 3.7% ($n = 8$; $p < 0.01$) of its control value in the presence of cytochalasin B (0.04 m*M*), such a percentage not being significantly different ($p > 0.35$) from that recorded in the prior set of experiments conducted at a lower concentration of the mould metabolite (0.02 m*M*). Even in the presence of cytochalasin B, however, the distribution space of 6-D^{125}IG remained much higher ($p < 0.001$) than the L-[1-^{14}C]glucose space, also in good agreement with our prior observations. Cytochalasin B decreased ($p < 0.01$) the distribution space of 3-*O*-[^{14}C]methyl-D-glucose to 70.8 ± 6.5% of its control value. The relative extent of such a decrease was comparable to that found with 6-D^{125}IG. Whether in the absence or presence of cytochalasin B, the distribution space of the ^{14}C-labeled D-glucose analog was not significantly different from that of 6-D^{125}IG. Pooling all available data, however, the distribution space of 3-*O*-[^{14}C]methyl-D-glucose only represented 84.0 ± 4.6% ($n = 16$; $p < 0.02$) of the mean corresponding value found under the same experimental conditions with 6-D^{125}IG(100.0 ± 4.2%; $n = 16$).

Uptake of 6-D^{125}IG

In order to assess the net uptake of 6-D^{125}IG by islets, the results obtained by the oil technique, used in all prior experiments, were compared to those recorded in islets (and pieces of either acinar tissue or whole pancreas) that underwent seven successive washes (about 5 min each) at 20°C before measuring their radioactive content. As illustrated in Fig. 2, in this procedure, the last washing media contained no more than about 0.1‰ of the initial radioactive content of the incubation medium.

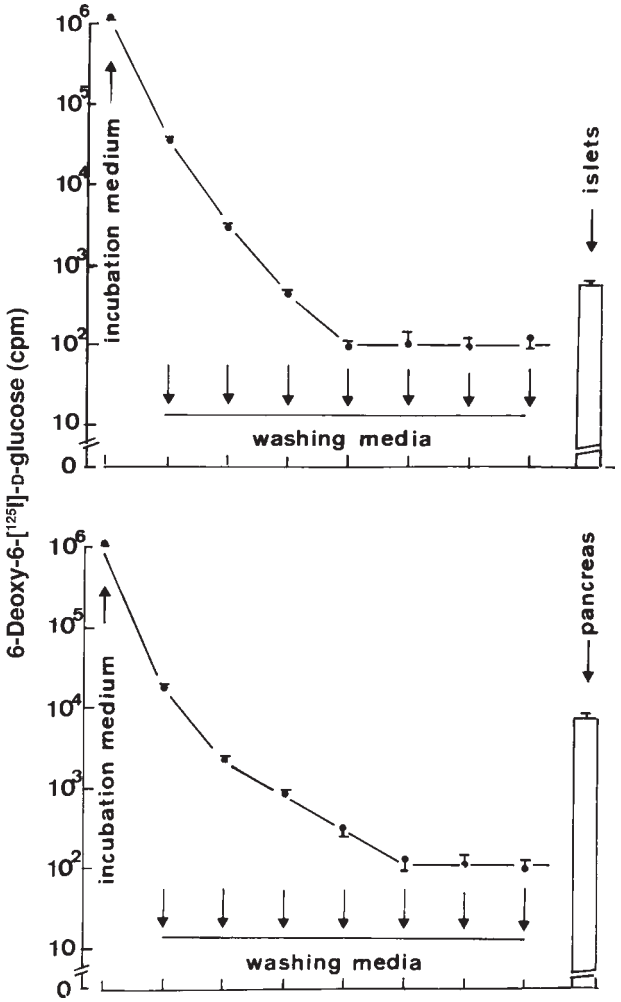

Fig. 2. Radioactive content of the incubation medium (0.3 mL), successive washing media (0.3 mL each) and either islets (upper panel) or pancreas pieces (lower panel) after incubation of groups of 100 islets each or pieces of pancreas (12.3 ± 2.7 mg wet wt) for 30 min in the presence of 6-D^{125}IG (10.0 μ*M*). Mean values (± SEM) refer to 8 (lower panel) and 16 (upper panel) individual determinations.

