The Structure-Function Relationship of GLP-1 Related Peptides in the Endocrine Function of the Canine Pancreas

AKIRA OHNEDA, KINUKO OHNEDA*, MAKOTO OHNEDA†, FUMIAKI KOIZUMI‡, SHINICHI OHASHI§, KOICHI KAWAI// and SEIJI SUZUKI//

Health Center, Tohoku University, *the Third Department of Internal Medicine, †the Second Department of Internal Medicine, and ‡the Department of Clinical and Laboratory Medicine, Tohoku University School of Medicine, Sendai 980, §Research Institute for Polymers and Textiles, Tsukuba, and // the Department of Internal Medicine, Institute of Clinical Medicine, University of Tsukuba, Tsukuba 305

OHNEDA, A., OHNEDA, K., OHNEDA, M., KOIZUMI, F., OHASHI, S., KAWAI, K. and SUZUKI, S. The Structure-Function Relationship of GLP-1 Related Peptides in the Endocrine Function of the Canine Pancreas. Tohoku J. Exp. Med., 1991, 165 (3), 209-221 — In order to clarify the relationship between the structure and function of glucagon-like peptide (GLP) 1 in the endocrine function of the pancreas, the response of insulin and glucagon to various synthetic GLP-1-related peptides was investigated in anesthetized dogs. GLP-1-related peptides were administered in a dosage of 400 pmol within 10 min into the pancreatic artery during glucose or arginine infusion and the changes in plasma insulin and glucagon in the pancreatic vein were studied. GLP-1 (7-36) and (7-37), as well as glucagon enhanced insulin release during glucose infusion, whereas neither GLP-1 (1-37), (7-20), (6-37) nor (8-37) stimulated insulin release. The administration of GLP-1 (1-37), (7-36) and (7-37) reduced glucagon release during glucose infusion. When arginine was infused, GLP-1 (7-20), (7-36), (7-37), and glucagon enhanced insulin release. In contrast, glucagon release was increased by the administration of GLP-1 (7-20), (8-37), and (7-37). The present study indicates that histidine at the 7th position of GLP-1 is important in eliciting biological action and that only truncated GLP-1 (7-36), (7-37), and (7-20) showed an insulinotropic action as strong as glucagon in dogs. Furthermore, it is suggested that the response of insulin and glucagon to GLP-1-related peptides is dependent on a background condition. —— insulin; glucagon; local circulation of pancreas

Research on preproglucagon revealed that the precursor of glucagon is processed in the A-cell of the pancreas and in the L-cell of the intestine, yielding glucagon-like peptides (GLP) 1 and 2 in addition to glucagon or glicentin (Mojsov

Received August 5, 1991; revision accepted for publication October 4, 1991.
et al. 1986; Ørskov et al. 1986). Although GLP-1 (1-37) has similarities in its amino acid sequence to glucagon, this peptide did not show any glucagon action, such as insulinotropic or glycogenolytic action (Ghiglione et al. 1984). However, it has been reported that a truncated GLP-1 (7-37) elicited a strong insulin stimulating action (Mojsov et al. 1987; Holst et al. 1987; Shima et al. 1988; Kawai et al. 1989). Furthermore, experimental studies revealed that GLP-1 is secreted during the ingestion of nutrients in both pig and man (Ørskov et al. 1986; Kreymann et al. 1987). Therefore, at present, the truncated GLP-1 (7-37) or (7-36) has been considered as a candidate of gut hormones in the enteroinsular axis (Mojsv et al. 1987; Holst et al. 1987; Shima et al. 1988). As shown in the in vitro studies, the difference in structure of the GLP-1 peptides revealed a large difference in their biological actions (Schmidt et al. 1985; Mojsv et al. 1987; Matsuyama et al. 1988; Shima et al. 1988; Suzuki et al. 1989). Therefore, in order to elucidate the structure/function relationship of GLP-1 related peptides in the endocrine pancreas, the present study was performed using an in situ perfusion of the canine pancreas.

