Glucagon like peptide 2

Glucagon-like peptide-2 (GLP-2) is a 33 amino acid peptide with the sequence HADGSFSDEMNTILDNLAARDFINWLIQTKITD (see Proteinogenic amino acid) in humans. GLP-2 is created by specific post-translational proteolytic cleavage of proglucagon in a process that also liberates the related glucagon-like peptide-1 (GLP-1). GLP-2 is produced by the intestinal endocrine L cell and by various neurons in the central nervous system. Intestinal GLP-2 is co-secreted along with GLP-1 upon nutrient ingestion.

When externally administered, GLP-2 produces a number of effects in humans and rodents, including intestinal growth, enhancement of intestinal function, reduction in bone breakdown and neuroprotection. GLP-2 may act in an endocrine fashion to link intestinal growth and metabolism with nutrient intake. GLP-2 and related analogs may be treatments for short bowel syndrome, Crohn's disease, osteoporosis and as adjuvant therapy during cancer chemotherapy.

In a study Iwai et al., characterized the mechanisms of GLP-2-induced hypotension. GLP-2 was administered peripherally or centrally to male Wistar rats anesthetized with urethane and α-chloralose. The rats were vagotomized or systemically pretreated with atropine, prazosin, or propranolol before the GLP-2 administration. The central and peripheral administration of GLP-2 reduced mean arterial blood pressure (MAP). The maximum change of MAP (maximum ΔMAP) was reduced by vagotomy or prazosin, but not propranolol. The effects of the central but not peripheral administration of GLP-2 were reduced by atropine. These results suggest that GLP-2 modulates vagal afferent inputs and inhibits the sympathetic nervous system in the brain to induce hypotension [1)].

Small bowel resection stimulates intestinal adaptive growth by a neuroendocrine process thought to involve both sympathetic and parasympathetic innervation and enterotrophic hormones such as glucagon-like peptide-2 (GLP-2).

Vagal afferents are not essential for GLP-2 secretion when the ileum has direct contact with luminal nutrients after resection. In summary, vagal afferent neurons are essential for maximal resection-induced intestinal adaptation through a mechanism that appears to involve stimulation by luminal nutrients [2)].

GLP-1 inhibited contractions at all sites. GLP-2 inhibited contractions in the pouch but did not affect motility in the neurally intact gastroduodenum. Glicentin had no effect on contractions at any site. Pretreatment with either a nitric oxide synthase inhibitor or phentolamine and propranolol reversed the inhibitory effect of glucagon, GLP-1 and GLP-2 on contractions in the pouch, but did not alter the inhibitory effect of glucagon and GLP-1 on motility in the neurally intact stomach and duodenum.

These results suggest that the effects of four peptides on gastroduodenal motility differ, and changes occur in the enteric neural modulation of motor activity after chronic surgical extrinsic denervation [3)].

1)
Iwai T, Kaneko M, Sasaki-Hamada S, Oka J. Characterization of the hypotensive effects of glucagon-

like peptide-2 in anesthetized rats. Neurosci Lett. 2013 Aug 29;550:104-8. doi: 10.1016/j.neulet.2013.07.004. Epub 2013 Jul 15. PubMed PMID: 23867714.

2) Nelson DW, Liu X, Holst JJ, Raybould HE, Ney DM. Vagal afferents are essential for maximal resection-induced intestinal adaptive growth in orally fed rats. Am J Physiol Regul Integr Comp Physiol. 2006 Nov;291(5):R1256-64. PubMed PMID: 17028287.

3) Shibata C, Naito H, Jin XL, Ueno T, Funayama Y, Fukushima K, Hashimoto A, Matsuno S, Sasaki I. Effect of glucagon, glicentin, glucagon-like peptide-1 and -2 on interdigestive gastroduodenal motility in dogs with a vagally denervated gastric pouch. Scand J Gastroenterol. 2001 Oct;36(10):1049-55. PubMed PMID: 11589377.