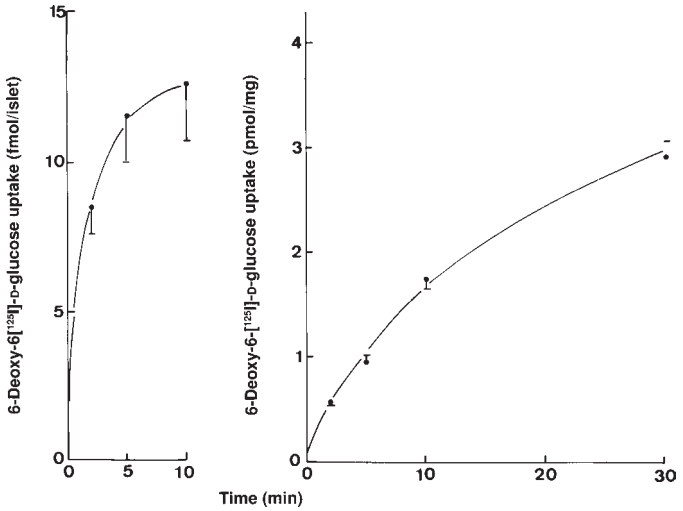

Fig. 3. Time course for the net uptake of 6-D^{125}IG (10.0 μ*M*) by isolated islets (left) and pieces of pancreatic tissue (right) incubated at 37°C. The measurements were made after either four washes (pieces of pancreas) or five washes (islets) at 20°C. Mean values (± SEM) refer to 10 (pieces of pancreas) or 16–17 (islets) individual measurements.

The results obtained by such a washing procedure were compared to those collected in the oil technique. However, in order to reach a meaningful comparison, only the pellet found at the bottom of the CsCl solution in HCl was now examined for its radioactive content, instead of the entire CsCl phase in previous experiments.

In pieces of exocrine tissue, the net uptake of 6-D^{125}IG (10.0 μ*M*) over 30 min incubation was not significantly different when estimated by either the oil separation procedure (0.220 ± 0.028 pmol/mg wet wt; $n = 5$) or extensive washing technique (0.229 ± 0.015 pmol/mg wet wt; $n = 3$). It was much lower, however, than that recorded in pieces of pancreatic tissue (*see below*), as expected from the interstitial edema of the acinar tissue caused by the injection of the Hank's solution in the procedure for the isolation of islets.

In pieces of pancreas tissue, the net uptake of 6-D^{125}IG (10.0 μ*M*) after 30 min incubation, as measured by the oil technique, indeed amounted to 1.096 ± 0.119 pmol/mg wet wt ($n = 7$). Moreover, this value was somewhat lower ($p < 0.05$) than that recorded, within the same experiments, after extensive washing, i.e., 1.581 ± 0.149 pmol/mg wet wt ($n = 8$), a difference probably attributable to the fact that, in the oil procedure, all pieces of pancreas did not always pass through the oil layer.

In isolated islets, also incubated for 30 min in the presence of 10.0 μ*M* 6-D^{125}IG, the corresponding values were 11.7 ± 0.8 fmol/islet ($n = 8$) in the oil technique and 14.7 ± 1.8 fmol/islet ($n = 16$) in the washing procedure, these two mean values not being significantly different from one another.

Assuming a wet weight of 5.0 μg/islet, these results yielded ratios between the net uptake of 6-D^{125}IG by isolated islets and pancreas pieces of 2.14 ± 0.27 (oil technique) and 1.86 ± 0.29 (washing procedure), with an overall mean value of 1.96 ± 0.21 (df = 35). In the third series of experiments mentioned above, such a ratio averaged 2.01 ± 0.18 (df = 46) when comparing the mean value for 6-D^{125}IG uptake by islets to that recorded after 30 min incubation in pancreas pieces (oil technique in both cases).