MATERIALS AND METHODS

The GLP-1 related peptides used in the study, GLP-1 (1-37) amide, (7-37), (7-36) amide, (7-20), (6-37) amide and (8-37) amide, were synthesized by the stepwise solid phase method, as described previously (Kawai et al. 1989; Suzuki et al. 1989). Porcine glucagon was donated by the Eli Lilly Co. (Indianapolis, IN, USA). In the present study 34 healthy mongrel dogs weighing 12 to 15 kg were used. After an overnight fast, the animals were anesthetized with sodium pentobarbital and an in situ local circulation preparation of the pancreas was made as reported previously (Ohneda et al. 1977). Briefly, the abdomen was opened by a midline incision. A glass T-cannula connected to a teflon catheter was inserted into the superior pancreaticoduodenal artery (PA). A plastic cannula was inserted into the superior pancreaticoduodenal vein (PV). Another plastic needle was inserted into the femoral artery (FA). After the completion of the operation, saline was infused into the PA at a rate of 2 ml/min. Approximately one hour after the operation was completed, the experiment was started. After the first samples were obtained, 0.5% glucose or 0.5% arginine solution with 0.2% bovine serum albumin was administered at a rate of 2 ml/min throughout the experiment. Twenty min after the infusion of glucose or arginine, the first GLP-1 peptide was infused into the PA for 10 min. The second and third peptides were similarly administered at 40 min-intervals. These peptides were administered in a dosage of 400 pmol. Blood samples were collected from the PV and FA before and 1, 3, 6, 10, 15, 20, 30 and 40 min after the start of the infusion of each peptide. Blood samples for hormone assay were drawn from the PV in amount of 4 ml, poured into a glass tube containing 1000 KIU of aprotinin (Trasylol®; Bayer Co., Leverkusen, Germany) and 10 mg of EDTA and refrigerated throughout the experiment. Plasma was separated by centrifugation at 4°C and kept at -20°C until the assay. Blood samples for glucose measurement were drawn from the FA and blood glucose was determined by the glucose oxidase method. Plasma insulin (IRI) was determined by immunoassay using the two-antibody system (Morgan and Lazarow 1963). Plasma glucagon (IRG) was measured by immunoassay using an antiserum (G21), specific to the C-terminal portion of glucagon, and porcine glucagon as a standard (Ohneda et al. 1975). In the present study, the mean values and standard errors of the mean ± s.e. were calculated. Statistical analyses for the changes in blood glucose and plasma hormones following each peptide were performed by multiple
comparison using analysis of variance. For a comparison of the response of insulin and glucagon, the maximal response of these hormones for 20 min after the start of the peptide infusion was calculated and compared with Student’s $t$-test. The p-value of less than 5% is considered significant.

**RESULTS**

The effect of GLP-1 related peptides upon insulin and glucagon release during glucose infusion

**GLP-1 (1-37), (7-37), and glucagon**

GLP-1 (1-37), (7-37), and glucagon were administered successively to a group of 6 dogs (Fig. 1). Fasting blood glucose was $6.7 \pm 0.47$ mmol/liter and did not change after glucose infusion into the PA. The infusion of GLP-1 (1-37) did not elicit any significant change in blood glucose. The plasma fasting IRI was $118 \pm 36.9 $ $\mu$U/ml and increased slightly to a level of $155 \pm 45.2 $ $\mu$U/ml after the glucose infusion. The plasma IRI decreased slightly 1 min after the GLP-1 (1-37) infusion but did not differ thereafter from the preinfusion level. The plasma IRG was $737 \pm 182 $ pg/ml at fasting and slightly decreased after the glucose infusion. The plasma IRG fell significantly to a level of $345 \pm 108 $ pg/ml 1 min following the infusion of GLP-1 (1-37) ($p < 0.01$). After the cessation of GLP-1 (1-37) the

Fig. 1. Effects of GLP-1 (1-37), (7-37), and glucagon upon the changes in blood glucose (BG), plasma insulin (IRI) and glucagon (IRG) during glucose infusion in a group of 6 dogs. Mean$ \pm $s.e.
plasma IRG returned to the preinfusion level.

Blood glucose did not change following the infusion of GLP-1 (7-37). The plasma IRI increased slightly from the preinfusion level of $145 \pm 51.5$ to $247 \pm 122 \mu U/ml$ 1 min after the infusion of GLP-1 (7-37), but the change did not reach statistical significance. The plasma IRG decreased slightly after the infusion of GLP-1 (7-37) ($p < 0.05$).

