# Product Data Sheet

Product Name: (Leu$^{15}$)-Gastrin I (human)
Cat. No.: GA20228

## Chemical Properties

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|---|---|---|---|
| Cas. No. | 39024-57-2 | | |
| Formula | $C_{98}H_{126}N_{20}O_{31}$ | M.Wt | 2080.2 |
| Solubility | DMSO : 100 mg/mL (48.07 mM; Need ultrasonic); $H_2O$ : 10.53 mg/mL (5.06 mM; ultrasonic and adjust pH to 11 with NaOH) | Storage | Store at -20°C |
| General tips | For obtaining a higher solubility , please warm the tube at 37 ℃ and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20℃ for several months. | | |
| Shipping Condition | Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request. | | |
| Structure | (Leu$^{15}$)-Gastrin I (human) | | |

## Protocol

**Kinase experiment [1]:**

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| Preparation Method | Enzymic hydrolyses of gastrin analogues were analysed by HPLC Enzyme (0.005 unit) was incubated with substrate (0.1mM) and buffer in a final volume of 0.1mL. Buffer was 100mM-Tris/HCl, pH7.5, containing 0.3M-NaCl. When specific inhibitors of ACE were used, they were preincubated with the enzyme for 5-15min at 37℃. Reactions were carried out at 37℃ for various times and then stopped by freezing in liquid nitrogen. Samples (20μL) were stored at -80℃ before HPLC analysis. In kinetic studies, ACE (0.005 unit) was incubated with gastrin analogues at ten different substrate concentrations (ranging from 10 to 1000μM), in a buffer containing 300mM-NaCl. |


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| Reaction Conditions | 10 to 1000μM |
| Applications | The initial and major site of hydrolysis was the penultimate peptide bond, which generated a major product, the C-terminal amidated dipeptide Asp-Phe-NH2. As a secondary cleavage, ACE subsequently released di- or tri-peptides from the C-terminal end of the remaining N-terminal fragments. Hydrolysis of [Leu$^{15}$]-gastrin-(14-17)-peptide in the presence of ACE was dependent on the chloride-ion concentration. Km values for the hydrolysis of [Leu$^{15}$]-gastrin-(11-17)-peptide and [Leu$^{15}$]-gastrin-(14-17)-peptide at an NaCl concentration of 300mm were respectively 420 and 3280μM, and the catalytic constants were about 115 and 885min-1. The kcat/Km for the reactions at 37℃ was approx. 0.28μM-1min-1. These results suggest that ACE might be involved in the metabolism in vivo of gastrin short fragments. |

**Animal experiment [2]:**

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| Animal models | Sprague-Dawley rats, weighing 200±225g |
| Preparation Method | Sprague-Dawley rats were given continuous subcutaneous infusion of human [Leu$^{15}$]-gastrin-17 (5nmol/kg•h) via osmotic minipumps, implanted in the neck under anaesthesia for 1, 2 or 6 days |
| Dosage form | 5nmol/kg•h |


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| Applications | Hypergastrinaemia was induced by continuous infusion of human [Leu$^{15}$]-gastrin-17 for 6 days. The treatment caused both vacuoles and lipofuscin bodies to appear in large numbers and the vacuoles disappeared promptly after interruption of the hypergastrinaemia, whereas the lipofuscin bodies remained. |


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References:

[1]. Dubreuil P, Fulcrand P, et al. Novel activity of angiotensin-converting enzyme. Hydrolysis of cholecystokinin and gastrin analogues with release of the amidated C-terminal dipeptide. Biochem J. 1989;262(1):125-130.

[2]. Zhao CM, Chen D, et al. ECL cells of the rat stomach: development of lipofuscin in response to sustained gastrin stimulation. Cell Tissue Res. 1998;291(2):315-323.

## Background

## Product Data Sheet

Gastrin is gastrointestinal hormones which is structurally similar in carboxy-terminal amino acids[1]. Gastrin are normally produced at high levels by endocrine (G) cells located in the gastric antrum and proximal duodenal mucosa. Gastrin can activate through the CCK2R several signaling pathways that have been linked to proliferation, cell adhesion, and antiapoptotic effects[2]. Human [Leu$^{15}$]-gastrin-17 is a synthetic analogue of human gastrin-17 and is considered more stable than natural human [Met$^{15}$]-gastrin-17 while having the same bioactivity[3]

[Leu$^{15}$]-Gastrin I can be synthesized use the Clt-resin[4]. Gastrin analogues can be hydrolyzed by angiotensin-converting enzyme(ACE), indicated that it is possible that administration of ACE inhibitors, used clinically as antihypertensive drugs, could affect the metabolism of gastrin fragments in vivo[5]

Human [Leu$^{15}$]-gastrin I directly modulated secretin binding to its receptors, that may involve in the inhibitory action of secretin on acid secretion induced by gastrin[1]. Continuous infusion of human [Leu$^{15}$]-gastrin-17 via osmotic minipumps increased the plasma levels of gastrin. In the rats given the high dose(2.4nmol/kg•h) of human [Leu$^{15}$]-gastrin-17, the ECL-cell density, the mucosal histamine concentration and HDC activity increased significantly[3]. Continuous infusion of human [Leu$^{15}$]-gastrin-17(5nmol/kg•h) for 6 days induces hypergastrinaemia, and caused both vacuoles and lipofuscin bodies to appear in large numbers, suggesting that gastrin stimulates the development not only of vacuoles but also of lipofuscin, perhaps through enhanced autophagocytosis and/or oxidative stress[6]

References:
[1]. Iwakawa S, Nomura H, et al. Direct modulation of secretin binding sites by gastrin in the rat stomach. J Pharmacobiodyn. 1992;15(8):437-441.
[2]. Ferrand A, Wang TC. Gastrin and cancer: a review. Cancer Lett. 2006;238(1):15-29.
[3]. Ryberg B, Axelson J, et al. Trophic effects of continuous infusion of [Leu$^{15}$]-gastrin-17 in the rat. Gastroenterology. 1990;98(1):33-38.
[4]. Barlos K, Gatos D, et al. Application of 2-chlorotrityl resin in solid phase synthesis of (Leu15)-gastrin I and unsulfated cholecystokinin octapeptide. Selective O-deprotection of tyrosine. Int J Pept Protein Res. 1991;38(6):555-561.


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[5]. Dubreuil P, Fulcrand P, et al. Novel activity of angiotensin-converting enzyme. Hydrolysis of cholecystokinin and gastrin analogues with release of the amidated C-terminal dipeptide. Biochem J. 1989;262(1):125-130.
[6]. Zhao CM, Chen D, et al. ECL cells of the rat stomach: development of lipofuscin in response to sustained gastrin stimulation. Cell Tissue Res. 1998;291(2):315-323.