Further experiments, conducted by the washing procedure, were aimed at scrutinizing the influence of some environmental factors on 6-D^{125}IG net uptake.

We have first investigated the time course for the net uptake of 6-D^{125}IG by islets and pieces of pancreatic tissue over short periods of incubation (Fig. 3). In the islets, the value recorded after only 2 min incubation already averaged 67.1 ± 17.1% (df = 31) of the mean reading at the tenth minute of incubation. As a matter of fact, the two series of measurements were not quite significantly different from one another ($p < 0.07$). A close-to-equilibrium value was reached within 5 min of incubation. In pieces of pancreatic tissue, the half-time for equilibration was much longer than in islets. The measurements made after 2 min incubation only represented 33.3 ± 3.5% (df = 18) of the mean value recorded after 10 min incubation, the net uptake of the iodinated hexose further and markedly increasing ($p < 0.001$) during a more prolonged incubation (30 min). Assuming that the net uptake of the iodinated D-glucose by the pieces of pancreas increased exponentially towards a steady-state value (U_{max}) corresponding to the equilibration between extracellular and intracellular concentrations, the K value for such an uptake (U) according to the equation $U = U_{max}(1 - e^{-Kt})$, was virtually identical when calculated from either the first two measurements (min 2 and 5) in Fig. 3 ($K = 0.022$ min^{-1}) or the last two measurements (min 30 and 60) in Fig. 1 ($K = 0.023$ min^{-1}), yielding a half-life close to 30 min.

In the last set of experiments in this series, we have investigated the influence of temperature and cytochalasin

B upon the release of 6-D^{125}IG during the washing procedure. For this purpose, groups of 100 islets each were first incubated for 30 min at 37°C in the presence of 6-D^{125}IG. The results obtained after 4 washes at 20°C were compared to those recorded after the same number of washes conducted at 4°C in the presence of cytochalasin B (0.1 m*M*). The final radioactive content of the islets in the former procedure averaged 47.6 ± 3.2% (n = 6; $p < 0.01$) of the mean value (60.2 ± 12.3 fmol/islet; n = 6) found, within the same experiments, in the latter protocol.

Such a protocol was used, therefore, to optimize the labeling of the islets in the perspective of autoradiographic studies. However, it was observed that only 2.4 ± 0.4% (n = 5) of the radioactivity present in the islets after the last of the four washes made at 4°C in the presence of cytochalasin B remained associated with the islet pellet after fixation with a 4% solution (v/v) of glutaraldehyde in Millonig buffer (1.0 mL) and two further washes in the same buffer (0.1 *M* phosphate buffer; pH 7.4) now containing 30 m*M* D-glucose. In these experiments, the total radioactivity recovered in the glutaraldehyde solution, the two further washes, and the islet pellet were comparable ($p > 0.25$) to that otherwise found in the islets after the four washes made at 4°C with the bicarbonate-buffer solution containing cytochalasin B (*see preceding paragraph*).

In the light of these findings, two other approaches were used to assess whether advantage could be taken from the vastly different time course for 6-D^{125}IG uptake by pancreatic islets and acinar tissue to achieve a preferential labeling of the islets after a short exposure of the pancreas to the iodinated hexose. In the first approach, pieces of pancreatic tissue from either control or STZ rats were incubated for only 2 min at 37°C in the presence of 10 μ*M* 6-D^{125}IG. In the second approach, the radioactive content of the islets and acinar tissue was measured in pancreases obtained 3 min after the intravenous injection of 6-D^{125}IG to normal rats.

After only 2 min incubation, the net uptake of 6-D^{125}IG (10.0 μ*M*) by pieces of pancreas averaged in control rats 1.10 ± 0.15 pmol/mg (n = 10), as distinct ($p < 0.025$) from only 0.68 ± 0.03 pmol/mg (n = 8) in STZ rats. It represented in the control and diabetic rats, respectively, 22.3 ± 3.0% (df = 18) and 15.6 ± 1.2% (df = 16) of the corresponding mean value (n = 10 in all cases) found after 60 min incubation. Thus, even when expressed relative to the paired value recorded after prolonged incubation of pieces of pancreas from the same animal, the early measurements made after 2 min incubation remained higher ($p < 0.06$) in control rats than diabetic animals. After 60 min incubation, the net uptake of 6-DIG averaged, in these experiments, 4.64 ± 0.14 pmol/mg (n = 20).