After the glucagon administration, blood glucose increased significantly from the preinfusion level of $6.8 \pm 0.75$ mmol/liter to a peak of $8.0 \pm 1.05$ mmol/liter at 20 min ($p < 0.01$). The plasma IRI rose from the preinfusion level of $150 \pm 27.1$ to $247 \pm 73 \mu U/ml$ at 3 min and fell immediately after the cessation of glucagon. However, these changes did not show a statistical significance. The plasma IRG increased immediately following the infusion of glucagon to a level of $3867 \pm 95$ pg/ml, decreasing after the cessation of glucagon ($p < 0.01$).

**GLP-1 (7-20), (7-36), and glucagon**

GLP-1 (7-20), (7-36), and glucagon were successively administered into the PA to a group of 5 dogs (Fig. 2). The preinfusion level of blood glucose was $6.3 \pm 0.41$ mmol/liter and did not change after the infusion of GLP-1 (7-20). The plasma IRI was $243 \pm 59.2 \mu U/ml$ at fasting and slightly increased to $376 \pm 97.0 \mu U/ml$ 20 min after the glucose infusion. Following the GLP-1 (7-20) infusion, the plasma IRI did not change significantly. The plasma IRG decreased slightly from the fasting level of $595 \pm 217$ to $495 \pm 243$ pg/ml after the glucose infusion.

![Fig. 2. Effects of GLP-1 (7-20), (7-36), and glucagon upon the changes in blood glucose (BG), plasma insulin (IRI) and glucagon (IRG) during glucose infusion in a group of 5 dogs. Mean±s.e.](image-url)
The infusion of GLP-1 (7–20) did not affect the plasma IRG in the PV significantly.

Blood glucose did not change following the administration of GLP-1 (7–36). The plasma IRI increased from the preinfusion level of 276±34 μU/ml to a peak of 400±67 μU/ml 3 min after the infusion of GLP-1 (7–36), returning to the preinfusion level after 30 min. However, these changes did not show a statistical difference. The plasma IRG fell slightly but significantly following the GLP-1 (7–36) administration (p<0.01).

Blood glucose increased slightly from the preinfusion level of 6.2±0.33 to a peak of 6.5±0.35 mmol/liter following the glucagon infusion (p<0.01). The plasma IRI increased from the preinfusion level of 319±50.9 to a peak of 604±78 μU/ml at 6 min, (p<0.05). The plasma IRG increased to a level of 3322±485 pg/ml following the glucagon administration (p<0.01).

GLP-1 (6–37), (8–37), and (7–37)

GLP-1 peptides (6–37), (8–37), and (7–37) were administered to a group of 6 dogs (Fig. 3). Blood glucose did not change following the infusion of GLP-1 (6–37). The plasma IRI increased slightly from 109±36 to 129±34 μU/ml after the glucose infusion, but did not elicit any significant change after the GLP-1 (6–37) administration. The plasma IRG decreased slightly following the infusion of GLP-1 (6–37), although not significantly.

Blood glucose did not change significantly following the infusion of GLP-1 (8–37). The plasma IRI increased from the preinfusion level of 150±28 to 309±
190 μU/ml after the GLP-1 (8-37) infusion, but these changes did not elicit any significant difference. The plasma IRG decreased transiently following the infusion of GLP-1 (8-37) \((p < 0.01)\).

Following the infusion of GLP-1 (7-37), blood glucose did not change. GLP-1 (7-37) induced an increase in the plasma IRI \((p < 0.01)\). The plasma IRG fell significantly following the GLP-1 (7-37) administration \((p < 0.05)\).

In these experiments with the glucose infusion, insulin release was enhanced by GLP-1 (7-37), (7-36) and glucagon. In contrast, glucagon secretion was not enhanced with the administration of these peptides investigated but was rather decreased in response to GLP-1 (1-37), (7-37), (7-36) and (8-37).

**The effect of GLP-1 related peptides upon insulin and glucagon release during arginine infusion**

In order to elucidate the effect of GLP-1 peptides upon the plasma IRI as well as IRG, GLP-1 peptides were administered into the PA during the infusion of 0.5% arginine.

**GLP-1 (1-37), (7-37), and glucagon**

These three peptides were administered successively to a group of 5 dogs (Fig. 4). Blood glucose rose slightly but significantly from the initial level of 5.1 ± 0.53 to 5.6 ± 0.59 mmol/liter following the infusion of 0.5% arginine \((p < 0.05)\). However, blood glucose did not change after the administration of GLP-1 (1-37).