As already mentioned, in the last series of experiments, six normal fed rats (229 ± 3 g body wt) were injected intravenously with 6-D^{125}IG (12 μCi; 0.04 μmol) in saline and killed by decapitation 3 min later. Prior to injection, 6-D^{125}IG had been purified by anion exchange chromatography, resulting in removal of about 14.8% of the initial radioactivity. The apparent volume of distribution of 6-D^{125}IG, as judged from the plasma radioactivity, averaged 2.23 ± 0.55 mL/g body wt (n = 6). Pancreatic islets (54 ± 13 islets/rat; n = 6) and pieces of acinar tissue (41.4 ± 2.2 mg wet wt; n = 18) from these rats were isolated using a Hank's solution maintained at 4°C (except for the period of incubation with collagenase) and containing 20 μ*M* cytochalasin B, and eventually sonicated (three times for 10 s each) in 1.0 mL of H_2O. Aliquots (0.1 mL each) of the homogenates were examined for their protein content, i.e., 2.45 ± 0.29 μg/islet (n = 6) and 84.6 ± 3.4 μg/mg wet wt for the edematous acinar pieces (n = 18). The rest of the homogenate (0.9 mL) was examined for its radioactive content. Relative to the paired plasma radioactive content and excluding one abnormally high value, the radioactive content of the islets corresponded to an apparent volume of distribution of 7.01 ± 1.24 nL/μg protein (n = 3), as compared ($p < 0.001$) to only 0.99 ± 0.09 nL/μg protein (n = 18) in the acinar tissue. Assuming that the protein content represents one-sixth of wet wt, the apparent volume of distribution in islets was compatible with the equilibration of 6-D^{125}IG concentration across the plasma membrane of islet cells, while not exceeding about 16.5 ± 1.5% of estimated wet wt in acinar pieces. The latter value is indeed close to that found in the whole pancreatic gland 3 min after injection of 6-D^{125}IG to streptozotocin-injected rats treated with insulin *(2)*. Such a low value also contrasts with that found in erythrocytes. Thus, 3 min after injection of 6-D^{125}IG, the paired erythrocyte/plasma ratio in radioactivity averaged, in the present experiments, 68.9 ± 4.3% (n = 6).

Discussion

The present results indicate that 6-deoxy-6-[^{125}I]iodo-D-glucose is taken up by both endocrine and exocrine pancreatic cells. No adverse effects of unlabeled 6-DIG upon either the metabolism or insulinotropic action of D-glucose (11.1 m*M*) was observed, at least up to a concentration of 0.1 m*M*, largely in excess of that required for labeling of the pancreas by 6-deoxy-6-[^{125}I]iodo-D-glucose whether in vitro or in vivo.

The time course for the uptake of the iodinated D-glucose analog differed vastly in islets and acinar pancreatic cells. It was also more severely affected by such agents as unlabeled 6-DIG, D-glucose, and cytochalasin B in the case of pancreatic pieces than in the case of isolated islets. In the islets, the apparent volume of distribution reached within 5 min a value identical to the intracellular ^3H_2O space. A different situation prevails, however, for the uptake of either D-[U-^{14}C]glucose or 3-*O*-[^{14}C]methyl-D-glucose by islets, in which case the apparent distribution space remains lower than the intracellular ^{3}HOH space *(3)*. Likewise, in the present study, the apparent distribution space of 6-deoxy-6-[^{125}I]iodo-D-glucose exceeded that of 3-*O*-[^{14}C]methyl-

D-glucose. This difference was unexpected since 6-DIG cannot undergo phosphorylation at variance with D-glucose and, albeit to a quite modest extent, 3-O-methyl-D-glucose *(1,4)*.