![Fig. 4. Effects of GLP-1 (1-37), (7-37), and glucagon upon the changes in blood glucose (BG), plasma insulin (IRI) and glucagon (IRG) during arginine infusion in a group of 5 dogs. Mean±S.E.](image-url)
There was a tendency to decrease in the plasma IRI following the infusion of GLP-1 (1-37), although not significantly. The plasma IRG did not change after the GLP-1 (1-37) infusion.

The administration of GLP-1 (7-37) did not elicit any changes in blood glucose. The plasma IRI increased from the preinfusion level of $177 \pm 52.6$ to $416 \pm 217 \mu U/ml$ 3 min after the infusion of GLP-1 (7-37), but the change did not show a statistical significance because of wide deviation. The plasma IRG increased from $897 \pm 395$ to a peak of $1116 \pm 352$ pg/ml 10 min after the infusion of GLP-1 (7-37), although the change was not significant.

The glucagon infusion induced a slight increase in blood glucose to a peak of $6.7 \pm 0.72$ mmol/liter after 15 min ($p < 0.01$). The plasma IRI increased from the baseline level of $168 \pm 79.2$ to a peak of $292 \pm 113 \mu U/ml$ after 6 min ($p < 0.01$). The plasma IRG reached a peak of $3010 \pm 6.7$ pg/ml after 3 min ($p < 0.01$) and remained elevated during the infusion of glucagon.

GLP-1 (7-20), (7-36), and glucagon

These three peptides were successively administered during the arginine infusion to a group of 6 dogs (Fig. 5). Blood glucose did not change significantly after the infusion of GLP-1 (7-20). The plasma IRI rose slightly from the preinfusion level of $97.5 \pm 18.2$ to a peak of $183 \pm 57.9 \mu U/ml$ 3 min after the GLP-1 (7-20) infusion, although not significantly. The plasma IRG gradually
increased following the GLP-1 (7-20) infusion \((p < 0.01)\).

Blood glucose did not change after the infusion of GLP-1 (7-36) but decreased slightly after 30 and 40 min. The plasma IRI rose from the initial level of \(97 \pm 26.4 \mu U/ml\) to a peak of \(344 \pm 156 \mu U/ml\) 1 min after the infusion of GLP-1 (7-36) \((p < 0.01)\). The plasma IRG increased slightly after the GLP-1 (7-36) administration, although not significantly.

Following the administration of glucagon, blood glucose rose slightly but this change did not show a statistical significance. The plasma IRI increased significantly after the glucagon infusion \((p < 0.01)\). The plasma IRG increased to a peak of \(3983 \pm 16 \text{ pg/ml}\) following the glucagon infusion \((p < 0.01)\).

**GLP-1 (6-37), (8-37), and (7-37)**

These three peptides were successively administered during the arginine infusion to a group of 6 dogs (Fig. 6). Blood glucose did not change at all after the GLP-1 (6-37) infusion. The plasma IRI increased slightly after the GLP-1 (6-37) infusion but the change did not show a statistical significance because of wide deviation. The plasma IRG did not change significantly following the GLP-1 (6-37) administration.

Blood glucose did not change after the GLP-1 (8-37) administration. The plasma IRI gradually decreased following the GLP-1 (8-37) infusion, but the change was not significant. The plasma IRG increased slightly after the administration of GLP-1 (8-37), although not significantly.

The administration of GLP-1 (7-37) did not elicit any changes in blood glucose (BG), plasma insulin (IRI) and glucagon (IRG) during arginine infusion in a group of 6 dogs. Mean ± s.e.

![Fig. 6. Effects of GLP-1 (6-37), (8-37), and (7-37) upon the changes in blood glucose (BG), plasma insulin (IRI) and glucagon (IRG) during arginine infusion in a group of 6 dogs. Mean ± s.e.](image-url)
glucose. The plasma IRI rose from the preinfusion level of 233 ± 74.2 μU/ml to a peak of 605 ± 299 μU/ml 6 min after the GLP-1 (7-37) infusion (p < 0.01). The plasma IRG decreased slightly following the GLP-1 (7-37) infusion, although not significantly.

From these experiments with the arginine infusion, it was demonstrated that insulin secretion was enhanced following the administration of GLP-1 (7-20), (7-36), (7-37) or glucagon. Contrary to the experiments with the glucose infusion, glucagon release was increased in response to the administration of GLP-1 (7-20), (7-36), (7-37) or (8-37).

A comparison of the effects of GLP-1 peptides on insulin and glucagon secretion

The effects of GLP-1 peptides upon insulin and glucagon secretion during glucose infusion are shown in Table 1. The maximum response indicated that among these seven peptides investigated, GLP-1 (7-37), (7-36), and glucagon significantly enhanced insulin release. However, there were no differences in the responses to these three peptides. In contrast, GLP-1 (1-37), (7-20), (6-37), and

<table>
<thead>
<tr>
<th>Peptides</th>
<th>N</th>
<th>Insulin (μU/ml)</th>
<th>Glucagon (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1-37)</td>
<td>6</td>
<td>21.6 ± 25.7</td>
<td>-225 ± 69.1*</td>
</tr>
<tr>
<td>(7-20)</td>
<td>5</td>
<td>-1.6 ± 16</td>
<td>228 ± 123</td>
</tr>
<tr>
<td>(7-36)</td>
<td>5</td>
<td>192 ± 41.5**</td>
<td>-34 ± 98</td>
</tr>
<tr>
<td>(6-37)</td>
<td>6</td>
<td>78.5 ± 61.2</td>
<td>-108 ± 75.5</td>
</tr>
<tr>
<td>(8-37)</td>
<td>6</td>
<td>73.6 ± 42.8</td>
<td>99.1 ± 51.5</td>
</tr>
<tr>
<td>(7-37)</td>
<td>12</td>
<td>114 ± 27.0**</td>
<td>-117 ± 40.8*</td>
</tr>
<tr>
<td>Glucagon</td>
<td>11</td>
<td>214 ± 48.7**</td>
<td>3021 ± 327**</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.01.

Table 2. Maximum response of insulin and glucagon to various GLP-1-related peptides during arginine infusion

<table>
<thead>
<tr>
<th>Peptides</th>
<th>N</th>
<th>Insulin (μU/ml)</th>
<th>Glucagon (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1-37)</td>
<td>5</td>
<td>-111 ± 117</td>
<td>112 ± 86.7</td>
</tr>
<tr>
<td>(7-20)</td>
<td>6</td>
<td>165 ± 58.5*</td>
<td>539 ± 85.7**</td>
</tr>
<tr>
<td>(7-36)</td>
<td>6</td>
<td>158 ± 31.3**</td>
<td>328 ± 524</td>
</tr>
<tr>
<td>(6-37)</td>
<td>6</td>
<td>249 ± 284</td>
<td>165 ± 103</td>
</tr>
<tr>
<td>(8-37)</td>
<td>6</td>
<td>-34 ± 69.5</td>
<td>226 ± 84.7*</td>
</tr>
<tr>
<td>(7-37)</td>
<td>11</td>
<td>407 ± 132*</td>
<td>220 ± 94.1*</td>
</tr>
<tr>
<td>Glucagon</td>
<td>11</td>
<td>331 ± 100**</td>
<td>1731 ± 325**</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.01.
(8–37) did not affect significantly the release of insulin. As far as glucagon secretion is concerned, GLP-1 (1–37) and (7–37) rather reduced glucagon release from the pancreas.

During the arginine infusion, in addition to GLP-1 (7–36), (7–37) and glucagon, GLP-1 (7–20) enhanced insulin secretion, as shown in Table 2. There were no significant differences between the responses of the plasma IRI to these four peptides. Neither GLP-1 (6–37), (1–37) nor (8–37) revealed the changes in insulin secretion. When arginine was infused, a significant glucagon release from the pancreas was observed during the infusion of GLP-1 (7–37), (7–20), and (8–37). The other GLP-1 peptides, (1–37), (7–36), and (6–37) did not elicit any significant changes in glucagon release.