The comparison between the uptake of 6-deoxy-6-[^{125}I]iodo-D-glucose, over 2 min incubation, by pancreatic pieces from control vs streptozotocin-injected rats, as well as the comparison between the radioactive content of isolated islets vs acinar tissue obtained from normal rats killed 3 min after the intravenous injection of 6-deoxy-6-[^{125}I]iodo-D-glucose, indicated that advantage could be taken of the above-mentioned difference in the time course for the uptake of the iodinated D-glucose analog by the two moieties of the pancreatic gland to label preferentially endocrine relative to exocrine cells. Thus, per μg protein, the net uptake of 6-deoxy-6-[^{125}I]iodo-D-glucose was about seven times higher in the islets than in the acinar tissue.

Further work is required, however, to investigate whether such a difference is sufficiently marked to allow a reliable assessment of the endocrine pancreatic mass in vivo by a non invasive imaging procedure. There are two arguments against such a view. First, because the endocrine pancreas represents only about 1% of the total pancreatic mass, even a sevenfold difference in 6-deoxy-6-[^{125}I]iodo-D-glucose uptake by endocrine and exocrine cells, when expressed per μg protein, would imply that the overall uptake of the iodinated D-glucose analog by the pancreatic gland would only be attributable for about 6.6% to its endocrine moiety. Second, even in the islets, the maximal apparent distribution space of 6-deoxy-6-[^{125}I]iodo-D-glucose did not exceed the total ^{3}HOH space. Hence, the in vivo distinction between intracellular and extracellular (e.g., plasmatic and interstitial) 6-deoxy-6-[^{125}I]iodo-D-glucose may be hampered by such a situation. Nevertheless, the present study may pave the way to the use of selected monosaccharides for imaging of the endocrine pancreas by non invasive imaging procedure. Indeed, advantage could conceivably be taken of the cell-specific expression of both the GLUT2 and glucokinase genes in insulin-producing cells (and hepatocytes) to allow for the uptake of selected monosaccharides by islet cells, at the exclusion of acinar cells, and for their further phosphorylation in the islet cells, in a manner somehow comparable to that prevailing for the labeling of several cell types by 2-deoxy-2-[^{18}F]fluoro-D-glucose *(5)*.

Materials and Methods

Unlabeled 6-deoxy-6-iodo-D-glucose (6-DIG) was kindly provided by Dr. C. Morin (Laboratoires d'Etudes Dynamiques et Structurales de la Sélectivité, Université Joseph Fournier, Saint-Martin-d'Hères, France) and 6-deoxy-6-[^{125}I]iodo-D-glucose by M. L. Mauclaire (CIS bio international, Gif-sur-Yvette, France).

All experiments were conducted in female Wistar rats (B & K Limited, Hull, UK or Iffa Credo, L'Arbresle, France) given free access to food (KM-04-k12; Pavan Service, Oud Turnhout, Belgium) and tap water up to the time of sacrifice. One set of experiments was conducted in rats injected intravenously with streptozotocin (0.25 μmol/g body wt) 3 d before sacrifice. The plasma D-glucose concentration *(6)* averaged in these animals 27.11 ± 1.05 m*M*, as compared to 9.82 ± 0.22 m*M* in control rats ($n = 2$ in both cases; $p < 0.005$). In such STZ rats, the insulin content of the pancreas is decreased to less than 5% of the control value.

The methods used to measure insulin release *(7)* and D-glucose metabolism *(8–10)* in isolated pancreatic islets, the apparent distribution space of selected molecules in biological samples separated, after incubation, from their surrounding medium by centrifugation through a layer of oil into a solution of CsCl in HCl *(3)*, and the protein content of tissue homogenates *(11)* were previously described in the cited references.

The present experiments were approved by the Commission d'Ethique du Bien-Etre Animal of our faculty.

All results, including those already mentioned, are expressed as mean values ± SE, together with the number of individual observations (n) or degree of freedom (df). The statistical significance of differences between mean values was assessed by the use of Student's two-tailed t-test.

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