**DISCUSSION**

Although GLP-1 (1–37) has similarities in 14 of the 37 amino acids compared with glucagon, this peptide did not elicit any insulinotropic action in anesthetized dogs, as originally reported by Ghiglione et al. (1984). In contrast, a truncated peptide (7–37) revealed clearly an insulinotropic action in the present experiment, confirming the findings reported previously (Holst et al. 1987; Mojssov et al. 1987; Matsuyma et al. 1988; Ørskov et al. 1988; Shima et al. 1988; Kawai et al. 1989; Suzuki et al. 1989). In the case of glucagon, N-terminal histidine has been considered important at the initiation of its biological action, since histidine is essential in binding the peptide to its receptor at the glucagon-sensitive cells (Assan and Slusher 1972). Therefore, the truncated GLP-1 (7–37), which has histidine at the N-terminal, would more easily be able to bind the B-cells in the islets than GLP-1 (1–37). To investigate the importance of histidine at the seventh of GLP-1, in the present experiment insulin releasing activity was compared using various truncated peptides, (6–37), (8–37), and (7–37). As shown in the results, the truncated GLP-1 (6–37) did not reveal any insulinotropic action, which is similar to the findings reported by Suzuki and his coworkers (1989). However, the truncated GLP-1 (8–37) induced an insulin releasing action during glucose infusion, although weak. The same finding was observed in the perfusion of the isolated rat pancreas (Gefel et al. 1990). These results suggest that the amino acid sequence following the 8th amino acid also stimulates insulin release, although histidine at the seventh position is necessary to initiate the biological action.

In the present study, both GLP-1 (7–37) and (7–36) prompted insulin secretion. This result suggests that glycine37 is not important in the insulin releasing action. This fact was reported in the experiment using the isolated rat pancreas (Yanaihara et al. 1988; Gefel et al. 1990). It is remarkable that the administration of GLP-1 (7–20) during arginine infusion revealed a significant increase in insulin release. However, this peptide did not affect the insulin release under glucose infusion. At present, it is not clear why GLP-1 (7–20) has an effect on
Effects of GLP-1 Peptides on Endocrine Pancreas

insulin release only during arginine administration. The fact that GLP-1 (7-20) promotes insulin secretion suggests that possible peptides with smaller amino acid sequences will elicit insulinotropic action.

As far as glucagon secretion is concerned, the glucagon response seems to be dependent on the basal condition. During glucose infusion, GLP-1 (7-37) reduced glucagon secretion, confirming previous findings (Kreymann et al. 1987; Matsuyama et al. 1988; Ørskov et al. 1988; Kawai et al. 1989). Similarly GLP-1 (1-37) reduced glucagon secretion during glucose infusion. This effect would be presumed as direct action of the peptide on A-cells of the pancreas, because the peptide did not affect insulin secretion. In contrast, GLP-1 (7-37), (7-20), and (8-37) enhanced glucagon secretion during arginine infusion. Therefore, the present study suggests that these peptides would promote arginine-induced glucagon secretion.

According to previous reports (Mojsov et al. 1987; Shima et al. 1988; Kawai et al. 1989), GLP-1 (7-37) or (7-36) elicits a remarkable insulinotropic action in the rat. However, in the present study, both the peptides (7-37) and (7-36) revealed as much insulinotropic action as glucagon. In the present study, GLP-1 related peptides were administered in a dosage of 400 pmol within 10 min, expecting to maintain approximately 1 nmol/liter in the PA by calculation from the blood flow of the PA (Ohneda et al. 1977). This was proved in the experiment with glucagon infusion, which showed a peak of approximately 1 nmol/liter of the plasma IRG in the PV. It was reported that GLP-1 (7-37) enhanced insulin release at the concentration of 1 nmol/liter in an isolated canine pancreas (Kawai et al. 1989). In contrast, insulin release was promoted by the administration of GLP-1 (7-37) at a concentration of 50 to 100 pmol/liter in the rat (Mojsov et al. 1987; Shima et al. 1988; Kawai et al. 1989). Therefore, there is a large variation in insulin response to GLP-1 peptides between animal species. Furthermore, the difference in experimental system, in vitro or in vivo, would account for the different results.

In the present study, GLP-1 (7-37) and (7-36) revealed the most remarkable insulinotropic action in the dog among GLP-1 related peptides investigated. In the present experiment, the maximum concentration of these peptides in the PA would reach as high as 1 nmol/liter. This level of GLP-1 peptides, it would be speculated, would be brought about after a meal in the physiological state from findings during oral glucose load in pigs (Ohneda 1987), although a plasma level of 50 pmol/liter of GLP-1 was observed after glucose ingestion in man (Kreymann et al. 1987). Therefore, some of these GLP-1 related peptides would modify the postprandial insulin secretion and would play an important role in the enteroinsular axis.
References


Effects of GLP-1 Peptides on Endocrine Pancreas
